ISSN: 2772-5170

Indian Pediatrics Case Reports

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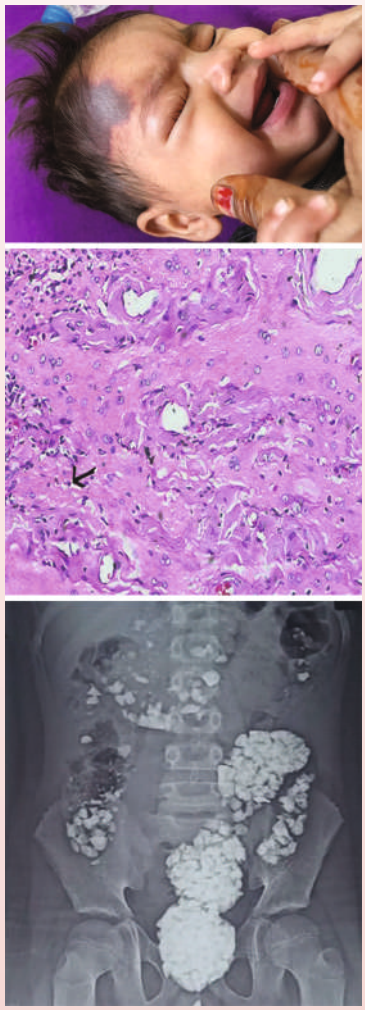
VOLUME 5 | ISSUE 1 | JANUARY-MARCH 2025 www.ipcares.org



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1. IQVIA TSA MAT Nov 2023
2. Menactra PI available at: https://www.sano.in/en/science-and-innovation/for-health[1]care-professionals/product-information
3. Su JR, et al. MMWR Morb Mortal Wkly Rep. 2016;65:161–162
4. Javaddekar B, Ghosh A, Kompithra RZ, et al. Indian Pediatr. 2018 Dec 15;55(12):1050-1055
5. Yadav S, et al. Indian Pediatr 2014. Jun;51(6):451-6
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Abnormal Behaviors in Adolescents: Diagnosis Not to be Based on Perceptions and Heuristics!

Adolescence is a remarkably unique stage in human life. Being a transition phase from childhood to adulthood, this period witnesses not only an obvious metamorphosis in physical and sexual development, but also a covert, yet significant, mental tumultuousness. With its bundle of psychological phenomena, stemming from the wild, passionate hot blood of youth, admixed with the innocence and immaturity of waning childhood, this period has always been a challenge to deal with, for parents, as also enigmatic for pediatricians.

Apart from mental perturbances, adolescents also tend to suffer from a myriad of bodily symptoms such as headache, abdominal and musculoskeletal pains, gastrointestinal disturbances, and subjective neurological sensations. These somatic symptoms are often overbearing, to the extent that they interfere with routine activities, causing truancy, social reticence, potentially affecting academic and psychosocial functioning. As much as it is distressing for the parents, so also it is baffling for the pediatricians, since the symptoms do not always conform to well-defined, common, organic pathologies, which the physicians are acquainted to, in clinical practice. While many of the somatic complaints are compatible with the criteria of "Functional Somatic Symptoms," some may be due to genuine underlying biological pathologies. The expected consequence of this ambiguity and overlap is an over or under-diagnosis of psychological functional disorders in adolescents.

There is increasing concern regarding the topic of unintended over or misdiagnosis of psychological disorders in adolescents, resulting in an escalating prevalence of mental disorders among children and adolescents over the past decades.[1] Reasons for such mis-labeling are many, including heuristics, biased informants, ambiguous symptoms, imprecise/overlapping diagnostic criteria or even health system driven compulsions. Unlike somatic disorders, there are no laboratory or genetic tests to confirm mental disorders, the latter being diagnosed based on research-supported consensus of expert-defined clusters of feelings and behaviors described in diagnostic manuals like DSM or the International Classification of Diseases. Thus, the clinical judgment may be affected by the perceptions of the physician or the caregivers.

This issue of *IPCaRes* includes two interesting reports in adolescents, dealing with phenomena mimicking psychological disorders: lithophagia[2] and anorexia nervosa.[3] Although such abnormal behaviors are likely to be taken as eccentric and psychological, the authors, in addition to psychologic assessment, have done a thorough workup for the possible etiologies, and eventually, both cases were found to have underlying organic biologic pathologies: lithophagia being a consequence of low iron stores in a covert celiac disease; food aversion and postprandial vomiting of anorexia nervosa being a result of superior mesenteric artery syndrome. This highlights the importance of being attentive to the complaints of adolescent children, however weird they may appear, and going ahead with all relevant investigations with an unbiased neutral mindset.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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References

1. Merten EC, Cwik JC, Margraf J, *et al*. Overdiagnosis of mental disorders in children and adolescents (in developed countries). Child Adolesc Psychiatry Ment Health 2017;11:5.
2. Kalvala K, Pandey S, Kokitkar SV, Bavdekar A. Lithophagia in a child: unraveling the puzzle of celiac disease. Indian Pediatr Case Rep 2025;5:30-2.
3. Reshmi YS, Basker MM, Ebenezer A. Superior mesenteric artery syndrome with anorexia nervosa: a rare case of postprandial vomiting in an adolescent. Indian Pediatr Case Rep 2025;5:47-50.

Submitted: 08-Feb-2025 **Accepted:** 08-Feb-2025
Published: 14-Feb-2025

Access this article online

Quick Response Code:

Website: www.ipcares.org

DOI: 10.4103/ipcares.ipcares_31_25

How to cite this article: Mishra K. Abnormal behaviors in adolescents: Diagnosis not to be based on perceptions and heuristics! Indian Pediatr Case Rep 2025;5:1.

Infantile Epileptic Spasms Syndrome in an Infant with *PHACTR1* Mutation Triggered by Whole-Cell-Pertussis Vaccine: A Case Report with Review of Literature

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Abstract

Background: Early-onset infantile epileptic spasm syndrome is a known feature of phosphatase and actin regulator 1 (*PHACTR1*) gene mutation. However, its association with whole-cell pertussis vaccination is unknown. **Clinical Description:** A 1-year-old child presented with history of recurrent seizures for the past 8 months, having onset within a few hours after third dose of pentavalent vaccination containing whole-cell pertussis vaccine. There was associated developmental delay. Examination revealed generalized hypotonia with preserved reflexes. **Management and Outcome:** Routine blood investigations were largely normal. Electroencephalography showed classical hypsarrhythmia, while magnetic resonance imaging of the brain was unremarkable. Whole exome sequencing showed c.1499T>C heterozygous mutation in exon 12 of the *PHACTR1* gene. The infant was treated with prednisolone, followed by vigabatrin, resulting in seizure-free state. **Conclusion:** Genetic analysis is advisable for infants with epileptic infantile spasms which are triggered by vaccination. *PHACTR1* gene mutation could be one of the genetic variations, predisposing infants to vaccine-triggered seizures.

Keywords: Genetic analysis, pentavalent vaccine, seizure

Vaccine-related seizures have been reported intermittently in the literature.[1] Mutations in various genes have been implicated in such seizures.[1,2] There have been several reports of SCN1A genetic mutation as a cause of seizure in children with epileptic encephalopathy with onset related to Diphtheria, Tetanus, and whole-cell Pertussis vaccination.[3,4] We report a 1-year-old child with an underlying heterozygous variant in the phosphatase and actin regulator 1 (*PHACTR1*) gene, who developed epileptic spasm with onset following the administration of the third dose of pentavalent vaccine containing whole-cell killed pertussis.

Clinical Description

A 1-year-old girl presented with a history of repeated episodes of abnormal body movements for the past 8 months. The child was apparently well till 4 months of age when she received the third dose of pentavalent vaccination (containing inactivated whole cell pertussis). Within 6 hours of vaccination, she developed fever and abnormal jerky movements of upper and lower limbs lasting for 5 minutes followed by postictal drowsiness for the next 1 hour. Seizures were aborted at a local hospital, but nature of treatment was not known. Subsequently, she developed sudden episodes of head drops, 1–2 such episodes per day, mostly upon waking from sleep. Later, the infant developed multifocal type of convulsions, for which she was started on oral levetiracetam by the local practitioner. There was no associated loss of consciousness, weakness, or tightness of limb, and no abnormal twisting movements in the body. There was no history of fever, head trauma, or ear discharge. The earlier pentavalent vaccinations had been uneventful and there were no other significant illnesses in the past. Following the onset of seizures, the baby gradually lost head control and social smile and did not achieve further milestones.

The infant was the first child of the parents, born through nonconsanguineous marriage, by vaginal delivery with a birth weight of 3 kg, with an uneventful antenatal, natal, and postnatal period. There was no family history of epilepsy. She was exclusively breastfed till 6 months, followed by complementary feeding; dietary recall revealed adequate calorie intake and a protein excess of 3 g/kg/day.

Access this article online

Quick Response Code:

Website: www.ipcares.org

DOI: 10.4103/ipcares.ipcares_135_24

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Submitted: 17-Jun-2024 **Revised:** 4-Oct-2024
Accepted: 16-Dec-2024 **Published:** 14-Feb-2025

How to cite this article: Sharma S, Khound M, Das BK, Kaushik JS. Infantile epileptic spasms syndrome in an infant with *PHACTR1* mutation triggered by whole-cell-pertussis vaccine: A case report with review of literature. Indian Pediatr Case Rep 2025;5:2-4.

At presentation to us, the child was conscious but not alert. She was afebrile with a pulse rate of 112/min, respiratory rate of 38/min, and blood pressure of 72/45 mmHg. Her weight was 9 kg (0–1 SD) and her length was 76 cm (1–2 SD), with mid-upper arm circumference of 13 cm. On general physical examination, there were no facial dysmorphism, nor any neurocutaneous markers. There was no pallor, icterus, cyanosis, clubbing, lymphadenopathy, or edema. On central nervous system examination, cranial nerves were intact, with generalized hypotonia and preserved reflexes. Other systemic examination was within normal limits. Based on the history and physical examination, a provisional diagnosis of infantile epileptic spasm syndrome was considered.

Management and Outcome

Routine investigations revealed hemoglobin of 10.2 g/dL, total leukocyte count 6500 IU/L, platelet count was 1.8 lakh/cumm, urea/creatinine 21/0.3 mg/dL, sodium/potassium/chloride 136/3.8/108 mmol/L, aspartate aminotransferase/alanine transaminase 36/28 U/L, and serum calcium level was 8.9 mg/dL. Electroencephalography showed classical hypsarrhythmia. Magnetic resonance imaging (MRI) of the brain was unremarkable. Her whole exome sequencing revealed c.1499T>C heterozygous mutation in exon 12 of the *PHACTR1* gene classified as likely pathogenic. The infant was diagnosed with infantile epileptic spasm due to mutation in the *PHACTR1* gene and started on oral prednisolone at 4 mg/kg/day but epileptic spasms persisted even at follow-up after 15 days. She was started on vigabatrin at 50 mg/kg, increasing gradually to 150 mg/kg/day, with tapering of steroids, following which spasms abated over the next 5 days. The infant has been seizure-free for the last 2 months.

Discussion with Review of Literature

Phosphatase and actin regulators (PHACTRs) are expressed in cardiovascular and neurological tissues, having a role in pre- and postnatal maturation, as well as angiogenesis. The PHACTRs consist of four proteins (*PHACTR1*-4) with different expression levels in both embryonic and adult brains, thought to be important in regulating cell shape and movement by impacting where PHACTRs are found inside cells.[5] Case reports with pathogenic mutations in the *PHACTR1* gene have rarely been reported [Table 1].

The clinical presentation of *PHACTR1* mutation includes early onset developmental encephalopathy, developmental delay, intellectual disability, coronary artery diseases, early onset myocardial infarction, and early onset parkinsonism [Table 1].[6-9] The age at onset of spasms, multifocal nature of seizures, and failure of oral steroids in earlier published cases,[6-9] were similar to our case. There were no cardiovascular symptoms in our case. While MRI findings were normal in our case, other cases have shown cortical atrophy or hypoplasia of the corpus callosum.[8,9]

Unlike previous reports of *PHACTR1* mutation, the present case highlights a possible temporal relationship between the whole-cell pertussis vaccination and the sudden onset of epileptic spasms in an infant with an underlying genetic predisposition; the onset of seizures being after the third dose of the vaccine, earlier two doses being uneventful. Various studies have reported diphtheria, tetanus, and pertussis vaccine as a potential trigger for the onset of Dravet syndrome,[3,4,10,11] but infantile epileptic spasm syndrome is seldom reported following a vaccination trigger. Whole-cell pertussis vaccine linked serious neurological disorders involves sodium channel gene mutations. The vaccine induces interleukin-1 β in the hippocampus and hypothalamus of vaccinated animals, causing a drop in inhibitory neurotransmitters gamma-aminobutyric acid and adenosine in the hippocampus, which leads to convulsive activity. The National Childhood Encephalopathy Study results showed that there is no direct causal relationship between infantile spasms and pertussis vaccination in children with structurally normal brains, but that the onset of spasms may be precipitated in those children who are prone to develop it.[12]

The nationwide 10-year follow-up study in the Netherlands, including 990 children with a temporal relation of seizures to vaccination in the first 2 years of life, reported that 52% of the children with vaccination-triggered epilepsy,

Table 1: Review of literature of published reports of individuals with *PHACTR1* gene mutation

Author, year	Gender, age of onset of seizures (months)	Clinical features	Treatment	Outcome
Hamada *et al*., 2018[6]	Male (3)	Epileptic spasm, focal seizures	Pyridoxal phosphate, ACTH	Partial response
Riazuddin *et al*., 2017[7]	NA	Intellectual disability	NA	NA
Marakhonov *et al*., 2021[8]	Case 1: Female (3)	Focal seizure with tonic component	Valproate, lamotrigine, levetiracetam, ACTH	NA
	Case 2: Female (3)	Epileptic spasms in clusters	ACTH, valproate	
	Case 3: Male (3.5)	Focal motor with secondary generalization	Valproate, ACTH, prednisolone, vigabatrin, oxcarbamazepine, levetiracetam	
Previtali *et al*., 2023[9]	Case 1: Female (2)	Asymmetric spasms in clusters	Valproate, BZDs, and ACTH	Partial response
	Case 2: Male (3)	Focal spasms	Vigabatrin, ACTH	No response
Present case	Female (4)	Multifocal, epileptic spasms in cluster	Prednisolone, vigabatrin	Good response

NA: Details not available in literature, ACTH: Adrenocortico trophic hormone, BZDs: Benzodiazepines

had epileptic encephalopathy, of which one case was diagnosed with West syndrome, which on follow-up turned into Lennox–Gastaut syndrome.[1] In our case, whether the seizure was coincidental or associated with the vaccine is unclear. The finding that the onset of seizures occurred only after the third vaccination argues against a major role for immune sensitization.

Conclusion

The present case creates awareness that early-onset developmental and epileptic encephalopathy due to *PHACTR1* mutation, may be triggered by whole-cell pertussis vaccination. Genetic analysis may thus be considered in infants developing persistent seizures post-vaccination.

Lesson learnt

- Early-onset developmental and epileptic encephalopathy may be triggered by whole-cell pertussis vaccination
- Genetic analysis is advisable in epileptic infantile spasms if they are persistent post vaccination
- Children with underlying *PHACTR1* gene mutations may have onset of epilepsy, following vaccination with whole-cell pertussis vaccine.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Verbeek NE, Jansen FE, Vermeer-de Bondt PE, *et al.* Etiologies for seizures around the time of vaccination. Pediatrics 2014;134:658-66.
2. Negi S, Sahu JK, Bhatia P, *et al.* Exploring the genetic landscape of diphtheria, tetanus and pertussis vaccination-associated seizures or subsequent epilepsies. Lancet Reg Health Southeast Asia 2023;8:100094.
3. Verbeek NE, van der Maas NA, Jansen FE, *et al*. Prevalence of SCN1A-related Dravet syndrome among children reported with seizures following vaccination: A population-based ten-year cohort study. PLoS One 2013;8:e65758.
4. Berkovic SF, Harkin L, McMahon JM, *et al. De-novo* mutations of the sodium channel gene SCN1A in alleged vaccine encephalopathy: A retrospective study. Lancet Neurol 2006;5:488-92.
5. Allen PB, Greenfield AT, Svenningsson P, *et al*. Phactrs 1-4: A family of protein phosphatase 1 and actin regulatory proteins. Proc Natl Acad Sci U S A 2004;101:7187-92.
6. Hamada N, Ogaya S, Nakashima M, *et al. De novo* PHACTR1 mutations in West syndrome and their pathophysiological effects. Brain 2018;141:3098-114.
7. Riazuddin S, Hussain M, Razzaq A, *et al.* Exome sequencing of Pakistani consanguineous families identifies 30 novel candidate genes for recessive intellectual disability. Mol Psychiatry 2017;22:1604-14.
8. Marakhonov AV, Přechová M, Konovalov FA, *et al.* Mutation in PHACTR1 associated with multifocal epilepsy with infantile spasms and hypsarrhythmia. Clin Genet 2021;99:673-83.
9. Previtali R, Leidi A, Basso M, *et al.* Case report: Early-onset parkinsonism among the neurological features in children with PHACTR1 variants. Front Neurol 2023;14:1181015.
10. Damiano JA, Deng L, Li W, *et al.* SCN1A variants in vaccine-related febrile seizures: A prospective study. Ann Neurol 2020;87:281-8.
11. McIntosh AM, McMahon J, Dibbens LM, *et al.* Effects of vaccination on onset and outcome of Dravet syndrome: A retrospective study. Lancet Neurol 2010;9:592-8.
12. Miller DC, Wadsworth MJ, Ross EM. Pertussis vaccine and severe acute neurological illnesses. Response to a recent review by members of the NCES team. Vaccine 1989;7:487-9.

Concurrent Manifestations of Type 1 Diabetes Mellitus and Nephrotic Syndrome in a Child with Unilateral Renal Hypo-dysplasia: A Case Report with Review of Literature

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Abstract

Background: Simultaneous occurrence of steroid-sensitive nephrotic syndrome (NS) and Type 1 diabetes mellitus (DM) in children is rare. **Clinical description:** A 21-month-old boy presented with generalized swelling with hypertension, with no significant illness in the past. Mother had type 1 DM from 11 years of age. **Management and Outcome:** Investigations revealed nephrotic range proteinuria, hypoalbuminemia along with raised blood sugar levels without ketoacidosis. Raised HbA1C and positive anti-glutamic acid decarboxylase confirmed type 1 DM. Ultrasonography detected a unilateral renal hypo-dysplastic kidney, which was non-functional on nuclear scan; vesico-ureteral reflux being ruled out by micturating cysto-urethrography. A therapeutic trial of steroids resulted in remission of proteinuria, insulin being titrated for glycemic control. Genetic analysis was negative and child remained relapse-free till last follow-up at one year. **Conclusion:** Nephrotic syndrome and DM may present concurrently. In the absence of genetic abnormality, and the presence of response to steroids, diabetic nephropathy as well as secondary focal segmental glomerulosclerosis are possibly ruled out.

Keywords: Anti-glutamic acid decarboxylase, congenital anomalies of kidney and urinary tract, genetics, prednisolone, remission

Simultaneous occurrence of steroid-sensitive nephrotic syndrome (NS) and type 1 diabetes mellitus (DM) in children is rare. The coexistence probably indicates an as yet unproven common genetic or immunological basis.[1] We report one such case here, who had an associated unilateral hypodysplastic kidney also.

Clinical Description

A 1-year-9-month-old boy presented with a history of increased thirst and frequency of micturition for 1 week. Four days later, edema was noted in both lower limbs, progressively increasing and associated with abdominal distension and mild facial puffiness. There was no history of fever, dysuria or discoloration of urine, breathing difficulty, jaundice, bleeding manifestations, rash, joint swelling, loose stools, headache, or seizures. There was no history of any chronic drug intake or recent vaccination. He was well in the past with no history of poor urinary stream. He was the first child of a nonconsanguineous parentage, born at term with a birth weight of 3 kg. His mother was diagnosed with type I DM at 11 years of age and was on insulin therapy with reasonably good glycemic control. The child had an uneventful antenatal period, with ultrasound scans being reported as normal. His developmental milestones were normal, and he had been immunized as per the national immunization schedule. He had an adequate intake of proteins but was deficient by 150 calories. There was no family history of renal disease.

On examination, he was conscious and afebrile with a pulse rate of 120/min, respiratory rate of 28/min, and blood pressure of 118/70 mmHg (Stage 2 hypertension as per American Academy of Pediatrics Hypertension guidelines[2]). His weight was 13 kg (between 50th and 85th percentile, as per WHO centiles), however, as per his mother, it was 11 kg before illness (between the 15th and 50th centiles). He had a length of 87 cm (between the 50th and 85th centiles), with no pallor, icterus, cyanosis, clubbing, or lymphadenopathy. He also had generalized edema and scrotal edema as well. Abdominal examination revealed

Access this article online

Quick Response Code:

Website: www.ipcares.org

DOI: 10.4103/ipcares.ipcares_213_24

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Submitted: 25-Aug-2024 **Revised:** 08-Dec-2024
Accepted: 10-Dec-2024 **Published:** 14-Feb-2025

How to cite this article: Marakkar S, Rahman RK, Soodhana D, Kumar S. Concurrent manifestations of type 1 diabetes mellitus and nephrotic syndrome in a child with unilateral renal hypo-dysplasia: A case report with review of literature. Indian Pediatr Case Rep 2025;5:5-8.

shifting dullness, with no organomegaly. Respiratory system examination revealed decreased breath sounds in the bilateral infrascapular area with dull percussion notes. Cardiovascular and neurologic examinations were normal.

Based on history and examination, a provisional diagnosis of NS was considered. However, the presence of increased urination in NS could not be correlated, hence we considered coexisting urinary tract infection, nephrogenic diabetes insipidus, or DM. Investigations [Table 1] showed a normal hemogram and negative C-reactive protein. The urine dipstick showed 3+ albuminuria and glucosuria, urine protein/creatinine ratio being 11 mg/mg. This, along with hypoalbuminemia and hypercholesterolemia with normal renal functions, confirmed NS. Blood sugar levels were raised (500 mg/dL), confirmed by rechecking. Furthermore, glycated hemoglobin (HbA1c) was 9.2%, suggestive of chronically high blood sugar levels. Blood gas analysis showed a pH of 7.32, HCO_3 of 19 mmol/L, pCO_2 of 33 mmHg, and blood ketones of 1.8 mmol/L. Ultrasonography showed a small (4 cm × 2.5 cm) dysplastic left kidney with poor corticomedullary differentiation (CMD) and a normal right kidney (9.6 cm × 4 cm) with maintained CMD, no pelvicalyceal or ureteral dilation, the urinary bladder being normal. There was mild ascites, other organs being normal.

The anti-glutamic acid decarboxylase-65 antibody was positive, suggestive of type 1 DM. The thyroid function test and serum cortisol were normal. Anti-tissue-transglutaminase levels were not checked as celiac disease is very uncommon in our part of the country and he had no symptoms. The Tc-99 m labeled dimercaptosuccinic acid renogram confirmed a nonfunctional left kidney with poor tracer uptake [Figure 1]. Renal artery doppler, echocardiogram, and ophthalmological evaluation done for assessing complications of hypertension and diabetes were within normal limits. A micturating cystourethrogram after 3 months was normal. Given the strong family history of type 1 DM, whole exome sequencing and multiplex ligation-dependent probe amplification analysis were done which were negative. Thus, the child was diagnosed with NS with Stage 2 hypertension, with an underlying hypoplastic left kidney, and associated type 1 DM. The NS was unlikely to be a result of diabetic nephropathy, rather, seemed distinct from DM, and consistent with secondary focal segmental glomerulosclerosis (FSGS) due to hyperfiltration damage in the single-functioning kidney.

Table 1: Baseline investigations of the child

Parameters	Values	Parameters	Values
Hemoglobin (g/dl)	12.3	FT3/FT4 (pmol/L)	4.8/15
TLC (/cumm) N// L (%)	9400; 22/78	TSH (mIU/L)	1.8
Platelets (/cumm)	6.2	Blood ketones (mmol/L)	1.8
S. albumin (mg/dl)	1.6	S. cholesterol (mg/dl)	320
AST/ALT (IU/L)	24/20	C3/C4 (mg/dl)	110/30
Urea/Creat (mg/dl)	28/0.4	S. Na/K (meq/L)	132/4.1
RBS (mg/dl)	500	HBsAg/Anti HCV/HIV	Negative

Urinalysis: albumin 3+, glucose ++, ketones +, white cells 3-4/hpf; red blood cells 0-1/hpf. Urine protein/creatinine ratio: 11mg/mg. TLC: total leukocyte count; N-neutrophil; L-lymphocyte; S-serum; AST/ALT: aspartate aminotransferase/alanine transaminase; RBS- random blood sugar; TSH- thyroid stimulating hormone; C-complement component; Na/K- sodium/potassium; HBsAg- hepatitis B surface antigen; creat-creatinine

The child was started on subcutaneous insulin therapy, a basal-bolus regimen with glargine once at night and aspart given before meals q8 hourly (0.8 units/kg/day), and oral nifedipine at 1 mg/kg/day (q6 hourly), followed by enalapril, under close monitoring. Blood sugars stabilized between 100 and 250 mg/dL by day 5. Renal biopsy was deferred, being a relative contraindication in a child with a solitary functioning kidney. Oral prednisolone (2 mg/kg/day) was started on day 3, after blood pressure was at 95th percentile. Oral nifedipine was gradually replaced with amlodipine. Following steroid intake, blood sugar levels increased from 180 mg/dL to above 400 mg/dL, requiring increase in insulin dosage to a maximum total daily dose of 3U/kg/day by 10 days of hospitalization. The patient attained complete remission of proteinuria by day 7 after starting steroids.

Although generalized edema subsided with albumin and furosemide infusions, the child developed asymmetric edema, more in his right leg on day 7 of admission. As he had a central venous catheter in the right femoral vein due to difficulty in peripheral venous access, an ultrasound Doppler was done, which revealed thrombosis of the common femoral vein. Unfractionated heparin infusion at 10U/kg/h was administered, followed by low-molecular-weight heparin (LMWH) at 1 mg/kg/dose twice daily subcutaneously.

He was discharged on prednisolone, advised at the same dose for 6 weeks, along with amlodipine, and LMWH (for 1½ months, Doppler having turned normal by then). His glycemic control improved after stopping steroids with insulin being maintained at 1.1 units/kg/day thereafter. He was under regular follow-up at the endocrinology and nephrology clinic. The child remained in remission and prednisolone was

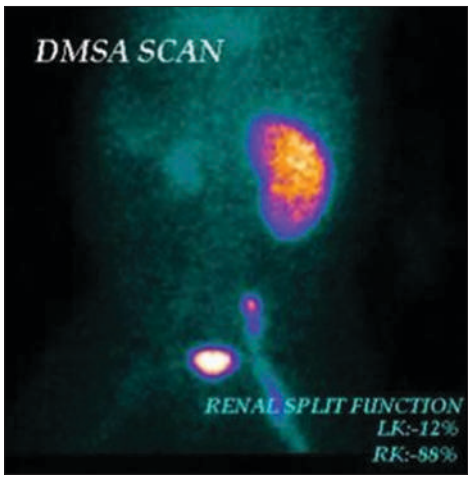

Figure 1: Dimercapto succinic acid renogram showing poor tracer uptake in left kidney

stopped after 12 weeks. Till the end of the year, he remained in remission, confirmed by urine protein/creatinine ratio checked intermittently, with blood sugar of 80–210 mg/dL (HbA1c of 7.7%) and blood pressure of 80/60 mmHg.

Discussion with Review of Literature

The above report is an interesting case of a child diagnosed concurrently with type 1 DM and NS associated with unilateral renal hypo-dysplasia. As the child had remained asymptomatic previously, probably both DM and NS co-manifested, the pathologies of both being independent of each other.

Nephrotic syndrome as a manifestation of diabetic nephropathy is well described in adults. While early diabetic nephropathy presenting as microalbuminuria, occurs around 5 years after the onset of type 1 DM, heavy proteinuria develops after another 10–15 years eventually resulting in end-stage renal disease.[3] Furthermore, DM is a known but usually transient complication of prolonged use of steroids and tacrolimus, in children with steroid-dependent NS.[4,5]

Diabetes mellitus associated with proteinuria due to nondiabetic nephropathy has rarely been described [Table 2].[1,6-11] In earlier reported cases, DM preceded NS by variable periods, except in two cases.[7,8] The short duration of DM and absence of any other target organ damage in all these cases implied that the NS was not a result of diabetes-induced kidney injury. Renal biopsies were done in 9/14 cases described [Table 2], with predominant histology being minimal change disease. As our patient had a solitary functioning kidney, we refrained from doing a renal biopsy at the outset and rather planned to perform it in the unfavorable event of steroid resistance, which, however, was not the outcome here.

Some of the prior case reports of concurrent NS and type 1 DM have demonstrated specific human leukocyte antigens, which may result in a genetic predisposition for the development of both disorders.[6,7,10] As our case additionally had a congenital dysplastic kidney with a positive family history, a genetic variation such as HNF1beta mutation causing maturity-onset diabetes of the young and congenital anomalies of kidney and urinary tract was suspected.[12] However, genetic analysis was negative. Other known associations like Hashimoto's thyroiditis were ruled out.[13]

A systematic review of a congenital solitary kidney, showed proteinuria in 10% after a mean follow-up of 7 years, none having NS,[14] Our patient fulfilled the triad of NS and even showed a response to steroids without the need for anti-proteinuric medications, thereby making secondary FSGS unlikely. As seen in many earlier reports [Table 2], the use of steroids in our child showed complete remission, though it was tough to adjust his insulin doses to maintain blood sugar levels during corticosteroid therapy. Daily, instead of alternate-day tapering of steroids has been suggested for better glycemic control.[8]

Conclusion

This case highlights the simultaneous presentation of type 1 DM and NS, in a child with unilateral renal hypodysplasia. Genetic

Table 2: Summary of prior reports of steroid-sensitive nephrotic syndrome in children with type 1 diabetes mellitus

Author (reference citation)	Cases	Age of diagnosis of DM	Age of diagnosis of NS	Associated disorders	Treatment	Outcome and follow-up
Urizar *et al*.[1]	Case 1	4 years	4 years (1 week after DM)	Nil	Insulin and steroids in all 5 cases	Relapses documented in cases 4 and 5 Renal biopsy done in all 5: Consistent with MCD in all
	Case 2	8 years	8 years			
	Case 3	3 years	4 years			
	Case 4	5 years	5 years			
	Case 5	2 months	10 months			
Agras *et al*.[6]		3 years	3 years 10 months	Nil	Steroid/insulin	Relapses documented Renal biopsy not done
Rego Filho *et al*.[7]		4 years (3 weeks after NS)	3 years 11 months	Nil	Steroid/insulin Cyclophosphamide	Relapses documented
Goldman *et al*.[8]	Case 1	3 years	3 years–5 months	Nil	Steroid and insulin in all cases	Relapses documented in all cases except case 3
	Case 2	9 years	15 years			
	Case 3	11 months	8 years		Cyclosporine in case 1	Renal biopsy done in cases 1 and 2 showed MCD
	Case 4	4 years–9 months (after NS)	4 years		Levamisole in case 4	Renal biopsy not done cases 3 and 4
Robinson *et al*.[9]		3 years	3 years–2 months	Nil	Insulin Steroid	Multiple relapses Renal biopsy: Immune complex glomerulonephritis
Otukesh *et al*.[10]		13 days	1 year	Nil	Insulin/steroid	Multiple relapses Renal biopsy: Membranous nephropathy
Bawahab *et al*.[11]		9 years	12 years	Nil	Insulin Steroid	Resolved Renal biopsy not done

MCD: Minimal change disease, NS: Nephrotic syndrome, DM: Diabetes mellitus

analysis being normal, and NS responding to steroids, possibly rules out diabetic nephropathy as also secondary FSGS.

Lessons learnt

- Type 1 diabetes mellitus (DM) may coexist with unilateral renal hypodysplasia and nephrotic syndrome
- Genetic analysis may be unremarkable in such a combination
- Nephrotic syndrome occurring concurrently with DM and responding to steroids, possibly rules out diabetic nephropathy and also secondary focal segmental glomerulosclerosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Urizar RE, Schwartz A, Top F Jr, *et al*. The nephrotic syndrome in children with diabetes mellitus of recent onset: Report of five cases. N Engl J Med 1969;281:173-81.
2. Flynn JT, Kaelber DC, Baker-Smith CM, *et al.* Clinical practice guideline for screening and management of high blood pressure in children and adolescents. Pediatrics 2017;140:e20171904.
3. Kopel J, Pena-Hernandez C, Nugent K. Evolving spectrum of diabetic nephropathy. World J Diabetes 2019;10:269-79.
4. Takahashi T, Okamoto T, Sato Y, *et al*. Glucose metabolism disorders in children with refractory nephrotic syndrome. Pediatr Nephrol 2020;35:649-57.
5. Dittrich K, Knerr I, Rascher W, *et al*. Transient insulin-dependent diabetes mellitus in children with steroid-dependent idiopathic nephrotic syndrome during tacrolimus treatment. Pediatr Nephrol 2006;21:958-61.
6. Agras PI, Kinik ST, Cengiz N, *et al*. Type 1 diabetes mellitus associated with nephrotic syndrome. J Pediatr Endocrinol Metab 2006;19:1045-8.
7. Rego Filho EA, Mello SF, Omuro AM, *et al*. Simultaneous onset of steroid-sensitive nephrotic syndrome and type 1 diabetes. J Pediatr (Rio J) 2003;79:557-60.
8. Goldman M, Hébert D, Geary DF. Management of steroid-sensitive nephrotic syndrome in children with type 1 diabetes. Pediatr Nephrol 2002;17:351-4.
9. Robinson LA, Howell DN, Wigfall DR, *et al*. Appearance of immune complex glomerulonephritis following the onset of type I diabetes mellitus in a child. Am J Kidney Dis 1997;30:713-6.
10. Otukesh H, Torabi A, Hoseini R, *et al*. Co-existence of type 1 diabetes mellitus and nephrotic syndrome with membranous glomerulonephritis in a 6 year old boy: Report of a case. Int J Child Adolesc 2016;2:25-7.
11. Bawahab NS, Safdar OY, Nagadi SA, *et al*. Nephrotic syndrome co-existing with type 1 diabetes in a 12-year-old boy: Case report and literature review. SAGE Open Med Case Rep 2019;7:2050313X19827734.
12. Raaijmakers A, Corveleyn A, Devriendt K, *et al.* Criteria for HNF1B analysis in patients with congenital abnormalities of kidney and urinary tract. Nephrol Dial Transplant 2015;30:835-42.
13. Dizdar O, Kahraman S, Gençtoy G, *et al.* Membranoproliferative glomerulonephritis associated with type 1 diabetes mellitus and Hashimoto's thyroiditis. Nephrol Dial Transplant 2004;19:988-9.
14. Hutchinson KA, Halili L, Guerra A, *et al*. Renal function in children with a congenital solitary functioning kidney: A systematic review. J Pediatr Urol 2021;17:556-65.

Tetanus in a Child Due to Otogenic Source: A Case Report with Review of Literature

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Abstract

Background: In adults, tetanus typically follows trauma, while in children, it often results from ear infection. **Clinical Description:** A 7-year-old boy presented with difficulty opening his mouth and generalized rigidity, developing over 10 days. He had a history of left ear discharge for a month, but no associated headache, vomiting, and abnormal movements. He was unvaccinated except for the birth dose. On examination, he was conscious and afebrile, but presented with generalized stiffness, risus sardonicus, and tachycardia, maintaining oxygen saturation. **Management and Outcome:** Tetanus was suspected clinically, and the child was kept in a sound-proof, dark isolation room. Equine immunoglobulin 10,000 IU and tetanus toxoid vaccine along with intravenous antibiotics were administered. Muscle spasms were managed with diazepam, chlorpromazine, and phenobarbitone. *Clostridium tetani* was confirmed from an ear swab culture. The child's muscle rigidity and spasms gradually decreased after 3 weeks, with improved oral intake. Intravenous sedation was transitioned to oral antispasmodics and he was discharged in a normal neurological status with no residual spasms. **Conclusion:** Tetanus in children is not obsolete, and needs to be kept in mind in case of chronic suppurative otitis media.

Keywords: Equine immunoglobulin, pediatric, risus sardonicus

Tetanus, a disease present since ancient times, is not yet obsolete. Despite vaccinations, the disease continues to occur in areas with low coverage, lack of immunity, and unhygienic predisposing conditions.[1] Not all cases of tetanus in children occur following trauma, with chronic suppurative otitis media being an important setting favoring entry and proliferation of the anaerobic bacilli *Clostridium tetani*, especially in unvaccinated children.[2] Although otogenic tetanus is well known, it is now a rare occurrence and hence is being reported to reiterate its incidence even in current day.

Clinical Description

A 7-year-old boy presented in the emergency department with stiffness of the whole body and difficulty opening mouth for 10 days. There was no associated fever, jerking of the limbs, altered sensorium, vomiting, headache, visual impairment, and history of trauma. There was a history of pus discharge from the left ear for 1 month, associated with ear ache and fever for 3 days. There was no history of bleeding from the ear nor use of pin for ear cleaning. The child had been treated for otitis media with oral medications by a local physician. After 1 week of oral medicines, the child developed difficulty opening his mouth and swallowing, gradually progressing over 10 days, followed by stiffness of the whole body. The stiffness was episodic, lasting for few minutes, increased with triggers like physical touch, feeding, and loud noise.

He was the first child of nonconsanguineously married parents, born at term, with a birth weight of 2.7 kg. Antenatally, pregnancy was booked, and mother received tetanus vaccinations and underwent routine ultrasound scans. The natal and postnatal periods were uneventful. The child had not been immunized, except the birth dose. His development was appropriate for age and he was on an average Indian diet. The parents were migrant laborers with no significant illness.

