CARE Checklist of information to include when writing a case report

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Topic	Item	Checklist item description	Reported on Line

Title **1** The diagnosis or intervention of primary focus followed by the words "case report" **COEXISTENCE OF HEREDITARY SPHEROCYTOSIS AND HYPERREACTIVE MALARIAL SPLENOMEGALY IN A CHILD FROM A MALARIA-ENDEMIC REGION: A CASE REPORT IN UGANDA.**

Key Words **2** 2 to 5 key words that identify diagnoses or interventions in this case report, including "case report" Hereditary spherocytosis; Hyperreactive malarial splenomegaly; Hemolytic anemia; Splenomegaly; Case report

Abstract (no references)

3a Introduction: What is unique about this case and what does it add to the scientific literature? Hereditary spherocytosis and hyperreactive malarial splenomegaly are important causes of anemia and splenomegaly, but their coexistence is rarely reported, particularly in malaria-endemic regions. This case highlights the diagnostic challenge of distinguishing inherited hemolytic disorders from malaria-related splenomegaly in low-resource settings and emphasizes the importance of considering dual pathology in children with persistent anemia and massive splenomegaly.

3b Main symptoms and/or important clinical findings A 7-year-old female presented with a 4-year history of progressive abdominal distension and a 5-day history of fever and abdominal pain. Examination revealed massive splenomegaly, moderate pallor, mild scleral jaundice, generalized lymphadenopathy, and severe anemia.

3c The main diagnoses, therapeutic interventions, and outcomes The patient was diagnosed with hereditary spherocytosis with probable coexisting hyperreactive malarial splenomegaly causing hypersplenism and severe hemolytic anemia. She received antimalarial therapy, blood transfusions, folic acid supplementation, and subsequently underwent splenectomy. Following surgery, the patient showed marked clinical and hematological improvement with resolution of anemia, no further epistaxis, and improved activity levels.

3d Conclusion—What is the main "take-away" lesson(s) from this case? This case highlights the importance of considering underlying inherited hemolytic disorders in children presenting with persistent anemia and massive splenomegaly in malaria-endemic regions. Early recognition of coexisting hereditary spherocytosis and malaria-related splenomegaly is essential for accurate diagnosis, appropriate management, and improved patient outcomes.

Introduction **4** One or two paragraphs summarizing why this case is unique (**may include** reference**s**) Hereditary spherocytosis (HS) is an inherited hemolytic anemia caused by defects in red blood cell membrane proteins, while hyperreactive malarial splenomegaly (HMS) is a chronic immune-mediated complication of repeated malaria exposure in endemic regions. Both conditions may present with anemia, jaundice, hemolysis, and splenomegaly, creating a significant diagnostic challenge, particularly in low-resource settings where splenomegaly is often initially attributed to malaria alone. The coexistence of HS and HMS is rarely reported in the literature, especially among children from sub-Saharan Africa.

This case is unique because it demonstrates how chronic malaria exposure may mask an underlying inherited hemolytic disorder, leading to delayed diagnosis and repeated hospitalizations. The report highlights the importance of maintaining a high index of suspicion for hereditary hemolytic anemias in children with persistent anemia and massive splenomegaly despite appropriate antimalarial treatment. It also emphasizes the role of careful clinical evaluation, family history, peripheral blood smear findings, and timely surgical intervention in improving outcomes in resource-limited malaria-endemic settings.

Patient Information **5a** De-identified patient specific information A 7-year-old female from western Uganda presented with a 4-year history of progressive abdominal distension and a 5-day history of fever and abdominal pain. She had multiple prior hospital admissions and a previous blood transfusion. Family history was significant for similar abdominal swelling in two siblings and the father.

5b Primary concerns and symptoms of the patient The primary concerns were progressive abdominal distension, recurrent fever, abdominal pain, generalized body weakness, dizziness, and reduced appetite. The caregiver was also concerned about persistent anemia and repeated hospital admissions.

5c Medical, family, and psycho-social history including relevant genetic information The patient had a history of multiple previous hospital admissions, including treatment for typhoid fever and prior blood transfusion for severe anemia. There was no known history of sickle cell disease or other chronic illnesses. Family history was significant for similar abdominal swelling in the father and two siblings, suggesting a possible inherited hematological disorder. The patient was from a malaria-endemic rural region in western Uganda with repeated exposure to malaria infection. No

significant psychosocial concerns were identified.

