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Coexistence of Hereditary Spherocytosis and Hyperreactive Malarial Splenomegaly in a Child From a Malaria-Endemic Region: A Case Report in Uganda

Abukar Hussein Mohamed
Maqaareey2011@gmail.com
Kampala International University
Mohamed Abdi Ahmed
Kampala International University
Mohamud Abdalla Hassan
Kampala International University
DJamila Magan Mohamed
Kampala International University
Mohamed Ali Ismail
Kampala International University
Maslah Osman Ali
Kampala International University
Jouyriah Adam mohamed
Kampala International University
Mohamed Ali Ahmed
Kampala International University
Abdirahman Ali Osobow
Kampala International University

Case Report

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COEXISTENCE OF HEREDITARY SPHEROCYTOSIS AND HYPERREACTIVE MALARIAL SPLENOMEGALY IN A CHILD FROM A MALARIA-ENDEMIC REGION: A CASE REPORT IN UGANDA.

Abukar Hussein Mohamed [1] ,Mohamed Abdi Ahmed[1] ,Mohamud Abdalla Hassan[1] ,DJamila Magan Mohamed[1],Mohamed Ali Ismail[1] , Maslah Osman Ali [2] , Jouyriah Adam mohamed[1] ,Mohamed Ali Ahmed[1] ,Abdirahman Ali Osobow [1]

1. Department of Pediatrics, faculty of clinical Medicine and Dentistry,

Kampala International University, Ishaka – Bushenyi – Uganda

2. Department of General Surgery , faculty of clinical Medicine and Dentistry,

Kampala International University, Ishaka – Bushenyi – Uganda

Author; Abukar Hussein, Department of Pediatrics, faculty of clinical Medicine and Dentistry, Kampala International University, Ishaka – Bushenyi – Uganda

Email; osobow.abdirahman@studwc.kiu.ac.ug

Corresponding Author; Abdirahman Ali Osobow , Department of Pediatrics, faculty of clinical Medicine and Dentistry, Kampala International University, Ishaka – Bushenyi – Uganda

Email; Maqaareey2011@gmail.com

ABSTRACT

Background:

Hereditary spherocytosis (HS) is a congenital hemolytic anemia caused by red blood cell membrane defects, while hyperreactive malarial splenomegaly (HMS) is an immune-mediated condition resulting from chronic malaria exposure in endemic regions. Both conditions present with anemia and splenomegaly, posing significant diagnostic challenges, particularly in low-resource settings where splenomegaly is often attributed to malaria alone.

Case Presentation:

We report a 7-year-old female from western Uganda who presented with a 4-year history of progressive abdominal distension and a 5-day history of fever and abdominal pain. Clinical

examination revealed massive splenomegaly, pallor, mild jaundice, and generalized lymphadenopathy. Laboratory findings showed severe anemia (hemoglobin 5.1 g/dL), elevated red cell distribution width, and peripheral blood smear demonstrating spherocytes. Malaria rapid diagnostic test was initially positive. Despite appropriate antimalarial therapy, the patient had persistent severe anemia and progressive splenomegaly requiring multiple blood transfusions. A positive family history of similar illness, together with hematological findings, supported a diagnosis of hereditary spherocytosis, while the presence of massive splenomegaly in a malaria-endemic region suggested concurrent HMS. The patient later underwent splenectomy with good clinical and hematological improvement.

Conclusion:
This case highlights the importance of considering underlying hematological disorders in children presenting with massive splenomegaly in malaria-endemic regions. Early recognition of dual pathology is essential to prevent misdiagnosis, guide appropriate management, and improve outcomes.

Keywords:
Hereditary spherocytosis; Hyperreactive malarial splenomegaly; Splenomegaly; Hemolytic anemia; Uganda; Case report

Background

Hereditary spherocytosis (HS) is a congenital hemolytic anemia caused by defects in red blood cell membrane proteins such as spectrin, ankyrin, band 3, or protein 4.2, leading to spherical red cells that are easily trapped and destroyed in the spleen(1). Clinically, HS commonly presents with anemia, jaundice, reticulocytosis, gallstones, and splenomegaly, although severity may vary from mild disease to severe childhood anemia(2). Diagnosis is supported by peripheral blood smear showing spherocytes, raised mean corpuscular hemoglobin concentration, reticulocytosis, negative direct antiglobulin test, and confirmatory tests such as eosin-5-maleimide binding or osmotic fragility testing (3).