On examination, the child was conscious and afebrile, in a state of generalized spasm of the body. All peripheral pulses were palpable with heart rate of 112/min, respiratory rate of 22/min, SpO_2 of 99% in room air, and blood pressure of

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Submitted: 12-Jul-2024 **Revised:** 09-Jan-2025
Accepted: 10-Jan-2025 **Published:** 14-Feb-2025

How to cite this article: Vikram A, Viagulam JC, Varadharajan P. Tetanus in a child due to otogenic source: A case report with review of literature. Indian Pediatr Case Rep 2025;5:9-11.

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Quick Response Code:

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DOI: 10.4103/ipcares.ipcares_161_24

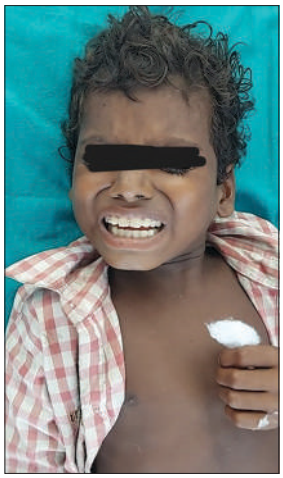

Figure 1: Risus sardonicus (sustained spasm of the facial muscles)

100/60 mmHg. He had severe spasms of the entire body with risus sardonicus [Figure 1]. The abdomen was rigid with no organomegaly, and cardiorespiratory system was normal. With this history and clinical presentation, a probable diagnosis of tetanus was kept.

Management and Outcome

The child was admitted in a sound-proof, dark, isolation room in the pediatric intensive care unit. The severity of tetanus, determined by modified Patel and Joag criteria,[2] had a score of 6 (moderate grade). Investigations revealed hemoglobin of 11.6 mg/dL, total leukocyte count 9000/mm^3, neutrophils 60.1%, lymphocytes 34.2%, C-reactive protein 14 mg/L, urea/creatinine 19/0.7 mg/dL, sodium/potassium/chloride 136/4.8/112 mEq/L, aspartate aminotransferase/alanine transaminase 24/28 IU/L, calcium 9.2 mg/dL, and creatinine phosphokinase of 480 units. Blood culture was negative. The child was started on maintenance intravenous fluids. The child developed respiratory failure on day 5 and was started on mechanical ventilation. Equine immunoglobulin (10,000 IU) was administered as a single intramuscular dose, after an intradermal test dose, since human antitetanus immunoglobulin (TIG) was not available. Tetanus toxoid vaccine was given intramuscularly. Ceftriaxone 100 mg/kg and metronidazole 30 mg/kg/day intravenously were given for 14 days. Muscle spasms were treated with diazepam 40 mg/kg/day intravenous bolus doses every 4 hours and chlorpromazine 0.5 mg/kg/dose 4 times a day. In view of persistent spasms, the child was further administered phenobarbitone 5 mg/kg/day twice daily. As per the advice of the otorhinolaryngologist, swab smear and culture were sent from the ear discharge, and a computed tomography of the brain was done. The latter was normal, while the ear swab was positive for *C. tetani*. Anaerobic Robertsons cooked meat broth was used as culture medium-the broth became turbid with gas formation and turned black color after 10 days of incubation, following which smear showed Gram positive bacilli with terminal, spherical bulging spores resembling drum stick appearance.

Ear toileting was done, and antibiotic ear drops were given. The child developed a lower respiratory tract infection on day 15, for which oral azithromycin and piperacillin–tazobactam was started. As muscle rigidity and spasms decreased gradually, the child was weaned from mechanical ventilation after 20 days. His oral intake improved by day 21. Antispasmodics were changed to oral forms (diazepam 1 mg/kg/day), and physiotherapy was started from the 4th week. The child was discharged after 35 days of hospitalization on diazepam. At 12 weeks follow-up, as the child was neurologically normal, with no residual spasms or neurodeficit, diazepam was tapered and stopped. Catch-up immunization for the child was advised.

Discussion with Review of Literature

The above is a successful story of management of a child with otogenic tetanus, a clinical condition now rarely observed by pediatricians.

Tetanus is a bacterial toxin-mediated, noncommunicable, potentially fatal neurological condition caused by *C. tetani*, affecting children primarily in developing countries with low vaccination coverage. There are around 56,000 estimated deaths related to tetanus worldwide.[2] Even in developed countries, cases of tetanus are being reported occasionally in current times, with over 300 tetanus patients reported in the USA between 2010 and 2022, and above 1500 cases of tetanus reported in the European Region since 2010.[3]

The anaerobic, spore-forming bacterium, commonly found in soil, dust, and animal excreta, enters the body through cuts or puncture wounds usually following trauma or crush tissue injury, rarely following insect bites and intravenous drug use.[1] In children, neonatal tetanus is most common, seen in the setting of home delivery, handling by untrained birth attendants, use of unsterile instruments, and other unclean traditional practices. In the absence of treatment, the mortality rate is 100% in neonatal tetanus.[4] The body, the bacteria produce a toxin, tetanospasmin, a potent neurotoxin that inhibits the release of glycine and GABA, leading to muscle spasms.

Otogenic tetanus is a rare form of tetanus, in which the portal of entry for the bacterium is via an ear infection. Persistent otorrhea in chronic otitis media causes *C. tetani* spores to enter the body through a perforation in the eardrum.[5] In such cases, the bacteria find an anaerobic environment conducive to producing tetanospasmin. A review of literature of published reports of children with otogenic tetanus over the last 20 years is presented in Table 1.

Differential diagnosis of tetanus infection in pediatric patients involves distinguishing from other conditions that may present with similar clinical features. Meningitis, with neck stiffness, fever, and irritability; hypocalcemia can also lead to muscle spasms and cramps; medications such as antipsychotics or antiemetics can cause dystonic reactions with muscle stiffness and spasms; rabies manifests with hydrophobia associated with muscle spasms with a history of animal exposure. Isolated trismus may be seen with

Table 1: Review of literature of the published reports of children with otogenic tetanus over the last 20 years

Author, year	Place	Number of cases	Age, gender	Outcome
Sharma and Kapoor, 2006[6]	India	1	2 years, female	Relapse
Mishra *et al*., 2012[7]	India	45/77 children with PNT	Mean age 8.65+2.5 years for all PNT cases; 40 male/37 female in all PNT cases	10/77 PNT cases expired
Adeel *et al*., 2012[8]	Pakistan	1	12 years, female	Improved
Kosam *et al*., 2015[9]	India	24	6.94±3.02 years, male: female: 1.4:1	Mortality rate 33.3%
Ogunkeyede *et al*., 2017[10]	Nigeria	23	Mean age 3.4 years±2.1 years, 13 male/10 female	3 deaths; rest recovered
Gupta and Vakharia, 2019[11]	India	1	8 years, female	Improved

PNT: Postneonatal tetanus

dental injuries/extraction/infections, zygomaticomaxillary trauma, or temporomandibular joint disorders. However, generalized rigidity and trismus, associated with intact consciousness, differentiates tetanus from the above conditions.[12]

Management of tetanus involves active and passive immunization with antibiotics and wound care, along with a dedicated supportive care. The TIG is most effective when administered preferably within 24 h after the diagnosis of tetanus. It should be given at a separate site from the tetanus toxoid vaccine to avoid interference. Human TIG is preferred compared to equine TIG due to less risk of hypersensitivity reactions. However, equine TIG is less expensive, making it a viable option in resource-limited settings. Sedation is crucial to avoid triggering muscle spasms. Antibiotics such as penicillin and metronidazole are recommended to eradicate the bacterial source.[1] Uncontrolled muscle spasms can lead to complications such as respiratory failure, fractures, and rhabdomyolysis. While if untreated, the condition has almost 100% fatality, treated cases have a case fatality of 10%–20%. Mishra *et al*., studying a large series of children with tetanus, reported mortality of 60% for neonatal tetanus and 12.9% for postneonatal tetanus, even among treated cases.[7]

Conclusion

The case reminds pediatricians about the continuing occurrence of tetanus in children, and must be kept as a possibility when a child presents with typical clinical features of tetanus, especially in the setting of chronic suppurative otitis media.

Lessons learnt

- Tetanus in children is still not obsolete and may be encountered by pediatricians
- As otogenic tetanus is an important source of Clostridium tetani, chronic suppurative otitis media in children should be treated promptly
- A dedicated supportive care in a sound-proof place, along with active and passive immunizations and antibiotics, can result in favorable outcome.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Afshar M, Raju M, Ansell D, *et al*. Narrative review: Tetanus-a health threat after natural disasters in developing countries. Ann Intern Med 2011;154:329-35.
2. Deniz M, Erat T. Generalized tetanus: A pediatric case report and literature review. Rev Inst Med Trop Sao Paulo 2023;65:e40.
3. World Health Organization. Tetanus reported cases and incidence. Available from: https://immunizationdata.who.int/global/wiise-detail-page/tetanus-reported-cases-and-incidence. [Last accessed 2024 Dec 24].
4. Hajaj H, Bahari H, Ayyad A, *et al*. Neonatal tetanus still exists: A case report and review of literature. Cureus 2024;16:e61410.
5. Akinbohun A, Ijaduola G. Otogenic tetanus among children in Ibadan, Nigeria. Internet J Otolaryngol 2008;10:14.
6. Sharma A, Kapoor S. Relapse in a child with otogenic tetanus. Trop Doct 2006;36:56-7.
7. Mishra K, Basu S, Kumar D, *et al*. Tetanus – Still a scourge in the 21st century: A paediatric hospital-based study in India. Trop Doct 2012;42:157-9.
8. Adeel M, Rajput SA, Awan MS, *et al*. A case of otogenic tetanus. BMJ Case Rep 2012;2012:bcr0320125976.
9. Kosam A, Durga K, Kumar H. Clinical profile and prognostic indicators of tetanus in children. Int J Med Res Rev 2015;3:601-607. doi: 10.17511/ijmrr.2015.i6.
10. Ogunkeyede SA, Daniel A, Ogundoyin O. Paediatric otogenic tetanus: An evidence of poor immunization in Nigeria. Pan Afr Med J 2017;26:177.
11. Gupta SR, Vakharia SD. Otogenic tetanus though immunisable but still existing. Indian J Otol 2019;25:37-9.
12. Santiago-Rosado LM, Lewison CS. Trismus. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK493203/. [Last updated on 2022 Oct 27].

Case Report

Methemoglobinemia and Glucose-6-phosphate Dehydrogenase Deficiency in a Neonate

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Abstract

Background: Methemoglobinemia is a condition where heme iron is oxidized from ferrous to ferric state, leading to hypoxia. Commonly due to drugs and toxins, it may rarely occur due to glucose-6-phosphate dehydrogenase (G6PD) deficiency. **Clinical Description:** A 20-day-old male neonate presented with lethargy, fever, loose stools, yellowish discoloration of skin, and dark urine. He had received ofloxacin earlier for diarrhea. On examination, neonate was in shock, with cyanosis and respiratory distress. Abdomen, chest, and cardiovascular system were normal. **Management and Outcome:** Despite increasing FiO_2 and supportive care for shock, SpO_2 did not improve. Chest X-ray, hyperoxia test, and echocardiography ruled out cyanotic cardio-pulmonary disease. Arterial blood gas showed PaO_2 >100 mmHg at SpO_2 84%. Co-oximetry confirmed elevated methemoglobin (MetHb) levels of 25.9%. The G6PD levels were low, precluding use of methylene blue. With high dose of Vitamin C and blood transfusion, the neonate recovered. **Conclusion:** Methemoglobinemia must be kept in mind while treating a patient with disproportionate hypoxia and cyanosis, not responding to oxygen therapy. Before giving methylene blue, G6PD deficiency should always be ruled out.

Keywords: Glucose-6-phosphate dehydrogenase, hemolytic anemia, newborn, saturation gap

Methemoglobinemia is a rare cause of cyanosis in an infant, which occurs when the iron in hemoglobin (Hb) is oxidized from the ferrous form (Fe^{2+}) to the ferric form (Fe^{3+}), thus hampering the ability of Hb to transport oxygen, resulting in tissue hypoxia.[1] We present an interesting clinical scenario of acquired methemoglobinemia in a neonate, the complexity of management getting escalated by the additional presence of an underlying glucose-6-phosphate dehydrogenase (G6PD) deficiency. Only few cases of methemoglobinemia have been reported associated with G6PD deficiency.[2]

Clinical Description

A 20-day-old male infant presented with history of fever, loose stools, and vomiting for 6 days, followed by development of yellowish discoloration, lethargy, and dark-colored urine over the past 3 days. The baby was exclusively breastfed and was apparently well till 14 days of life, when he became symptomatic, after undergoing a circumcision. The baby was prescribed oral ondansetron, ofloxacin, metronidazole, and herbal liver enzyme drops by a local practitioner. Three days later, the infant developed jaundice, dark-colored urine, and lethargy. The stools remained yellow, whereas the urine caused an orangish-brown color on the diaper.

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DOI: 10.4103/ipcares.ipcares_29_24

The baby was born full-term, weighing 3.16 kg, to a G2P1 L1 mother from a second-degree consanguineous marriage. The antenatal and natal periods were unremarkable. Although there was a history of neonatal jaundice on day 4, the infant did not receive any phototherapy.

At the time of admission, the baby was euthermic with a weight of 3.05 kg, heart rate 150/min, respiratory rate 52/min, with SpO_2 of 78%–82% in room air. His anterior fontanelle was depressed, skin turgor slow, capillary refill >3 seconds, peripheral pulses weak, peripheries cold and cyanosed, pallor present, with icterus present till abdomen. Systemic examination revealed an irritable but consolable neonate with normal tone and spontaneous activity in all four limbs. The abdomen was soft with no organomegaly, cardio-respiratory system examination being normal. The provisional diagnosis was kept as late-onset sepsis with shock and respiratory failure, associated with jaundice and acute gastroenteritis.

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Submitted: 06-Feb-2024 **Revised:** 02-Jun-2024
Accepted: 16-Dec-2024 **Published:** 14-Feb-2025

How to cite this article: Aggarwal S, Garg S, Sehgal MJ, Bhatia JS. Methemoglobinemia and glucose-6-phosphate dehydrogenase deficiency in a neonate. Indian Pediatr Case Rep 2025;5:12-4.

Management and Outcome

High-flow oxygen therapy was initiated along with intravenous fluids and antibiotics. Initial laboratory investigations [Table 1] revealed anemia with a hemoglobin of 8.2 g/dL, slightly elevated C-reactive protein (13.7 mg/dL), indirect hyperbilirubinemia (total/direct bilirubin 17.3 / 0.95 mg/dL), and mild respiratory acidosis on venous blood gas analysis (pCO_2 of 26 mmHg, paO_2 93 mmHg, pH 7.4, HCO_3 18.7 meq/L). Despite increasing FiO_2 to 95%, SpO_2 did not improve. Hence, congenital cyanotic heart disease (CCHD) was suspected; hyperoxia test was negative and two-dimensional-echocardiography was normal ruling out CCHD. A chest radiograph was normal. As arterial blood gas showed "saturation gap" with PO_2 >100 mmHg with a concurrent SpO_2 of 84%, a possibility of methemoglobinemia was considered. Co-oximetry was done which revealed elevated methemoglobin (MetHb) levels of 25.9%, confirming the diagnosis. Further, baby was noticed to pass cola-colored urine after the initial fluid bolus, suggestive of intravascular hemolysis. Hence, diagnosis was revised to hemolytic anemia with methemoglobinemia.

Before administration of methylene blue, which is the first-line treatment for methemoglobinemia, a quantitative estimation of G6PD was done, showing a value of 4.37 U/g Hb (normal range 7.0–20.5 g Hb), suggesting G6PD deficiency. As methylene blue is contraindicated in G6PD deficiency, the neonate was given high dose of Vitamin C (5 mg/kg q 6 h) orally for 4 days. Furthermore, as serial investigations showed progressive anemia (Hb reaching 3 g/dL), packed red blood cells (RBCs) was transfused. The clinical condition of the neonate gradually improved and serial co-oximetry also showed a fall in MetHb level to 0.3% by 36 hours. The patient was discharged with normal oxygen saturation, no active hemolysis, and good weight gain on breast and formula feed. Parents were counseled regarding medication and other agents leading to hemolysis in G6PD deficiency. The patient is on regular outpatient department follow-up, thriving well and is asymptomatic.

Table 1: Results of investigations done at admission

Test	Value
Hemoglobin (g/dL)	8.2
Total leucocyte count (/mm^3)	36.4
Platelets (/mm^3)	234
C-reactive protein (mg/L)	13.7
Urea/creatinine (mg/dL)	39.5/0.83
Bil (total/unconjugated) (mg/dL)	17.3/16.4
AST/ALT (IU/L)	165/25
Alkaline phosphatase	279
LDH (U/L)	1134
Albumin	3.4
Na/K/Cl (meq/L)	138/4.9/98
Calcium	10.1
Direct Coombs test	Negative
Reticulocyte count (%)	8.9
G6PD (U/g hemoglobin)	4.34

G6PD: Glucose-6-phosphate dehydrogenase, LDH: Lactate dehydrogenase, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase

Discussion

Methemoglobinemia occurs when the iron within the Hb oxidizes from its usual ferrous (Fe^{2+}) to a ferric (Fe^{3+}) state, impairing oxygen carrying capacity,[3] thus leading to cyanosis. The condition may be acquired or congenital. Congenital MetHb is due to deficiency of cytochrome b5 reductase (CYB5R) in RBCs which physiologically maintains low methemoglobinemia levels by converting ferric iron back to ferrous form.[4] Acquired methemoglobinemia, which is more common, can result from exposure to oxidizing agents.[5] As newborns have low CYB5R activity compared to adults, they are prone to develop methemoglobinemia.[6]

Glucose-6-phosphate dehydrogenase deficiency is an X-linked disorder, with a global prevalence of 4.9%, being the most common human enzyme defect. This enzyme reduces nicotinamide adenine dinucleotide phosphate (NADP) to NADPH, thus protecting the RBCs against oxidative stress. In individuals with G6PD deficiency, oxidizing stresses such as sepsis, or certain drugs can cause hemolytic anemia.[3] Such oxidative stress in the setting of G6PD deficiency can also lead to methemoglobinemia, as methemoglobin reductase is dependent on NADPH, which is unavailable in G6PD deficiency.

In our case, ofloxacin which was prescribed to the baby by a rural medical practitioner for fever and loose stools, is classified as high-risk drug for causing hemolysis in individuals with G6PD deficiency. Thus, this seems the most likely trigger for hemolysis and methemoglobinemia in this patient, a scenario closely aligning with the findings described by Titheradge *et al*.[5]

The clinical features of methemoglobinemia correlate with MetHb levels, which are often reported as a percentage of total hemoglobin.[7] Levels of 10%–20% present with cyanosis only, while at 20%–30% MetHb levels, symptoms of mild breathing difficulty, tachycardia, and headache develop. Above 50%, severe dyspnea, arrhythmia may develop, eventually being fatal.[1] Our patient, with a measured MetHb level of 25%, exhibited cyanosis, moderate respiratory distress, and shock,–symptoms more severe than typically expected at this level due to his underlying anemic status. When MetHb levels are beyond 30%, SpO_2 plateaus at around 85%, despite high FiO_2, though oxygen saturation in arterial blood gas analysis corresponds to increasing FiO_2.[8] Confirmatory diagnosis can be made by co-oximetry which was done in our case;[8] the other test being the Evelyn-Malloy test.[9]

Treatment aims at eliminating the offending agent and supportive care, the drug of choice being methylene blue.[10] Ours was a difficult case to treat, as the newborn was G6PD deficient, a situation in which methylene blue is contraindicated. Thus, Vitamin C was administered as an alternative,[7] results

being favorable. Exchange transfusion and hyperbaric oxygen are also used in refractory cases.[1]

Conclusion

This case emphasizes the importance of considering methemoglobinemia as a potential diagnosis in neonates presenting with persistent cyanosis after excluding respiratory and cardiac causes. In addition, methylene blue should be avoided in methemoglobinemia when G6PD deficiency is suspected.

Lessons learnt

- Methemoglobinemia should be considered in neonates with persistent cyanosis
- Glucose-6-phosphate dehydrogenase (G6PD) levels need to be assessed before treating with methylene blue
- Ascorbic acid should be used instead of methylene blue in the presence of G6PD deficiency.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that his name and initials will not be published and due efforts will be made to conceal his patient identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Kaminecki I, Huang D. Methemoglobinemia. Pediatr Rev 2021;42:164-6.
2. Ludlow JT, Wilkerson RG, Nappe TM. Methemoglobinemia. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537317/. [Last updated on 2023 Aug 28].
3. Lyle AN, Spurr R, Kirkey D, *et al.* Case report of congenital methemoglobinemia: An uncommon cause of neonatal cyanosis. Matern Health Neonatol Perinatol 2022;8:7.
4. Percy MJ, Lappin TR. Recessive congenital methaemoglobinaemia: Cytochrome b (5) reductase deficiency. Br J Haematol 2008;141:298-308.
5. Titheradge H, Nolan K, Sivakumar S, *et al.* Methaemoglobinaemia with G6PD deficiency: Rare cause of persistently low saturations in neonates. Acta Paediatr 2011;100:e47-8.
6. Iolascon A, Bianchi P, Andolfo I, *et al.* Recommendations for diagnosis and treatment of methemoglobinemia. Am J Hematol 2021;96:1666-78.
7. Wright RO, Lewander WJ, Woolf AD. Methemoglobinemia: Etiology, pharmacology, and clinical management. Ann Emerg Med 1999;34:646-56.
8. Haymond S, Cariappa R, Eby CS, *et al.* Laboratory assessment of oxygenation in methemoglobinemia. Clin Chem 2005;51:434-44.
9. Arnaud F, Higgins A, McCarron R, *et al.* Determination of methemoglobin and hemoglobin levels in small volume samples. Artif Cells Nanomed Biotechnol 2017;45:58-62.
10. Skold A, Cosco DL, Klein R. Methemoglobinemia: Pathogenesis, diagnosis, and management. South Med J 2011;104:757-61.

Case Report

Incomplete Kawasaki Disease Presenting as Anterior Mediastinitis and Neck Cellulitis

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Abstract

Background: While classical Kawasaki disease (KD) is easily diagnosed by a well-established set of diagnostic criteria, the diagnosis of incomplete KD remains elusive. **Clinical Description:** A 1-year-old girl presented with high fever, painful swelling, and redness over the anterior part of the neck, associated with swallowing difficulty. There was no rash, redness of eyes, or lymphadenopathy. **Management and Outcome:** Considering cellulitis of the neck, antibiotics were initiated. She developed stridor and received dexamethasone. Fever subsided, dysphagia and neck swelling improved by 3 days, but fever re-appeared on day 5, with progressively rising total leukocyte counts, platelets, and C-reactive protein. Magnetic resonance imaging neck showed features of anterior mediastinitis. Bacillus Calmette–Guérin reactivation was noted on day 8. Suspecting atypical KD, echocardiography was done thereafter, which showed left main coronary artery aneurysm. Intravenous immunoglobulin and aspirin were started. Because of medium sized aneurysm at repeat echo, increasing in size, treatment was intensified with infliximab and prednisolone. Follow-up echo after 2 weeks, showed diminution in the size of aneurysm with complete regression by 2 months. **Conclusion:** The case highlights yet another atypical manifestation of KD. Only a high index of suspicion in an unusual course of febrile illness in a child can diagnose such incomplete forms of KD.

Keywords: Atypical Kawasaki disease, bacillus Calmette–Guérin reactivation, coronary aneurysm

Kawasaki disease (KD) is the most common cause of acquired heart disease among children. Coronary artery aneurysms can lead to myocardial ischemia, infarction, and sudden death. The definition of atypical KD should be reserved for patients who have clinical manifestations not fulfilling the criteria for classic KD.[1,2] The potentially severe outcome of either classic or incomplete KD without therapy emphasizes the importance of early identification and treatment of all patients with the disease. We report a case of incomplete KD with a rare presentation.

Clinical Description

A 1-year-old girl presented with fever and cough for 5 days, painful swelling, and redness at the front of the neck, associated with difficulty in swallowing for 1 day. There was no rash, lymphadenopathy, altered sensorium, redness of eyes, icterus, vomiting, diarrhea, or urinary symptoms. She was being treated by a local practitioner with oral amoxicillin/clavulanic acid along with paracetamol since the first day of illness. Past history and family history were insignificant, and she had received all her vaccines till date.

On admission, the child was conscious but irritable with a temperature of 101°F, heart rate of 130/minute, respiratory rate of 32/min, SpO_2 of 97% in room air, and normal volume pulses with a blood pressure of 86/68 mmHg. Her anthropometry was appropriate for age. Mild pallor was present, but icterus, cyanosis, clubbing, edema, and lymphadenopathy were absent. The swelling on the anterior part of the neck was diffuse, 10 cm × 5 cm, with erythema of overlying skin and tender on palpation. Examination of the throat and oral cavity was unremarkable, and systemic examination was normal.

Management and Outcome

Considering a possible diagnosis of cellulitis of the neck, she was started on intravenous ceftriaxone and flucloxacillin. Initial investigations [Table 1] revealed anemia, a high total leukocyte count (TLC), and raised C-reactive protein (CRP). The throat swab did not yield any pathogen, and the blood culture was sterile. The child

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Submitted: 14-Jun-2024 **Revised:** 01-Jan-2025
Accepted: 03-Jan-2025 **Published:** 14-Feb-2025

How to cite this article: Dey S, Das B, Pal P, Lalbiakzuali N. Incomplete Kawasaki disease presenting as anterior mediastinitis and neck cellulitis. Indian Pediatr Case Rep 2025;5:15-7.

Access this article online

Quick Response Code:

Website: www.ipcares.org

DOI: 10.4103/ipcares.ipcares_131_24

developed stridor on day 2, and considering a possibility of acute laryngotracheobronchitis, he received a single dose of intravenous dexamethasone along with adrenaline nebulization. Because of dysphagia and stridor being present in the background of neck cellulitis, magnetic resonance imaging (MRI) [Figure 1] of the neck was performed, which showed a diffuse increase in signal intensity of subcutaneous tissue on fat-suppressed images with multiple enlarged lymph nodes bilaterally. T2 fat suppressed (T2FS) screening of the anterior chest showed edema of the mediastinum with enlarged anterior mediastinal lymph nodes, suggesting anterior mediastinitis.

Fever subsided on day 3 of hospitalization, stridor subsided, dysphagia improved, and the child started accepting oral feeds. In view of the symptomatic improvement, otorhinolaryngology opinion was deferred. The neck swelling gradually subsided, but fever recurred on day 5, with an increase in TLC and platelets. Along with persistent fever, TLC and platelets continued to rise, with the CRP almost doubling from 67.3 mg/l to 126 mg/l from days 6–8. Furthermore, on day 8, erythema and edema of bacillus Calmette–Guérin (BCG) site were noticed, suggesting BCG reactivation. Our patient initially presented as neck cellulitis and anterior mediastinitis was unresponsive to antibiotics, continued to have high TLC and CRP with progressively increasing platelets. BCG reactivation and echo cardiography showing coronary artery aneurysm finally clinched the diagnosis of KD. A two-dimensional (2D) echocardiography was advised which showed small left main coronary artery (LMCA) aneurysm (+2.9 Z). Thus, the diagnosis was revised to atypical KD with LMCA small aneurysm presenting as neck cellulitis and anterior mediastinitis.

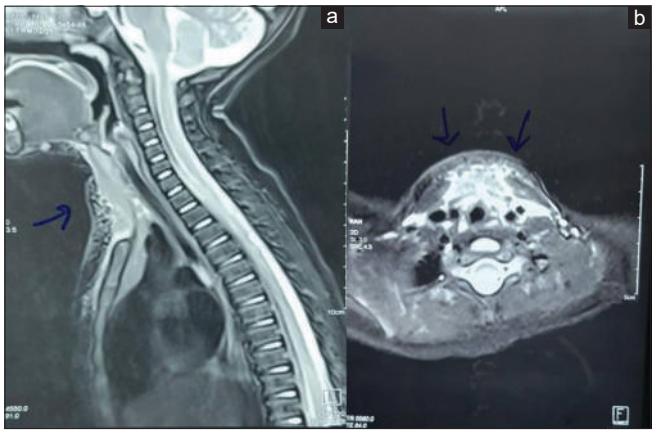

Figure 1: (a and b) Magnetic resonance imaging neck showing edema of the anterior mediastinum, enlarged lymph nodes, and cellulitis suggestive of anterior mediastinitis. The arrows show the cellulitis of the anterior chest wall

The child was started on intravenous immunoglobulin (IVIg) 2 g/kg over 16 hours over along with aspirin 5 mg/kg as per institutional protocol on day 8 of admission. The child became afebrile within 24 hours of completion of IVIg therapy. Repeat echocardiography after 2 days showed an increase in the size of LMCA aneurysm (+6.9 Z). Considering the presence of a medium-sized aneurysm, treatment was intensified with infliximab (10 mg/kg single dose) on day 10. On day 12, LMCA aneurysm showed some regression (+5.8 Z), but CRP remained high (67.7 mg/l). Hence, oral prednisolone 2 mg/kg was started, and the child was discharged on prednisolone and aspirin, with plan to taper off prednisolone over 15 days. Progressive regression in the size of LMCA aneurysm was seen after 15 days (+4.6 Z) with complete regression by 2 months.

Discussion

Kawasaki disease, predominantly an acute-onset vasculitis of medium vessels, primarily affecting children below 5 years of age, though known in the literature for over 50 years, still puzzles pediatricians with its ever-evolving atypical manifestations. The exact cause remains unknown, with no single pathognomonic clinical or laboratory finding for

Table 1: Serial investigations of the index child

Investigations/treatment	Day 1	Day 3	Day 6	Day 8	Day 10	Day 12	After 2 weeks	After 8 weeks
Hb (g/dL)	9.3	8.9	9.0	8.6		8.1		
TLC (/mm^3)	12,000	1,3980	18,700	18,500		14,300		
DLC (%)	N52L41	N37L59	N75L45	N61L32		N24L70		
Platelets (/mm^3)	446,000	556,000	683,000	873,000		992,000		
CRP (mg/L)	109.2	53.6	67.3	126		67.7		
Na/K (mg/dL)	138/5.05							
Urea/creatinine (mg/dL)	19/0.23							
TP/albumin (mg/dl)	6.6/3.9							
AST/ALT (IU/L)	70/74							
Bilirubin (total/direct) (mg/dl)	0.38/0.2							
Echocardiography				LMCA + 2.93Z	LMCA + 6.91Z	LMCA + 5.8 Z	LMCA + 4.18Z	LMCA + 2.07Z
Therapy				IVIg + Aspirin	Infliximab	Prednisolone		

Hb: Hemoglobin, TLC: Total leukocyte count, DLC: Differential count, CRP: C-reactive protein, Na: Sodium, K: Potassium, TP: Total protein; AST/ALT: Aspartate aminotransferase/alanine transaminase, LMCA: Left main coronary artery, IVIg: Intravenous immunoglobulin

making the diagnosis. The standard diagnostic criteria of KD are based on a set of symptoms and signs developed by the American Heart Association (AHA)[1] or the Japanese Kawasaki Disease Research Committee.[2] Atypical KD was used for patients who did not meet the classical criteria but had coronary complications, but recently, it was proposed to use atypical KD interchangeably with incomplete KD, regardless of coronary complications. The incidence of incomplete KD ranges from 15% to 36.2%, being relatively more common in children at extremes of age (<1 year old or >5 years).[3] No other factor has been found to be associated with the incidence of incomplete KD.

As per AHA, a diagnosis of incomplete KD is possible in children with fever and two principal features (according to the Japanese criteria, three principal symptoms), along with six additional laboratory and echocardiographic criteria. To diagnose atypical KD, a patient should have more than three laboratory abnormalities, which include anemia for age, sterile pyuria, hypoalbuminemia (≤3 gm/dl), leukocytosis (≥15000/mm^3), and elevation of alanine aminotransferase (ALT) and platelet cell count.[4,5] In our case, we found anemia, leukocytosis, and elevated platelet count, though sterile pyuria, hypoalbuminemia, and elevated ALT features were absent.

Other findings which support the diagnosis of atypical KD are inflammation at the BCG inoculation site (found in our case), anterior uveitis, elevated levels of brain natriuretic peptide (BNP) and N-terminal pro-BNP, hyponatremia, elevation of left ventricular mass, and diastolic dysfunction of the left ventricle.[6-8] Hua *et al*.[9] reported that in patients <6 months old, total fever duration of ≥8 days, delayed diagnosis, and albumin ≤3.5 mg/dl were independent risk factors for coronary artery lesions in KD. Mediastinal lymphadenopathy is a rare finding associated with KD.[10] Our patient initially presented as neck cellulitis and anterior mediastinitis was unresponsive to antibiotics, continued to have high TLC and CRP with progressively increasing platelets. BCG reactivation and echo cardiography showing coronary artery aneurysm finally clinched the diagnosis of KD.

Conclusion

The case creates awareness among pediatricians to consider the possibility of incomplete KD in children who have had an unresolving, unexplained fever, unresponsive to antibiotics for more than 5 days, meeting some of the clinical criteria of KD, especially with clues like BCG reactivation. Incomplete KD can easily be missed, if not suspected, and delayed diagnosis may result in a higher risk of developing coronary artery lesions. Treatment needs to be intensified in the presence of coronary aneurysms.

Lessons learnt

- Index of suspicion should be high for incomplete KD in young children presenting with unexplained fever for more than 5 days associated with some evidence of systemic inflammation
- Incomplete and atypical presentations are common in infantile KD, and a 2D echocardiography should be performed at the earliest suspicion
- Treatment needs to be intensified in the presence of coronary aneurysms.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Council on Cardiovascular Disease in the Young, Committee on Rheumatic Fever, Endocarditis, *et al*. Diagnostic guidelines for Kawasaki disease. Circulation 2001;103:335-6.
2. Japan Kawasaki Disease Research Center, Japan Kawasaki Disease Research Committee. Tokyo: Japan Kawasaki Disease Research Center, Japan Kawasaki Disease Research Committee; c2012. Diagnostic guidelines of Kawasaki disease. Available from: https://kawasaki-disease.org/diagnostic/. [Last accessed on 2001 Jan 09].
3. Sonobe T, Kiyosawa N, Tsuchiya K, *et al.* Prevalence of coronary artery abnormality in incomplete Kawasaki disease. Pediatr Int 2007;49:421-6.
4. Newburger JW, Takahashi M, Gerber MA, *et al.* Diagnosis, treatment, and long-term management of Kawasaki disease: A statement for health professionals from the committee on rheumatic fever, endocarditis, and Kawasaki disease, council on cardiovascular disease in the young, American Heart Association. Pediatrics 2004;114:1708-33.
5. Jun HO, Yu JJ, Kang SY, *et al.* Diagnostic characteristics of supplemental laboratory criteria for incomplete Kawasaki disease in children with complete Kawasaki disease. Korean J Pediatr 2015;58:369-73.
6. Sinha R, Balakumar T. BCG reactivation: A useful diagnostic tool even for incomplete Kawasaki disease. Arch Dis Child 2005;90:891.
7. Bang S, Yu JJ, Han MK, *et al.* Log-transformed plasma level of brain natriuretic peptide during the acute phase of Kawasaki disease is quantitatively associated with myocardial dysfunction. Korean J Pediatr 2011;54:340-4.
8. Muta H, Ishii M, Egami K, *et al.* Serum sodium levels in patients with Kawasaki disease. Pediatr Cardiol 2005;26:404-7.
9. Hua W, Ma F, Wang Y, *et al.* A new scoring system to predict Kawasaki disease with coronary artery lesions. Clin Rheumatol 2019;38:1099-107.
10. Javadi V, Shiari R, Rahmani K, *et al*. Mediastinal lymphadenopathy in a child with Kawasaki disease. Open Access Rheumatol 2020;12:87-9.

Case Report

Moyamoya Disease: A Cerebrovascular Involvement in a Child with Wiskott–Aldrich Syndrome

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Abstract

Background: Wiskott–Aldrich syndrome (WAS) is a rare X-linked disorder characterized by immunodeficiency, thrombocytopenia, and eczema, with a risk of autoimmune phenomena. **Clinical Description:** A 3-year-old boy presented to us with a history of recurrent skin and mucosal bleeds, itchy skin lesions, and recurrent purulent ear discharge. He had been hospitalized for pneumonia and meningitis earlier, having developed left-sided hemiplegia associated with a cerebral infarct. On examination, he was growth retarded with pallor, hepatosplenomegaly, multiple purpuric spots, and infected scalp lesions. In addition, he had spastic hemiparesis in the left side. **Management and Outcome:** Investigation revealed microcytic hypochromic anemia, eosinophilia, thrombocytopenia, and very high IgE titer (10,433). Coagulation profile was normal. Tuberculosis work-up was negative. The mean platelet volume was low normal (7.3) and bone marrow showed decreased number and size of megakaryocytes. Exome sequencing showed pathogenic mutation of *WAS* gene in exon 3 hemizygous XLR variant. The patient received weekly intravenous immunoglobulin therapy and cotrimoxazole. The eczema, thrombocytopenia, and infections improved. Later, he developed sudden-onset bilateral loss of vision. Magnetic resonance (MR) imaging brain revealed acute infarct on the left occipital region and gliosis in the right cerebral hemisphere with MR angiography showing middle and posterior cerebral artery thrombosis and narrowing of bilateral distal internal carotid arteries suggestive of moyamoya disease. Immunosuppressive agents and antiplatelets could not be administered, so the child was kept under supportive care. **Conclusion:** This case makes pediatricians aware of the possibility of cerebrovascular events as a manifestation of autoimmune vasculitis in children with WAS. Optimal treatment for such cases needs research.

Keywords: Autoimmune vasculitis, autoimmunity, eczema, immunodeficiency

Wiskott–Aldrich syndrome (WAS) is a rare X-linked immune deficiency disorder characterized by thrombocytopenia, eczema, and susceptibility to infections. Approximately 50% of *WAS* gene mutations have classical-WAS phenotype, others have XLT (X-Linked Thrombocytopenia) phenotype.[1] Apart from usual manifestations, there is an increased risk of autoimmune phenomena and lymphoreticular tumors in WAS.[2] Here, we present a unique case of WAS with cerebral vessel involvement consistent with moyamoya disease. Such association of WAS with moyamoya syndrome has perhaps not been reported before.

Clinical Description

A 3-year-old boy presented to us with a history of multiple episodes of bleeding from the nose and bleeding spots in various parts of the body, occurring since infancy. The bleeding spots appeared in crops, without any history of trauma. There was a history of intermittent epistaxis and gum bleeding. His parents also complained of increasing pallor as well as gradual distension of the abdomen for 1 year. There was no associated fever, bone pain, or jaundice.

The child had been hospitalized multiple times in the past, receiving multiple blood and platelet transfusions. He was suspected and managed as a case of immune thrombocytopenia or inherited marrow failure syndromes, without reaching a final diagnosis. In addition, the child had a history of recurrent purulent discharge from both ears, since the age of 3 months, responding each time to oral antibiotics. Since the age of 8 months, the child had itchy lesions over the scalp with serous discharge, often turning purulent with scratching. He received topical steroids and oral antihistaminic drugs regularly for these. There was a history of hospitalization for one episode of meningitis and another for bronchopneumonia at the age of 15 months and 24 months, respectively, as per previous discharge certificates.

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DOI: 10.4103/ipcares.ipcares_139_24

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Submitted: 20-Jun-2024 **Revised:** 24-Dec-2024
Accepted: 26-Dec-2024 **Published:** 14-Feb-2025

How to cite this article: Das E, Pati S, Jesmin S, Paul A. Moyamoya disease: A cerebrovascular involvement in a child with Wiskott–Aldrich syndrome. Indian Pediatr Case Rep 2025;5:18-22.

There was no history of similar illness in any family member. The patient was the first and only child of his parents, born out of nonconsanguinous marriage, at term. Antenatal, natal and postnatal periods were uneventful. Developmental history was normal up to the age of 15 months, following which he had meningitis and developed weakness of left side of body. By 2 years of age, he could walk dragging the left leg. He spoke few words with meaning, though hearing was apparently intact. He was immunized as per national schedule.

On examination, the child was conscious, with pallor, but no icterus, cyanosis, edema, or clubbing nor significant lymphadenopathy. He was afebrile with a heart rate of 98/min and respiratory rate of 29/min. Head-to-toe examination showed evidence of epistaxis, petechial spots all over the body, and multiple infected lesions over the scalp and face and evidence of epistaxis [Figure 1]. He had a weight of 10.5 kg, height 79 cm (both <−3 SD as per the WHO growth charts) head circumference being 47 cm (5th percentile). His abdomen was distended, umbilicus inverted, without venous prominence; liver palpable 5 cm below the right costal margin, firm and nontender, while spleen was 4 cm palpable along splenic axis. There was left-sided hemiparesis, with no cranial nerve involvement; tone being increased in both upper and lower limbs with brisk deep tendon reflexes on the left side. Power in both upper and lower limbs of left side was 3/5. Examination of cardiorespiratory system was within normal limits. Based on history and clinical examination, possible differentials considered were chronic immune thrombocytopenia, Evans syndrome, and primary immunodeficiency.

Management and Outcome

Routine investigations [Table 1] showed anemia, with reticulocyte 1.5%, red cell distribution width 22.9, and low platelets (34,000/mm^3). Peripheral smear showed hypochromic microcytic red cells, MCV 82%, MCH 22, MCHC 24.4, with mean platelet volume 7.3 fl (7.9–12 normal). Alkaline phosphatase was 177 IU/L, lactate dehydrogenase was 950 IU/L. Serum iron (50 µg/dL), ferritin (104 ng/mL), and total iron binding capacity (400 µg/dL) were normal. High-performance liquid-chromatography testing for thalassemia was negative (HbA 97%, HbA2 2%, Hb-F 1%). The Direct Coombs Test was negative and coagulation profile was within normal limits. Integrated counseling and testing was nonreactive.

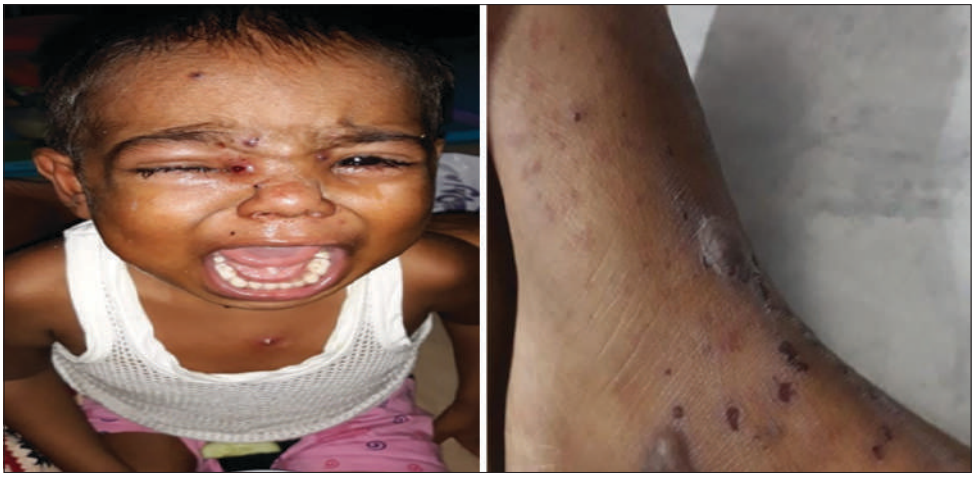

Figure 1: Child with infected eczematous skin lesions and purpuric spots in lower legs

Table 1: Results of serial investigations of the child done during hospitalization

Parameters	Day 1 (at hospitalization)	Day 3	Day 7 (after platelet transfusion)	Day 14	Day 21	Day 55 (at discharge)
Hb (g/dL)	6.6	4.6	12.1	12	12	11.9
TLC (/mm^3)	14,000	19,000	17,400	16,800	14,100	13,000
Platelet (/mm^3)	34,000	<10,000	60,000	40,000	20,000	60,000
Neutrophil/lymphocytes/eosinophils (%)	50/22/30	45/17/34	46/15/32	40/20/28	45/28/26	48/25/22
CRP/ESR	85/2.39	82/3.4	54/1.8	44/1.5	40/0.9	34/0.9
Bilirubin (total/conjugated) (mg/dL)	0.5/0.3	0.5/0.2	0.4/0.2	0.6/0.3	0.5/0.1	0.4/0.1
Urea/creatinine (mg/dL)	26/0.6	26/0.5	20/0.7	22/0.9	24/0.5	14/0.5
Na/K/Cl (mEq/L)	139/4.1/100	142/3.8/103	137/3.1/98	138/3.4/98	140/3.5/99	144/3.8/101
AST/ALT (IU/L)	46/38	40/31	44/30	38/30	46/28	48/20

Hb: Hemoglobin, TLC: Total leukocyte count, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, Na: Sodium, K: Potassium, Cl: Chloride, AST/ALT: Aspartate aminotransferase/alanine transaminase

Thus, the differential diagnoses considered in a child with chronic anaemia, hepatosplenomegaly, recurrent sino-pulmonary infections and itchy skin rashes were primary immunodeficiency like common variable immunodeficiency, Langerhans cell histiocyosis(LCH) and disseminated tuberculosis. Immunoglobulin profile showed raised IgE: 10,433 IU/ml (0–60 IU/mL) and IgG: 3270 mg/dL (range 700–1700 mg/dl), slightly raised IgA: 524 mg/dl (72–350 mg/dL) and low IgM: 48 mg/dL (50–300 mg/dl) levels. Neutrophil oxidative index was 1.33 (normal value: <2). Skeletal survey revealed no punched out osteolytic lesions characteristic of LCH. As seborrhea scalp and characteristic rash of LCH were absent, skin biopsy was not planned. Mantoux test and gastric lavage for CBNAAT were negative. Chest X-ray was noncontributory. A bone marrow examination was done, which showed decreased number and size of megakaryocytes with cellular reactive marrow with a myeloid to erythroid ratio of 1.5:1 and eosinophilic preponderance. Our primary suspicion was WAS, though the platelet size was not small. A whole-exome sequencing was advised. Meanwhile, the child was managed with intravenous co-amoxiclav and topical antibiotics for the folliculitis on the scalp and face along with oral antihistaminic drugs. Packed red blood cells and platelets were transfused as Hb dropped to 4.6 gm/dL after massive epistaxis. Platelet counts remained between 10,000 and 40,000/mm^3 [Table 1], with high eosinophil counts and IgE > 2500 IU/mL.

Whole-exome sequencing showed pathogenic mutation of *WAS* gene exon 3 splice variant c.326_327 del hemizygous, XLR variant. Thus the child was diagnosed as a case of WAS with failure to thrive, anaemia, hepatosplenomegaly along with classical triad. Spastic hemiplegia could be explained as a sequel of previous meningitis. Computed tomography brain done at that time had shown focal hypodensity in the right parietal lobe. The child was planned for weekly intravenous immunoglobulin (IVIG) therapy 400 mg/kg, starting on Day 55 of hospitalization. He was discharged on cotrimoxazole thrice weekly as prophylaxis against pneumocystis jiroveci pneumonia. After receiving 4 cycles of IVIG, the petechiae disappeared, platelet count gradually increased, and plateaued at 1lakh/mm; eczema also improved.

However, on attaining 4 years of age, the patient presented with sudden onset, painless loss of vision in both eyes. There was no

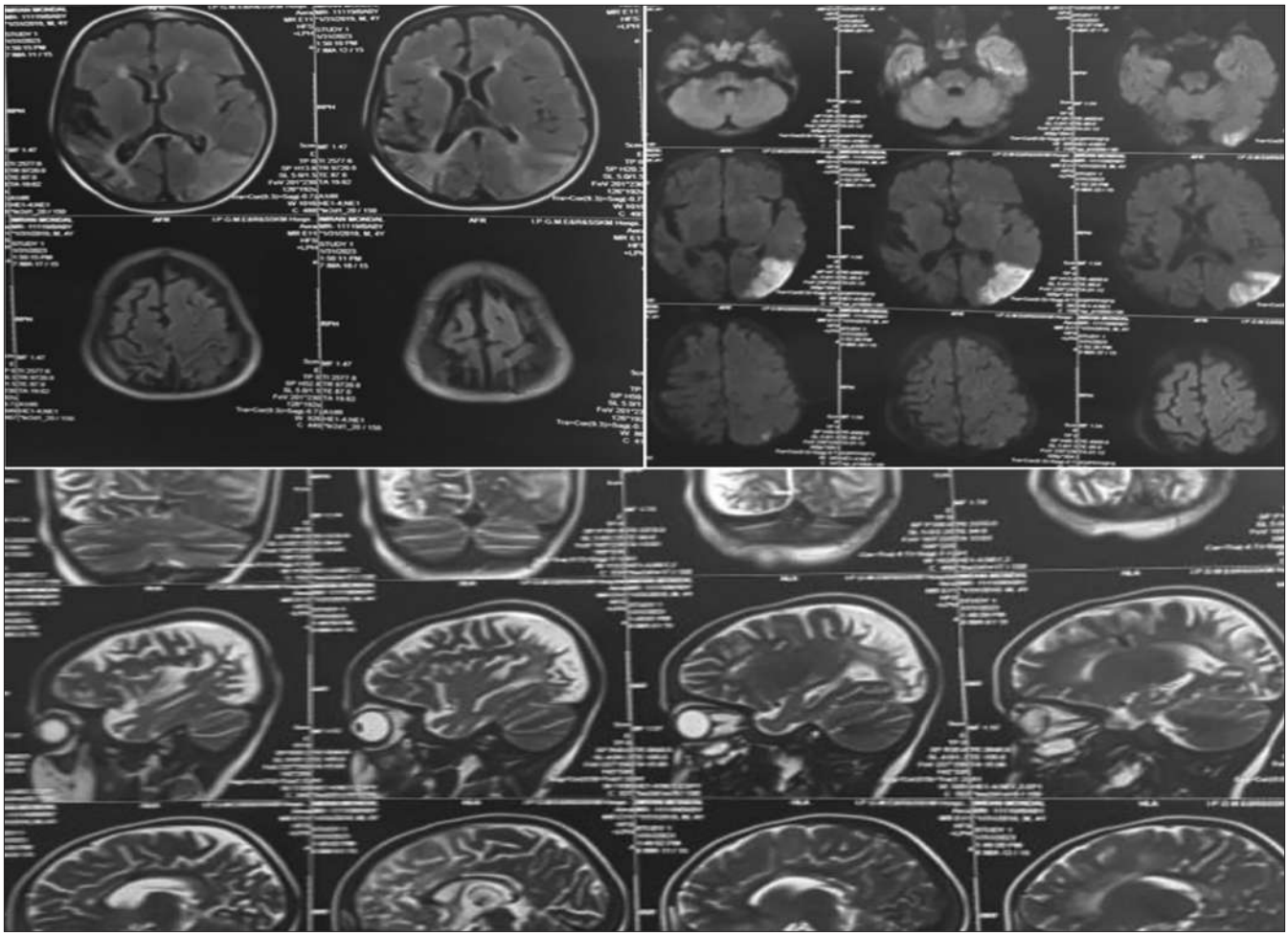

Figure 2: MRI Brain (contrast) Coronal and sagittal view: Large area of diffusion restriction in DWI with T2 weighted hyperintensity involving left parieto-occipital lobe s/o acute infarct. Diffuse moderate gliosis and atrophy seen involving lower lobes of right cerebral hemisphere. Old infarct not showing any enhancement in post contrast study seen in right parieto-temporal region

associated fever, vomiting, headache, convulsions, trauma, or any new weakness, nor recurrence of bleeding manifestations. On examination, the child was conscious with stable vitals. Blood pressure was 100/70 mmHg (50th–90th percentile). Fundus examination showed mild disc pallor. Systemic examination was uneventful. As the classic variety of WAS is prone to autoimmune manifestations, we considered the possibility of optic neuritis. However, an absent visual evoked potential suggested cortical blindness. MRI orbit was normal. MRI brain revealed acute infarct on left occipital region with T2-hyperintensity, gliosis seen in right cerebral hemisphere indicative of old infarct [Figure 2]. MR Angiography showed narrowing of bilateral internal carotid artery with thrombosis in right middle cerebral artery and posterior cerebral artery suggestive of Moyamoya disease [Figure 3]. This explained the old infarct and current cortical blindness. Lipid and coagulation profile were normal. Serum antinuclear antibody, antiphospholipid antibodies, and p-anti-neutrophic cytoplasmic antibody (p-ANCA) were negative. Echocardiography was also noncontributory. Antiplatelet therapy or neurosurgical interventions could not be planned due to underlying WAS. The final diagnosis was WAS complicated with moyamoya disease. Even at 6 months follow up he had complete absence of vision in right eye with only light perception in left eye.

Discussion

Wiskott–Aldrich syndrome is a rare X-linked disorder with caused by mutations on the short arm of chromosome XP11.22-p11.23. Exclusively seen in males, with an incidence of about 1 in every 100000 live births, it comprises a characteristic triad of immunodeficiency, thrombocytopenia, and eczema, though the disorder may have a wide spectrum of severity of presentation.[1] The gene product WASp, expressed in non-erythroid hematopoietic cells, is an ultrastructural component of the cellular architecture responsible for cell morphology, signaling, cell-locomotion, and immune-synapse formation.[3] T-cell dysfunction, impaired B-cell homeostasis and impaired phagocytosis and chemotaxis of monocytes, macrophages, and dendritic cells occur in this disorder. Intrinsic platelet abnormalities result in increased ineffective thrombocytopoiesis and reduced platelet survival.[4]

Bleeding manifestations due to thrombocytopenia may present since early age, manifesting as umbilical stump bleeding, later as skin and mucosal bleeds. Susceptibility to recurrent infections like otitis media, sinusitis, pneumonia, meningitis, and sepsis results in failure to thrive. Nearly half of the affected children develop eczema since the 1st year of life.[1,5] In a study of 95 children with definite WAS from India,[6] the median age of onset of symptoms was 3 months, with median age of diagnosis being 12 months. Over 90% of them manifested bleeding episodes, with infections and eczema reported in around 80%. Our patient showed bleeding, eczema, as well as recurrent infections since infancy.

Multiple studies worldwide have documented autoimmune manifestations in 26%–72% of patients with WAS,[2,7] like hemolytic anemia, vasculitis involving both small and large vessels, inflammatory bowel disease, and renal diseases. Autoimmune hemolytic anemia (AIHA) is the most common autoimmune manifestation in children with WAS, associated with ANA and sometimes Coomb's test positivity.[2] Though our child had anemia with hepatosplenomegaly, Coomb's test and ANA were negative. Vasculitis is the second common among the autoimmune manifestations in WAS; medium-and-small-vessels of skin, renal, coronary, cerebral, or hepatic arteries, as well as large vessels like aorta can be involved.[2,8,9] Nearly 40% of the Indian

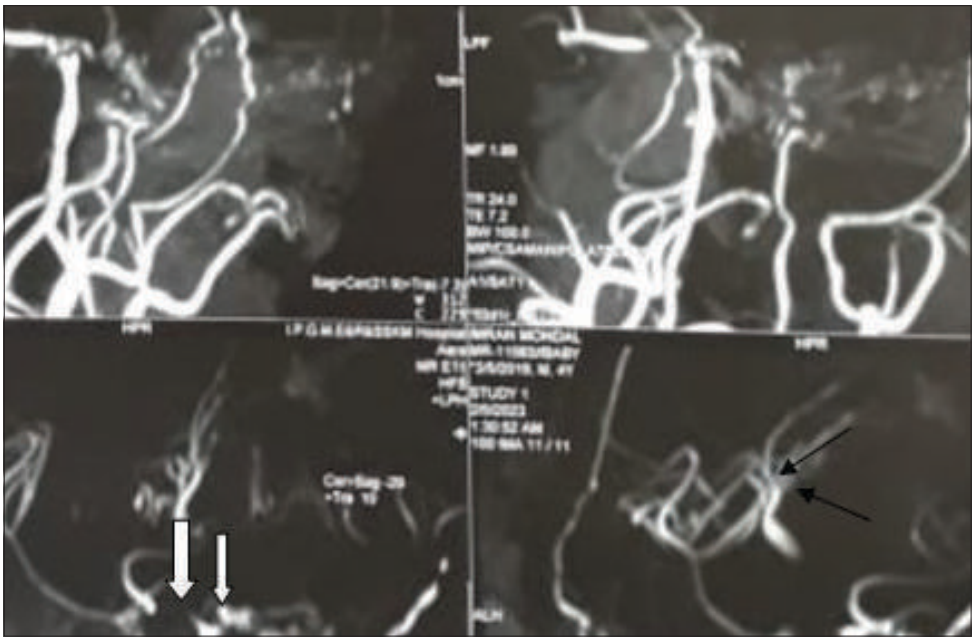

Figure 3: MRA s/o Moyamoya disease. Narrowing of B/L Internal Carotid Arteries (shown by white arrows). Small vessels seen around circle of Willis suggestive of puff of smoke appearance (black arrows)

cohort of patients with WAS[6] had autoimmune phenomena, AIHA was the commonest disorder (9.5%), Takayasu vasculitis was reported in one child.[6] There is a dearth of reports regarding cerebral vasculitis in WAS and almost none with moyamoya disease. We postulate autoimmune vasculitis leading to thrombosis and narrowing in cerebral arteries, could be the possible mechanism.

Diagnosis of WAS in our case was suspected based on the early onset of the triad of clinical manifestations, confirmed by genetic analysis. Micro-platelets (MPV < 5fl), a characteristic finding of WAS, was not seen in our case. The Indian study found 10 out of 65 patients having normal MP.[6] Baharin *et al*. also reported a 9-month-old infant with WAS and normal platelet volume.[10]

Management of the disorder is mainly supportive, with antibiotics, platelet transfusions, and skin care and IVIG therapy.[11] Despite IVIG doses, our patient developed cerebral vessel thrombosis. Due to anticipated risk of complications, neurosurgery, anti-platelet therapy and corticosteroids could not be considered. Hematopoietic cell transplantation is curative,[11] which, again was not feasible in our case.

Conclusion

The case reported here highlights cortical blindness due to cerebral vessel thrombosis, consistent with moyamoya disease, as an unusual complication of the rare WAS. Being a primary immunodeficiency disorder, treatment of autoimmune phenomena like vasculitis/vascular thrombosis is tough, with not many available therapeutic options.

Lessons learnt

- Unexplained persistent thrombocytopenia and recurrent infections may be due to Wiskott- Aldrisch Syndrome (WAS)
- Neurological manifestations in WAS may be due to autoimmune vasculitis
- Treatment of cerebral thrombosis in WAS is challenging due to risk of infections and bleeding.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Acknowledgment

We would like to acknowledge our respected Professors, Prof M.KDas and Prof.Supratim Datta for their guidance and support.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Massaad MJ, Ramesh N, Geha RS. Wiskott-Aldrich syndrome: A comprehensive review. Ann N Y Acad Sci 2013;1285:26-43.
2. Sudhakar M, Rikhi R, Loganathan SK, *et al*. Autoimmunity in Wiskott-Aldrich syndrome: Updated perspectives. Appl Clin Genet 2021;14:363-88.
3. Jin Y, Mazza C, Christie JR, *et al.* Mutations of the Wiskott-Aldrich syndrome protein (WASP): Hotspots, effect on transcription, and translation and phenotype/genotype correlation. Blood 2004;104:4010-9.
4. Westerberg LS, de la Fuente MA, Wermeling F, *et al.* WASP confers selective advantage for specific hematopoietic cell populations and serves a unique role in marginal zone B-cell homeostasis and function. Blood 2008;112:4139-47.
5. Suri D, Singh S, Rawat A, *et al.* Clinical profile and genetic basis of Wiskott-Aldrich syndrome at Chandigarh, North India. Asian Pac J Allergy Immunol 2012;30:71-8.
6. Suri D, Rikhi R, Jindal AK, *et al.* Wiskott Aldrich syndrome: A multi-institutional experience from India. Front Immunol 2021;12:627651.
7. Dupuis-Girod S, Medioni J, Haddad E, *et al.* Autoimmunity in Wiskott-Aldrich syndrome: Risk factors, clinical features, and outcome in a single-center cohort of 55 patients. Pediatrics 2003;111:e622-7.
8. Kawakami C, Miyake M, Tamai H. Kawasaki disease in a patient with Wiskott-Aldrich syndrome: An increase in the platelet count. Int J Hematol 2003;77:199-200.
9. Filipovich AH, Krivit W, Kersey JH, *et al*. Fatal arteritis as a complication of Wiskott-Aldrich syndrome. J Pediatr 1979;95:742-4.
10. Baharin MF, Dhaliwal JS, Sarachandran SV, *et al*. A rare case of Wiskott-Aldrich syndrome with normal platelet size: A case report. J Med Case Rep 2016;10:188.
11. Worth AJ, Thrasher AJ. Current and emerging treatment options for Wiskott-Aldrich syndrome. Expert Rev Clin Immunol 2015;11:1015-32.

Case Report

Lutembacher Syndrome in a Child with Chronic Tonsillopharyngitis

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Abstract

Background: Lutembacher syndrome (LS) is a condition where congenital atrial septal defect (ASD) and acquired rheumatic mitral stenosis (MS) co-occur, seen mainly in adult population. We report LS incidentally detected in a child, while seeking medical care for unrelated problem. **Clinical Description:** A 13-year-old boy presented with chronic throat pain and was planned for tonsillectomy. During pre-anesthetic checkup, a cardiac murmur was detected and sent for cardiac evaluation. He was otherwise asymptomatic in the past. On examination, he was underweight with stable vitals, without edema, cyanosis, clubbing, or engorged neck veins. Auscultation revealed normal S1, wide split S2 with A2 >P2, and short ejection systolic in pulmonary area. **Management and Outcome:** Routine laboratory investigations were normal. Electrocardiogram showed sinus rhythm, with normal PR and QT intervals. QRS axis – Right axis, normal "*P*" axis, incomplete RBB (V1–V3 leads) with right ventricle dominant forces. Echocardiography showed a 20 mm ASD, along with MS, thickened anterior mitral leaflet, thickened and fixed posterior mitral leaflet, and chordal thickening, consistent with rheumatic MS, thereby confirming LS. The child was started on regular penicillin prophylaxis, and was advised tonsillectomy. **Conclusion:** This case creates awareness among pediatricians regarding the possible occurrence of LS in children having a chronic source of streptococcal infection like tonsillopharyngitis. Knowledge about this condition and astute echocardiographic evaluation can identify this condition.

Keywords: Atrial septal defects, congenital heart disease, mitral stenosis, pediatric, rheumatic heart disease

Lutembacher syndrome (LS), commonly seen in adults, is a structural cardiac abnormality that includes a combination of atrial septal defect (ASD) and mitral stenosis (MS). While ASD is usually a congenital defect, MS is invariably acquired post rheumatic fever.[1,2] We report a rare case of a child with LS, where this condition was incidentally detected during workup for an unrelated symptom.

Clinical Description

A 13-year-old boy was referred to our pediatric cardiology department for evaluation. The boy had complaints of throat pain persisting for 3 months with difficulty in swallowing food and not gaining adequate weight in the last few months. There was no history of fever, cough, hemoptysis, hoarseness of voice, contact with tuberculosis, bleeding, or joint swelling. He was evaluated in the otorhinolaryngology (ENT) department and was found to have chronic tonsillitis. As he was symptomatic affecting weight gain, a tonsillectomy was planned. During the pre-anesthetic evaluation, the patient was found to have an abnormal S2, and a murmur was heard in the pulmonary area. Tonsillectomy was deferred; he was advised 12-lead electrocardiogram (ECG) and two-dimensional echocardiography and was sent to the pediatric cardiac clinic. On questioning, he was found to be active like his peers. There was no history of palpitations, syncope, or hospitalization, nor any cardiac evaluation done in the past. He was second born to nonconsanguineous parents. His development was age appropriate, with an average school performance. He was immunized appropriately till the age of 5 years; his family medical history was insignificant.

On examination, in the cardiac clinic, the patient was conscious, with no respiratory distress. He was medium built with a weight of 25 kg, height of 141 cm, and body mass index of 12.6 (<3rd percentile). He was afebrile with normal volume pulses at 80/min, respiratory rate of 20/min, blood pressure of 98/70 mmHg, and SpO_2 of 100% in all four limbs. No pallor, cyanosis, icterus, edema, clubbing, cervical lymphadenopathy nor thyromegaly was observed. Jugular venous pressure was not elevated. Cardiac auscultation revealed a regular heart rate of 80 beats/min, with normal S1 and wide split S2 with A2 > P2. There was no S3 or mid-diastolic murmur. Short ejection systolic (flow murmur) was heard in pulmonary area. Throat

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DOI: 10.4103/ipcares.ipcares_168_24

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Submitted: 16-Jul-2024 **Revised:** 31-Dec-2024
Accepted: 02-Jan-2025 **Published:** 14-Feb-2025

How to cite this article: Vemala V, Reddy JP. Lutembacher syndrome in a child with chronic tonsillopharyngitis. Indian Pediatr Case Rep 2025;5:23-5.

examination showed enlarged tonsils with no teeth caries. Chest and abdominal examinations were unremarkable. Based on the presentation, history, and examination, a clinical diagnosis of chronic tonsillitis with growth failure and an acyanotic congenital heart disease was suspected.

Management and Outcome

Investigations revealed a hemoglobin of 13 g/dL, total leukocyte count of 13,500/mm^3, neutrophils 55%, lymphocytes 40%, and platelets 2.45 lakhs/mm^3. Biochemical parameters showed a serum creatinine of 0.8 mg/dL, negative C-reactive protein, and erythrocyte sedimentation rate of 8 mm/hour. Serum electrolyte levels were normal. Chest radiography revealed normal situs with levocardia, with no cardiomegaly with normal pulmonary blood flow and normal lung fields. The ECG [Figure 1] showed sinus rhythm, and the PR and QT intervals were normal. QRS axis showed right axis, normal "*P*" axis, incomplete RBB (V1–V3 leads) with right ventricle (RV) dominant forces.

Echocardiography showed a 20 mm moderate, unrestrictive ASD [Figure 2] with a dilated right atrium and RV, without vegetations on the valves. He had MS of moderate severity according to the World Heart Federation (WHF) criteria,[3] along with thickened anterior mitral leaflet, thickened and fixed posterior mitral leaflet, and chordal thickening, which are all classical findings on echocardiography of rheumatic MS[3] [Figure 3]. Even in established cases of rheumatic heart disease, 50% of patients do not have a history of acute rheumatic fever.[4] Even in the present case, there was no history of acute rheumatic fever, and echocardiographic findings were typical of rheumatic etiology. Thus, based on history, clinical presentation, and investigations, the child was diagnosed as a case of moderate rheumatic MS with large ostium secundum ASD, consistent with pediatric LS, along with chronic tonsillitis with growth failure.

The child was started on prophylaxis with benzathine penicillin, 1.2 lakh IU intramuscularly every 21 days. As he was asymptomatic, no medications were started for the LS. He was advised to undergo tonsillectomy as this could have been a source of streptococcal infection, causing recurrent damage to cardiac valves. The child was kept under follow-up and planned for balloon mitral valvotomy and ASD device closure if the child became symptomatic. He was last seen 3 months after tonsillectomy, when he was asymptomatic and was in functional Class I.

Discussion

This is an interesting report of a child with LS, a condition rarely encountered in pediatric practice. According to the latest modified definition, the condition is a combination of ASD (congenital or iatrogenic) and MS (congenital or acquired), with the size of the ASD being typically >15 mm.[1] Common in young adults, LS is seen more frequently in geographical regions with higher incidence of RHD. While rheumatic fever occurs at

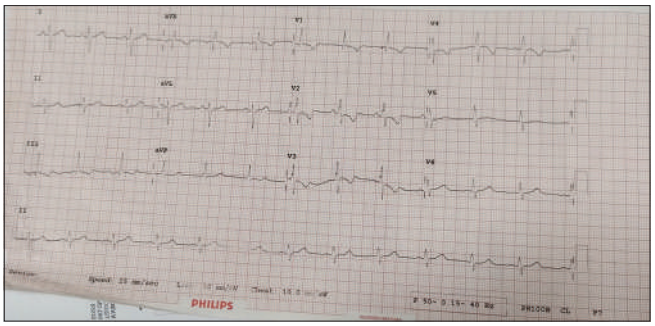

Figure 1: Twelve-lead electrocardiogram shows sinus rhythm, PR and QT intervals are normal. QRS axis – Right axis, normal "*P*" axis, Incomplete RBB present with right ventricle dominant forces

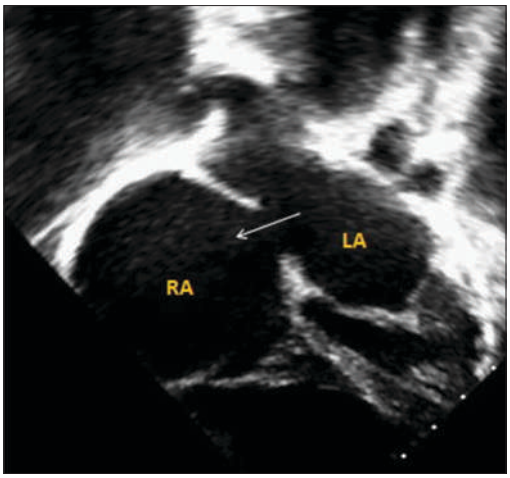

Figure 2: Four-chamber view of the heart. Arrow points to an atrial septal defect (size = 20 mm). RA: Right atrium, LA: Left atrium

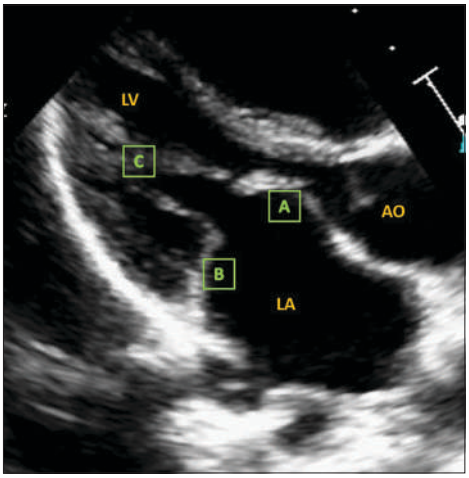

Figure 3: Parasternal long-axis view of the heart. All morphological features of rheumatic mitral stenosis are present as per the World Heart Federation criteria[3] (A: Thickened anterior mitral leaflet, B: Thickened and fixed posterior mitral leaflet, and C: Chordal thickening). LA: Left atrium, LV: Left ventricle

5–15 years of age, symptomatic MS usually develops 20 years after rheumatic fever, thus being exceptionally rare to diagnose LS in the pediatric age.[5,6] Our case had none of the Jones

criteria; such criteria may be ascertained in only 50% of patients with RHD or LS patients.[4] The rheumatic etiology of MS here is based on the characteristic echocardiographic findings, as per WHF criteria.[3] The explanation for MS at such an early age in our patient is probably chronic tonsillopharyngitis, which known to cause recurrent episodes of rheumatic fever, causing progressive damage to the cardiac valves.[4]

Hemodynamics in LS is unique. In cases with restrictive ASD with severe MS, the ASD is small and unable to decompress the left atrium, thereby resulting in early development of symptoms of pulmonary venous hypertension, paroxysmal nocturnal dyspnea, and orthopnea. In cases with nonrestrictive ASD and mild MS, hemodynamics resembles that of an isolated ASD, presenting only in adulthood, when severity of MS increases. The hemodynamics in severe MS with nonrestrictive ASD is most interesting, where the left atrium, though overloaded, decompresses through the ASD, thereby keeping left atrial pressures low, delaying development of pulmonary venous hypertension. However, due to amplified left to right shunting across the ASD there is progressive dilatation of the right atrium and RV with increased pulmonary blood flow and eventually right ventricular failure.[2] In our case ASD was large and MS was probably moderate. The child was asymptomatic, as the left atrium was getting decompressed by the large ASD.

Cardiac auscultation shows a wide split S2 and flow murmurs in tricuspid and pulmonary areas. The characteristic auscultatory findings of MS such as loud first heart sound, opening snap, and a mid-diastolic rumbling murmur may not be apparent in LS because of reduced gradient across the mitral valve due to decompression through ASD. Even in echocardiography, MS severity assessment by mitral inflow Doppler is fallacious. Rather, morphological evaluation of leaflets and chordae along with mitral valve area by planimetry helps in correct assessment of MS severity. In our case, based on Doppler criteria, MS was mild. However, the morphological criteria and planimetry assessment suggested moderate MS. As illustrated in the case by Karadawi and Ali,[5] LS can progress to multivalvular affection. In most cases of LS, balloon mitral valvotomy is technically difficult due to large size of ASD;[7] hence, traditionally, it is treated with open-heart surgery with mitral valve repair/replacement and patch closure of ASD. Prognosis is excellent if the patient is diagnosed early, before the onset of pulmonary hypertension and heart failure. Any focus of streptococci needs to be eliminated and penicillin prophylaxis should be continued lifelong.[4]

Conclusion

The case described here creates awareness that LS may rarely be seen in pediatric age group, especially in regions endemic for rheumatic fever. Although typical auscultatory and clinical findings of MS may be absent, the knowledge of this condition and its hemodynamics will enable pediatricians to make a diagnosis of LS. Penicillin prophylaxis needs to be given lifelong to prevent long-term complications.

Lessons learnt

- Leutembacher syndrome, a combination of large atrial septal defect (ASD) and mitral stenosis (MS), may rarely be seen in children
- Early-onset MS may be attributed to recurrent undetected rheumatic fever episodes due to chronic tonsillopharyngitis.
- Presence of ASD may keep symptoms of MS at bay. Only a detailed echocardiography can identify this potentially serious cardiac disorder.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Vaideeswar P, Marathe S. Lutembacher's syndrome: Is the mitral pathology always rheumatic? Indian Heart J 2017;69:20-3.
2. Bashi VV, Ravikumar E, Jairaj PS, *et al*. Coexistent mitral valve disease with left-to-right shunt at the atrial level: Clinical profile, hemodynamics, and surgical considerations in 67 consecutive patients. Am Heart J 1987;114:1406-14.
3. Rwebembera J, Marangou J, Mwita JC, *et al.* 2023 World Heart Federation guidelines for the echocardiographic diagnosis of rheumatic heart disease. Nat Rev Cardiol 2024;21:250-63.
4. Kumar RK, Tandon R. Rheumatic fever and rheumatic heart disease: The last 50 years. Indian J Med Res 2013;137:643-58.
5. Karadawi N, Ali SK. Lutembacher syndrome variant: Rheumatic heart disease involving all four valves and associated with an atrial septal defect in a child. Sudan J Paediatr 2017;17:64-7.
6. Horstkotte D, Niehues R, Strauer BE. Pathomorphological aspects, aetiology and natural history of acquired mitral valve stenosis. Eur Heart J 1991;12 Suppl B:55-60.
7. Bhambhani A, Somanath HS. Percutaneous treatment of Lutembacher syndrome in a case with difficult mitral valve crossing. J Invasive Cardiol 2012;24:E54-6.

Case Report

Purpura Fulminans Due to Inherited Protein-C Deficiency in an Infant, in the Setting of MIS-C

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Abstract

Background: Although multisystem inflammatory syndrome in children (MIS-C) may be associated with various mucocutaneous features, purpura fulminans (PF) has rarely been associated with it in children. **Clinical Description:** A 10-month-old female infant presented with multiple ecchymotic patches on bilateral lower limbs and scalp gradually progressive over 5 months, associated with fever and irritability for 5 days. On examination, she was alert, hemodynamically stable, with severe pallor and corneal opacity in the left eye, along with the skin lesions, systemic examination being unremarkable. **Management and Outcome:** Investigations revealed severe anemia, normal leukocyte, and platelet counts, elevated inflammatory markers, raised ferritin and NT pro-BNP levels. D-dimer was 5 times the normal range, COVID-19 real-time reverse transcriptase-polymerase chain reaction test was negative, but COVID-19 serology was positive >400 AU/ml. Echocardiography ruled out coronary dilatation. Ophthalmological evaluation revealed permanent hyperplastic vitreous in the left eye with retinal detachment in the right eye. The patient was managed along the lines of MIS-C with PF with broad-spectrum antibiotics, methylprednisolone, fresh frozen plasma, later adding cyclosporine, aspirin, and infliximab therapy. The baby showed remarkable improvement. Genetic analysis showed likely pathogenic heterozygous variant in the *PROC* gene which results in protein C deficiency. **Conclusion:** This case highlights an inherited protein C deficiency manifesting as PF, in a setting of MIS-C in an infant. Prompt and aggressive management can be lifesaving.