Hyperreactive malarial splenomegaly (HMS), previously called tropical splenomegaly syndrome, is a chronic immune-mediated complication of repeated malaria exposure, especially in malaria-endemic regions. It is characterized by massive splenomegaly, high antimalarial antibody levels, markedly elevated IgM, and clinical improvement after prolonged antimalarial therapy or prophylaxis (4). HMS is an important cause of massive splenomegaly in endemic areas, but diagnosis is often difficult because malaria parasites may be absent on routine blood smear at presentation and other causes of splenomegaly must be excluded(5).

The coexistence of HS and HMS is clinically important because both conditions can present with anemia, jaundice, hemolysis, and splenomegaly. In malaria-endemic countries such as Uganda, massive splenomegaly may easily be attributed to recurrent malaria alone, potentially delaying recognition of an underlying inherited hemolytic disorder. Case reports from African settings have shown that HS may be missed for years and present later with complications such as massive splenomegaly, gallstones, repeated transfusions, or inappropriate iron therapy(6). Therefore, this case report highlights the need to consider both chronic malaria-related immune splenomegaly and inherited red cell membrane disorders when evaluating a child with persistent anemia and massive splenomegaly in a malaria-endemic region.

Case presentation

We describe the case of A 7-year-old female from Kyenjojo District, Uganda, presented with a 5-day history of abdominal pain and fever. The abdominal pain was gradual in onset, generalized but more pronounced in the left upper quadrant, non-radiating, moderate in severity, and worsened by eating, coughing, and walking, but relieved by lying on her side. The pain was associated with loss of appetite.

The current symptoms were preceded by a 4-year history of progressive abdominal distension, described by the caregiver as a slowly enlarging abdominal mass, more prominent in the left upper abdomen, with no associated changes in bowel habits.

She also had a 5-day history of high-grade intermittent fever, worse in the evenings and partially relieved by tepid sponging. This was associated with generalized weakness, headache, and dizziness, but there were no convulsions or loss of consciousness.

Her past medical history was significant for four prior hospital admissions, including three for typhoid fever and one for an unspecified illness. She had previously received a blood transfusion for an unknown indication. There was no known history of chronic illnesses such as sickle cell disease.

Notably, the family history was significant, as two siblings and the father had similar abdominal swellings, suggesting a possible hereditary condition.

On examination, the child was fully conscious and oriented but had moderate pallor and mild scleral jaundice, indicating ongoing hemolysis. She had generalized lymphadenopathy involving posterior cervical, mandibular, and inguinal nodes. Vitals: PR 98, RR 33, SpO_2 96%, Temp 35.6°C. .

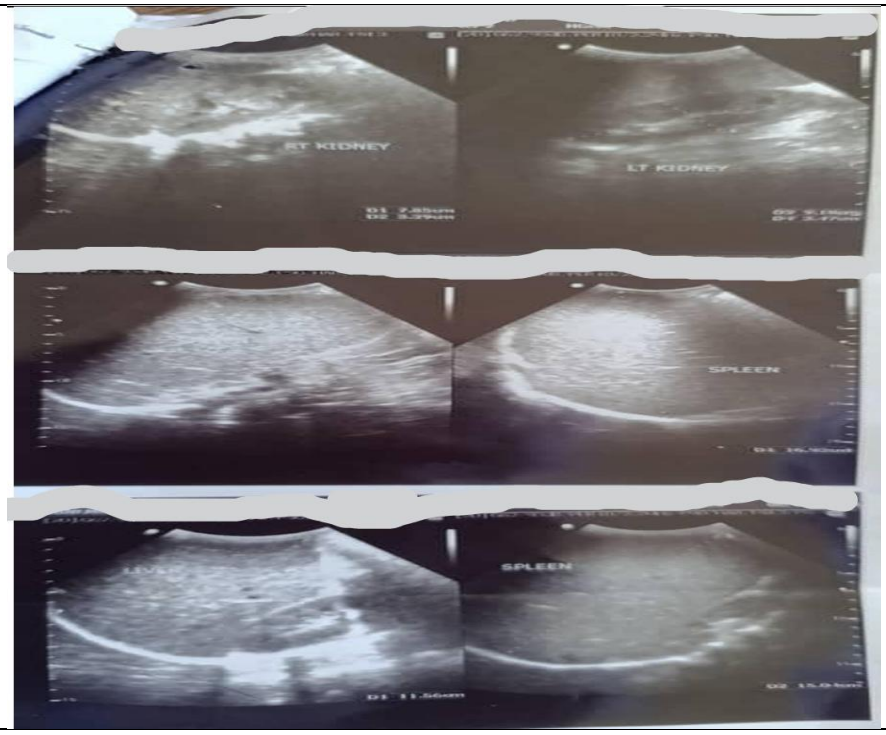
Abdominal examination revealed marked asymmetrical distension with a massive splenomegaly, the spleen extending up to 16 cm below the left costal margin at admission and progressing to 22 cm during hospitalization. The spleen was firm, smooth, and tender. Mild hepatomegaly was also noted.