Keywords: COVID-19, fresh frozen plasma, thrombophilia

Multisystem inflammatory syndrome in children (MIS-C) is a hyperinflammatory syndrome affecting children who have previously been infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus.[1] The condition can present with diverse mucocutaneous manifestations, but purpura fulminans (PF), characterized by rapidly progressive hemorrhagic infarction of the skin is a rare complication, reported mostly in adults,[2,3] only rarely in children.[4,5] We report an infant presenting to us in the immediate post-COVID pandemic period, with MIS-C and PF, later found to have an underlying protein C deficiency.

Clinical Description

A 10-month-old female infant presented with fever for 5 days, irritability, and multiple ecchymotic patches on both lower limbs and the scalp, which had gradually progressed over 5 months, recently developing blisters over the lesions [Figure 1]. In addition, the parents noticed the absence of visual fixation and signs of vision impairment in the child, for 3 months. There was no history of cough, coryza, diarrhea, vomiting, photophobia, drug intake, oral ulceration, joint swelling, yellowish discoloration of the skin or urine, abnormal body movements, trauma, previous hospitalization, bleeding manifestations, or conjunctival swelling or redness. The child had multiple outpatient visits to ophthalmologists for vision impairment. The child was admitted to a local hospital for 2 days for the treatment of skin lesions, during which she received packed red cell and fresh frozen plasma (FFP) transfusions before being referred to our hospital.

The infant was the second in birth order, born from a nonconsanguineous marriage, at term, through Cesarean section, due to oligohydramnios, with a normal birth weight; antenatal and postnatal periods being uneventful. The child was immunized according to age. There was a developmental delay in the motor domain due to restricted movement caused by painful lesions on both lower limbs, along with poor visual

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Submitted: 30-Jul-2024 **Revised:** 20-Oct-2024
Accepted: 12-Dec-2024 **Published:** 14-Feb-2025

How to cite this article: Gupta A, Maheshwari A, Mahto D, Dhankar M. Purpura fulminans due to inherited protein-C deficiency in an infant, in the setting of MIS-C. Indian Pediatr Case Rep 2025;5:26-9.

fixation. The infant had been started on complementary feeding at 6 months of age. There was no family history of chronic illness or bleeding disorders.

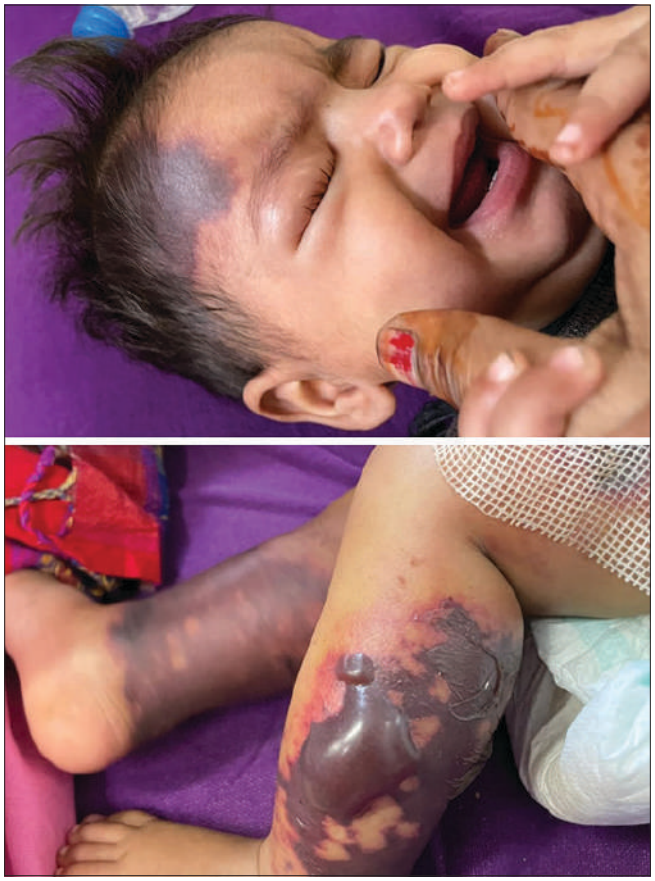

Figure 1: Scalp Ecchymosis (Above), Lower limb ecchymosis with blisters (below)

On examination, the child was alert, active, but febrile (temperature 102°F), with normal volume pulses of 128/min, respiratory rate 42/min, capillary refilling time <2 s, and blood pressure 92/64 mm/Hg taken in left upper arm and consistent across all four limbs. Pallor was present, but no clubbing, cyanosis, icterus, or lymphadenopathy. The infant had a weight 7.8 kg (25^{th}–50^{th} centile), length 68 cm (10^{th}–25^{th} centile), and head circumference 43 cm (25^{th}–50^{th} centile). There were multiple ecchymotic patches on bilateral lower limbs associated with blister formation. The left eye had corneal opacity. Systemic examination was within normal limits. Based on history and examination findings, we kept some of the differentials such as inherited thrombophilia with severe PF with left eye leukocoria, atypical Kawasaki disease, and severe sepsis with disseminated intravascular coagulation.

Management and Outcome

Investigations [Table 1] revealed severe anemia with increasing platelets from 250,000/mm^3 to 550,000/mm^3 over 5 days. Biochemical parameters, including renal and liver function and serum sodium and potassium, were within the normal range. Inflammatory markers including C-reactive protein (CRP) and ferritin were elevated, but procalcitonin was low. The coagulation profile was normal, but the D-dimer level was five times the upper limit of normal. The fibrinogen level was elevated at 1100 mg/dL. Triglycerides, troponin T, creatinine phosphokinase, and lactate dehydrogenase were normal, with no evidence of macrophage activation syndrome. The initial NT-pro BNP was markedly raised at 10,208 pg/mL, indicating cardiac dysfunction. Blood, urine as well as skin swab cultures were sterile.

Echocardiography showed a z-score of (+0.45) in the left main coronary artery, (+1.27) in the left anterior descending

Table 1: Serial investigations of the infant during disease course

Lab parameters	At admission	At discharge (after 2 weeks)	Re-admission	Follow up (at 2 weeks)
Hemoglobin (g/dL)	5.42	9.45	9.8	10.6
TLC (cells/mm^3)	11,500	10,770	9560	9270
DLC (%)				
Neutrophils	50	50	44	35
Lymphocytes	40	43	46	50
Platelet (lakhs/mm^3)	250,000	450,000	360,000	282,000
ESR (mm/h)	28	14	24	16
TP/albumin (g/dL)	6.8/4.5	7/4.2	7.1/3.8	7.2/4.4
AST/ALT (IU/L)	38/34	32/34	36/34	28/21
BUN/creatinine (mg/dL)	22/0.39	24/0.33	26/0.42	15/0.3
CRP (mg/dL)	83.6	2.2	63	1.19
NT-pro BNP (pg/dL)	10,208	5647	3298	236.3
INR	0.91	1.2	1.8	1.4
D-dimer (ng/mL)	>1050			
Fibrinogen (mg/dL)	1100			
Ferritin (ng/dL)	457.7			

TLC: Total leukocyte count, DLC: Differential count, ESR: Erythrocyte sedimentation rate, TP: Total protein, AST: Aspartate aminotransferase, ALT: Alanine transaminase, BUN: Blood urea nitrogen, CRP: C-reactive protein, NT-pro BNP: N-terminal pro B-type natriuretic peptide, INR: International normalized ratio

artery, and (−0.19) in the right coronary artery, with no evidence of left ventricular dysfunction or pericardial effusion. Complement components C3/C4 were 54/16 mg/dl, and the immunoglobulin profile was normal. Antinuclear antibodies and antiphospholipid antibodies were negative. The COVID-19 Real-time reverse transcriptase-polymerase chain reaction test was negative, but COVID-19 serology was positive at >400 AU/ml (>15AU/ml-positive). Ophthalmologic evaluation revealed persistent hyperplastic primary vitreous (PHPV) with anterior segment agenesis in the left eye and retinal detachment in the right eye. Doppler study of the bilateral lower limbs was unremarkable. The presentation and investigations strongly suggested MIS-C with mucocutaneous manifestations and cardiac dysfunction.

We initiated treatment with broad-spectrum antibiotics, packed red cell transfusion, pulse doses of methylprednisolone, and FFP transfusions twice daily. There was significant improvement in the existing lesions, but new lesions began to appear on the 5th day of hospitalization. One dose of intravenous immunoglobulin (IVIG) at 2 g/kg was administered, and aspirin and cyclosporine were added to the treatment regimen due to the ongoing inflammation. Progressive improvement was observed in the old lesions, and the new lesions started to heal by 10 days of hospitalization [Figure 2]. Repeat NT-pro BNP levels decreased to 5647 pg/ml by 2 weeks and inflammatory markers

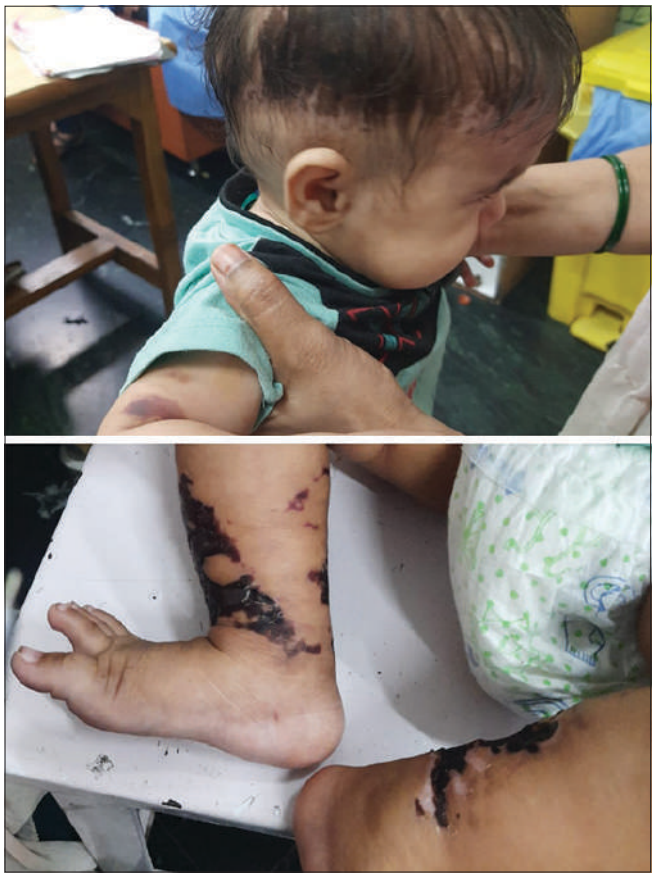

Figure 2: Scalp lesions recovered (Above). Healing stage in ecchymotic patches of lower limbs (Below)

such as CRP and erythrocyte sedimentation rate returned to normal ranges by day 14 [Table 1]. The patient improved clinically and was discharged after 14 days of hospitalization.

A follow-up echocardiogram at 7 days postdischarge showed no coronary artery dilation or aneurysm. However, the child presented after 1 week of discharge with new lesions on the abdomen and scalp. Routine investigations and a coagulation profile were repeated, revealing an international normalized ratio of 1.8 [Table 1]. Along with FFP transfusion, a second dose of IVIG was administered. However, as the lesions showed minimal improvement, infliximab (5 mg/kg) infusion was administered, following which, the infant showed complete resolution of lesions with no residual scarring, by 3–4 days post infliximab. In view of severe PF, we also sent genetic testing for underlying procoagulant state. Subsequent prothrombotic workup done 6 weeks after the resolution of acute illness, revealed protein C deficiency with 15% activity (normal range 70%–130%) and normal protein S activity (132%). The whole exome sequencing report identified a heterozygous mutation in the *PROC* gene on exon 7 (c.658C>T, p. Arg220Trp), which is associated with an autosomal dominant variant of thrombophilia type 3, resulting in protein C deficiency. The parents were prognosticated and advised genetic testing but the cost was the limiting factor.

Discussion

The above is an interesting case of a rapidly progressive PF in an infant, where clinical and laboratory investigations indicated MIS-C, with subsequent prothrombotic workup revealing protein C deficiency, confirmed by genetic testing. While acute infection with SARS-CoV-2 virus in children often goes undetected as they typically remain asymptomatic or exhibit mild symptoms,[6] children can present later, manifesting as MIS-C that mimics Kawasaki disease shock syndrome.[7,8] Purpura fulminans associated with MIS-C in an infant has rarely been reported. We postulate that the underlying procoagulant condition in our child was exacerbated by MIS-C, leading to a life-threatening condition of PF.

Dermatologic complications known to be associated with SARS-CoV-2 virus infection include chilblains, maculopapular rash, urticaria, erythema multiforme, and papulovesicular eruptions.[9,10] While PF associated with COVID-19 infection has been reported in adults,[2,3] it is hardly reported in children. While Pereira *et al*. reported PF in a 2-year-old girl, 3 weeks after a possible COVID-19 infection,[4] a 12-year-old boy was reported by Parappil *et al*.,[5] with PF in a setting of diabetic ketoacidosis with MIS-C. The older child also developed left hemiparesis due to the right middle cerebral artery territory infarct.

A rapidly progressive condition, with acute necrosis and infarction of the skin, PF occurs due to three underlying pathophysiology: inherited or acquired abnormalities of the protein C or other coagulation systems, acute infectious PF, and idiopathic.[11] While majority are due to inherited or acquired abnormalities of the

protein C and protein S factors, Gram-negative organisms have been implicated in most of the acute infectious variety.[12] A study involving 12 Chinese children with severe congenital protein C deficiency (protein C activity <10%) showed that PF manifesting within 24–48 h after birth in most cases,[13] while in our case, the disorder manifested at 10 months of age, following a COVID-19 infection. In addition, in the same study, three patients were found to have concurrent protein S deficiency, whereas our patient had normal protein S levels.[13]

Ophthalmic manifestations of congenital thrombophilia include nonreactive pupils, leukocoria, chemosis, periorbital edema, shallow anterior chamber, dilated iris vessels, posterior synechia, and microphthalmos.[14] Park *et al*.[15] reported a neonate with bilateral leukocoria, PHPV, and retinal dysplasia in both eyes, associated with protein C deficiency. Our patient had PHPV and anterior segment agenesis in the left eye, along with retinal detachment in the right eye.

Prompt diagnosis and treatment are crucial to prevent permanent disability and mortality. In a resource-limited country like India, where activated protein C concentrate is unavailable, ongoing thrombosis can be managed with FFP transfusion with or without anticoagulants. The adolescent with PF, reported by Parappil *et al*.,[5] responded well to IVIG, methylprednisolone pulse, and aspirin therapy. In our patient, although initial treatment with these measures along with steroids and IVIG showed improvement, recurrence of lesions required further escalation of treatment with infliximab, which showed favorable outcome. Siblings should be screened for protein C, protein S, and antithrombin levels, as parents can be asymptomatic carriers. Pregenetic counseling should be conducted before planning subsequent pregnancies.

Conclusion

An underlying inherited protein C deficiency may manifest as a life-threatening PF, triggered in the setting of MIS-C. Prompt treatment is necessary to prevent progression and sequelae. In resource-limited settings, where activated protein C concentrate is unavailable, FFP transfusion, supplemented with steroids and other immunotherapy, may be beneficial.

Lessons learnt

- MIS-C should be suspected in a child presenting with fever and purpura fulminans (PF) especially in a peri-COVID-19 period
- Genetic analysis to be considered in refractory PF-may reveal underlying inherited protein C deficiency
- Prompt and aggressive intervention can halt progression of disease and prevent significant morbidity and mortality.

Declaration of patient consent

The authors confirm that they have received all necessary patient consent forms. The legal guardian has granted permission for the publication of images and other clinical details in the journal. The guardian understands that personal identifiers, such as names and initials, will not be disclosed, and reasonable steps will be taken to protect the individual's identity.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Multisystem Inflammatory Syndrome in Children and Adolescents with COVID 19: Scientific Brief. Available from: https://WHO/2019-nCoV/Sci_Brief/Multisystem_Syndrome_Children/2020. [Last accessed on 2025 Jan 10].
2. Pangburn J, Gibbs J. Two cases of COVID-19 patients with associated purpura fulminans. J Burn Care Res 2023;44:485-6.
3. Khan IA, Karmakar S, Chakraborty U, *et al*. Purpura fulminans as the presenting manifestation of COVID-19. Postgrad Med J 2021;97:473.
4. Pereira RA, Mundkur SC, Neminathan A, *et al*. Purpura fulminans-a rare complication post COVID-19 infection in children. Int J Contemp Pediatr 2023;10:1342-4.
5. Parappil P, Ghimire S, Saxena A, *et al.* New-onset diabetic ketoacidosis with purpura fulminans in a child with COVID-19-related multisystem inflammatory syndrome. Infect Dis (Lond) 2022;54:522-8.
6. Dong Y, Mo X, Hu Y, *et al.* Epidemiology of COVID-19 among children in China. Pediatrics 2020;145:e20200702.
7. Suratannon N, Dik WA, Chatchatee P, *et al*. COVID-19 in children: Heterogeneity within the disease and hypothetical pathogenesis. Asian Pac J Allergy Immunol 2020;38:170-7.
8. Nejad Biglari H, Sinaei R, Pezeshki S, *et al*. Acute transverse myelitis of childhood due to novel coronavirus disease 2019: The first pediatric case report and review of literature. Iran J Child Neurol 2021;15:107-12.
9. Panda M, Agarwal A, Hassanandani T. Dermatological manifestations of COVID-19 in children. Indian Pediatr 2022;59:393-9.
10. Young TK, Shaw KS, Shah JK, *et al.* Mucocutaneous manifestations of multisystem inflammatory syndrome in children during the COVID-19 pandemic. JAMA Dermatol 2021;157:207-12.
11. Adcock DM, Brozna J, Marlar RA. Proposed classification and pathologic mechanisms of purpura fulminans and skin necrosis. Semin Thromb Hemost 1990;16:333-40.
12. Darmstadt GL. Acute infectious purpura fulminans: Pathogenesis and medical management. Pediatr Dermatol 1998;15:169-83.
13. Tang X, Zhang Z, Yang H, *et al.* Clinical and genetic features of Chinese pediatric patients with severe congenital protein C deficiency who first presented with purpura fulminans: A case series study and literature review. Thromb Res 2022;210:70-7.
14. Ghassemi F, Abdi F, Esfahani M. Ophthalmic manifestations of congenital protein C deficiency: A case report and mini review. BMC Ophthalmol 2020;20:282.
15. Park UC, Choung HK, Kim SJ, *et al*. Bilateral retinal dysplasia and secondary glaucoma associated with homozygous protein C deficiency. Korean J Ophthalmol 2005;19:112-5.

Case Report

Lithophagia in a Child: Unraveling the Puzzle of Celiac Disease

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Abstract

Background: Celiac disease (CD) is known to present with a wide spectrum of gastrointestinal and non-gastrointestinal manifestations. Although pica may be associated with low iron stores in CD, lithophagia as an extreme form of pica, is rarely reported in CD. **Clinical Description:** A 9-year-old boy presented with abdominal pain, without any vomiting, constipation, or diarrhea. On examination, he was overweight with mild pallor, and diffuse abdominal tenderness, without any palpable lump. **Management and Outcome:** Investigations revealed hemoglobin of 10.7 g/dL, with microcytic hypochromic red blood cells and very low ferritin levels. The abdominal radiograph showed radio-opaque foreign bodies in the entire large bowel and rectum. A review of history revealed lithophagia. These findings in a child with adequate nutrition, with no psychological disorder, raised suspicion of CD. Raised tissue transglutaminase antibody along with villous atrophy on duodenal biopsy confirmed the diagnosis of CD. The patient was treated with lactulose enemas, followed by iron supplementation and a gluten-free diet. Lithophagia resolved with these measures. **Conclusion:** The case highlights that lithophagia may be the only symptom in a child with CD. A high index of suspicion for CD needs to be kept in an otherwise psychologically normal, nutritionally adequate child having lithophagia.

Keywords: Atypical symptom, extraintestinal, iron-deficiency anemia, low ferritin, pica

Celiac disease (CD) is an immune-mediated enteropathy occurring in individuals with a genetic predisposition, triggered by the consumption of gluten proteins. Among the wide spectrum of clinical features of CD, pica is known to be a manifestation in nonclassic forms of CD, often associated with low iron stores.[1] Lithophagia, an exceptionally uncommon form of pica, is an abnormal desire to eat pebbles, stones, or stone fragments.[2,3] We describe a boy with CD with lithophagia as the presenting feature.

Clinical Description

A 9-year-old boy presented with lower abdominal pain for 1 week. The pain was moderate-to-severe in intensity, diffuse, intermittent in nature, lasting for few hours, and associated with a decrease in appetite and affecting sleep. There was no fever, vomiting, loose stools, constipation, abdominal distension, urinary complaints, or recent weight loss. There was no contributory history in the past except for history of pica at 3 years of age, which responded to oral iron supplementation. The patient was born at term, via normal vaginal delivery, with a birth weight of 3.1 kg with no adverse antenatal or perinatal events. He was completely immunized as per the national immunization schedule. He was developmentally appropriate for his age. Family history was unremarkable.

On examination, the child was conscious, alert with stable vitals (pulse rate 90/min, blood pressure 108/72 mmHg, temperature 98.2 F). There was mild pallor but no icterus, cyanosis, clubbing, edema, or lymphadenopathy. He was overweight for his age (32.4 kg, 75th-90th percentile), had a height of 135 cm (50th–75th percentile), and a body mass index of 17.7 kg/m2 (85th–95th percentile). The abdomen showed generalized distension with central adiposity, and the umbilicus was inverted. There was diffuse tenderness in the hypogastrium, with normal bowel sounds. There was no obvious, palpable lump, organomegaly, or free fluid in the abdomen. Per rectal examination was normal. Based on the history and examination, the possible differentials kept were acute gastritis, pancreatitis, mesenteric cyst, or volvulus, and investigations were carried out accordingly.

Management and Outcome

Investigations revealed hemoglobin of 10.7 g/dL with a mean corpuscular volume of 58 fL, total leucocyte count of 11,380/cumm, and platelets of 4.6 lakhs/cumm. The

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Submitted: 31-Jul-2024 **Revised:** 27-Dec-2024
Accepted: 31-Dec-2024 **Published:** 14-Feb-2025

How to cite this article: Kalvala K, Pandey S, Kokitkar SV, Bavdekar A. Lithophagia in a child: Unraveling the puzzle of celiac disease. Indian Pediatr Case Rep 2025;5:30-2.

Access this article online

Quick Response Code:

Website: www.ipcares.org

DOI: 10.4103/ipcares.ipcares_185_24

peripheral smear showed microcytic hypochromic anemia with aniso-poikilocytosis, increased red-cell distribution width (22%), and normal reticulocyte count (1.1%). The liver function and kidney function tests were within normal limits (serum bilirubin [total/conjugated] 0.45/0.23 mg/dL, total protein/albumin 7.4/4.4 mg/dL, aspartate aminotransferase/alanine transaminase 27/20 IU/L, urea/creatinine 25/0.39 mg/dL, sodium/potassium/chloride 138/4.2/102 mg/dL). C-reactive protein was 3.2 mg/L, and erythrocyte sedimentation rate was 12 mm/h. On further investigating the cause of anemia, serum ferritin was found to be very low (6.6 ng/mL; normal range 15–200 ng/mL), suggestive of iron-deficiency anemia.Stool routine and microscopy showed the absence of pus cells, parasites, or occult blood. The ultrasonogram showed echo-reflective lesions in the sigmoid colon, rectum, and anal canal. A radiograph of the abdomen showed multiple, well-defined radio-opaque foreign bodies in the entire large bowel and rectum. With such an abnormal abdominal X-ray, the boy was further probed, and the boy confessed to consuming stones and pebbles in large quantities in the last few weeks.

The patient was kept nil by mouth, started on intravenous maintenance fluids and started on lactulose enemas. Over a period of the next 7 days, the patient passed stools with stones and stone fragments of different sizes. Serial abdominal radiographs [Figure 1a and b] showed a decrease in the stone load with the resolution of the abdominal pain. In view of his abnormal eating practices, a detailed intellectual and psychological assessment was done which showed above average intelligence quotient and normal psychological evaluation.

Considering the constellation of symptoms of severe and unusual pica (lithophagia) in a boy with normal intelligence and normal psychological assessment, with iron deficiency anemia with otherwise normal nutrition pattern, nonnutritional causes of iron deficiency were considered and an upper gastrointestinal endoscopy was performed. The gastroduodenoscopy showed decreased duodenal mucosal folds with scalloping of the mucosa [Figure 1c]. Duodenal biopsy showed increased intraepithelial lymphocytes, crypt hyperplasia and mild villous atrophy suggestive of CD and classified as Modified Marsh Grade 3A [Figure 1d]. Tissue transglutaminase IgA was raised (159.7 U/mL; normal range: 8–20 U/mL).

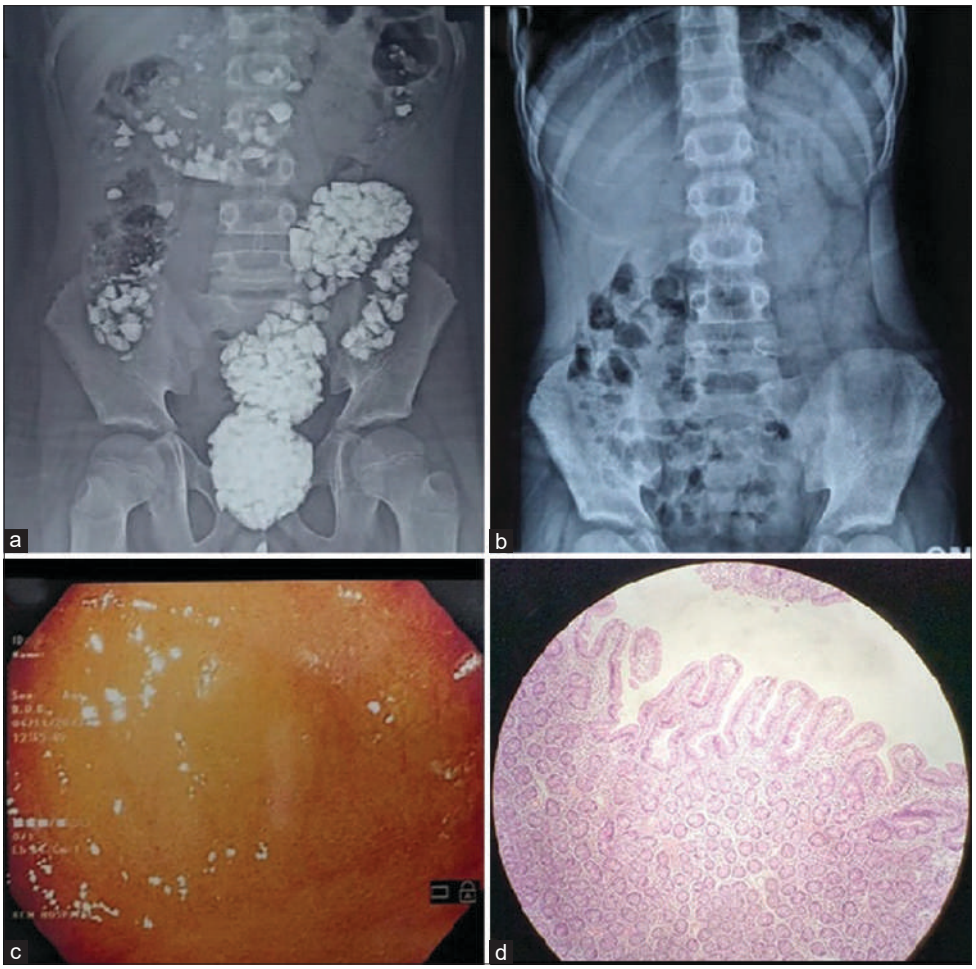

Figure 1: (a) Radiograph of the abdomen depicting extensively loaded colon due to lithophagia at presentation; (b) Clearance of stones after enemas and oral laxatives; (c) Upper gastrointestinal endoscopy picture showing decreased duodenal mucosal folds with extensive scalloping of mucosa, (d) Duodenal biopsy depicting increased intraepithelial lymphocytes, crypt hyperplasia and mild villous atrophy

The patient was started on a gluten-free diet. As the patient did not respond to oral iron therapy, parenteral iron therapy was given. Psychological consultation was done, and the family was counseled.

Discussion

The above report is an extraordinary case of a child with a relatively covert CD, who had developed pica to the extent of lithophagia, before being diagnosed with this underlying condition.

Celiac disease is a chronic immune-mediated enteropathy, triggered by the ingestion of gluten-containing foods, with predilection in genetically susceptible individuals who express specific human leukocyte antigens (HLA-DQ2, HLA-DQ8).[1] It is a common disorder, prevalent in 0.5%–1% of the general population, with the highest prevalence in Europe. With a female preponderance, the disease can begin at any age, though usually there are two peaks for onset: One in first 2 years of life after the introduction of gluten in weaning foods and the other in the second or third decades of life.[4]

Though the classic intestinal form of CD, characterized by diarrhea, anorexia, abdominal pain, distention, bloating, failure to thrive, or weight loss, is easily identifiable, the diagnosis of the extraintestinal nonclassic forms may be challenging.[4,5] Children with the latter form may present with nonspecific features such as iron deficiency anemia with low ferritin, short stature, aphthous stomatitis, constipation, overweight/obesity, neurological symptoms, delayed puberty, or even infertility.[4-7]

Lithophagia, a habit of eating pebbles or rocks, is a form of geophagia, and has rarely been reported in patients with CD.[8-10] The presenting features in all these cases were refractory iron deficiency anemia, growth failure, diarrhea, or constipation. However, in our case, an overweight boy presented with acute abdominal pain due to lithophagia and was later found to be iron deficient with positive serology and histology for CD. The highlighting point here is that the boy had almost no features of a typical CD, except iron deficiency leading to lithophagia. The underlying etiology of CD could be made only based on a strong suspicion of the cause of anemia in an otherwise nutritionally healthy child.

The potential complications associated with lithophagia include intestinal obstruction or colon perforation.[11] In our case, fortunately, there were no signs of intestinal obstruction and conservative management with lactulose enemas helped in the removal of the stones. The fact that the habit of lithophagia waned after the introduction of a gluten-restricted diet, proves that the abnormal habit was not psychological, but related to CD with low iron stores.

Conclusion

This case highlights lithophagia as yet another atypical manifestation of CD. A child with CD may remain apparently healthy without typical features of CD, with pica being the only symptom, which may reach an extremely unusual form of lithophagia.

Lessons learnt

- Pica may reach the extreme form of lithophagia in a child with relatively covert underlying celiac disease (CD)
- Diagnosis of CD is challenging in children with nonclassical extra-intestinal forms of the disease
- Low iron stores and abnormal pica/lithophagia in an otherwise nutritionally healthy child should raise suspicion of CD.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

Acknowledgement

We are grateful to Dr. Ashish Bavdekar for their expert advice and support throughout this case report. We extend our thanks to Dr. Snehavardhan Pandey for their dedication and assistance in data gathering and manuscript preparation. We are deeply thankful to the patient and their family for their cooperation and consent to share this case.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Sahin Y. Celiac disease in children: A review of the literature. World J Clin Pediatr 2021;10:53-71.
2. Borgna-Pignatti C, Zanella S. Pica as a manifestation of iron deficiency. Expert Rev Hematol 2016;9:1075-80.
3. Nachan YS, Pande SD, Deshmukh AS, *et al*. A comprehensive review on pica. Int J Creat Res Thoughts 2023;11:78-83.
4. Caio G, Volta U, Sapone A, *et al.* Celiac disease: A comprehensive current review. BMC Med 2019;17:142.
5. Oliveira GN, Mohan R, Fagbemi A. Review of celiac disease presentation in a pediatric tertiary centre. Arq Gastroenterol 2018;55:86-93.
6. Lal SB, Venkatesh V, Aneja A, *et al.* Clinical spectrum and changing presentation of celiac disease in Indian children. Indian J Med Res 2023;158:75-84.
7. Jericho H, Guandalini S. Extra-intestinal manifestation of celiac disease in children. Nutrients 2018;10:755.
8. Shahryar M, Shahramian I, Dehghani SM, *et al*. Lithophagia as a clue for celiac disease: A case report and literature review. Gastroenterol Hepatol Bed Bench 2017;10:70-2.
9. Altamimi E. Lithophagia in iron-deficient patient with celiac disease. J Pediatr Gastroenterol Nutr 2014;59:e49.
10. Korman SH. Pica as a presenting symptom in childhood celiac disease. Am J Clin Nutr 1990;51:139-41.
11. Narayanan SK, Akbar Sherif VS, Babu PR, *et al*. Intestinal obstruction secondary to a colonic lithobezoar. J Pediatr Surg 2008;43:e9-10.

Case Report

Giant Axonal Neuropathy in a Child with Stop-Gain Variant in *GAN* Gene

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Abstract

Background: Giant axonal neuropathy (GAN) type 1 is a rare autosomal recessive, progressive neuro-degenerative disorder, caused by biallelic variants in Gigaxonin *(GAN)* gene. **Clinical Description:** An 11-year-old boy born out of consanguineous marriage presented with features of regression of milestones, initially motor, followed by cognitive and speech abnormality, associated with seizures and hearing impairment progressing over past 2–3 years. On examination, he had kinky hair, nystagmus, with diffuse muscle atrophy, absent tendon reflexes, positive cerebellar signs as well as impairment of higher mental functions. **Management and Outcome:** Laboratory investigations were largely normal, with magnetic resonance imaging showing features of diffuse white matter abnormality with signal changes noted in the dentate nuclei. Exome sequencing identified a homozygous likely pathogenic stop-gain variant in *GAN* gene. Parents were counselled and child was provided supportive care. **Conclusion:** The case creates awareness among pediatricians regarding the rare disorder of GAN. A thorough neurological assessment with careful physical examination along with a knowledge of this disorder will help in making an early diagnosis.

Keywords: Cognitive impairment, hair abnormality, India, neuroregression, peripheral neuropathy

Giant axonal neuropathy type-1 (GAN) is an early-onset, chronic, slowly progressive, primarily motor neuropathy, affecting both peripheral and central nervous systems. The characteristic tightly curled or kinky hair is a pathognomonic feature of GAN.[1,2] To date, less than 50 families have been reported worldwide with exact prevalence not known.[3] Here, we present a patient from northern part of India with this rare disorder.

Clinical Description

An 11-year-old boy was presented with complaints of multiple episodes of falls over last 3 years, associated with gradual loss of ability to do multiple daily activities, along with decline in academic performance in school, observed for last 2 years. The acute complaint for seeking our consultation was inability to walk for last 1 month.

The falls began at around 8 years of age, on the 3rd day of an episode of fever; the instability progressed over the next 1 year, resulting in various motor impairments like inability to wear shoes, climbing up and down stairs and squatting, associated with apathy, slow speech and unusual behavioral and emotional expressions. He also was noted to have blunted hearing ability at 10 years of age, although his vision was apparently intact. By the age of 11 years, the child had become physically incapacitated with loss of independent walking. With a decline in scholastic performance, he was discontinued from school at 9 years of age. At around 9 years of age, he had two episodes of abnormal body movements involving all limbs with loss of consciousness, without fever, which subsided spontaneously and no treatment was taken. The child had a gradual decrease in appetite and underwent significant weight loss.

Before these developments, the boy had no medical or surgical illness. He was the second child of parents, born out of third-degree consanguineous marriage, in a North Indian Hindu family, at term, with uneventful antenatal, natal and postnatal period. There was no similar illness in the family. He had attained his developmental milestones at appropriate ages and was immunized for age.

On examination, the child was conscious, afebrile with heart rate of 90/min, respiratory rate of 15/min, and blood pressure 100/60 mmHg. His head circumference was 51 cm, weight was 30 kg (−0.64 IAP z score), and height was 132 cm (−1.48 IAP z score). Head-to-toe examination showed tightly curled, lusterless, kinky hair with sparse eyebrows [Figure 1a and b], multiple scars on the knees due to recurrent falls, hyperpigmentation of

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Quick Response Code:

Website: www.ipcares.org

DOI: 10.4103/ipcares.ipcares_241_24

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Submitted: 06-Oct-2024 **Revised:** 05-Jan-2025
Accepted: 07-Jan-2025 **Published:** 14-Feb-2025

How to cite this article: Srinivasan VM, Manisha R, Nilay M, Bhakhri BK, Singh DK. Giant axonal neuropathy in a child with stop-gain gigaxonin variant in *gan* gene. Indian Pediatr Case Rep 2025;5:33-6.

knuckles, and angular cheilitis, but no specific neurocutaneous markers. There was no pallor, cyanosis, clubbing, icterus, edema, or lymphadenopathy. A mini–mental state examination showed he was not oriented to time (0/5) but could identify the place (3/5), with impairment of immediate memory (3/6), and impaired simple calculations; language domain could not be assessed adequately. Cranial nerve examination was normal except horizontal nystagmus in both eyes, fundus examination showing mild disc pallor bilaterally. Motor system examination showed diffuse atrophy across all muscles, reduced tone, Grade 3/5 power in distal muscles of upper and lower limbs and proximal muscle of upper limbs, with Grade 2/5 in proximal muscles of lower limb. There was generalized areflexia, dynamic ankle contractures; Babinski sign could not be elicited. Sensory system examination was normal. Cerebellar signs were positive. Brainstem evoked response audiometry done showed mild sensorineural hearing loss. Other system examinations were normal, with no contractures, scoliosis, foot deformities, or other orthopedic issues.

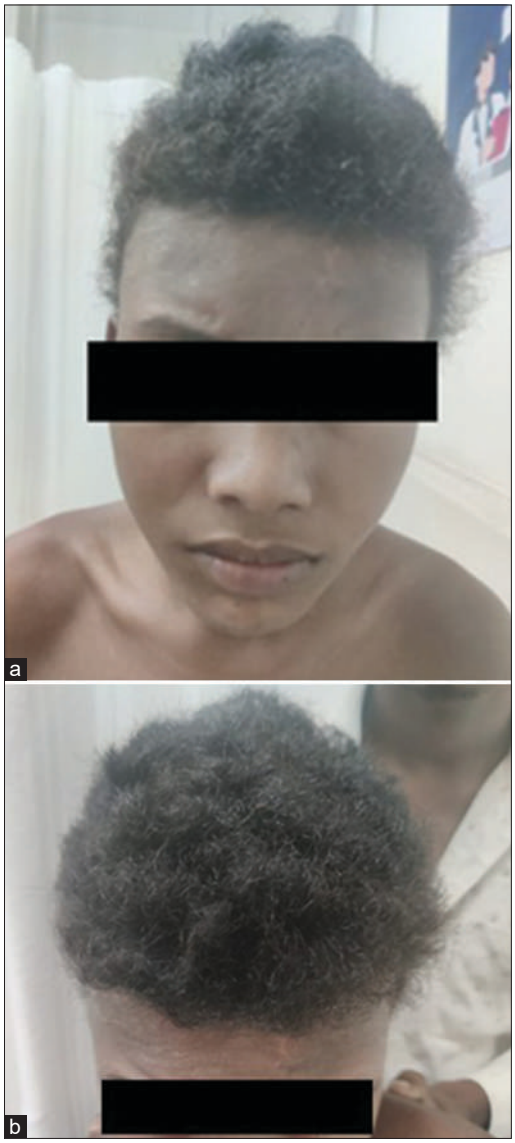

Figure 1: (a and b) Clinical photographs and hair changes of proband

Based on the history and examination, possibilities were neurodegenerative disorder or neuropathy, with differentials being metachromatic leukodystrophy of juvenile onset, peroxisomal disorder, GAN, and mitochondrial leukoencephalopathy.

Management and Outcome

Investigations revealed hemoglobin 12.2g/dL, total leukocyte count 9000/mm^3 and platelet count of 3.5 lakhs/mm^3, urea/creatinine: 25/0.8 mg/dL, sodium/potassium/chloride 134/4.5/99 meq/L, AST/ALT 30/25 IU/L, total protein/albumin 6.2/4.0mg/dL, fasting blood glucose 90mg/dL, lactate 15mg/dL (normal: 4.5–19.8), Vitamin B12 was 200 pg/mL (160–950), and creatinine kinase was 51 (10–120 µg/L). Hair examination on light microscopy, done in view of suspected GAN, showed features of pili torti [Figure 2].

Magnetic resonance imaging (MRI) of brain, without contrast, showed white matter abnormalities including the periventricular as well as subcortical white matter along with signal changes noted in internal capsule, thalami, and the dentate nuclei [Figure 3a-c], suggestive of dysmyelination; cerebellum being normal. Cerebrospinal fluid examination and electroencephalogram were not done. Blood lactate being normal, mitochondrial disorder was unlikely. Arylsulphatase A enzyme testing for metachromatic leukodystrophy was not done due to cost constraints. Exome sequencing was performed as it can screen mutations in all genes mentioned in the differentials as a one-time test and proved cost-effective. It identified a homozygous stop-gain variant c.724C>T[p.(Arg242Ter)] in exon-4 of *GAN* gene (NM_022041.4) classified as likely pathogenic (PVS1, PM2) as per the ACMG 2015 classification [Figure 4]. Thus, the child was diagnosed as a case of GAN.

Parents were counseled and the child was provided supportive care in the form of physiotherapy, speech therapy, and advised hearing aids.

Discussion

We present an interesting scenario of a child who presented with features of peripheral neuropathy in the form of generalized muscle wasting, hypotonia, areflexia, along with features of central nervous system involvement in the form of seizures and cognitive impairment. This combination is a unique scenario, the differentials narrowing to: late infantile/juvenile form of metachromatic leukodystrophy, Krabbe disease, *PLA2G6* associated neuroaxonal dystrophy and GAN. The characteristic kinky hair with pili torti in our child was an important clue indicating the diagnosis of GAN.

Giant Axonal Neuropathy is caused by mutations in the *GAN* gene located on the 16q23.2, which encodes for the protein gigaxonin, of the ubiquitin-proteasome system, highly expressed in brain, heart, and skeletal muscle. Loss of function mutation leads to accumulation of intermediate filaments in muscle fibers, Schwann cells, astrocytes and neurons of

peripheral and central nervous system, histopathologically evident as "giant axonal swellings."[4]

The disorder usually has early onset, followed by progressive distal weakness of limbs, culminating in loss of ambulation by the end of the first decade.[5] The study of 45 individuals with genetically confirmed GAN,[3] reported a mean age at symptom onset of 2.9 years, with mean age of loss of independent ambulation being 8.3 years. The child reported by us had a relatively higher age of onset of 8 years, similar to the case reported by Vijaykumar *et al*.[6] Other neurological impairments include impaired sensation, intellectual disability, epilepsy, dysarthria, dysphagia, oculomotor apraxia, nystagmus, and vision loss, many of which were present in our case. Bony involvements in the disorder include joint contractures, foot deformities and scoliosis, the latter being present in 44% of the children studied by Bharucha-Goebel *et al*.[3]

The findings of pili torti may be observed in many genetic conditions, but those associated with neurological features include, GAN, occipital horn syndrome, Netherton syndrome, metabolic disorders such as citrullinemia, mitochondrial disorders, Menkes disease, Argininosuccinic aciduria, and congenital disorder of glycosylation type-1a.[7] Neuroimaging can help us in excluding the differentials. Metachromatic leukodystrophy usually has periventricular involvement with tigroid appearance of involved white matter. Krabbe disease usually has features of signal changes in the thalami, along cranial nerves and deep white matter involvement. *PLA2G6* related disorder usually have cerebellar atrophy with associated hypertrophy of clivus and changes in globus pallidus. In GAN, involvement of dentate nuclei, cerebellar white matter, periventricular white matter, and middle cerebellar peduncles are seen.[8,9] The current case had features of dentate involvement with involvement of periventricular and cerebellar white matter along with signal changes in the corticospinal tracts which favored the diagnosis of GAN over others. Bamaga *et al*.[10] reported a 7-year-old male child with progressive gait abnormality, weakness with electrodiagnostic studies showing axonal motor and sensory neuropathy, although unusually the MRI brain was normal. The current case had similar features but neuroimaging had multiple abnormalities. Both the cases were diagnosed with exome sequencing.

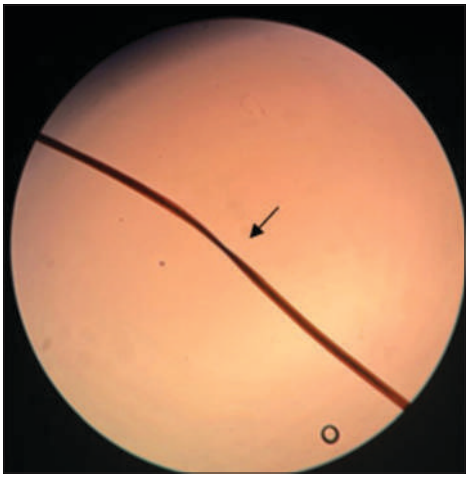

Figure 2: Pili torti seen on light microscopy of hair (black arrow)

Exome sequencing identified a stop-gain homozygous variant p.(Arg242Ter) in *GAN*. This variant is absent in the gnomAD (https://gnomad.broadinstitute.org/variant/16-81356875-C-T?dataset=gnomad_r4). This variant is in a gene where loss of function is a known mechanism of disease causation. This variant has two entries on ClinVar (https://www.ncbi.nlm.nih.gov/clinvar/) and affects the linker + kelch domains of the protein[11] Treatment includes mainly supportive care. Autologous bone marrow has been successful in some patients.[12] In a latest study of intrathecal injection of AAN vector containing GAN transgene transfer in 14 patients, showed some adverse events with improvement in motor function.[13]

Conclusion

Neuroregression in a child with involvement of both peripheral and central nervous system should raise suspicion of GAN.

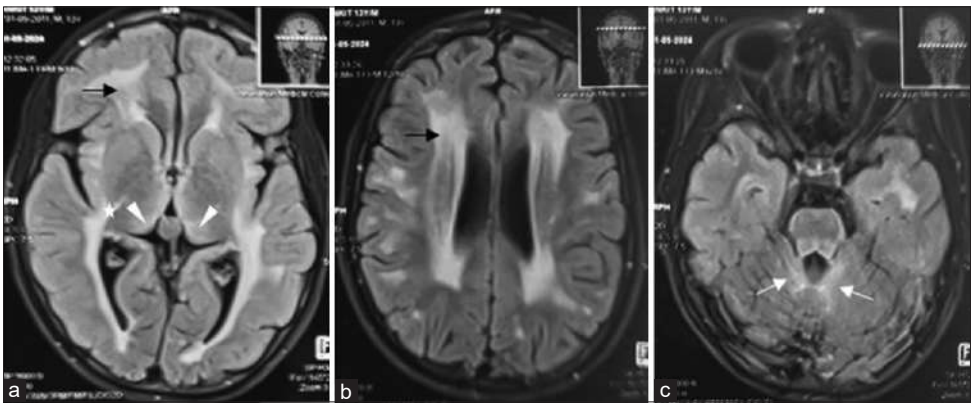

Figure 3: (a-c) Magnetic resonance imaging brain T2 FLAIR imaging shows periventricular hyperintensities (black arrow), internal capsule (white star), thalami (white arrow head), subcortical white matter abnormalities, and dentate nuclear changes (white arrow)

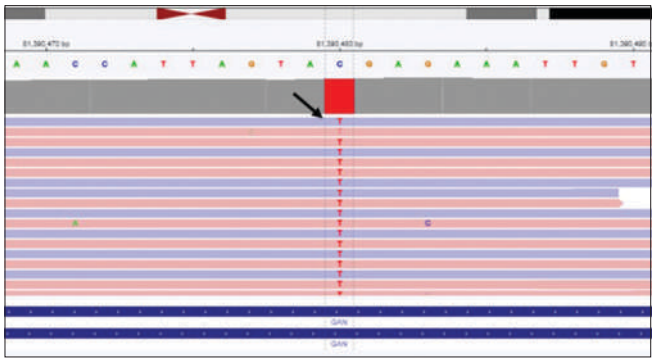

Figure 4: Integrative genomics viewer, a tool to visualize the exome sequencing data showing the mutation (black arrow points to a column where the reference nucleotide is C which is seen in blue on top which is changed to T, which is the mutation of interest)

The pathognomonic kinky hair helps in clinching the diagnosis, confirmed by genetic studies. Treatment is chiefly supportive.

Lessons learnt

1. Features of peripheral neuropathy as well as central nervous system involvement in a child with neuroregression, should raise suspicion of giant axonal neuropathy (GAN)
2. An astute clinical examination can corroborate the neurological findings with the kinky hair, to diagnose GAN
3. Neuroimaging and genetic analysis confirm the diagnosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

Acknowledgments

The authors are grateful to the patient and his family for their precious cooperation in this study and also grateful to Neuberg laboratories for performing the test.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Johnson-Kerner BL, Roth L, Greene JP, *et al*. Giant axonal neuropathy: An updated perspective on its pathology and pathogenesis. Muscle Nerve 2014;50:467-76.
2. Tazir M, Nouioua S, Magy L, *et al.* Phenotypic variability in giant axonal neuropathy. Neuromuscul Disord 2009;19:270-4.
3. Bharucha-Goebel DX, Norato G, Saade D, *et al.* Giant axonal neuropathy: Cross-sectional analysis of a large natural history cohort. Brain 2021;144:3239-50.
4. Bomont P, Cavalier L, Blondeau F, *et al.* The gene encoding gigaxonin, a new member of the cytoskeletal BTB/kelch repeat family, is mutated in giant axonal neuropathy. Nat Genet 2000;26:370-4.
5. Hentati F, Hentati E, Amouri R. Giant axonal neuropathy. Handb Clin Neurol 2013;115:933-8.
6. Vijaykumar K, Bindu PS, Taly AB, *et al.* Giant axonal neuropathy. J Child Neurol 2015;30:912-5.
7. Hoffmann A, Waśkiel-Burnat A, Żółkiewicz J, *et al.* Pili torti: A feature of numerous congenital and acquired conditions. J Clin Med 2021;10:3901.
8. Al-Maawali A, Yoon G, Feigenbaum AS, *et al.* Validation of the finding of hypertrophy of the clava in infantile neuroaxonal dystrophy/PLA2G6 by biometric analysis. Neuroradiology 2016;58:1035-42.
9. van der Knaap MS, Bugiani M. Leukodystrophies: A proposed classification system based on pathological changes and pathogenetic mechanisms. Acta Neuropathol 2017;134:351-82.
10. Bamaga AK, Muthaffar OY, Alyazidi AS, *et al*. Giant axonal neuropathy: A case report of subclinical childhood manifestations. Cureus 2024;16:e54368.
11. Bomont P, Ioos C, Yalcinkaya C, *et al.* Identification of seven novel mutations in the *GAN* gene. Hum Mutat 2003;21:446.
12. Sharma A, Gokulchandran N, Kulkarni P, *et al*. Application of autologous bone marrow stem cells in giant axonal neuropathy. Indian J Med Sci 2010;64:41-4.
13. Bharucha-Goebel DX, Todd JJ, Saade D, *et al.* Intrathecal gene therapy for giant axonal neuropathy. N Engl J Med 2024;390:1092-104.

Case Report

Extensive Facial Hemangioma with Dandy-Walker Malformation in an Infant: A Rare Case Report of PHACE Syndrome

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Abstract

Background: The acronym PHACE has been used for a rare neurocutaneous syndrome encompassing congenital malformations such as posterior fossa defect (P), infantile hemangioma (H), arterial abnormality (A), cardiac defect (C), and eye (E) abnormality. Although hemangiomas are common, the risk of having PHACE increases with size of hemangioma. **Clinical Description:** A 7-month-old female baby presented with multiple large hemangiomas over the face, scalp, extending inside oral cavity, neck, and upper chest which were increasing in size gradually, with ulcerations. Birth and development were unremarkable. She had macrocephaly and respiratory distress with a pansystolic murmur. **Management and Outcome:** Echocardiography revealed ventricular septal defect and brain imaging showed communicating hydrocephalus with empty posterior fossa, suggestive of Dandy–Walker Malformation. These findings along with large facial hemangioma are consistent with PHACE syndrome. **Conclusion:** The case highlights the importance of having a knowledge regarding such an important but rare condition of PHACE syndrome, which may be missed if not evaluated for, in an infant with hemangioma.

Keywords: Hydrocephalous, posterior fossa abnormality, segmental hemangioma, ventricular septal defect

Although hemangioma is a common finding in children, extensive lesions of the face or involving entire anatomical segments may be associated with abnormalities in other organ systems. The posterior fossa anomalies, hemangioma, arterial lesions, cardiac abnormalities/coarctation of the aorta, and eye anomalies (PHACE syndrome) is an important condition to be considered in such hemangiomas. Diagnostic criteria for PHACE syndrome were first described in 2009,[1] further modified in 2016.[2] Based on these criteria, we report an infant with extensive hemangioma with Dandy–Walker malformation, consistent with PHACE syndrome.

Clinical Description

A 7-month-old baby girl was admitted to our hospital with multiple large reddish lesions over the face, scalp, and neck present since birth, associated with feeding difficulty as well as some breathing problem. The lesions, initially small, gradually increased in size, and in number over 2 weeks, and ultimately coalesced covering both sides of the face, neck, and over the scalp. Her parents also noticed lesions over mouth and nose. The child gradually developed feeding difficulty both for semisolid food and breast milk, due to these lesions. She had some breathing difficulty with cough and fever for 3–4 days before presenting to us. Though extremely irritable, there were no associated abnormal movements, no history of trauma, and no similar lesions elsewhere in the body, currently or in the past. No similar history was found in any family member. The infant had a birth weight of 2.6 kg, appropriate for gestational age. The antenatal and postnatal course was uneventful. The child's development was normal as per her age and had received routine immunizations as per age. Her thyroid screening at birth was normal following birth.

On examination, the infant had an axillary temperature of 99°F, normal volume pulses palpable in all four limbs, heart rate of 90/min, blood pressure 90 / 60 mmHg, and capillary refill time of 3 seconds. The infant had respiratory distress with a respiratory rate of 56/min, moderate chest retractions, and SpO_2 90%. Pallor, cyanosis, icterus, clubbing, and edema were

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DOI: 10.4103/ipcares.ipcares_224_24

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Submitted: 13-Sep-2024 **Revised:** 21-Dec-2024
Accepted: 24-Dec-2024 **Published:** 14-Feb-2025

How to cite this article: Sinha D, Ray SK, Kundu S, Karim R, Sai GV. Extensive facial hemangioma with dandy-walker malformation in an infant: A rare case report of PHACE syndrome. Indian Pediatr Case Rep 2025;5:37-40.

absent. Her weight was 5.5 kg (*Z* score: 2.75, <3rd percentile), length of 52 cm, with a gross structural deformity over the head, specifically deforming the occipital bone with macrocephaly (head circumference was 49 cm).

We found multiple large facial hemangiomas, extending over the scalp, neck as well as over the inner side of the mouth [Figure 1]. There were widespread ulcerations with bleeding points over the face, with extensions to mouth and palatal mucosa. There were no other neurocutaneous markers. Chest auscultation showed bilateral wheeze. On cardiovascular examination, apex beat was shifted laterally with pansystolic murmur over the left 4th and 5th intercostal space. Abdominal and neurological examinations were unremarkable. Fundus examination was also normal. Based on history and clinical examination, the infant was considered likely to be suffering from a syndrome linked with hemangioma, possibilities being PHACE or Sturge–Weber syndrome.

Management and Outcome

The infant was started on supportive care with maintenance fluids, antibiotics, and moist oxygen. Investigations showed hemoglobin 9.5 mg/dL, raised total leukocyte count 19,300 cells/mm^3 (neutrophil 73% and lymphocytes 20%), platelets 3.6 lac/mm, and C-reactive protein was 6.5 mg/dL. Biochemical parameters were within normal limits. Chest X-ray was normal. A two-dimensional-echocardiography revealed 4 mm perimembranous ventricular septal defect (VSD) with left-to-right shunt and normal left ventricular function without any pulmonary artery hypertension. To evaluate the cause of gross posterior skull bone deformity, we planned magnetic resonance imaging brain but failed twice owing to lack of sedation. Hence, computed tomography angiography was performed [Figure 2], which showed the fourth ventricle to be grossly enlarged along with communicating hydrocephalus. Empty posterior fossa signified agenesis of cerebellar vermis, hence Dandy–Walker malformation was confirmed [Figure 3]. This structural brain defect together with the large facial hemangioma was consistent with PHACE syndrome.

Figure 1: Extensive facial and oral hemangioma (before and after use of beta-blocker therapy)

Oral propranolol (1 mg/kg/dose) was started to control the large hemangiomas. Topical timolol was also administered over palatal and oral mucosal hemangioma with gradually increasing dose of propranolol. Topical antibiotic along with dressing of the ulcerative wound was performed regularly. Ryles tube feeding followed by oral feeding was initiated. Oral hemangioma size regressed in due course over 4 weeks; treatment was continued [Figure 1]. The infant was referred to the neurosurgery department for specialized management of the brain malformation.

Discussion

The diagnostic criteria of PHACE syndrome had been established by a multidisciplinary team in 2009, [1] according to which, "Definite PHACE" is considered in the presence of a characteristic segmental hemangioma or hemangioma >5 cm on the face or scalp plus 1 major criterion or 2 minor criteria; and "Possible PHACE" is diagnosed in the presence of a hemangioma >5 cm on the face or scalp plus 1 minor criterion. The term "segmental" was used for a lesion covering an anatomic region, rather than a single focal point. This was updated in 2016[2] adding that patients with large segmental hemangioma of the neck, upper trunk, or trunk and proximal upper extremity having 2 other major criteria should also be considered to have "Definite PHACE." The organ systems included in major/minor criteria encompass arterial anomalies, structural brain lesions, cardiovascular, ocular, and anomaly of midline of the chest and abdomen. Our case presented with very large facial, oral, and scalp hemangioma along with a structural defect in the posterior fossa of the brain and Dandy–Walker malformation (one "major") and VSD (one "minor"), confirming definite PHACE syndrome.

An infant with hemangioma has 2%–3% risk of having PHACE, the risk increasing proportionate with size of hemangioma and having a predilection for females.[2] The pathogenesis of PHACE is not well understood. Any insult during embryogenesis between 3 and 12 weeks, as well as on neural crest derivatives might have a role in developing hemangioma and other organ system defects. The condition is not hereditary and no genetic etiology has not been identified.[3]

Congenital vascular anomalies are the most common extracutaneous associations in PHACE, with aorta and medium-sized arteries of the chest, neck, and head having highest potential for morbidity, especially the risk of acute ischemic stroke in those with cerebral vascular anomalies.

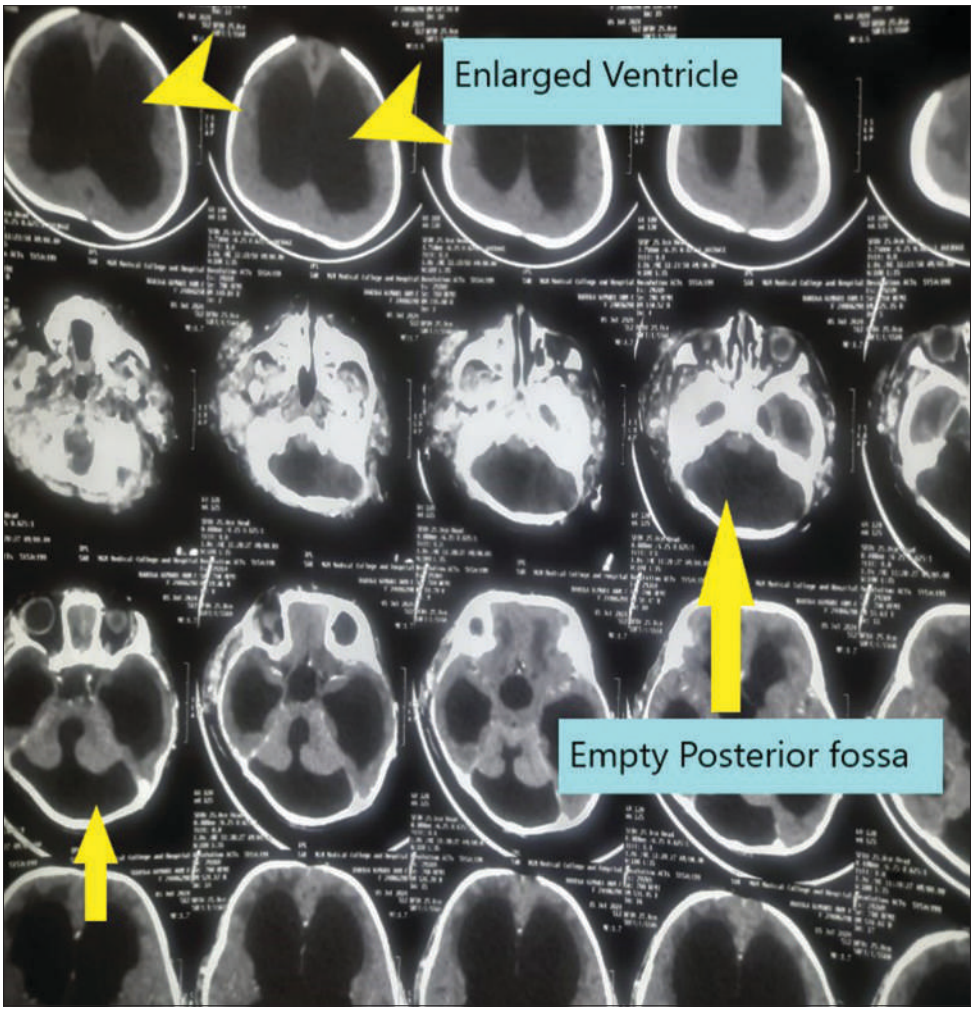

Figure 2: Computed tomographyangiogram showing empty postfossa along with enlarged ventricle

Risk stratification and surveillance have been recommended accordingly by experts.[2] Rare cases of PHACE syndrome associated with moyamoya vasculopathy have been reported.[4]

The prevalence of posterior fossa abnormalities ranges from 30.4% to 81%; the spectrum extending from focal cerebellar dysplasia to various cystic malformations including the Dandy–Walker complex.[2] Similar to our case, recently, William *et al*. reported Dandy–Walker variant malformation in a child with PHACE syndrome.[5] The Dandy–Walker malformation in PHACE scenario reported by Tiwary *et al*.[6] had associated hearing loss with microphthalmia and leukocoria. Some authors[7] have detected Dandy–Walker malformation in antenatal fetal neuroimaging, with PHACE syndrome being diagnosed by observing hemangioma following birth.

Congenital heart disease in this condition occurs in 41% to 67%.[2] The International PHACE Syndrome Registry showed the aberrant origin of a subclavian artery being the most common cardiovascular anomaly, with coarctation being the second-most common anomaly.[8] The long-term follow-up study of 104 individuals with PHACE syndrome, found that nearly half of the patients had anomalies of the heart, aortic arch, or brachiocephalic arteries. Of these, 18.5% had VSD, also seen in our case.[9]

Haggstrom *et al*., divided the face into four developmental segments (frontotemporal, frontonasal, maxillary, and mandibular). Frontotemporal and frontonasal segmental hemangiomas are linked more with ocular and central nervous system involvement, whereas mandibular segment is linked with midline and cardiovascular defect.[3] Other associations with PHACE syndrome include auditory impairment, speech delay, endocrine involvement, and dental abnormalities.[10] Differential diagnosis of PHACE syndrome includes Struge–Weber syndrome (parietal and occipital lobe leptomeninges involved, seizure episodes in almost every case, and cardiac defects are rare), LUMBAR syndrome (lower body hemangioma), and Wyburn–Mason syndrome (arteriovenous malformation in eye, brain and skin).[10]

Multidisciplinary management is necessary. For hemangioma, propranolol is the only drug approved by the US Food and Drug Administration for the management of problematic

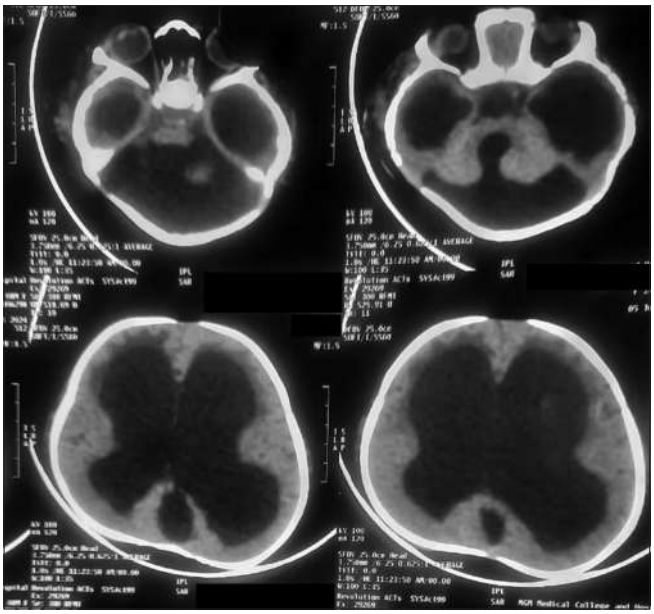

Figure 3: Zoomed picture of computed tomographyangiogram showing enlarged ventricle as well as hydrocephalus and postfossa defect-signify Dandy–Walker Malformation

infantile hemangioma, usually starting at 0.5–1 mg/kg daily dose and gradually increased. However, its use in PHACE with cerebrovascular anomalies is controversial, due to the risk of stroke. Lower doses and a slower escalating schedule should be considered,[2] We used both oral and topical beta-blocker drugs (propranolol and timolol) synergistically.

Conclusion

This case creates awareness among pediatricians to keep in mind the possibility of PHACE syndrome, in an infant presenting with a large hemangioma, especially with a skull deformity. A comprehensive evaluation including neuroimaging and echocardiography will help in diagnosing this interesting syndrome. Multidisciplinary management under regular monitoring can help to prevent morbidities.

Lessons learnt

- A possibility of PHACE syndrome is to be considered in a child with infantile hemangioma
- Imaging including angiography of the brain and neck, echocardiography along with careful evaluation for associated abnormalities, can help in diagnosis
- Multidisciplinary approach is required for the management of such child.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Metry D, Heyer G, Hess C, *et al.* Consensus statement on diagnostic criteria for PHACE syndrome. Pediatrics 2009;124:1447-56.
2. Garzon MC, Epstein LG, Heyer GL, *et al.* PHACE syndrome: Consensus-derived diagnosis and care recommendations. J Pediatr 2016;178:24-33.e2.
3. Haggstrom AN, Lammer EJ, Schneider RA, *et al*. Patterns of infantile hemangiomas: New clues to hemangioma pathogenesis and embryonic facial development. Pediatrics 2006;117:698-703.
4. Tortora D, Severino M, Accogli A, *et al.* Moyamoya vasculopathy in PHACE syndrome: Six new cases and review of the literature. World Neurosurg 2017;108:291-302.
5. William M, Bhusal A, Umar SM, *et al*. PHACE syndrome: A case report and a comprehensive review. Ann Med Surg (Lond) 2024;86:2286-91.
6. Tiwary AK, Mishra DK, Jha G. A rare face of "PHACE" syndrome with dandy-walker malformation, microphthalmia with leukocoria, hearing loss and involuting segmental facial hemangioma. Indian J Paediatr Dermatol 2017;18:223-6.
7. Sepulveda W, Sepulveda F. Fetal neuroimaging findings in PHACE syndrome: Case report and review of the literature. J Matern Fetal Neonatal Med 2022;35:2751-8.
8. Bayer ML, Frommelt PC, Blei F, *et al.* Congenital cardiac, aortic arch, and vascular bed anomalies in PHACE syndrome (from the international PHACE syndrome registry). Am J Cardiol 2013;112:1948-52.
9. Braun M, Frieden IJ, Siegel DH, *et al.* Multicenter study of long-term outcomes and quality of life in PHACE syndrome after age 10. J Pediatr 2024;267:113907.
10. Keith L. PHACE syndrome: A review. Semin Pediatr Neurol 2024;51:101152.

Case Report

Fever in a Neonate – To Keep Neonatal Malaria in Mind

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Abstract

Background: Malaria is seldom suspected and diagnosed in neonates. Although India is endemic for malaria, there are few reports of neonatal malaria. **Clinical Description:** A 20-day-old, term, exclusively breast-fed, neonate, presented with high-grade fever for 1 day, without any abnormal movements. Antenatally, the mother had fever transiently for 2 days during the second trimester, but not investigated. Examination revealed pallor with hepatosplenomegaly, with normal tone and reflexes. **Management and Outcome:** Investigations revealed anemia (7.1 g/dL) and thrombocytopenia (30,000/µL), with bilirubin (total/conjugated) 5.8 / 0.5 mg/dL. Peripheral blood showed schizonts of *Plasmodium vivax.* The baby was treated with chloroquine, following which he became afebrile and was discharged on the 5th day. **Conclusion:** The case reiterates the importance of suspecting malaria in neonates presenting with symptoms mimicking neonatal sepsis and born to mothers in malaria-endemic areas. Prompt diagnosis and treatment can lead to a favorable outcome.

Keywords: Congenital malaria, hepatosplenomegaly, *Plasmodium vivax*, sepsis, vertical transmission

Neonatal malaria may be congenital or acquired. While congenital malaria is typically defined as the presence of asexual forms of malarial parasites in the peripheral blood smear or cord blood of the newborns from birth to 7 days of life, neonatal malaria refers to malaria in an infant up to the age of 28 days.[1,2] However, the distinction is not clear. Although a serious condition with potential morbidity and mortality, it is treatable. Here, we report a case of neonatal malaria, which was timely diagnosed and treated.

Clinical Description

A 20-day-old male neonate, from western Rajasthan, India, presented with high-grade fever for 1 day, not associated with lethargy, refusal to feed, vomiting, or abnormal movements. The baby was born at term, through normal vaginal delivery, cried immediately after birth, started breastfeeding within one hour, and was immunized with polio, BCG, and hepatitis B vaccines. The mother was a booked case, had receiving tetanus vaccination and iron supplementation. She reported having high-grade fever lasting 2 days during the second trimester, which subsided spontaneously, without medical consultation. There was no family history of recent fever.

The baby was alert, febrile (axillary temperature: 37.6°C), heart rate 166/min, respiratory rate 50/min, capillary refill time <3 sec, mean blood pressure of 43 mmHg, and SpO_2 96% on room air. He had some pallor but no icterus or cyanosis with weight of 3 kg (<3rd percentile as per WHO standards at day 20 of life), length of 51 cm (3rd to 15th percentiles), and head circumference was 35 cm (3rd to 15th percentiles). There were no rash, petechiae, or any mosquito bites on exposed parts. The abdomen was distended, liver and spleen were both palpable 4 cm below the costal margin, and the anterior fontanelle was at level. Examination of the cardiorespiratory and central nervous systems including neonatal reflexes were within normal limits. Based on this clinical presentation, our differential diagnosis included late-onset sepsis, congenital malaria, and intrauterine infections.

Management and Outcome

Investigations showed anemia (7.1 g/dL) and thrombocytopenia (30,000/µL), with normal total leukocyte count (7800/mm^3) and C-reactive protein of 38 mg/dL. Biochemical parameters showed serum bilirubin (total/conjugated) 5.8/0.5 mg/dL, aspartate aminotransferase/alanine transaminase 31 / 12 IU/L, urea/creatinine 36 / 0.2 mg/dL, sodium/potassium/chloride 137/4.2/105 meq/L, and calcium 8.5 mg/dL and the rapid diagnostic test for malaria was positive. Direct Coomb's test

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Submitted: 30-Aug-2024 **Revised:** 19-Dec-2024
Accepted: 24-Dec-2024 **Published:** 14-Feb-2025

How to cite this article: Dara PK, Mohta D, Choudhary A, Choudhary N, Soni RK. Fever in a neonate – to Keep neonatal malaria in mind. Indian Pediatr Case Rep 2025;5:41-2.

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DOI: 10.4103/ipcares.ipcares_219_24

was negative. The peripheral blood film revealed schizonts of *Plasmodium vivax*, with a parasite density of 6800 parasites/μL (3+). Blood culture was sterile.

The neonate was started on intravenous ampicillin and gentamicin. After the diagnosis of malaria was confirmed, antibiotics were discontinued, and the neonate was treated with oral chloroquine. After the first dose of chloroquine, the neonate became afebrile, his general condition improved, hepatosplenomegaly started reducing, and he resumed breastfeeding. A repeat peripheral blood film showed no parasites. The neonate was discharged on the 5th day of admission. However, the patient did not come for follow-up.

Discussion

Although malaria is an important public health problem in tropical and subtropical areas of the world, its occurrence in neonates is seldom encountered by physicians.[3,4] As per a systematic review of 22 studies including 28,083 neonates, the overall prevalence of clinical neonatal malaria was 12.0%.[5] While congenital malaria is defined as the presence of malarial parasites in the blood of newborn within the 1st week of life and is due to the transfer of malaria parasites from mother to fetus during pregnancy or delivery, neonatal malaria is the connotation used for malaria in an infant up to the age of 28 days.[1] However, these definitions are not very rigid and may overlap. In our case, although the mother had a febrile episode antenatally, she was not investigated, so it is unclear whether the neonate had congenital or acquired malaria.

It has been reported that the placenta serves as an effective barrier against malaria parasite transmission protecting the fetus. Further, maternal antibodies, breast milk constituents, and high fetal hemoglobin protect the neonates against heavy parasitemia. However, placental infestation with malarial protozoa leads to syncytiotrophoblast disruption, syncytial knot formation, and fibrinoid deposition, increasing the risk of perinatal morbidity and mortality, such as intrauterine growth restriction, premature labor, and intrauterine fetal death.[6]

Fever is the most common presenting feature in neonatal malaria, others being respiratory distress, pallor, hepatomegaly, poor feeding, jaundice, and diarrhea. Unusual presentations may include recurrent apnea, cyanosis, jaundice, and multi-organ dysfunction.[3-5,7] Our case presented with fever associated with pallor.

Treatment for congenital malaria includes chloroquine and artemisinin-based therapy. Primaquine is not used in congenital malaria as it is a transfusion-related infection without an exoerythrocytic phase. Although a hepatic phase is present in acquired neonatal malaria, primaquine is contraindicated in newborns because of G6PD deficiency. Chloroquine is used for uncomplicated *P. vivax* malaria, while artemisinin-based therapies are indicated for severe malaria.[3,8] Early diagnosis and treatment led to a favorable outcome in this case. Prevention of congenital malaria requires prompt diagnosis and treatment of malaria in pregnant women, along with malaria control measures.

Conclusion

The case creates awareness among pediatricians that malaria may be a possibility in a sick neonate presenting as sepsis, especially in endemic regions. Unless suspected, neonatal malaria, which is otherwise treatable, may remain undetected and untreated.

Lessons learnt

- Neonatal malaria should be kept in the differential diagnoses of a newborn presenting with fever and sepsis-like features
- Unless suspected and specifically looked for in the peripheral smear, neonatal malaria may be missed
- Neonatal malaria due to *P. vivax* is easily treatable if diagnosed early.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Mohan K, Omar BJ, Chacham S. Malaria in newborn: A missed entity for primary care physician. J Family Med Prim Care 2023;12:1511-5.
2. Tahirou I, Zara MO, Moustapha ML, *et al.* Congenital malaria and its associated factors at Issaka Gazobi maternity of Niamey in Niger. Int J Pediatr 2020;2020:1-6.
3. Tesso ZG, Gossaye TY, Bekana DS, *et al*. *Plasmodium falciparum* neonatal malaria with atypical presentation: A case series from Southwestern Ethiopia. Malar J 2024;23:178.
4. Nagaraj N, Berwal PK, Sharma M, *et al.* Congenital and neonatal malaria in Asian Indian population. Int J Community Med Public Health 2015;2:639-42.
5. Danwang C, Bigna JJ, Nzalie RN, *et al*. Epidemiology of clinical congenital and neonatal malaria in endemic settings: A systematic review and meta-analysis. Malar J 2020;19:312.
6. Crocker IP, Tanner OM, Myers JE, *et al*. Syncytiotrophoblast degradation and the pathophysiology of the malaria-infected placenta. Placenta 2004;25:273-82.
7. Choudhury S, Das J. Case series on congenital malaria from a tertiary care hospital in North Eastern India. Asian J Med Sci 2021;12:166-8.