On 2nd June 2025 Our Diagnosis wa **Moderate splenomegaly with hypersplenism (Hyperreactive Malarial Splenomegaly)**

Initial laboratory investigations showed:

Full Blood Count , MRDT , LFT								
CBC	Lymphocytosis 6.49	Monocytosis 1.09	Neutropenia 18.3%	RBCS 1.86	HB 5.1	RDW 71.6	PLT 150	
LFT	Low albumin : 3.47			High Direct bilirubin : 0.67				
RFT	Creatinine low : 0.37			Urea normal : 12.0				
RCT	Reactive(Determine and STAT PAK)							
Hep B sAg	Negative							

Abdominal Ultrasound	
	• The Spleen is moderately enlarged but maintain normal shape and echopattern with no focal lesions seen. • Its outline is regular and smooth. Spleen =16.9 cm^3 • **NOTE:** • < 15 cm^3 …Mild splenomegaly • > 22 cm^3 ……Severe splenomegaly

Initial Management:

- Establish IV access, Start Tab. Paracetamol 250 mg TDS, Give start dose of IV Artesunate 60 mg
- Mother Refused Blood

Review--3rd June 2025, 10am

- Reported episode of right-sided epistaxis during the night. Abrupt onset, resolved with application of cotton swabs. No trauma history, amount blood loss couldn't be quantified .
- **On examination:** CRT < 2 secs, Vitals: PR 108 bpm, Temp 37.1°C, RR 25 bpm
- **Nasal Exam:**
  - No active bleeding
  - Clot noted on medial aspect of right nostril Left nostril clean and dry
  - No signs of systemic bleeding (no petechiae or purpura on skin or mucosa)

PLAN:

Similar 2nd June 2025

4th June 2025

- No new complaints reported.
- O/E: Patient alert; moderate pallor (conjunctiva, palms, soles).Vitals: PR 112 bpm, RR 22bpm, SpO_2 99%, Temp 36.3°C.

5th June 2025

- Pt reported gradual, intermittent right knee pain (4/10), worsened by touch and movement, relieved by paracetamol.
- No swelling or trauma history.
- **O/E:**
    - Soft tissue injury signs absent, pt hard, moderate pallor.
    - Vitals: PR 98 bpm, SpO_2 96% RA, RR 24 bpm, Temp 36.4°C.

Plan:

- Continue artemether/lumefantrine
- Tab paracetamol 250 mg TDS

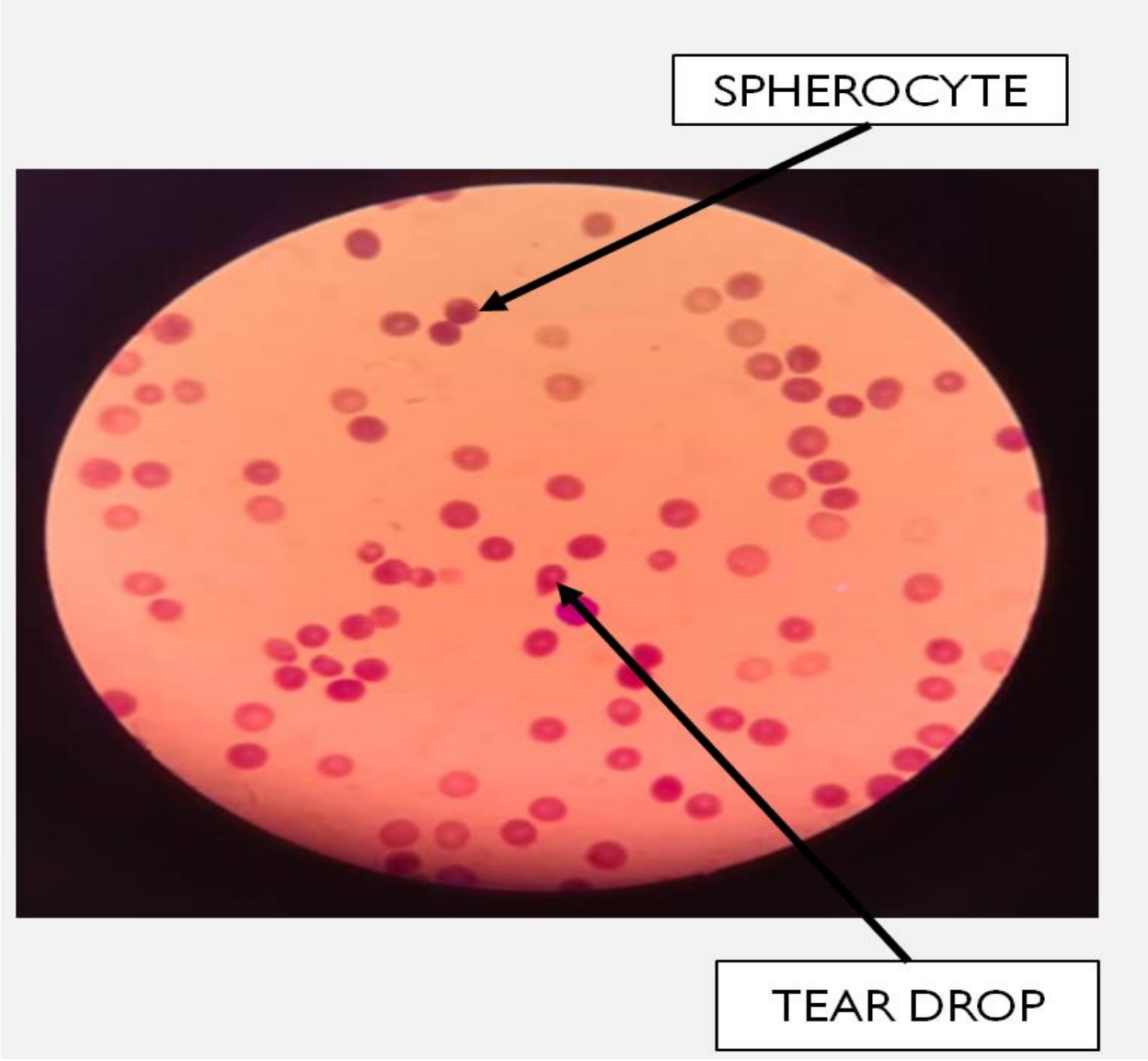
6th June 2025

- Reported episode of right-sided epistaxis during the night. Abrupt onset, stopped with pressure using a handkerchief.
- O/E: Fair general condition, mild scleral jaundice, moderate pallor (conjunctival, palms, soles).Vitals: Temp 36.6°C, PR 116 bpm, RR 24 bpm, SpO_2 100% on RA.
- Plan:
- Continue artemether/lumefantrine
- Tab paracetamol 250 mg TDS

We repeated CBC also we did Peripheral Blood film

CBC							
CBC	WBC : Normal	Lymphocytosis	Neutropenia	RBC	HB	RDW	PLT
		7.33	13.7	1.28	3.5	71.0	131

Peripheral Blood film



Cont.….6th June 2025

Diagnosis:

- Moderate splenomegaly with hypersplenism secondary to hereditary spherocytosis and Hyperreactive Malarial Splenomegaly)
- Resolving malaria

- Plan
  - Transfused 100 mL O-negative packed RBCs.
  - Cont. with Treatment
  - Re-discussed referral due to ongoing transfusion needs and blood unavailability at KDH; mother declined against advice.

Initiated tab folic acid ½ tablet.