Nasal Glial Heterotopia: An Unusual Cause of Lump on the Nose in a Child- A Case Report

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Abstract

Background: Glial heterotopia is a rare, nonneoplastic extracranial displacement of the brain tissue, most commonly seen on the nose. **Clinical Description:** A 2-year-6-month-old boy presented with a nasal mass gradually increasing since birth, being otherwise asymptomatic. The mass was firm, tense, predominantly skin-colored with some bluish discoloration, with no signs of inflammation, present on the left side of the bridge of the nose. Systemic examination and vitals were normal. **Management and Outcome:** Contrast-enhanced magnetic resonance imaging scan showed features suggestive of nasal glial heterotopia (NGH), with a thin linear T2-weighted hyperintense stalk extending from the mass up to the foramen cecum. Complete surgical excision, with ligation and cauterization of the fibrous communicating tract, was done close to intracranial entry. Histopathology confirmed the diagnosis of glial heterotopia, with immunohistochemistry showing glial fibrillary acid protein positivity. **Conclusion:** Pediatricians need to be aware that a slow-growing external nasal mass, present since birth, may be a NGH. Imaging can delineate intracranial connections with confirmation by histopathology after complete excision.

Keywords: Extranasal glioma, glial fibrillary acid protein, neuroglial heterotopia, pediatric

Neuroglial heterotopias are rare, nonneoplastic masses containing brain tissue outside the central nervous system.[1] The most common location of neuroglial heterotopias is in the nose, either externally or internally, and are known as nasal glial heterotopia (NGH) or nasal gliomas. Although benign, they are often cosmetically or clinically unacceptable and surgical excision is recommended. We report a child with an extranasal NGH, a condition less known among pediatricians due to its rare occurrence.

Clinical Description

A 2-year-and 6-month-old boy presented with a lump on the nose, present since birth. Parents noticed a small lump over the root of the bony nasal bridge soon after birth, which gradually increased in size over the next 24 months. Although parents had been advised evaluation and follow-up at birth, they sought otorhinolaryngology opinion when the child was 1 year of age. An imaging of the head was then advised but was deferred as the child was apparently asymptomatic and also due to the prevailing COVID-19 pandemic. Subsequently, he was brought to us for evaluation. At the time of presentation, the child had no other associated symptoms such as pain or discomfort, bleeding or discharge from the lump, or any breathing difficulties. There was no other significant past medical history.

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DOI: 10.4103/ipcares.ipcares_235_24

The child was born out of a nonconsanguineous marriage, at term, by an emergency cesarean section, done in view of nonprogression of labor. He cried immediately after birth with good Apgar scores and weighed 3 kg. Antenatal and postnatal periods were uneventful. The child had received vaccinations as per the National Immunization Schedule, and his development was age appropriate.

On examination, the child was alert and active. His weight was 12.9 kg (3rd–50th centile), height was 93 cm (50th–97th centile), and head circumference was 47 cm (50th centile). He was afebrile, with heart rate of 110/min, respiratory rate of 24/min, and SpO_2 99% in room air. There was no pallor, cyanosis, clubbing, pedal edema, or lymphadenopathy. A tense, predominantly skin-colored mass, approximately 2 cm × 2 cm in size, with a small area of bluish discoloration was noted on the left side of the bridge of the nose. It was firm, nontender, nontransilluminant with no signs of inflammation [Figure 1a]. No other gross external anomalies were noted on the face or

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Submitted: 27-Sep-2024 **Revised:** 09-Jan-2025
Accepted: 10-Jan-2025 **Published:** 14-Feb-2025

How to cite this article: Pusapati S, Gudipudi UD, Penumetcha KR. Nasal glial heterotopia in a child: An unusual cause of lump on the nose. Indian Pediatr Case Rep 2025;5:43-6.

Figure 1: (a) Black arrow pointing towards a skin-colored mass with bluish discoloration over the left side of the bridge of the nose; (b) Post operative picture showing healed scar

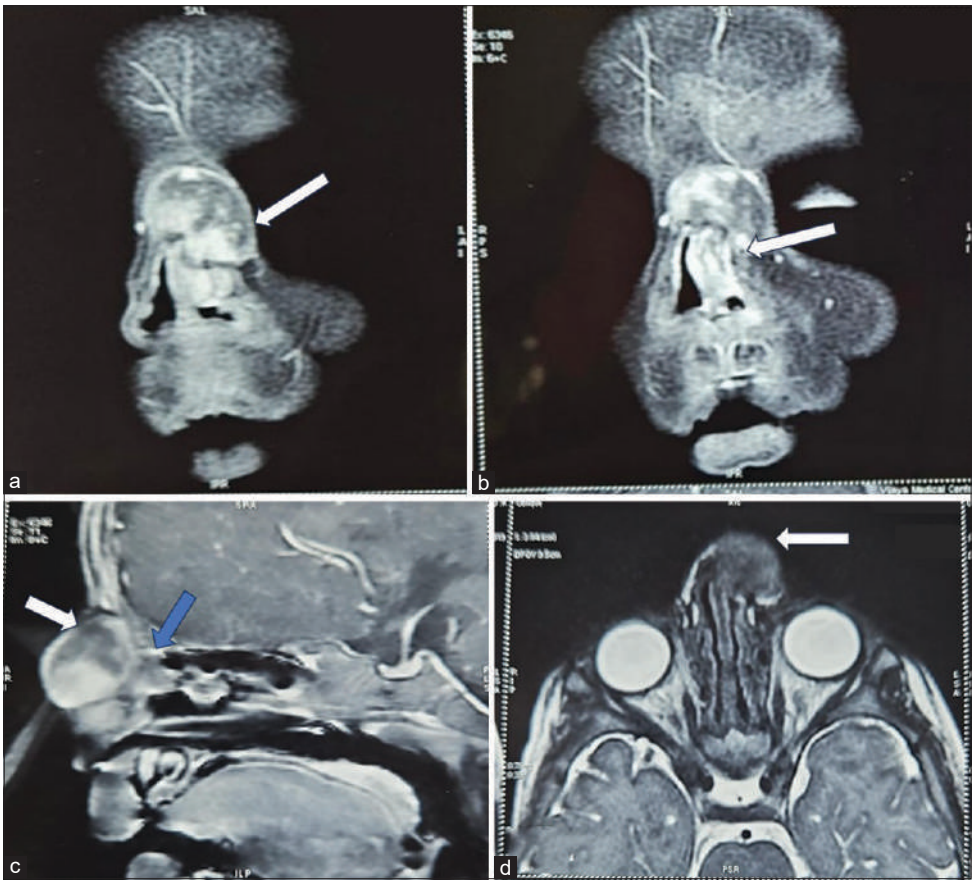

Figure 2: Contrast-enhanced magnetic resonance imaging (MRI) T1 images of paranasal sinuses in the coronal sections (in anterior most plane) showing (a) widening of the nasal dorsum and minimally enhancing mass within the prenasal space on the left side (white arrow); (b) truncation of anterior nasal septum with asymmetry of left nasal cavity (white arrow); Contrast-enhanced MRI (c) T1 sagittal reformatted image in the midline showing extension of a thin soft-tissue signal intensity stalk from the mass up to the foramen cecum (blue arrow), white arrow indicates the nasal mass; (d) T2 axial image revealing the epicenter and extension of the mass

the rest of the body. The oral cavity was normal without any cleft lip or palate. Examination of the nose showed adequate nasal passages, and both ears were normal. He had normal heart sounds, chest was clear, abdomen was soft without any organomegaly, and his neurological examination was normal. The possible differential diagnoses considered were nasal dermoid cyst, nasal glioma, or encephalocele.

Management and Outcome

Basic routine laboratory investigations revealed hemoglobin 10.9 g/dL, total leukocyte count 7800 cells/mm^3 and platelets 1.67 lakhs/mm^3, urea/creatinine 20/0.3 mg/dL, random blood sugar 92 mg/dL, and thyroid-stimulating hormone of 5.5 mIU/mL. The plain and contrast-enhanced magnetic resonance imaging (CE-MRI) of the nose and brain showed a 2.3 cm × 2.4 cm × 3.2 cm mass within the soft tissues of the nasal dorsum. Truncation of the anterior nasal septum, splaying of nasal bones, and asymmetry of the left nasal cavity but no extension into nasal cavity was reported. A thin linear hyperintense stalk-like structure extending from the mass up to the foramen cecum was noted [Figure 2a-d]. High-resolution computed tomography (HRCT) scan of the paranasal sinuses (PNS) showed no communication with ethmoid sinuses. While the CE-MRI delineates the mass and evaluates its intracranial extension and dural communication if any, the HRCT of the PNS was done to evaluate the association of the lump with the sinuses and other nasal bony structures. Experts from otorhinolaryngology and neurosurgery departments provisionally diagnosed the mass as a nasal glioma with minimal intracranial extension and surgical excision was planned under general anesthesia.

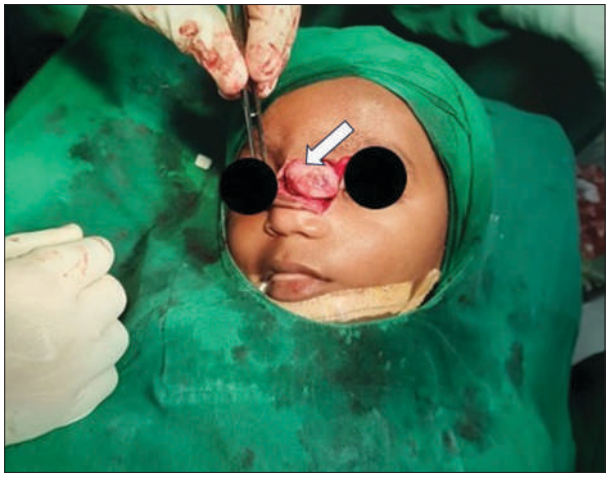

Figure 3: Intraoperative image showing the nasal mass (white arrow) exposed through lateral rhinotomy incision

The preoperative electrocardiogram, chest X-ray, and two-dimensional echocardiography were normal, the tests being done to rule out any associated congenital heart disease. The child underwent complete surgical excision of the nasal lump through a lateral rhinotomy approach [Figure 3]. The nasal bridge which was in contact with the mass was depressed on the left side with splaying of nasal bones. A tract of fibrous tissue was seen extending intracranially. The glioma was excised completely, and the tract was ligated and cauterized close to its intracranial entry into the foramen cecum. No cerebrospinal fluid (CSF) leak was observed during the procedure. Histopathology [Figure 4a and b] of the excised mass showed gliosis with mature astrocytes. There was no cytological atypia. Immunohistochemistry [Figure 4c] done with glial fibrillary acidic protein (GFAP) was positive confirming the clinical diagnosis of glial heterotopia/nasal glioma. The postoperative period [Figure 1b] was uneventful, and the patient was discharged 3 days after surgery. Thereafter, the patient was under regular follow-up for 2 years, with no recurrence, nor symptoms.

Discussion

Glial heterotopia is a rare, noninherited, benign, congenital anomaly, in which mature glial cells grow outside the central nervous system. Although the most common location is nose, it has also been reported on the scalp, orbit, middle ear, palate,

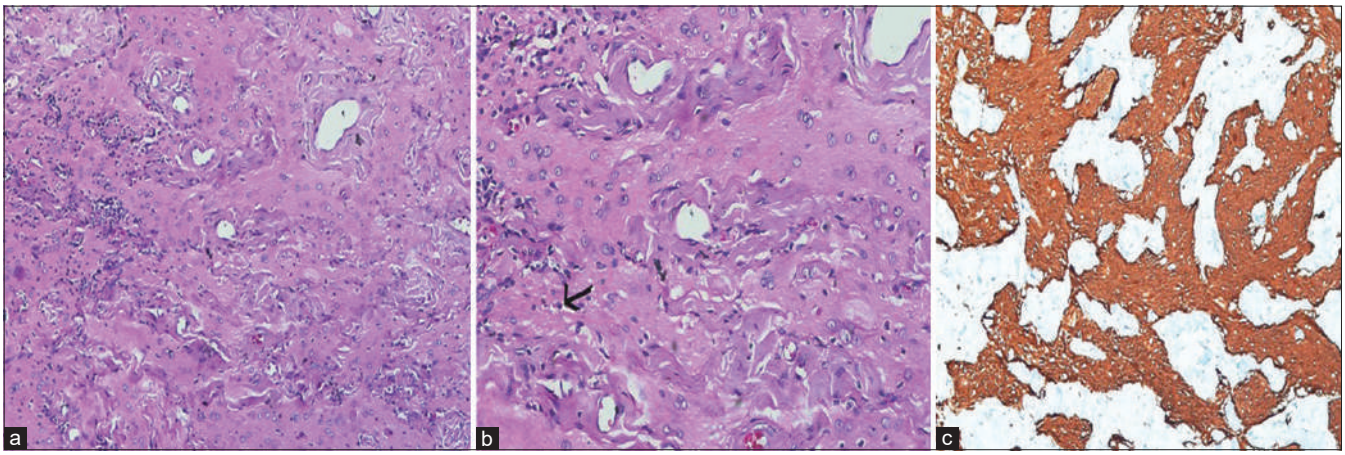

Figure 4: Histopathology images: (a) Glial tissue with dense intervening vascular collagenous stroma (×10); (b) Fibrillary glial tissue with cells showing variable cytoplasm and oval nuclei (black arrow), with no mitotic activity (×20); (c) Glial fibrillary acidic protein positive (×20)

and tongue. Nasal gliomas constitute about 5% of all congenital nasal masses, the latter having an overall estimated incidence of 1 in 20,000–40,000 live births, clearly having an extremely rare occurrence.[1]

The systematic review[2] of 152 reports of NGH showed that 130 were diagnosed in childhood, being more common in males. Location may be extranasal (36%), intranasal (45%), or mixed (19%). Nearly half of the children with NGH remain asymptomatic, with the rest manifesting mostly with nasal congestion, especially in intranasal type. Choking, feeding difficulties, rhinorrhea, and rarely even meningitis have been reported. Extranasal gliomas appear as a firm, red-to-bluish, slow-growing mass, covered by the skin.[3,4] The absence of pulsations and no increase in size with Valsalva maneuver rules out a vascular etiology. Our case too had a skin-covered mass and remained asymptomatic due to which medical attention was delayed.

Imaging can determine whether a congenital midline mass is associated with any bone defect or not. MRI is helpful in identification of intracranial communication when present, and the lesions exhibit high signal intensity on T2W images which lacks enhancement. Anterior osseous structures and bone flaws can be better appreciated in CT. X-ray alone was done in few cases but of not much diagnostic value.[5] Studies state that due to the possibility of CSF leakage in the presence of intracranial link, diagnostic biopsies are not recommended. The review done by Gallego Compte *et al*.,[2] showed that MRI and CT were done in nearly 40% and 20% of cases, respectively, with another 20% having undergone both. We conducted both CE-MRI and high-resolution CT scan, which showed a mass connected with thin linear T2W hyperintense stalk-like structure extending up to the foramen cecum radiologically suggestive of nasal glial heterotropia.

Neurogenic tumors, encephaloceles, ectodermal tumors, and teratomas are the differential diagnosis of a congenital nasal midline mass. Although nasal encephalocele and nasal glioma originate from the brain tissue, an encephalocele remains connected to the brain by a pedicle, while a nasal glioma usually has no connection to the central nervous system. Only 10%–15% of gliomas may be connected to the dura mater, and this is more common among the intranasal type of gliomas.[6] In our case, there was no direct intracranial communication despite the presence of a fibrous tract from the mass to the foramen cecum, which was ligated and cauterized.

Complete surgical excision is preferred for cosmetic reasons and to prevent further deformity of the nose, with external rhinotomy being the most common approach, as done in our case. Other surgical methods include endoscopic resection or combination approach.[2] If previously undetectable tract is found intraoperatively, neurosurgical consultation may be needed. Histopathology is essential for the diagnosis – presence of astrocytes and neuroglial fibers in fibrovascular connective tissue stroma, along with the presence of glial fibrillary acid protein (GFAP), is confirmative of glial tissue.[7]

Conclusion

Rarely pediatricians may encounter a child with an external nasal mass, present since birth, growing slowly, which could be a NGH. Knowledge about this rare condition will enable timely imaging, differentiating from other nasal masses and confirming the diagnosis by excision and histopathological examination. A multidisciplinary team approach is required for successful outcome.

Lessons learnt

- A slow-growing external nasal mass, present since birth, may be a nasal glial heterotopia, of which pediatricians are less familiar
- Imaging by MRI and HRCT are important to delineate intracranial connections and associations with the paranasal sinuses. Histopathology confirms the diagnosis
- Surgical resection can result in full recovery with no recurrence.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Maharaj S. Pediatric nasal glial heterotopia. Ear Nose Throat J 2022;101:P83-5.
2. Gallego Compte M, Menter T, Guertler N, *et al*. Nasal glial heterotopia: A systematic review of the literature and case report. Acta Otorhinolaryngol Ital 2022;42:317-24.
3. Bailey NA. A congenital extranasal glioma in a newborn. SAGE Open Med Case Rep 2022;10. doi:10.1177/2050313X221144515.
4. Yan YY, Zhou ZY, Bi J, *et al*. Nasal glial heterotopia in children: Two case reports and literature review. Int J Pediatr Otorhinolaryngol 2020;129:109728.
5. Abdel Razek AA, Gamaleldin OA, Elsebaie NA. Peripheral nerve sheath tumors of head and neck: Imaging-based review of World Health Organization classification. J Comput Assist Tomogr 2020;44:928-40.
6. Adil E, Robson C, Perez-Atayde A, *et al.* Congenital nasal neuroglial heterotopia and encephaloceles: An update on current evaluation and management. Laryngoscope 2016;126:2161-7.
7. Kathuria P, Agarwal S. Nasal glial heterotopy in childhood: A case report highlighting the morphological and immunohistochemical features. Indian J Pathol Microbiol 2006;49:612-4.

Case Report

Superior Mesenteric Artery Syndrome with Anorexia Nervosa: A Rare Case of Postprandial Vomiting in an Adolescent

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Abstract

Background: Superior mesenteric artery (SMA) syndrome is an underdiagnosed complication of acute, severe weight loss, usually seen among adolescents. Reduction of mesenteric fat causes SMA to compress the duodenum against the abdominal aorta. It is a known complication of restrictive eating disorder like anorexia nervosa (AN). **Clinical Description:** An 11-years-8-month-old girl presented with vomiting after feeds, and avoidance of food over 1.5 years, with weight loss, fatigue, and excessive sleepiness over the past 5 months. She attained menarche 10 months ago, preceded by an apparent spurt in height, but developed amenorrhea following two cycles. On examination, she was tall, relative to her weight with a low body mass index (BMI) of 12.3 kg/m^2, Tanner stage 3. She showed exaggerated orthostatic pulse and blood pressure changes. Her general physical and systemic examinations were otherwise normal. **Management and Outcome:** Routine blood investigations were unremarkable. Abdominal X-ray and barium swallow were normal. Investigations for common chronic infections were negative, and she fulfilled the criteria for AN binge-purge type. Further, ultrasound abdomen showed reduction in the aortomesenteric distance and upstream dilation of the second and third part of the duodenum, suggestive of SMA syndrome, confirmed by computed tomography abdomen. Nutritional rehabilitation was done initially via nasogastric tube, later through nasojejunostomy, with high-calorie diet, gradually being shifted to oral. With multidisciplinary team management, the child recovered, with weight gain of 2.67 kg over 3 weeks. **Conclusion:** Pediatricians need to keep in mind SMA syndrome as a rare cause of intractable vomiting and food aversion, especially during growth spurt with drastic fall in BMI due to eating disorders. Nutritional rehabilitation and counseling are enough to reverse all symptoms.

Keywords: Adolescent, body mass index, growth spurt, puberty

Superior mesenteric artery (SMA) syndrome is a rare cause of intractable vomiting, caused by the compression of the third part of the duodenum between the aorta posteriorly and the SMA anteriorly.[1] Although it is a known complication developing subsequent to the eating disorder anorexia nervosa (AN) in teenagers, SMA syndrome may also occur primarily due to acute pubertal growth spurt and drastic fall in body mass index (BMI) as well as due to multiple other causes. .[2] Here, we describe the interesting combination of SMA syndrome and AN developing in a girl at the onset of puberty.

Clinical Description

An 11-year-8-month-old girl presented with food aversion over 1½ years. Mother perceived the food refusal to be intentional and when forced to eat, she would get agitated and vomit, the vomiting becoming worse over the last 5 months. Vomitus was nonbilious, nonprojectile containing food particles. As per records, she apparently had lost 5 kg over the past 5 months. There was associated constipation, abdominal discomfort, fatigue, excessive sleepiness, dizziness, and palpitation on exertion over the last few months. She had attained menarche 10 months ago and had menstrual cycles for 2 consecutive months followed by amenorrhea. The mother also reported truancy, lack of interest in her surroundings, and avoidance of friends for the last 3 months. Evaluations in various hospitals over 3 months, did not yield a diagnosis. There was no associated fever, night sweats, cough, breathlessness, diarrhea, abdominal pain, swallowing difficulty, swelling of feet, abnormal movements, jaundice, bulky stools, excessive thirst, or increased micturition.

She was the first child of parents, born out of a third-degree consanguineous marriage, at term, with a birth weight of 3 kg.

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Website: www.ipcares.org

DOI: 10.4103/ipcares.ipcares_261_24

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Submitted: 14-Nov-2024 **Revised:** 14-Jan-2025
Accepted: 17-Jan-2025 **Published:** 14-Feb-2025

How to cite this article: Reshmi YS, Basker MM, Ebenezer A. Superior mesenteric artery syndrome with anorexia nervosa: A rare case of postprandial vomiting in an adolescent. Indian Pediatr Case Rep 2025;5:47-50.

The antenatal, natal, and neonatal periods were uneventful. She had appropriate development, studying in grade 6 with good scholastic performance, and was adequately immunized for age. She had no similar or other significant illnesses in the past. Her family history was insignificant, with a 10-year-old healthy, younger sister.

On examination, she looked malnourished and emotionally distressed. She had tachycardia (120/min), respiratory rate was 22/min, temperature 98.4°F. Anthropometry showed a weight of 29.8 kg (10^{th}–25^{th} centile), height 152 cm (75^{th}–90^{th} centile), and BMI 12.73 kg/m^2 (<3^{rd} centile), (as per Indian Academy of Pediatrics 2015 growth centiles). She had no pallor, acrocyanosis, icterus, clubbing, lymphadenopathy, edema, or knuckle hyperpigmentation. The skin was dry, with thinning of scalp hair. Tanner's stage was 3. The abdomen was soft and nontender, with no organomegaly. The cardiorespiratory examination was normal. She was conscious, oriented, and had normal tone, power, and reflexes, with no focal neurological deficits. She was diagnosed with severe malnutrition, probably due to upper gastrointestinal (GI) obstruction or a primary eating disorder.

Management and Outcome

Initial investigations revealed hemoglobin of 14.2 g %, probably secondary to hemoconcentration following excessive vomiting, reduced fluid intake, and dehydration; total leukocyte count 7100/mm^3, neutrophil 61%, lymphocytes 28%, and platelet count 4.22 L/mm^3. Serum sodium and potassium levels were normal (140/4.2 meq/L, respectively), as also the hepatic and renal function tests (total/conjugated bilirubin 0.6/0.19, aspartate aminotransferase/alanine aminotransferase 320/7.4 U/L, total protein 6.6 g/dL, albumin 4.3 g/dL, alkaline phosphatase 73 U/L, and creatinine 0.35 mg/dL), amylase 46 U/L and lipase 30 U/, calcium/phosphorus were 10.4/4 mg/dL, and magnesium being 2.17 mg/dL. C-reactive protein was negative. The erythrocyte sedimentation rate at 1 hour was low (1 mm). There were no air-fluid levels on X-ray abdomen, and barium swallow showed no reflux. Other causes for weight and height loss were ruled out: HIV ELISA, Mantoux test were negative, and chest X-ray had no evidence of tuberculosis. The random blood sugar was 82 mg %. Thyroid stimulating hormone was 3.25 µIU/mL, T4–14.4 µg% and Free T4 1.62 ng%, stool for ova, parasites, cyst, and occult blood were negative.

As per opinion of pediatric gastroenterologist, she was referred to specialists in adolescent medicine, to rule out a possible eating disorder in view of negative results for organic causes. On re-evaluation, it was found that the child had a fear of weight gain, and vomited after every meal to relieve the distress she experienced after eating, though Russel's sign (calluses on the dorsum of knuckles due to induced vomiting) was absent. Orthostatic changes were present: pulse rate, supine, and standing were 120 and 153/min, respectively; blood pressure supine and standing were 118/80 and 100/62 mmHg, respectively. Investigations for psychiatric causes and eating disorder mimics were carried out: antinuclear antibody was negative, ruling out systemic lupus erythematosus. Magnetic resonance imaging of the brain to rule out diencephalic lesions, a mimic of AN, revealed features of generalized cerebral atrophy [Figure 1].

Finally, the child was diagnosed as AN binge-purge type (AN-BP), with the presence of all the three mandatory criteria according to diagnostic and statistical manual (DSM-5)[3] On evaluation for complications of severe malnutrition in AN-BP, microcardia (cardio-thoracic ratio: 38.3%) was delineated in chest X-ray [Figure 2]. There was no evidence of arrhythmias on electrocardiogram. Investigations in view of secondary amenorrhea revealed luteinizing hormone 7.50 mIU/mL, (normal: ≤4.38 mIU/mL) follicular stimulating hormone 9.40 mIU/mL (normal: 0.87–9.16 mIU/mL), prolactin 12.0 ng/mL (normal: 2.8–29.2 ng/mL), and estradiol 25.55 pg/mL (normal: 21–85 pg/mL), Vitamin D level was 8.2 ng/mL, Vitamin B12 158 pgm/mL, iron 47 µg% and folic acid 5.3 ng/mL, all significantly low. Bone mineral density done in view of prolonged duration of the illness of more than a year and amenorrhea for 8 months, revealed severe osteopenia [Figure 3].

Ultrasound abdomen revealed normal sized liver with increased echotexture, other organs being normal. There was a reduction in the aorto-mesenteric distance and upstream dilation of the second and third parts of the duodenum. This was suggestive of SMA syndrome causing compression of the third part of the duodenum between the abdominal aorta and SMA. Subsequently, CT abdomen with angiogram revealed an aorto-mesenteric distance of 4.6 mm and aorto-mesenteric angle of 14 confirming SMA syndrome, a well-known complication of restrictive ED such as AN-BP [Figure 4].

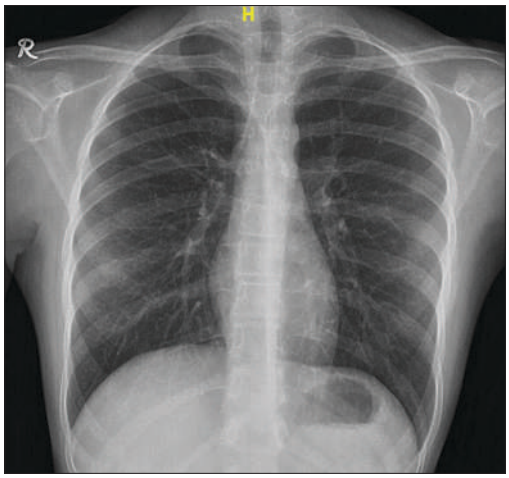

Figure 1: Chest X-ray showing microcardia (computed tomography ratio: 38.3%)

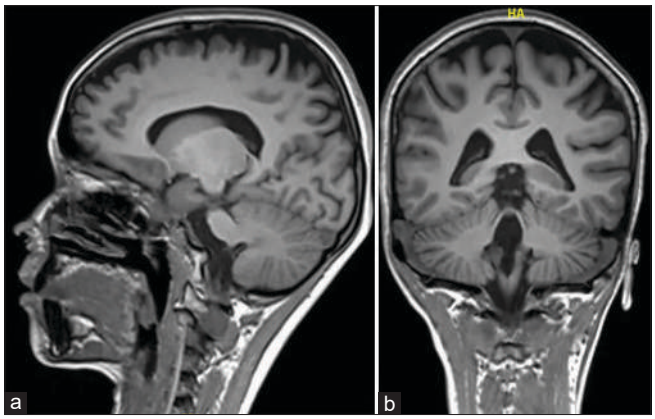

Figure 2: Magnetic resonance imaging brain showing mild diffuse cerebral atrophy. (a) Sagittal plane, (b) Coronal plane

Initially, nasogastric feeding was initiated. On day 6, a nasojejunostomy (NJ) tube was inserted under fluoroscopic guidance, and high-calorie special feeds (500 kcal/250ml) were started via continuous infusion at a rate of 250 ml over 4 hours with 2 hours of bowel rest, feeds being increased every 3 days to reach a maximum of 3000 kcal. She was also started on calcium 1000 mg/day, cholecalciferol 60,000 IU a week, methylcobalamine 500 µg a day, iron, and multivitamin supplements. On Day 11, she developed refeeding syndrome with hypophosphatemia and hypokalemia (serum phosphorus 2.4 mg%; serum potassium 3 mmol/L), managed by appropriate supplementation. A multidisciplinary team comprising specialists in adolescent medicine, child psychiatrists, psychologists, dieticians, and adolescent nurses were involved. Over 3 weeks, abdominal pain and vomiting resolved, NJ feeds were gradually stopped and oral feeds increased. She gained 2.67 kg over 3 weeks and was discharged after a total of 1 month of hospitalization. At review 1 week later, she was hemodynamically stable, tolerating oral feeds with no vomiting. The family opted to continue further management in their hometown. Transfer of her care was arranged for Maudsley family-based therapy, the most effective treatment for adolescent-onset AN.[3]

Discussion

The above is an interesting case of persistent vomiting in a child which turned out to be due to SMA syndrome, developing as a result of an acute fall in BMI as a consequence of her pubertal growth spurt and the subsequent weight loss due to food avoidance due to her classic features of AN.

The SMA syndrome is an extremely rare phenomenon with an incidence of barely 0.013%–0.3%, most commonly seen in adolescents and young adults, predominantly in females.[1,4] The pathophysiology involves an overall reduction of mesenteric and retroperitoneal fat resulting in decrease in the fat plane between the duodenum and the SMA, leading to compression and obstruction of the

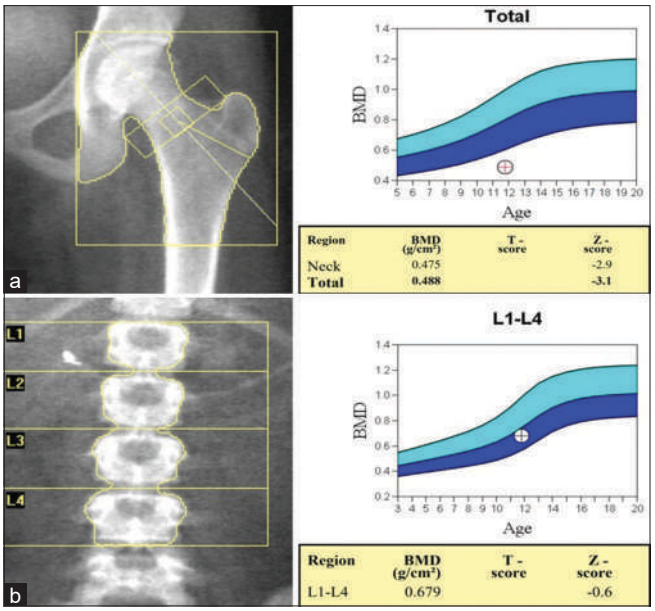

Figure 3: Dual energy X-ray Absorptiometry scan showing bone mineral density. (a) Lumbar spine, (b) Hip: Severe osteopenia. (Z-score: < -3.1)

duodenum. The SMA syndrome is known to occur with no or minimal weight loss, especially during pubertal growth spurt when there is lesser weight gain relative to height, thus reducing body mass.[5-7] The patient in this report had a height >75th centile, had attained menarche at 10 years and 10 months, with an acute weight loss of around 5 kg, thus creating the setting for SMA syndrome. SMA is a complication which has been described among many adolescents with AN. Watters et. al. has described SMA as a complication following AN in 8 patients. Bozzola et. al reported this complication among 12 adolescent patients. Thus, SMA is a known complication of AN.[1,4] A pubertal growth spurt followed by the significant weight loss as a result of the diet restrictions due to AN was the reason which led to the development of SMA in our case.

The condition typically presents with postprandial abdominal pain, nausea, vomiting, and weight loss.[1,5] Other causes leading to reduction in angulation between the SMA and the aorta include hypercatabolic state, external compression by belts or spica casts, corrective spinal surgery for scoliosis, congenital abnormalities like high insertion of the duodenum at the ligament of Treitz, neurological injury such as spine hyperextension, exaggerated lumbar lordosis, with 40.4% of cases being idiopathic.[1,5] After ruling out common causes of vomiting and weight loss, diagnosis of SMA syndrome may be considered in unexplained severe abdominal symptoms in adolescents around their pubertal growth. Upper GI barium swallow may show delayed transit of contrast through the third portion of the duodenum. A contrast-enhanced CT scan confirms the diagnosis demonstrating an aortomesenteric angle <25° and aortomesenteric distance <8 mm (normal: mean angle 38°–56°; mean aortomesenteric distance 10–28 mm). Upper GI endoscopy should be done to rule out intraluminal obstruction.[8]

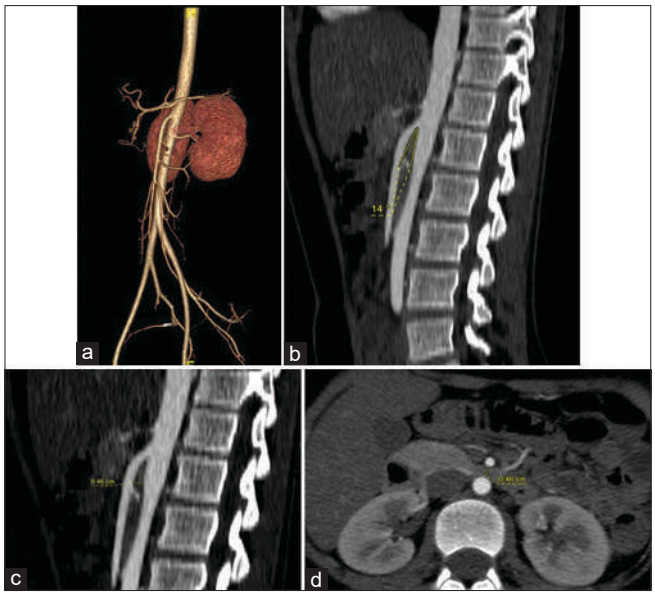

Figure 4: Contrast-enhanced computed tomography (CT) scan of abdomen; (a) CT angiogram of the abdomen showing aorta-superior mesenteric artery axis; (b) Reduced aortomesenteric angle (14°); (c) Reduced aortomesenteric distance (4.6 mm) in the sagittal plane; (d) Reduced aortomesenteric distance (4.6 mm) in horizontal plane

Management is conservative and symptoms resolve with weight gain, goal being to restore the abdominal pad of fat around the aortomesenteric axis.[1] Nasogastric or naso-jejunal tube feeding is required initially to bypass the obstruction. If the obstruction is complete, parenteral nutrition is necessary. Surgical intervention should be reserved for those who are refractory to medical therapy even after 3–4 weeks.[1,9] In our patient, NJ feeding was successful resulting in improvement of weight and symptom resolution.

Conclusion

This case creates awareness to consider the possibility of SMA syndrome in a child with intractable postprandial vomiting, especially in the setting of a pubertal growth spurt with drastic fall in BMI due to AN. After ruling out organic causes of obstruction, an astute observation of aortomesenteric angulation in CT images can clinch the diagnosis of SMA syndrome. Focusing on nutritional rehabilitation may be sufficient to reverse the phenomenon and relieve symptoms.

Lessons learnt

1. Superior mesenteric artery syndrome may be suspected in a child with intractable postprandial vomiting, especially in the setting of a pubertal growth spurt with drastic fall in BMI.
2. Significant weight loss following restrictive eating disorders like anorexia nervosa can cause SMAS as a complication.
3. Diagnosis is confirmed by assessing the aortomesenteric angulation in CT images; successful resolution occurs with nutritional rehabilitation.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Bozzola E, Irrera M, Cirillo F, *et al.* Superior mesenteric artery syndrome in anorexia nervosa: A case report and a systematic revision of the literature. Nutrients 2024;16:541.
2. Bloomberg L, Hoscheit M, Hendler S, *et al*. Superior mesenteric artery syndrome in an adolescent female with anorexia nervosa. Clin Med Res 2023;21:46-8.
3. Hornberger LL, Lane MA, Committee on Adolescence. Identification and management of eating disorders in children and adolescents. Pediatrics 2021;147:e2020040279.
4. Watters A, Gibson D, Dee E, *et al*. Superior mesenteric artery syndrome in severe anorexia nervosa: A case series. Clin Case Rep 2020;8:185-9.
5. Biank V, Werlin S. Superior mesenteric artery syndrome in children: A 20-year experience. J Pediatr Gastroenterol Nutr 2006;42:522-5.
6. Gharti SB, Shrestha N, Thapa KS, *et al.* Superior mesenteric artery syndrome in an 11-year-old boy: A case report. Clin Med Insights Case Rep 2024;17:1-2.
7. Okamoto T, Sato T, Sasaki Y. Superior mesenteric artery syndrome in a healthy active adolescent. BMJ Case Rep 2019;12:e228758.
8. Merrett ND, Wilson RB, Cosman P, *et al*. Superior mesenteric artery syndrome: Diagnosis and treatment strategies. J Gastrointest Surg 2009;13:287-92.
9. Singh S, Contrucci AL. Superior mesenteric artery syndrome and anorexia nervosa: A case report. J Med Case Rep 2023;17:459.