7TH June 2025

- Reported another episode of spontaneous right nostril bleeding, stopped with pressure using a handkerchief.
- O/E: Moderate conjunctival and palmar pallor, Vitals: SpO_2 99% on RA, Temp 37.1°C, RR 22 bpm, PR 126 bpm.
- **Abdomen:** Marked asymmetric distension, splenomegaly extending 22 cm below costal margin.
- Local exam: No active bleeding from right nostril; left nostril clean and dry.
- Plan:
- Cont. treatment
- Perform post-transfusion CBC

Test	RESULT		RANGE
CBC	WBC normal	11.86	3.00-15.00
	Lymphocytosis	6.31	1.0-3.7
	RBC	1.43	2.50-5.50
	Low HB	3.9	12.0-17.0
	Low PLT	99	150-450

Cross-match compatible with O positive blood

Transfused 200 mL(2 units) packed cells (O positive)

Consult surgical team to evaluate for possible splenectomy

Note: At 7pm complaints of high-grade fever (39.6) following transfusion that was of gradual onset, slightly relieved by paracetamol and tepid sponging.

SURGICAL REVIEW

7th July at 1:40 pm

- Reviewed a 7-yr-old/F being managed for mod splenomegaly with hypersplenism 2º to hereditary spherocytosis (R/O HMS), Resolving malaria; on oral anti-malarials, PCM, folic acid, and BT.
- **On exam:** sick-looking, lying spine, in mild resp distress, on active transfusion with obvious abdominal distension.
- Severely Pale (palmar + conjunctival), with a tinge of jaundice. Noted post cervical, mandibular, and inguinal lymphadenopathy, mild facial puffiness, and dry lips. CRT <2 secs.
- **Vitals:** PR 112 bpm, weak synchronous; RR 28 bpm; Temp 37.8°C (axillary); SpO_2 96% on RA; BP N/D.
- **Abdominal exam**
    - Asymmetrically distended abdomen with abdominal-thoracic pattern; everted umbilicus; no scars, distended veins, petechiae, or purpura. Tender LUQ with palpable, firm, smooth mass [=22cm below left costal margin with dull percussion note (likely spleen)]; RUQ mass palpable 5cm below costal margin (likely liver); no shifting dullness or succussion splash.
- **Plan (Surgery + Pead teams)**
    - Perform red cell osmotic fragility test
    - Cont. with treatment above
    - Administer pneumococcal vaccine (PCV23, 0.5 mL)
    - Prepare for elective splenectomy once clinically stable
    - Book platelets in advance(obtained)
    - RESULTS

- Red cell osmotic fragility test(NOT DONE)

8TH JUNE 2025 (PEAD/SURGICLAL)

- Reported no complaints. However mother still insisted on discharge, and declined splenomegaly.
- **O/E:** Pt in FGC**,** Moderate conjunctival and palmar pallor,
- Vitals: SpO_2 99% on RA, Temp 35.7°C, RR 21 bpm, PR 120 bpm.
- **Abdomen:**
    - Marked asymmetric distension, splenomegaly extending 22 cm below costal margin.
- **Plan;**
    - Continue with above treatment.
    - Consider counselling mother.
    - Consider Surgery on 8th June





Postoperative Course and Follow-up

The patient underwent an elective splenectomy after appropriate preoperative preparation, including blood transfusion optimization and administration of pneumococcal vaccination. The procedure was uneventful.

In the immediate postoperative period, the child was closely monitored for complications. She remained hemodynamically stable, with no evidence of bleeding, infection, or respiratory distress. Pain was adequately controlled with analgesics, and she was started on prophylactic antibiotics as per hospital protocol.

Over the subsequent days, there was marked clinical improvement. The patient's pallor gradually resolved, and her energy levels improved significantly. Repeat laboratory investigations showed a progressive rise in hemoglobin levels and stabilization of platelet counts, consistent with resolution of hypersplenism.

She was discharged in stable condition with the following recommendations:

- Daily folic acid supplementation
- Infection prevention counseling, including prompt care for febrile illness
- Education on the risk of post-splenectomy infections
- Scheduled follow-up visits

At follow-up visits, the child remained clinically well with:

- No recurrence of anemia
- No further episodes of epistaxis
- Improved growth and activity levels

Discussion

Hereditary spherocytosis (HS) is the most common inherited hemolytic anemia in many populations and is characterized by defects in red blood cell membrane proteins, leading to

chronic hemolysis, anemia, jaundice, and splenomegaly. Similarly, hyperreactive malarial splenomegaly (HMS) is a well-recognized complication of chronic or repeated malaria exposure in endemic regions, resulting from an exaggerated immune response with persistent antigenic stimulation. Both conditions share overlapping clinical features, including anemia, jaundice, hemolysis, and splenomegaly, which can create significant diagnostic challenges, particularly in resource-limited, malaria-endemic settings such as Uganda (7).

In malaria-endemic areas, massive splenomegaly is often initially attributed to malaria or its complications, including HMS. However, HMS is characterized by massive splenomegaly, markedly elevated IgM levels, high antimalarial antibody titers, and clinical improvement following prolonged antimalarial therapy. Importantly, malaria parasites are frequently absent on routine peripheral blood smear at presentation, reflecting the chronic and low-grade nature of the infection. This may lead clinicians to rely heavily on clinical history and epidemiological context, potentially overlooking other coexisting or alternative causes of splenomegaly (7).

The coexistence of HS and HMS, as demonstrated in this case, is clinically important because the presence of HMS may mask the underlying diagnosis of HS. In such settings, the hemolysis and splenomegaly observed may be incorrectly attributed solely to malaria-related pathology. As a result, diagnosis of HS may be delayed, especially when access to specialized diagnostic tests such as eosin-5-maleimide binding assays or osmotic fragility testing is limited. This diagnostic delay can lead to repeated hospital visits, inappropriate management, and avoidable complications(3).

Several case reports from African settings have highlighted that HS may remain undiagnosed for years due to misattribution of symptoms to more common conditions such as malaria or nutritional anemia. Patients may present later with complications including massive splenomegaly, pigment gallstones, severe anemia requiring repeated transfusions, and in some cases inappropriate iron supplementation, which may worsen iron overload. These findings emphasize the importance of maintaining a high index of suspicion for inherited hemolytic disorders in children with persistent or recurrent hemolysis, even in malaria-endemic areas(8).

From a diagnostic perspective, HS should be considered in any child with chronic hemolysis, especially when peripheral blood smear shows spherocytes, there is reticulocytosis, and the direct antiglobulin test is negative. The presence of a family history, although not always reported, can further support the diagnosis. In contrast, HMS diagnosis relies on a combination of clinical, immunological, and therapeutic criteria, including exclusion of other causes of splenomegaly. Therefore, careful clinical evaluation and targeted investigations are essential to differentiate and identify coexisting conditions (3).

Management of patients with coexisting HS and HMS requires a comprehensive approach. While HMS responds to prolonged antimalarial therapy or prophylaxis, HS management is largely supportive, including folic acid supplementation, monitoring for complications, and consideration of splenectomy in severe cases. Failure to recognize HS may delay appropriate interventions and increase morbidity(7).

This case highlights the need for clinicians working in malaria-endemic regions to consider alternative or coexisting diagnoses in children presenting with massive splenomegaly and hemolytic anemia. Strengthening diagnostic capacity, increasing awareness of inherited hemolytic disorders, and adopting a systematic approach to evaluation can improve early diagnosis and patient outcomes (8).

Conclusion

This case highlights the rare coexistence of hereditary spherocytosis and hyperreactive malarial splenomegaly in a child from a malaria-endemic region. It underscores the importance of considering underlying hematological disorders in patients presenting with massive

splenomegaly and persistent anemia, rather than attributing findings to malaria alone. Early recognition of dual pathology is essential to guide appropriate management, including timely splenectomy where indicated, and to improve clinical outcomes.

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Declarations

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Conflicts of interest/Competing interests

The authors declare that they have no competing interests.

Ethics approval

Ethical clearance for this case report was obtained from the Ethics Committee at Kisoro Regional Referral Hospital (Approval Number: KRRH-EC-2025-20-93).

Consent to participate

Written informed consent to participate was obtained from the patient's parent/legal guardian.

Written consent for publication

Written informed consent for publication of this case report and accompanying clinical details was obtained from the patient's parent/legal guardian. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

Availability of data and material

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability

Not applicable.

Authors' contributions

A.H.M participated in the clinical management of the patient and drafted the initial manuscript. M.A.A., M.A.H.,MAA, M.O.A., B.Y. A.A.O, and I.D. contributed to data collection, case documentation, and literature review. D.J.M.M. and M.A.A. supervised the study and critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Supplementary Files

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