Case Report

Allgrove Syndrome with Absent Adrenal Gland in a Child: A Case Report

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Abstract

Background: Allgrove syndrome is an autosomal recessive disorder caused by mutation in *AAAS* gene and characterized by alacrimia, achalasia, and adrenal insufficiency. Subtle clinical features may be the only findings and need good workup. **Clinical Description:** A 5-year-old boy, product of third-degree consanguineous marriage, presented with diffuse hyperpigmentation of the skin for the past 2 years, along with difficulty in swallowing and absence of tears. He was conscious, with average built, stable vitals, and a normal neurological examination. There was marked hyperpigmentation of the skin, lips, and nails. Rest of the examination was noncontributory. **Management and Outcome:** Investigations revealed normal hemogram, renal and liver functions with normal electrolytes. There was marked cortisol deficiency and high adrenocorticotrophic hormone with low normal serum aldosterone. Barium studies suggested achalasia, confirmed on esophagoscopy and manometry. The contrast-enhanced computed tomography of the abdomen revealed a complete absence of adrenals. Clinical exome sequencing revealed a pathogenic homozygous missense mutation in *AAAS* gene confirming the diagnosis of Allgrove syndrome. The child was started on oral hydrocortisone supplementation with low-dose fludrocortisone, along with lubricating eye drops. Endoscopic myotomy has been planned for achalasia. **Conclusion:** Allgrove syndrome, a rare disorder, needs keen clinical suspicion to detect and prevent devastating complications.

Keywords: Achalasia, adrenal insufficiency, alacrimia, cortisol, hyperpigmentation

Allgrove syndrome or Triple A syndrome (TAS) is an autosomal recessive disorder caused by mutation in *AAAS* gene that codes for ALADIN or alacrimia, achalasia, adrenal insufficiency, and neurologic disorder protein.[1] The penetrance of the gene defect is close to 100%, though with variable clinical expression.[2] The heterozygote carriers are asymptomatic. [2] It is characterized by adrenal insufficiency (AI), failure of lower esophageal sphincter to relax (achalasia), and absence of tear secretion (alacrimia). The triad of manifestations could be accompanied by autonomic dysfunction (4A) and also with spinal amyotrophy (5A).[3]

Although uncommon, TAS must be considered in the presence of any of its component features and should prompt a search for other manifestations. We present a child who was brought to attention because of darkening of skin color. A thorough history and systematic search together with genetic analysis led to the diagnosis of Allgrove syndrome.

Case Description

A 5-year, 4-month-old boy presented with complaints of progressive darkening of the skin, nails, and lips for the past 2 years, associated with poor weight gain. The darkening of the skin was diffuse, involving generalized skin, without any lesions or scratching. There was no history of episodes of lethargy or seizures. On specific enquiry, the parents revealed that there was difficulty in swallowing, and the child used to bend backwards while eating food, preferring soft, and home-cooked foods. If offered solids such as *chapatti*, he would have difficulty in swallowing and often vomit. Similarly, on specific enquiry regarding tears, the mother said that he never had any tears even when he cried and often rubbed his eyes. There was neither photophobia nor any complaint of increased or decreased sweating. As per mother, his vision and speech were clear, and he had no difficulty or clumsiness in walking. There had not been any illness requiring hospitalization in the past.

The child was the second child of his parents, born out of a third-degree consanguineous marriage at term, with antenatal, natal, and postnatal periods being uneventful. The child had been gaining milestones consistent with age and had average

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Submitted: 12-Dec-2024 **Revised:** 09-Jan-2025
Accepted: 14-Jan-2025 **Published:** 14-Feb-2025

How to cite this article: Mittal M, Agrawal I, Rai A, Singh G, Prasad P, Gulati P. Allgrove syndrome with absent adrenal gland in a child: a case report. Indian Pediatr Case Rep 2025;5:51-4.

scholastic performance. All the family members were in good health and did not have similar complaints.

On examination, weight was 15.7 kg (*z* score – 1.0), height 110 cm (*z* score – 0.36), and body mass index 12.98 (*z* score – 1.18). He was afebrile, with good volume pulses at a rate of 90/min, respiratory rate was 26/min, and blood pressure was 90/70 mmHg with no postural drop. There was no dysmorphism; hydration was fair, and there was no pallor, icterus, cyanosis, or lymphadenopathy. The skin had generalized hyperpigmentation that was more evident over the lips, tongue, knuckles, palms, and nail beds [Figure 1]. There was no wasting of thenar or hypothenar eminences. The back and spine were normal. The child was alert and responsive to surroundings, with a clear speech and normal cranial nerve examination. Power, tone, and tendon reflexes were normal for age, and his gait was also normal. The other systemic examination was noncontributory. Based on the history and examination, it appeared to be a possible case of primary adrenal insufficiency (in view of hyperpigmentation) with associated dysphagia and dryness of eyes and warranted further workup.

Management and Outcome

Laboratory workup revealed hemoglobin of 11.7 g/dL, total leukocyte count 9940/cumm, neutrophils 56.4%, lymphocytes 38.8%, platelets 293,000/cu.mm, urea/creatinine 21/0.4 mg/dL, sodium/potassium 136/4.14 mEq/L, bilirubin (total/conjugated) 1.0/0.3 mg/dL, aspartate transaminase/alanine aminotransferase 47/43 IU/L, and calcium/phosphorus/alkaline phosphatase 8.1/4.2 mg/dL/323 IU/L. Specific investigations done for adrenal function (by electrochemiluminescence method) [Table 1] showed very low levels of morning basal serum cortisol (0.063 µg/dl [normal 5-23 µg/dl]) and post adrenocorticotropic hormone (ACTH) stimulation 0.321 µg/dl (peak cortisol levels <18 µg/dL indicate adrenal insufficiency). Due to financial constraints, only the serum cortisol was done initially, and the other tests could be done only after 8–10 months.

Ophthalmologic evaluation revealed dryness of eyes, reduced thickness of tear film, and Schirmer's test suggestive of decreased lacrimation in both eyes; fundus being normal. Barium swallow using thin liquid barium revealed smooth distal narrowing of cardiac portion of the esophagus with prestenotic dilatation giving bird-beak appearance [Figure 2a]. Esophagoscopy allowed negotiation to the stomach with mild resistance at gastroesophageal junction, ruling out mechanical stricture. High-resolution esophageal manometry was performed using 24-channel water-perfused system, and it showed panesophageal pressure pattern with integrated relaxation pressure of 63.4 mmHg. This was suggestive of achalasia type 2 [Figure 2b]. A contrast-enhanced computed tomography (CT) performed on a 16-slice multislice scanner revealed complete nonvisualization of the adrenal tissue on both the sides, the space for adrenals being filled with fat showing low attenuation [Figure 3]. Genetic studies were suggestive of a pathogenic homozygous missense variant c.43C>A in exon 1 of the *AAAS* gene that results in change of amino acid glutamine to lysine at codon 15(p.Gln 15Lys; ENST00000209873.9), which is responsible for formation of frameshifted truncated ALADIN protein p.G14Vfs*45 causing TAS. Thus, the child was confirmed as a case of Allgrove or TAS with adrenal insufficiency (AI), with achalasia type 2 and alacrimia with no features of autonomic dysfunction.

The child was started on hydrocortisone 10 mg/m^2/day, orally, in three divided doses and lubricating eye drops. Considering the increased plasma renin activity and CT findings, fludrocortisone was added in low dose of 50 µg/day, orally, a single daily dose. Further, written instructions were provided for the doses of hydrocortisone to be doubled during stress situations. The child has been under follow-up for about 15 months, his hyperpigmentation is reducing, and his electrolytes and blood pressure are within the normal limits. The child has been planned for endoscopic myotomy for achalasia management. Parents were counseled, and the serum cortisol done for siblings and parents was normal. The genetic analysis of parents and siblings could not be done due to financial constraints.

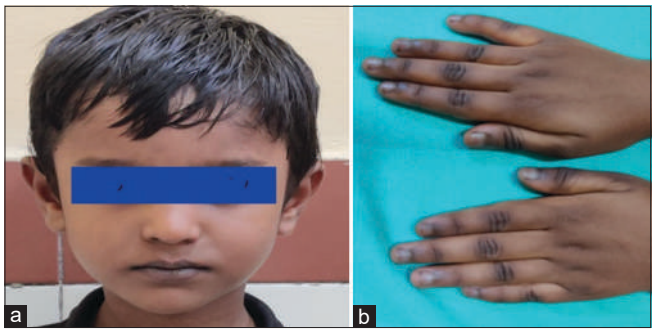

Figure 1: (a) Face of the child showing hyperpigmentation, especially apparent in the lips. (b) Hands of the child showing hyperpigmentation, especially evident over the knuckles

Discussion

We have described a child with TAS (Allgrove) syndrome who was brought to attention because of hyperpigmentation. The AI, an isolated glucocorticoid deficiency, prompted a search for other associations which completed the puzzle. The child had AI, alacrimia, and achalasia with no evidence of autonomic

Table 1: Adrenal function tests in the index case

Test parameter	Level	Reference values
Cortisol (basal) (µg/dL)	0.063	5–23
Post-ACTH cortisol (µg/dL)	0.32	>18
ACTH (pg/mL)	96	10–50
17 hydroxyprogesterone (ng/mL)	0.1	0.1–1
DHEAS (µg/dL)	1.3	0.1–1.5
Plasma renin activity (ng/mL/h)	5.8	0.05–5
Aldosterone (ng/dL)	6.3	2–20

DHEAS: Dehydroepiandrosterone, ACTH: Adrenocorticotrophic hormone

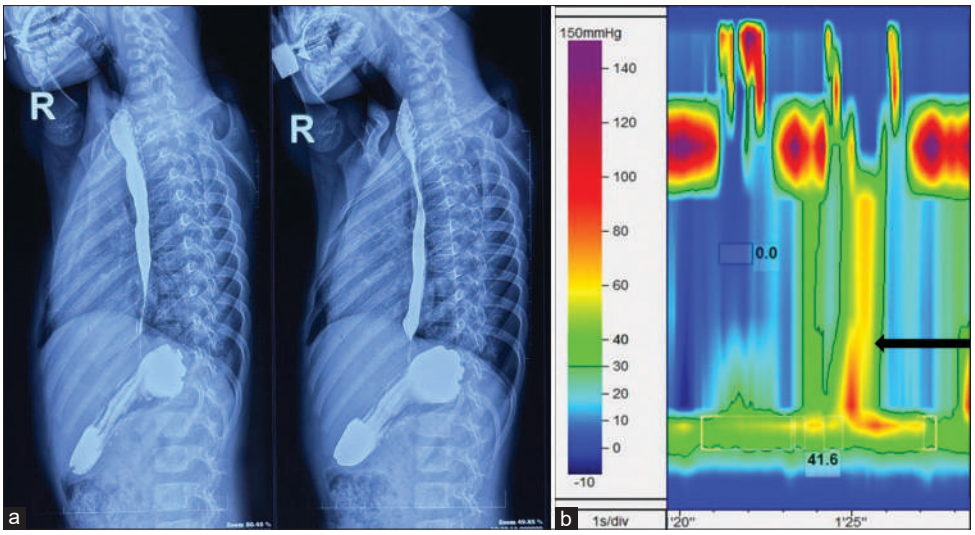

Figure 2: (a) Oblique view of barium swallow images showing dilated esophagus with smooth distal narrowing giving a bird-beak appearance suggestive of achalasia. (b) High-resolution manometry showing evidence of type 2 achalasia (Chicago classification): Integrated relaxation pressure – 63.4 mmHg, lack of normal esophageal peristalsis and pan-pressure zone in response to normal swallowing of water (arrow)

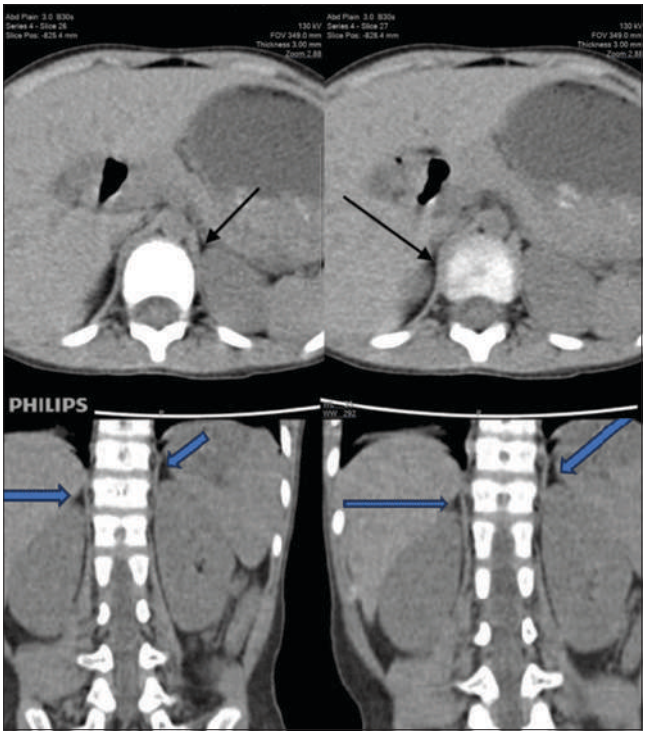

Figure 3: Axial (upper row) and coronal (lower row) computed tomography images of the upper abdomen reveal nonvisualization of the adrenal on both the sides. The space for adrenals (marked with arrows) is empty and is filled with fat

dysfunction. The complete absence of adrenal glands on CT scan seems to be a hitherto undescribed association.

Triple A syndrome (TAS), an important cause of primary AI, is a rare genetic disorder causing adrenal unresponsiveness to ACTH (ACTH resistance), described mainly as sporadic case reports and case series with no clear prevalence rates available. The median age at presentation was 4.7 years in one series from India.[4] The systematic review of cases reported a median age at presentation of 5 years, with 80% within the first decade and 8% beyond the third decade.

Dysphagia is the most common presenting symptom of achalasia; other symptoms could be regurgitation of undigested food, retrosternal chest pain, heartburn, weight loss, and change in posture during swallowing to help propel food down the esophagus as was observed in this case too.[4,5] The hyperpigmentation in AI is due to the similarity of alpha subunits of ACTH (which is raised) and melanocyte-stimulating hormone. Alacrimia is present in almost all cases and from early infancy onward but interestingly does not lead to the diagnosis by itself. It may lead to punctiform corneal destruction if left untreated.[6] Neurological manifestations such as chorea, dysarthria, dystonia, ataxia, hyperreflexia, and dementia are usually after 18 years of age. There could be muscle weakness and hypoplasia of palm muscles and foot flexors. Autonomic dysfunction may be present in 30% presenting as postural hypotension, impaired cardiovascular reflexes, cardiac dysrhythmias, anisocoria, and reduced sweating. Occasional cases have been reported to develop bulbospinal amyotrophy, optic nerve atrophy, and epilepsy.[5,7]

The diagnosis of primary AI requires documenting a low morning serum cortisol (<5 μg/dL) with poor response to ACTH stimulation (<18 μg/dL) which is often accompanied with a very high plasma ACTH (>300 pg/mL). Barium studies, esophagoscopy, and high-resolution manometry studies are useful for diagnosing and classifying achalasia. The CT scan in our case showed complete absence of the adrenals which was not reported in the published literature, although they are often severely atrophied.[8] However, we suspect that there might be some functioning adrenal tissue, considering that plasma renin activity was only mildly increased, and serum aldosterone levels were only mildly reduced.

The causative *AAAS* gene present on chromosome 12q13 is present ubiquitously in all cells with enhanced expression in adrenal cells, gastrointestinal cells, and pituitary gland.[9] The ALADIN protein, encoded by the gene, is a constituent of nuclear pore complex, involved in the nucleocytoplasmic movement of multimolecular complexes, the impairment of which predisposes to oxidative cell injury, affecting the steroidogenesis in adrenal cells with accumulation of precursors. In about 15% of cases, the mineralocorticoid production is also reduced.[10,11] Patients with mutations that result in formation of a truncated protein have higher likelihood of having symptomatic AI and at a younger age than the nontruncating group. Nontruncating mutations have a higher likelihood of having neurological dysfunction though at a later age than those with truncating mutations.[4] Prevalence and presentation of AI and achalasia are similar with either mutation type. The differences in the phenotype have been recognized only recently, and more research is warranted in this area. The differences could be attributed to different cellular processes with a functionally impaired protein in the nontruncating group and a truncated protein (that is likely to undergo degradation) in the other group. Compound heterozygous mutations with at least one nontruncating mutation show a milder phenotype. Clustering of mutations among geographical regions has been noted similarly with other mutations, and this includes c.1331 + 1G>A in North Africa and USA; c.1432C>T, p.R478* and c.787T>C, p.S263P in Europe; c.771delG, p.R258Gfs*33 in China; and c.43C>A, c.762delC; p.S255Vfs*36 in India.[4] For a given mutation, intrafamilial variability in phenotype is marked due to the effect of other modifying genes or environmental factors. Our patient had a pathogenic mutation (truncating) c.43C>A, p.G14Vfs*45, which has been previously noted, particularly in Indian and European families.[4]

If not recognized timely, it could result in hypoglycemic episodes including seizures, adrenal crisis, and even sudden death.[5] The AI requires immediate substitution with steroids that was started as oral hydrocortisone in this case. Treatment options for achalasia include pneumatic dilatation, laparoscopic Heller's myotomy, and peroral endoscopic myotomy.[12] Our patient received timely diagnosis and replacement hydrocortisone doses along with eye care and is planned for the definitive management for achalasia.

Conclusion

The patient was brought to attention due to the marked hyperpigmentation and correlation with other symptoms together with a low serum cortisol, and genetic studies clinched the diagnosis. Being alert to the possibility of TAS and the need for adrenal function testing could save lives.

Lessons learnt

- Generalized hyperpigmentation may be the clue to a serious underlying illness.
- Presence of adrenal insufficiency should prompt search for associated symptoms of alacrimia and achalasia.
- Confirmation of diagnosis by genetic analysis and prompt initiation of treatment can prevent life threatening complications.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Allgrove J, Clayden GS, Grant DB, *et al*. Familial glucocorticoid deficiency with achalasia of the cardia and deficient tear production. Lancet 1978;1:1284-6.
2. Sandrini F, Farmakidis C, Kirschner LS, *et al.* Spectrum of mutations of the AAAS gene in Allgrove syndrome: Lack of mutations in six kindreds with isolated resistance to corticotropin. J Clin Endocrinol Metab 2001;86:5433-7.
3. Goizet C, Catargi B, Tison F, *et al.* Progressive bulbospinal amyotrophy in triple A syndrome with AAAS gene mutation. Neurology 2002;58:962-5.
4. Patt H, Koehler K, Lodha S, *et al.* Phenotype-genotype spectrum of AAA syndrome from Western India and systematic review of literature. Endocr Connect 2017;6:901-13.
5. Milenkovic T, Zdravkovic D, Savic N, *et al.* Triple A syndrome: 32 years experience of a single Centre (1977-2008). Eur J Pediatr 2010;169:1323-8.
6. Brooks BP, Kleta R, Caruso RC, *et al*. Triple-A syndrome with prominent ophthalmic features and a novel mutation in the AAAS gene: A case report. BMC Ophthalmol 2004;4:7.
7. Babu K, Murthy KR, Babu N, *et al*. Triple A syndrome with ophthalmic manifestations in two siblings. Indian J Ophthalmol 2007;55:304-6.
8. Yadav P, Kumar D, Bohra GK, *et al*. Triple A syndrome (Allgrove syndrome) – A journey from clinical symptoms to a syndrome. J Family Med Prim Care 2020;9:2531-4.
9. Handschug K, Sperling S, Yoon SJ, *et al*. Triple A syndrome is caused by mutations in AAAS, a new WD-repeat protein gene. Hum Mol Genet 2001;10:283-90.
10. Tsigos C. Isolated glucocorticoid deficiency and ACTH receptor mutations. Arch Med Res 1999;30:475-80.
11. Clark AJ, Weber A. Adrenocorticotropin insensitivity syndromes. Endocr Rev 1998;19:828-43.
12. Tashiro J, Petrosyan M, Kane TD. Current management of pediatric achalasia. Transl Gastroenterol Hepatol 2021;6:33.

Endoscopic View of Common Gastrointestinal Diseases in Children

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Endoscopy is the cornerstone of modern pediatric gastroenterology. It has revolutionized the diagnosis and treatment of gastrointestinal (GI) diseases. These procedures allow gastroenterologists to visualize inside the GI tract helping

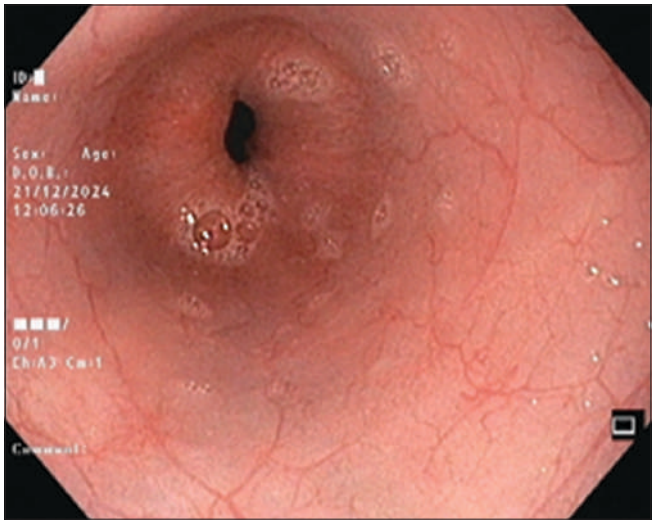

Image 1: Normal distal esophagus as a smooth, pale pink, and glossy mucosa with gastroesophageal junction at the end

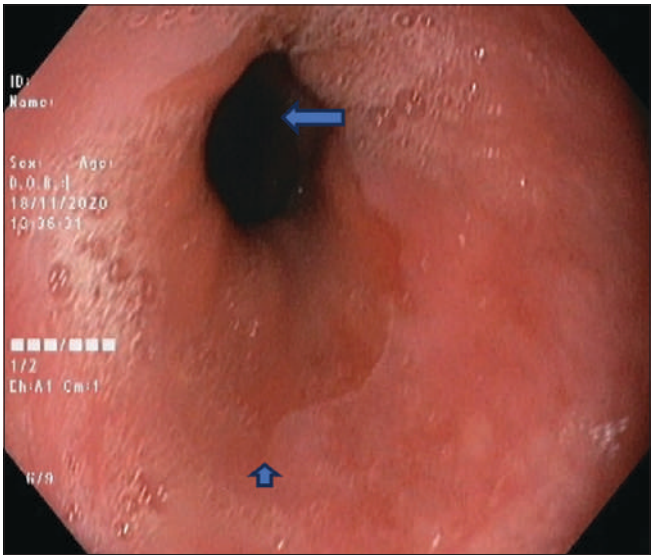

Image 2: Lower end of the esophagus. Big arrow shows diaphragmatic indentation, and small arrow shows Z line. This is esophageal mucosa in a child with Hiatus Hernia and gastroesophageal reflux disease, endoscopically described as a more than 2-cm separation of the upward displaced esophagogastric junction and diaphragmatic impression

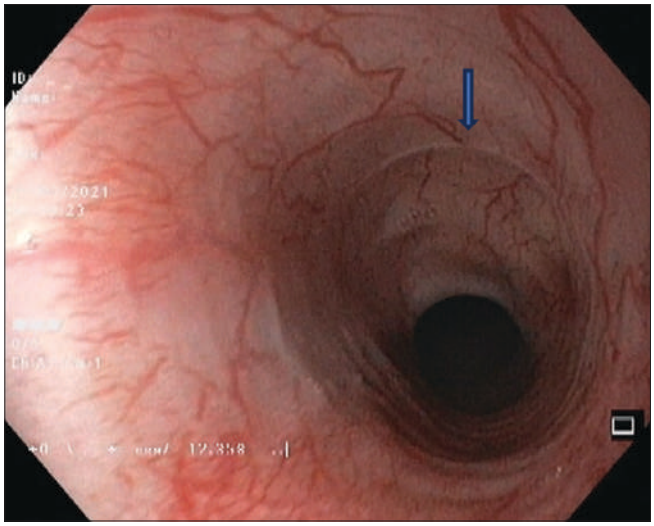

Image 3: Early trachealization (arrow) of the esophagus in a child, which is a characteristic finding of an inflammatory condition known as eosinophilic esophagitis, characterized by intense eosinophilic infiltration of the esophagus. This child had recurrent vomiting, failure to thrive, and feeling of food being stuck in the chest

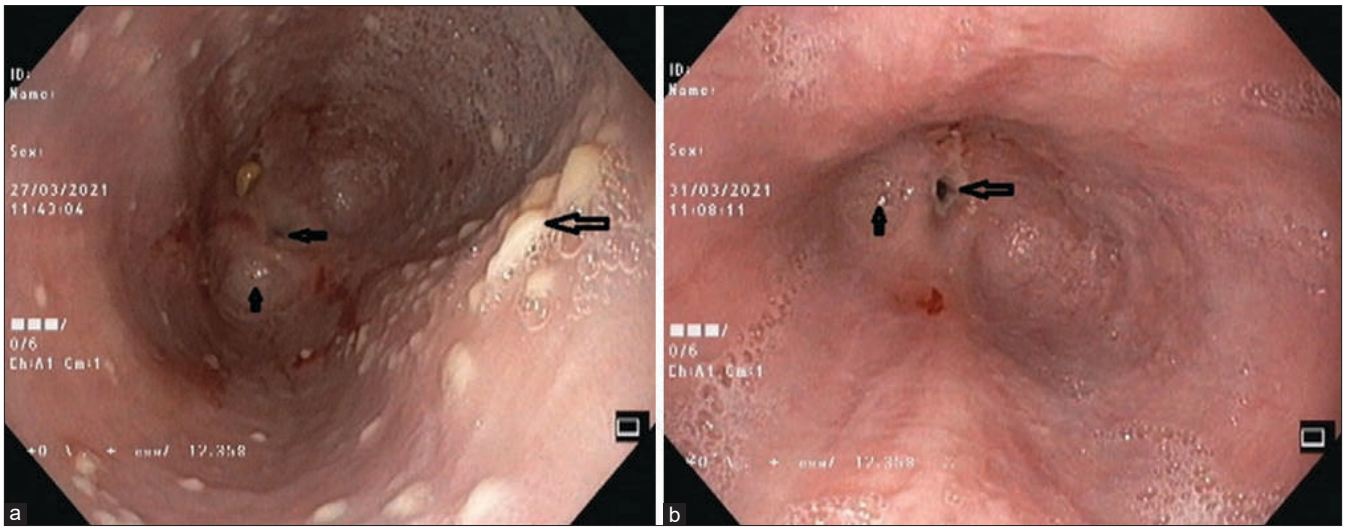

Image 4: (a) Esophageal candidiasis with esophageal stricture with pseudodiverticulum (small arrow), the most prevalent cause of infectious esophagitis, causes dysphagia, odynophagia, and retrosternal pain. The candida proliferates and adheres to the esophageal mucosa, forming white-yellow plaques (big arrow). The plaques are seen on upper endoscopy as seen in this image, and do not wash from the mucosa with water irrigation. (b) Posttreatment of esophageal candidiasis showing the clearing of white-yellow plaques, stricture (big arrow), which needs dilatation

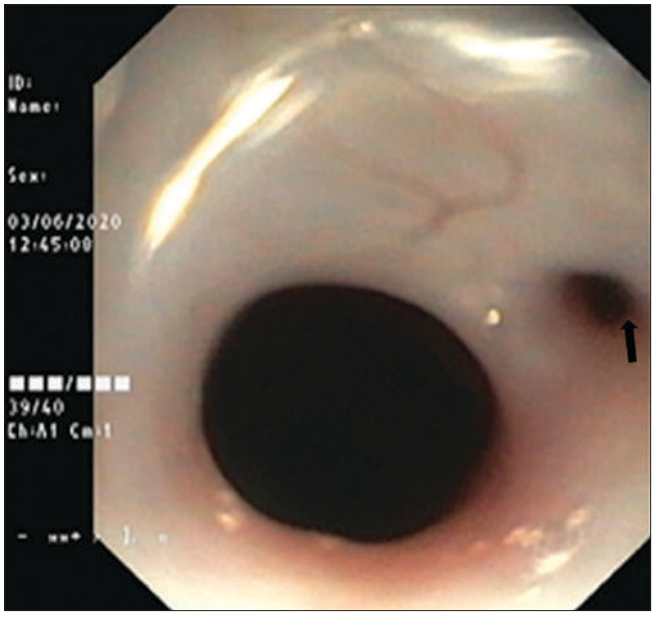

Image 5: Tracheoesophageal Fistula type E: Isolated fistula (H-type, black arrow) identified on upper gastrointestinal endoscopy in a 2-month-old male child having persistent cough with choking during feeding. This anomaly accounts for about 4% of tracheoesophageal malformations and has an incidence of around 1:50,000–80,000 births

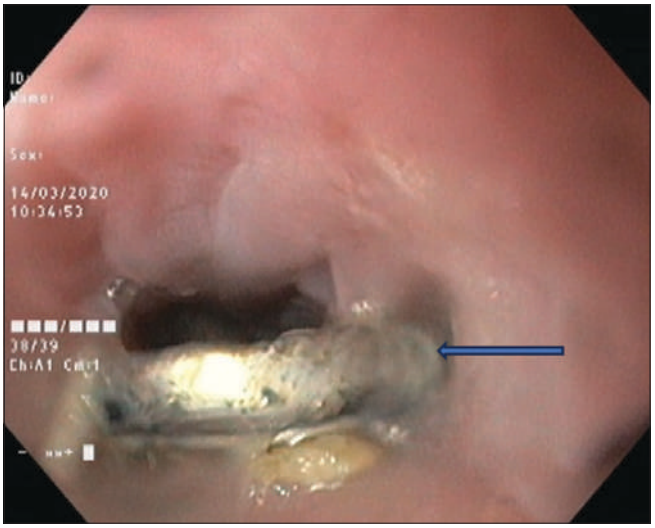

Image 6: Button battery (BB, blue arrow) impacted in esophagus which is swollen, and its rim has started separating. Endoscope provides means for the removal of foreign body and esophageal evaluation simultaneously. Damage to the mucosa is caused by local pressure necrosis, corrosive damage from leakage of battery content, heavy metal toxicity, electric injury, and electrolysis. Mucosal damage can occur within 2 h after BB lodgment. Battery in esophagus needs immediate endoscopic removal preferably <2 h

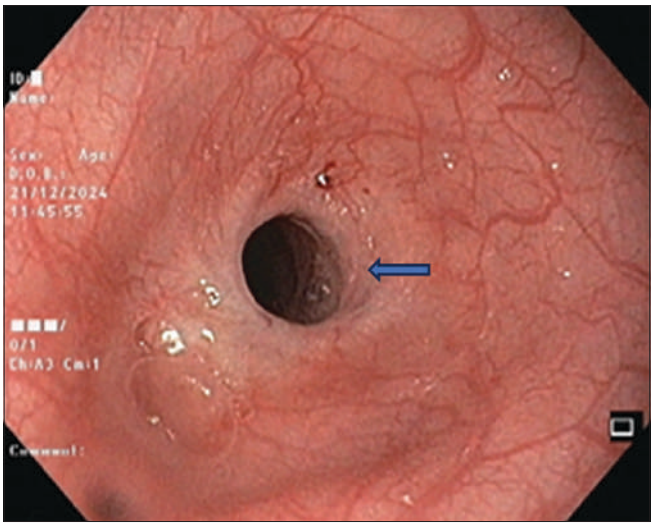

Image 7: Anastomotic stricture (blue arrow), which is the most common complication following operative repair of congenital tracheoesophageal fistula. The cornerstone of treatment is endoscopic dilation, whose primary aims are to achieve symptom relief, allow age-appropriate capacity for oral feeding, and reduce the risk of pulmonary aspiration

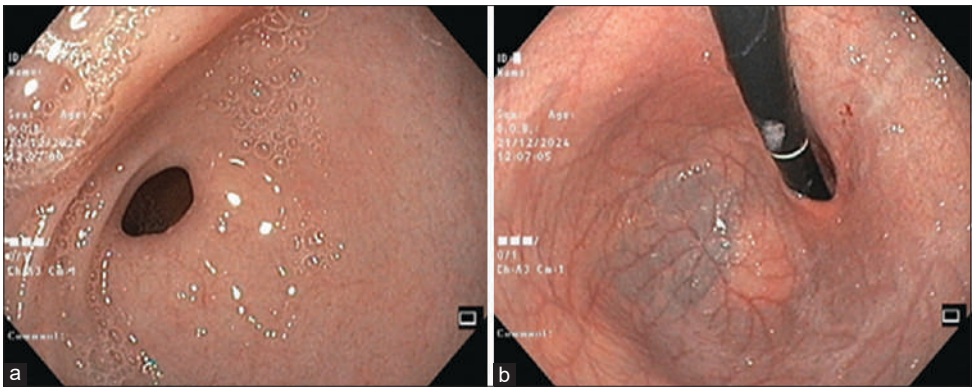

Image 8: (a) Normal view of the gastric antrum and pylorus; (b) Normal cardia and fundus of the stomach in inversion

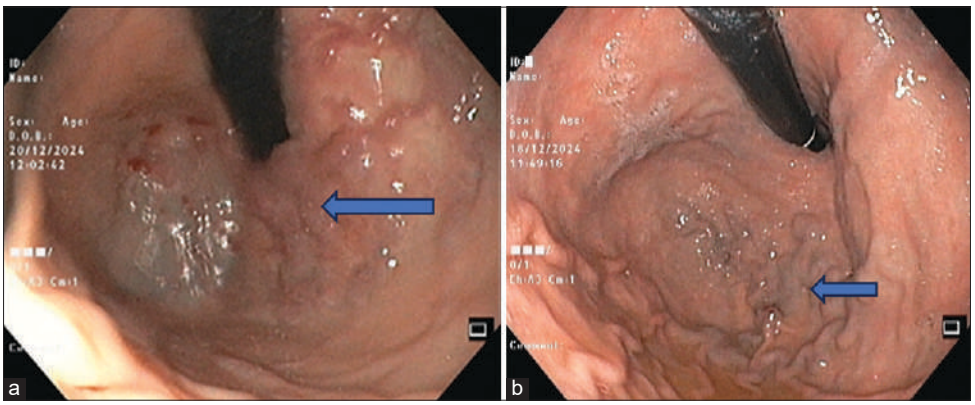

Image 9: Sarin classification, grades of gastric varices (GV) based on their location and relationship to esophageal varices. Gastroesophageal varices (GOV) 1 (a blue arrow): These varices extend along the lesser curvature of the stomach. They are the most common type of GV, accounting for about 70% of all cases. GOV2: These varices extend along the greater curvature of the stomach and may extend into the cardia. Isolated GV (IGV) 1: These varices (b blue arrow) are located in the fundus of the stomach. They are also known as fundal varices. IGV2: These varices are located in other parts of the stomach. They are also known as ectopic varices

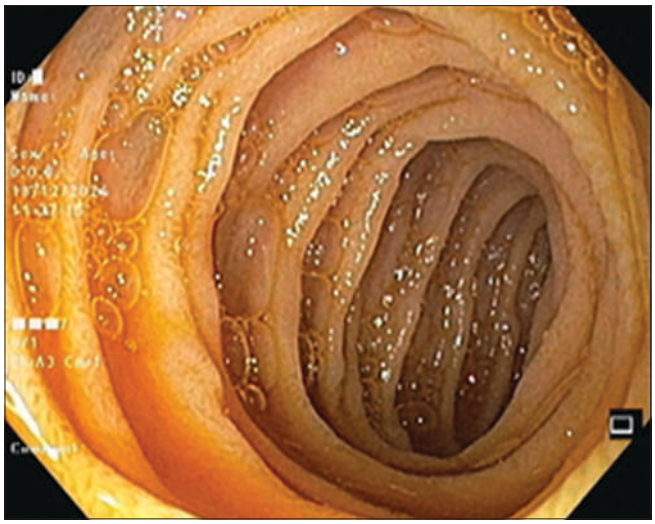

Image 10: Normal appearance of the duodenum: Pinkish mucosa, with regular well-defined and evenly spaced mucosal/Kerckring's folds. Sometimes, bile can also be seen, changing the color of the mucosa

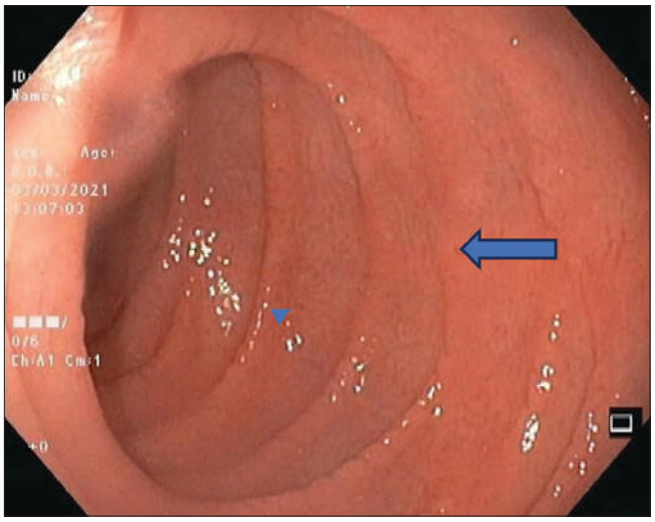

Image 11: Endoscopic image of celiac disease reduction in number and height of duodenal folds, or loss of Kerckring's folds (blue arrow) is the most sensitive (76%) and specific (98%) single endoscopic change indicating celiac disease. Scalloping (arrowhead) of the duodenal folds is an endoscopic finding that indicates injury to the duodenum's mucosal layer. It is often caused by villous atrophy

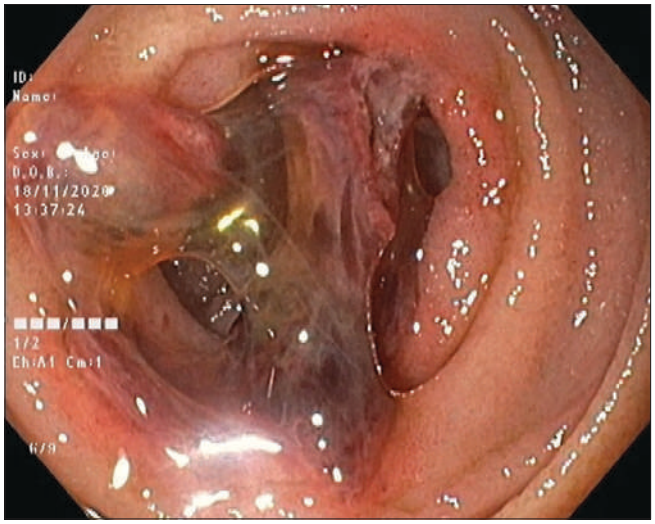

Image 12: Henoch–Scholein Purpura: It shows erythema, swelling, hemorrhagic erosions, and ulcerations with clots adhering to opposite walls of duodenum in a child with Henoch Scholein Purpura having severe abdominal pain. The most affected area is the descending part of the duodenum. These pathologies within the bowel wall and mesentery lead to abdominal symptoms

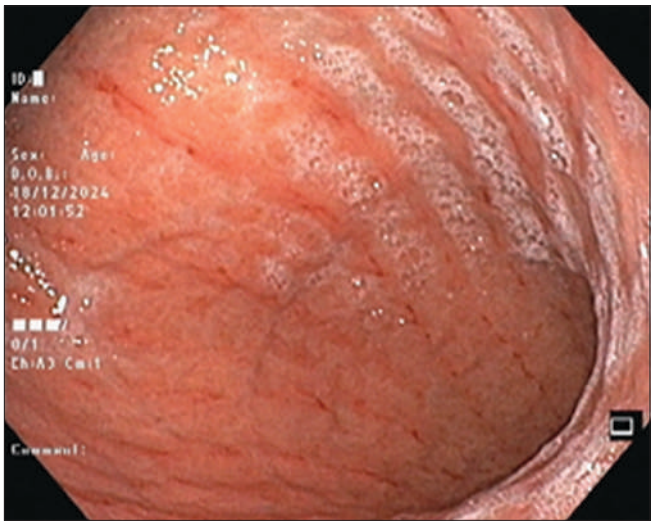

Image 13: Raised linear erythema in a child with portal hypertension (early gastric antral vascular ectasia). Portal hypertension related increase in the portal vein pressure leads to hyperdynamic congestion in the gastric, small intestinal, and colonic mucosa. The mucosa undergoes microcirculatory changes, such as submucosal angiogenesis and vascular ectasia, that impair its integrity and promote its susceptibility to damage

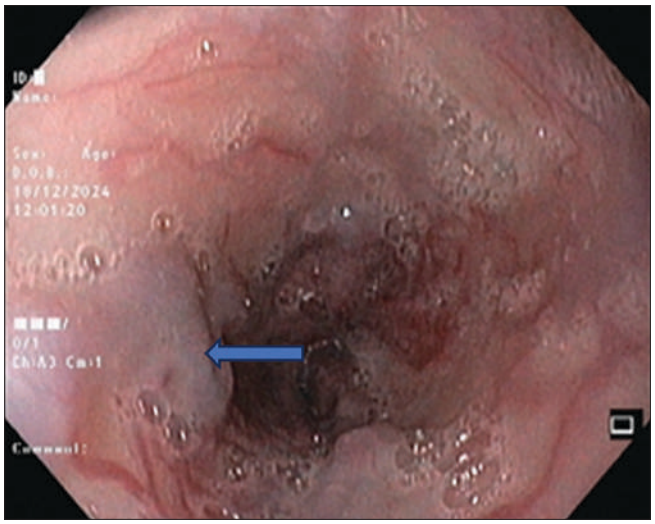

Image 14: Esophageal varices (F2, blue arrow) in a child with portal hyperstension. Classification of esophageal varices according to the Japanese Research Society for Portal Hypertension. F1: Straight-shaped varices do not disappear with insufflation. F2: Slightly enlarged tortuous varices occupying less than one-third of the esophageal lumen. F3: Large-sized varices occupying more than one-third of the esophageal lumen

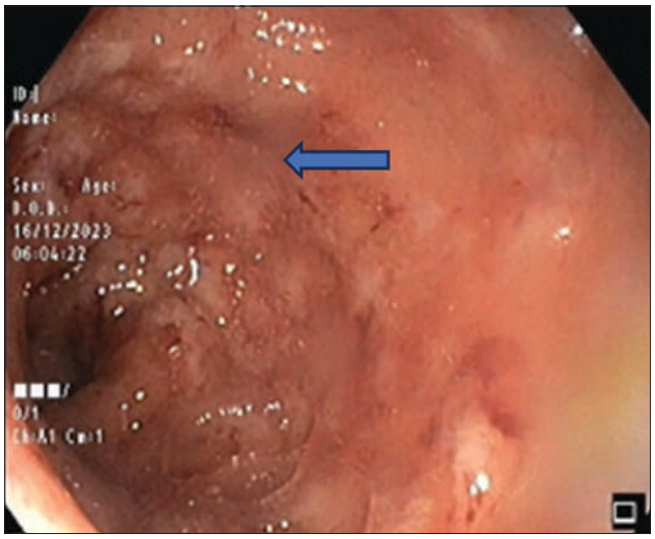

Image 16: Marked erythema, loss of vascular markings, erosions, ulcers, and early cobblestone (arrow) appearance in a child with Crohn's disease who had chronic diarrhea, bleeding per rectum, and abdominal pain for 3 months. Colonoscopy is principal test in diagnosis of inflammatory bowel disease

in both diagnosis and treatment. Some of the indications requiring endoscopy are dysphagia, odynophagia, unexplained weight loss, abdominal pain, recurrent vomiting, GI bleeding, anemia, and chronic diarrhea. Some of the common GI disorders are shown here for a basic understanding of pediatricians.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

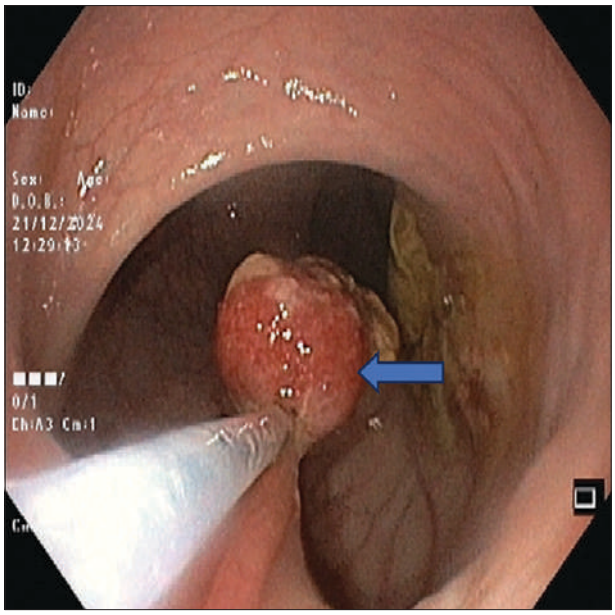

Image 15: Juvenile pedunculated single rectal polyp with polypectomy snare around its stalk (blue arrow) in a child having painless rectal bleeding for 1 year. Ninety percent of gastrointestinal polyps are juvenile polyps, which usually cause painless perrectal bleeding in children. Treatment involves polypectomy and removal of polyp

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Suggested Readings

1. Al-Hussaini AA, Semaan T, El Hag IA. Esophageal trachealization: A feature of eosinophilic esophagitis. Saudi J Gastroenterol 2009;15:193-5.
2. Tambucci R, Angelino G, De Angelis P, *et al.* Anastomotic strictures after esophageal atresia repair: Incidence, investigations, and management, including treatment of refractory and recurrent strictures. Front Pediatr 2017;5:120.
3. Han Y, Jin SY, Kim DW, *et al.* Endoscopic and microscopic findings of gastrointestinal tract in Henoch-Schönlein purpura: Single institute experience with review of literature. Medicine (Baltimore) 2019;98:e15643.
4. Pallio S, Melita G, Shahini E, *et al.* Diagnosis and management of esophagogastric varices. Diagnostics (Basel) 2023;13:1031.

Submitted: 04-Feb-2025 **Accepted:** 04-Feb-2025
Published: 14-Feb-2025

Access this article online

Quick Response Code:

Website: www.ipcares.org

DOI: 10.4103/ipcares.ipcares_28_25

How to cite this article: Rai A. Endoscopic view of common gastrointestinal diseases in children. Indian Pediatr Case Rep 2025;5:55-9.

Right Pulmonary Artery Aplasia Associated with Right-sided Congenital Pulmonary Cystic Adenomatoid Malformation

A 51-day-old male infant presented with runny nose, fast breathing, and poor feeding, but no fever. He was born at 36 weeks' gestation by vaginal delivery, with a birth weight of 3.2 kg, and an APGAR score of 8 and 8 at 1 and 10 min, respectively. Antenatally, obstetric follow-ups were irregular, and no scans were done. She denied taking any teratogenic medication or having any infection.

On examination, the baby had a weight of 4.35 kg, head circumference of 37 cm, and length 55.5 cm. He was normothermic, with respiratory rate of 48/min, heart rate of 140/min, SpO_2 of 96% in room air, and a capillary filling time <2 seconds. On auscultation, there were normal vesicular breath sounds in bilateral lung fields. The S1 and S2 sounds were normal, and there was a soft 1/6–2/6 ejection systolic murmur over the upper left sternal edge. The abdomen was soft, liver was just palpable. Tone and reflexes were normal. A provisional diagnosis of bronchiolitis was kept.

Baseline counts showed hemoglobin 11.3 mg/dl, hematocrit 30.4%, total leukocyte count 9640/cm^3, neutrophils 2501/cm^3, lymphocytes 6266/cm^3, and platelets 379,000. Respiratory panel was negative for respiratory syncytial virus, adenovirus, and influenza, sodium/potassium/chloride 138/4.8/101 mmol/l, calcium 10.3 mg/dl, urea/creatinine 15/0.24 mg/dl, and aspartate aminotransferase/alanine transaminase 25/12 IU/l.

Chest X-ray showed atelectasis of the right upper lobe with a cystic formation, with septations. An echocardiogram showed normal left ventricular dimensions and contractility (left ventricular end-diastolic volume 25.5 mm, intraventricular septum 3.8 mm, left ventricular posterior wall 32 mm, and ejection fraction 74%). The ventricular and atrial septa and semilunar and atrioventricular valves were normal. The pulmonary artery trunk was visualized as a continuation of the left pulmonary artery with slightly increased velocity of 1.65 m/seconds. The right pulmonary artery was not visualized [Figure 1 and Video 1]. The pulmonary veins were draining to the left atrium. There was a left aortic arch with slightly increased velocity of 2.12 m/seconds. A computed tomogram angiography showed absence of right pulmonary artery and normal left pulmonary artery. There were collateral branches from the right subclavian artery and intercostal arteries [Figure 2a-c]. The lung parenchyma showed a multilobular cystic malformation on the right mid and lower lobe measuring approximately 4.5 cm as well as atelectasis of the right upper and lower lobe [Figure 2d and e].

A diagnostic catheterization was undertaken which showed aplasia of the right pulmonary artery, normal drainage of the pulmonary veins, normal contractility of the left ventricle, patent foramen ovale, and normal coronary arteries [Video 2]. There were small collateral vessels from the right subclavian artery to the right lung [Video 3]. The pulmonary pressures were mild to moderately increased with a maximum pressure gradient (PG) of 42 mmHg, diastolic PG of 11 mmHg, mean PG of 27 mmHg, and pulmonary resistance of 6 Woods units. The systemic arterial pressures were 59/35 mmHg and 24.26 Woods units.

Thus, the diagnosis of right-sided congenital pulmonary cystic adenomatoid malformation (CCAM) associated with right pulmonary artery aplasia was confirmed. As oxygen saturation was maintained in room air, the baby was kept under observation and discharged on regular follow-up.

Congenital cystic adenomatoid malformation is a rare developmental disorder of the lung parenchyma, with an incidence estimated at 1 in 25,000–1 in 35,000 births,[1] caused by abnormal arrest in lung development at various stages of embryogenesis. Airway anomalies are identified in around 4%–8% of children with congenital heart disease.[2] However, only rarely, CCAM has been reported to be associated with vascular abnormalities. Earlier, a 2.5-year-old girl has been reported[3] with absent right pulmonary artery and hypoplastic right lung with CCAM in the right lower lobe, associated with left vocal cord palsy secondary to severe pulmonary hypertension, consistent with Ortner's syndrome. Recently, an adult male was reported[4] with absence of left pulmonary artery and right aortic arch with mirror image branching, associated with type 2 CCAM. The treatment of choice is surgical resection, be it thoracoscopic or open surgery.[1] However, the operation of asymptomatic neonates remains controversial.[5]

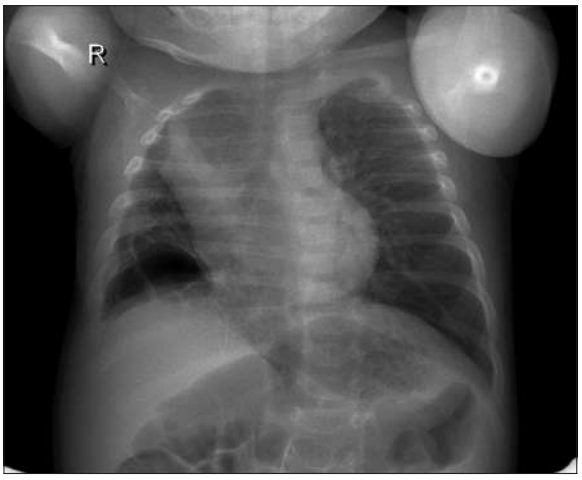

Figure 1: Multilobular cystic malformation on the right mid and lower lobe measuring approximately 4.5 cm as well as atelectasis of the right upper and lower lobe

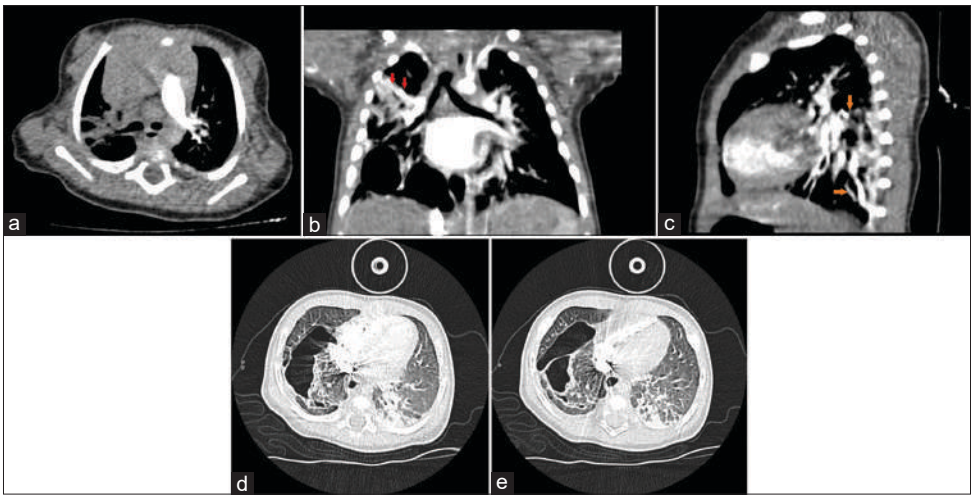

Figure 2: (a) Computed tomography (CT) angiogram showing the absence of the right pulmonary artery. (b) CT angiogram showing collaterals arising from the right subclavian artery and (c) intercostal arteries. (d and e) Contrast-enhanced CT of lung parenchyma showing a multilobular cystic malformation on the right mid and lower lobe as well as atelectasis of the right upper and lower lobe. The red arrows show the collaterals

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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References

1. Aryal K, Regmi PR, Adhikari G, *et al*. Congenital pulmonary airway malformation (CPAM): A case report and review of the literature. Radiol Case Rep 2023;18:3483-6.
2. Gailson T, Singh R, Bhatia A, *et al*. Bridging bronchus – An unsuspected airway anomaly associated with congenital heart disease: A case report with review of literature. Indian Pediatr Case Rep 2024;4:11-4.
3. David JJ, Mohanlal S, Sankhe P, *et al*. Unilateral right pulmonary artery agenesis and congenital cystic adenomatoid malformation of the right lung with Ortner's syndrome. Lung India 2016;33:553-5.
4. Padmanaban E, Nibhanupudi KM, Amirthalingam U, *et al*. Congenital cystic adenomatoid malformation associated with right aortic arch with mirror image branching and absence of left pulmonary artery in an adult. Egypt J Radiol Nucl Med 2021;52:221.
5. Downard CD, Calkins CM, Williams RF, *et al.* Treatment of congenital pulmonary airway malformations: A systematic review from the APSA outcomes and evidence based practice committee. Pediatr Surg Int 2017;33:939-53.

Submitted: 27-Jul-2024 **Revised:** 01-Jan-2025
Accepted: 02-Jan-2025 **Published:** 14-Feb-2025

Videos available on: www.ipcares.org

Access this article online

Quick Response Code:

Website: www.ipcares.org

DOI: 10.4103/ipcares.ipcares_177_24

How to cite this article: Anagnostopoulou A, Andreou N, Eleftherakis N. Right pulmonary artery aplasia associated with right-sided congenital pulmonary cystic adenomatoid malformation. Indian Pediatr Case Rep 2025;5:60-1.

A Newborn with Dysmorphic Features with Congenital Abnormality of Skin (Questions)

An 11-day-old baby girl, born out of nonconsanguineous marriage, to a 29-year-old woman at 35 weeks of gestation, through Cesarean section due to oligohydramnios, was received at our institution with shock and late-onset sepsis. The mother was G4P3 with one spontaneous abortion in the first trimester. Routine antenatal checkups, and ultrasound evaluation in the third trimester revealed a low amniotic fluid index (4 cm). Mother had received iron, folic acid, and calcium supplements, along with two doses of tetanus toxoid injections. There was no history of maternal hypertension, gestational diabetes, thyroid disorders, any leaking or bleeding per vaginum, or uterine tenderness. There was no history of neonatal death nor skin problems in the family. Double and quadruple marker screening tests were not performed antenatally.

The baby cried immediately after birth with APGAR scores of 8 and 9 at 5 and 10 minutes, respectively. She was admitted in a private hospital for 10 days due to mild respiratory distress, receiving oxygen and breast milk through an orogastric tube. She was transferred to our hospital on the 11th day of life due to worsening general condition.

Upon admission, the newborn was very sick and lethargic in respiratory distress with dysmorphic features. Her weight was 1.18 kg (small for gestational age), length

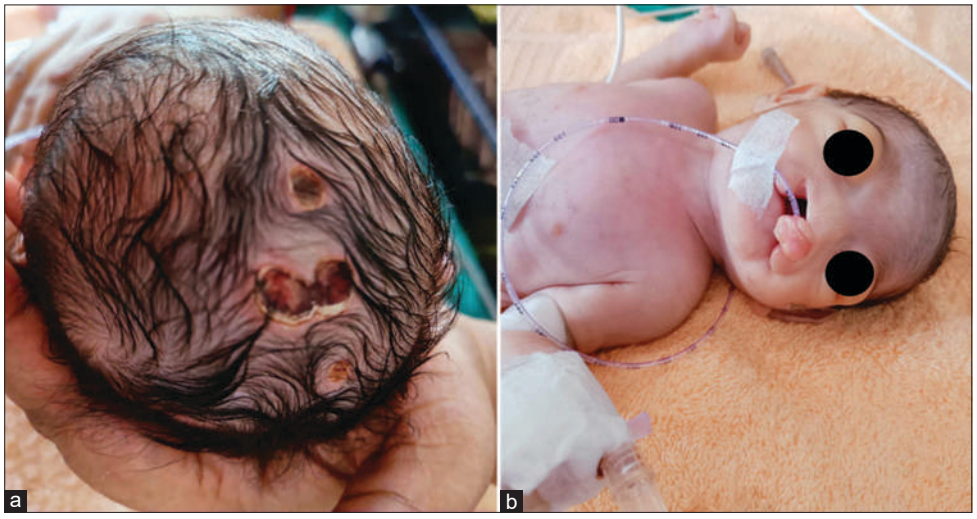

Image 1

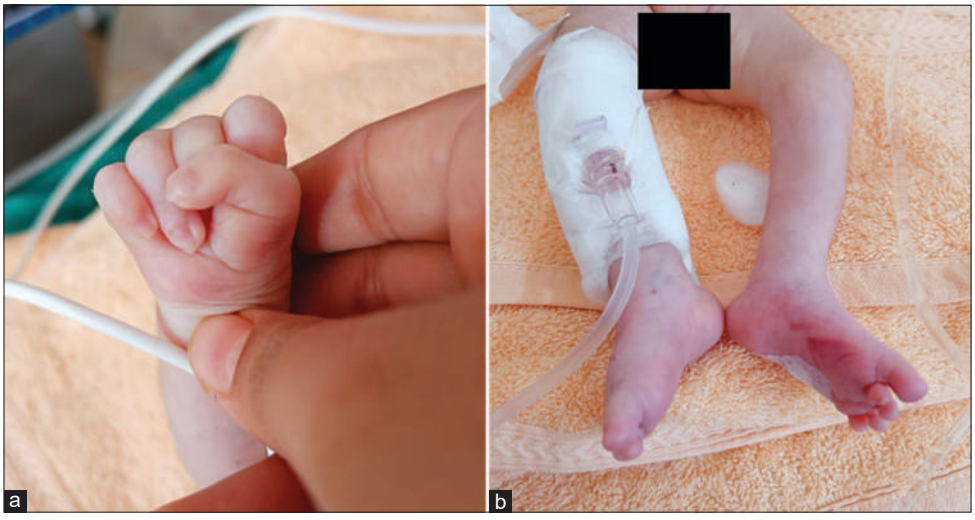

Image 2

42 cm (<3rd percentile), and head circumference 28 cm (<3rd percentile). The newborn was afebrile with a respiratory rate of 80/minute, heart rate of 180/minute, oxygen saturation of 89% on room air with Downe's score of 4/10. Poor perfusion was evident with a prolonged capillary refill time of 3 seconds, weak central and peripheral pulses, and cold extremities with mottled skin. Anterior fontanelle was at level. Random blood glucose level was 86 mg/dL, with no pallor, icterus, or cyanosis. The newborn had many congenital anomalies including multiple scalp defects (around 2 cm each) located at the midline and extended to both parietal regions of the cranial vertex [Image 1a], cleft lip, cleft palate, microcephaly, hypertelorism [Image 1b], clenched hands with the outer finger on top of inner fingers [Image 2a], and foot deformities [Image 2b], indicating a syndromic disorder. The scalp revealed three lesions with full-thickness defects of the epidermis, dermis, subcutaneous tissue, and bone and one lesion with partial thickness defect of the epidermis and dermis. There was no cerebrospinal fluid leakage, nor grossly dilated veins surrounding the defect. Cardiorespiratory examination revealed a pan-systolic murmur over precordium and subcostal retractions with equal air entry in bilateral lungs. The abdomen was soft with generalized hypotonia in all the extremities.

Investigations revealed hemoglobin 14.2 g/dL, total leukocyte count 12,000/mm^3, platelet 100,000/mm^3, urea/creatinine 28/0.9 mg/dL, bilirubin (total/conjugated) 3.2/0.4 mg/dL, aspartate aminotransferase/alanine aminotransferase 45/39 IU/L, and sodium/potassium/chloride 138/4.2/102 meq/L. The chest X-ray showed significant cardiomegaly (cardiothoracic ratio >0.65), bilateral diffuse pulmonary infiltrates with perihilar congestion and normal lung volumes. The newborn was started on piperacillin–tazobactam and meropenem, with caffeine (5 mg/kg loading dose, followed by 1.5 mg/kg of maintenance dose every 8 hours by slow intravenous infusion) and dopamine. Dressing of the scalp defects was done with saline-soaked gauze and mupirocin ointment. Pediatric surgery consultation was taken for scalp defects, cleft lip, and cleft palate. Echocardiography and genetic testing were declined by parents due to financial constraints. As the shock worsened with fall in SpO2-86% on day 2, adrenaline infusion along with oxygen therapy by heated, humidified high-flow nasal cannula was started. Despite aggressive management, the newborn expired on the 12th day of life.

Question 1: Identify the scalp lesions.
Question 2: Name the classification proposed for this skin condition.
Question 3: Identify the syndrome based on the Image 1, 2 and the features described in text.
Question 4: Name one autosomal dominant and one autosomal recessive condition associated with this skin disorder.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

Acknowledgment

The authors acknowledge the contribution of all physicians who contributed to the management of this case. We extend our heartfelt gratitude to the parents for consenting to the submission of their child's image, which will enhance our understanding, and we honor the memory of the lost baby.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Submitted: 30-Aug-2024 **Revised:** 04-Jan-2025
Accepted: 07-Jan-2025 **Published:** 14-Feb-2025

Access this article online

Quick Response Code:

Website: www.ipcares.org

DOI: 10.4103/ipcares.ipcares_218_24

How to cite this article: Rani S, Bharath N, Nayak S. A newborn with dysmorphic features with congenital abnormality of skin (questions). Indian Pediatr Case Rep 2025;5:62-3.

Erythematous Subcutaneous Nodules and Plaques in a Young Infant (Answers)

Winner of the Clinical Quiz
Dr. Rinku Sharma,
Resident (Department of Pediatrics),
Vardhaman Mahavir Medical College and Safdarjung Hospital, New Delhi.

Question 1: Identify the skin condition in Image 1a and b.

Answer: Subcutaneous fat necrosis of newborn. It is a rare inflammatory disorder of subcutaneous fat tissue affecting newborns. Hypoxia and hypothermia are probable risk factors.[1-3] Interestingly, term healthy babies with no risk factors may also be affected. Clinically, it appears as erythematous or violaceous well-circumscribed, mobile, subcutaneous nodules, or plaques noted over bony prominences such as shoulders, buttocks, back, and thighs. Differential diagnoses include sclerema neonatorum. Key differences between these two conditions are summarized in Table 1.

Question 2: What investigation would confirm the skin condition; name one biochemical derangement associated with this condition?

Answer: Skin biopsy should be done for histopathological examination, which reveals lobular panniculitis, with infiltrates comprising lymphocytes, histiocytes, multinucleated giant cells, and sometimes eosinophils. Triglyceride crystallization in adipocytes and giant cells results in characteristic refractile, radially arranged, needle-shaped clefts inside cytoplasm.[1]

Hypercalcemia is a serious potential biochemical complication needing immediate recognition and management, found in 25% of cases, and may appear even after regression of lesions. Other associated laboratory abnormalities include thrombocytopenia, hypoglycemia, and hypertriglyceridemia.[2] Our patient did not have hypercalcemia but had thrombocytopenia.

Question 3: Name two maternal and fetal risk factors for this skin condition.

Answer: Maternal risk factors include: umbilical cord prolapse, meconium aspiration, placenta praevia, preeclampsia, maternal diabetes mellitus, maternal medications (calcium channel blockers, and cocaine), passive smoking during pregnancy, and maternofetal Rh incompatibility. Neonatal risk factors include: perinatal asphyxia, seizures, congenital heart disease, hypothermia, anemia, obstetric trauma, intestinal perforation, sepsis, and therapeutic hypothermia used in neonates of perinatal asphyxia.

Question 4: What is the management of the skin condition?

Answer: It is a self-limiting disorder and does not require any intervention. Complications should be monitored and managed. Our patient's cutaneous lesions healed gradually after ulceration. For the sepsis and meningitis with ventriculitis, the baby was provided mechanical ventilation, intravenous

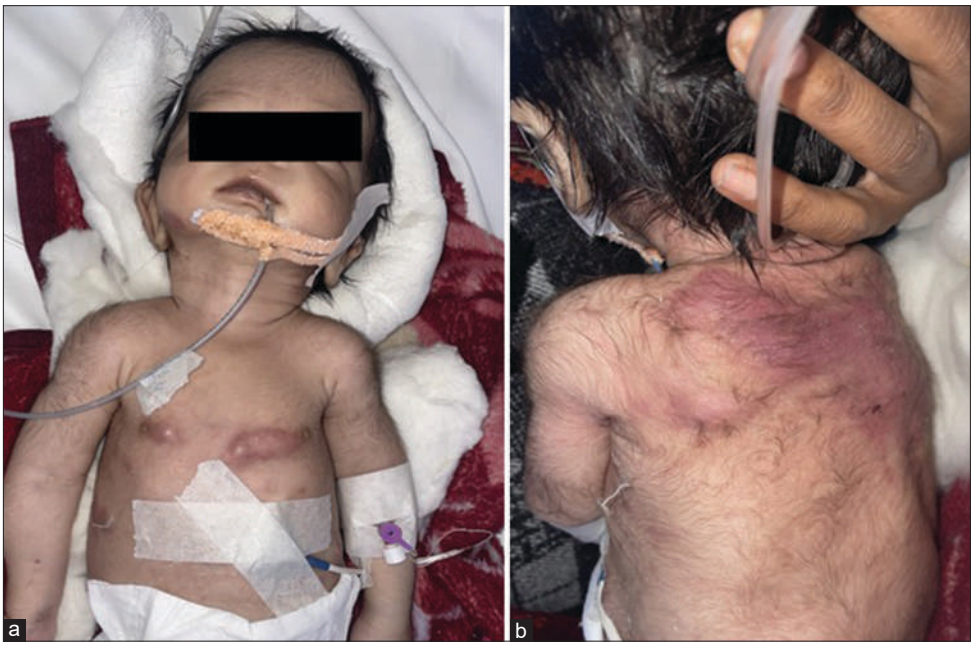

Image 1

Table 1: Differences between subcutaneous fat necrosis of newborn and sclerema neonatorum

	Subcutaneous fat necrosis of newborn	Sclerema neonatorum
Predisposing factors	Can occur in normal infants as well as infants with perinatal risk factors like cold/hypothermia, etc.	Affected infants are almost always sick
Onset	First few days to weeks after birth	First few days after birth
Clinical presentation	Erythematous or violaceous, mobile, well-circumscribed nodules or plaques	Mottled purplish, woody hard indurated skin which is cold to touch Skin can't be pinched as it is bound down to subjacent subcutaneous tissue, including muscle and bone
Sites affected	Usually over bony prominences on shoulders, buttocks, thighs, back, arms, neck and cheeks	Usually begins in buttocks and thighs but known to progress rapidly to involve entire skin. There is immobility of extremities and mask-like expression on face
Course and prognosis	Lesions resolve spontaneously or may ulcerate to discharge oily contents followed by resolution or calcification	Prognosis is poor, most affected infants die within few days
Histopathology	Necrosis of subcutaneous adipocytes with intense inflammation, consisting of lymphocytes, histiocytes, multinucleate giant cells, and eosinophils	There is destruction of normal fat lobules with sparse inflammatory infiltrate without fat necrosis
Management	No treatment is required for the lesions. Associated hypercalcemia to be treated	Underlying disease to be treated. Exchange transfusion and intravenous immunoglobulin have been tried

antiepileptics, antibiotics, and packed red blood cell transfusion. Head circumference monitoring was done for hydrocephalus. Platelet count and calcium levels were also monitored. Gradually, the general condition of child improved and he was shifted to humidified high-flow nasal cannula and then weaned off. Oral feeds were started and the child was discharged and referred to neurosurgery.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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References
1. Muzy G, Mayor SA, Lellis RF. Subcutaneous fat necrosis of the newborn: Clinical and histopathological correlation. An Bras Dermatol 2018;93:412-4.
2. Rubin G, Spagnut G, Morandi F, *et al*. Subcutaneous fat necrosis of the newborn. Clin Case Rep 2015;3:1017-20.
3. Frank L, Brandt S, Wabitsch M. Subcutaneous fat necrosis in newborns: A systematic literature review of case reports and model of pathophysiology. Mol Cell Pediatr 2022;9:18.

Comments by Dr. Ankita Patel (Section Editor)
We were happy to see such strong understanding demonstrated by the quiz answers, most of you got the quiz answers right. The quiz had some intriguing questions but despite that the engagement with the quiz has been lower than anticipated. We look forward to seeing even greater participation in the next quiz.

Submitted: 24-Jun-2024 **Revised:** 10-Jan-2025
Accepted: 10-Jan-2025 **Published:** 14-Feb-2025

Access this article online

Quick Response Code:

Website: www.ipcares.org

DOI: 10.4103/ipcares.ipcares_144_24

How to cite this article: Dhattarwal N, Dabas S. Erythematous subcutaneous nodules and plaques in a young infant (answers). Indian Pediatr Case Rep 2025;5:64-5.

Munchausen by Proxy: A Haunting Encounter

The memory of that 7-month-old boy, admitted with seemingly endless health issues, still haunts me, years later. His initial hospitalization in the medical unit where I was working, was due to hypocalcemic seizures, which resolved with standard treatment. However, I remember his discharge got postponed multiple times due to persistent complaints by mother of recurring seizures in child, unwitnessed by hospital staff. Despite numerous tests and neuroimaging, no cause was found. The boy, paradoxically, remained remarkably active and playful between these episodes and hence was discharged. Subsequently, the boy was admitted in different wards of the hospital, each time with a different complaint. A pattern emerged: the mother would insist on symptoms warranting admission and invasive treatments. She seemed more interested in medical procedures than the child's actual well-being.

The turning point came when the boy was admitted to our ward again, with persistent high fever spikes. He was started on parenteral antibiotics and underwent a battery of tests, all noncontributory. Fever spikes persisted and our quest for the cause found no answers. Every day in the rounds it puzzled us how such an active child was getting a daily fever spike of 103°F.

One day, when I was on duty during an ongoing strike in the hospital, I got enough time to take detailed rounds of the limited number of patients admitted, including this boy with fever. The boy conspicuously seemed happier to spend time with the doctors and the nurses than with his mother. The same evening the mother complained that the boy had a fever. I was told the mother always insisted on checking the temperature herself as she believed the boy would not cooperate with the nurses. I grew suspicious, and one of our staff nurses volunteered to closely monitor the boy. To our surprise, it was found that the mother had manipulated the thermometer by dipping it in hot tea, and was probably doing this always. This revelation, coupled with the child's consistently playful demeanor, exposed a disturbing truth: Munchausen syndrome by proxy.

Such fabrication by the mother not only exposed her innocent child to unnecessary medical interventions and potential harm, but also caused a painful breach of trust between the doctor and the patient. As healthcare providers, though we are bound by the sacred oath to believe in a patient, rarely, we are confronted with such ethical dilemmas, where our pledge to care is marred by doubts regarding the validity of the complaints. However, for the protection of the victim, in this case, a child, every effort must be taken to elicit the truth, maintaining confidentiality, as the impact of revelation may be profound. In cases of suspected Munchausen Syndrome by Proxy, every effort should be made to gather as much information as possible within the scope of professional responsibility with the aim to uncover the full truth of the child's medical condition. This may help assist parents in resolving their conflicts and seek appropriate support to provide the best possible care for their child.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Submitted: 29-Nov-2024 **Revised:** 30-Dec-2024
Accepted: 31-Dec-2024 **Published:** ***

Access this article online

Quick Response Code:

Website: www.ipcares.org

DOI: 10.4103/ipcares.ipcares_271_24

How to cite this article: Muralidhar AP. Munchausen by proxy: A Haunting encounter. Indian Pediatr Case Rep 2025;XX:XX-XX.

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Abbreviation: ACVIP: Advisory Committee on Vaccines and Immunization Practices; DTP: Diphtheria tetanus and pertussis; HEP-B: Hepatitis B; Hib: Haemophilus influenzae type b

References:
1. Rao M IS, Kasi SG, Dhir SK, Wadhwa A, Rajsekhar B, Kumar CM, et al. Indian Academy of Pediatrics (IAP) Advisory Committee on Vaccines and Immunization Practices (ACVIP): Recommended Immunization Schedule (2023) and Update on Immunization for Children Aged 0 Through 18 Years. Indian Pediatr. 2024 Feb 15;61(2):113-125. 2. Pertussis vaccination: use of acellular pertussis vaccines among infants and young children. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 1997 Mar 28;46(RR-7):1-25. Erratum in: MMWR Morb Mortal Wkly Rep 1997 Aug 1;46(30):706. 3. World Health Organization (WHO) [Internet]. The immunological basis for immunization series: module 4: pertussis, update 2017; [cited 2023 Feb 8]. Available from: https://www.who.int/publications/i/item/ the-immunological-basis-for-immunization series-module-4-pertussis-update-2017 4. Hexavalent Vaccine Market Study [Internet]. A White Paper To Understand The Market Structure Of Pediatric Pertussis Combination Vaccines. ReportLinker [Internet]. 2020; November. Available from: https://ai.reportlinker.com/en/resources/blog/market-trends/sanofi-pasteur-is-the-global-market-leader-in- all-categories-of-ap-based-pediatric-combination-vaccines Accessed on: 10/11/2022

Indian Pediatrics Case Reports

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The Journal

The journal's full text is available online at https://www.ipcares.org. and issues are published quarterly in February, May, August, November. The journal's full text is available online at https://www.ipcares.org. The journal publishes case reports related to pediatrics, neonatology, pediatrics surgery.

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115/4 Ground floor, Gautam Nagar,
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Published by
Wolters Kluwer India Private Limited,
Fourth Floor, East Wing, Marisoft III, Marisoft Premises,
Part of Software Technology Park, S. No. 15, Vadgaon Sheri,
Kalyani Nagar, Pune – 411 014, Maharashtra, India.
Website: www.medknow.com

Printed at
Nikeda Art Printers Pvt. Ltd.,
Building No. C/3 - 14,15,16, Shree Balaji Complex, Vehele Road,
Village Bhatale, Taluka Bhiwandi, District Thane - 421302, India.