5d Relevant past interventions with outcomes The patient had previously received treatment for presumed malaria and typhoid fever during multiple hospital admissions, with temporary symptomatic improvement but persistent abdominal distension and anemia. She had also undergone prior blood transfusion for severe anemia. Despite antimalarial therapy during the current admission, the patient continued to have worsening splenomegaly and severe anemia requiring repeated blood transfusions, which prompted further evaluation and eventual splenectomy with subsequent clinical improvement.

Clinical Findings

Timeline

Diagnostic Assessment

Therapeutic Intervention

Follow-up and Outcomes

6 Describe significant physical examination (PE) and important clinical findings On examination, the patient was fully conscious and oriented but appeared moderately pale with mild scleral jaundice. She had generalized lymphadenopathy involving the posterior cervical, mandibular, and inguinal lymph nodes. Abdominal examination revealed marked asymmetrical abdominal distension with massive splenomegaly extending up to 22 cm below the left costal margin and mild hepatomegaly. The spleen was firm, smooth, and tender on palpation. Vital signs showed tachycardia and mild tachypnea, while oxygen saturation remained within normal range on room air.

7 Historical and current information from this episode of care organized as a timeline

Date/Period	Clinical Events and Interventions
4 years before admission	Progressive abdominal distension noted by caregiver, predominantly in the left upper abdomen.
Previous years	Multiple hospital admissions for presumed typhoid fever and severe anemia; previous blood transfusion received.
5 days before admission	Developed high-grade intermittent fever, generalized abdominal pain, weakness, dizziness, and poor appetite.
2 June 2025	Admitted with massive splenomegaly, pallor, mild jaundice, and severe anemia (Hb 5.1 g/dL). Malaria rapid diagnostic test positive. Started on antimalarial therapy and supportive care.
3–6 June 2025	Persistent severe anemia and progressive splenomegaly despite treatment. Recurrent episodes of epistaxis occurred. Peripheral blood smear demonstrated spherocytes suggestive of hereditary spherocytosis. Blood transfusions administered.
7 June 2025	Surgical review performed due to worsening hypersplenism and transfusion dependence. Splenectomy planned after stabilization and pneumococcal vaccination.
8 June 2025	Continued supportive management and counseling before surgery.
Postoperative period	Elective splenectomy performed successfully without complications. Clinical and hematological improvement observed with resolution of anemia and no recurrent epistaxis.
Follow-up	Patient remained clinically stable with improved activity, no recurrent severe anemia, and no further hospital admissions reported.

8a Diagnostic testing (such as PE, laboratory testing, imaging, surveys Diagnostic evaluation included detailed physical examination, complete blood count, liver and renal function tests, malaria rapid diagnostic test, abdominal ultrasound, and peripheral blood smear analysis. Physical examination revealed massive splenomegaly, pallor, mild jaundice, and lymphadenopathy. Laboratory investigations showed severe anemia (hemoglobin 5.1 g/dL), elevated red cell distribution width, thrombocytopenia, and lymphocytosis. Malaria rapid diagnostic test was positive. Abdominal ultrasound demonstrated splenomegaly with preserved splenic architecture and mild hepatomegaly. Peripheral blood smear revealed numerous spherocytes consistent with hereditary spherocytosis. Surgical review recommended osmotic fragility testing, although this was not performed due to resource limitations.

8b Diagnostic challenges (such as access to testing, financial, or cultural) iagnosis was challenging because the patient presented in a malaria-endemic setting where massive splenomegaly and anemia are commonly attributed to malaria-related conditions. Limited access to specialized hematological investigations such as eosin-5-maleimide binding assay, direct antiglobulin testing, and osmotic fragility testing further complicated confirmation of hereditary spherocytosis. Financial and resource limitations also restricted advanced diagnostic evaluation. In addition, the caregiver initially declined blood transfusion and referral, which delayed optimal management.

severe malaria with hypersplenism, hematological malignancy, sickle cell disease, chronic liver disease, and other causes of massive splenomegaly and hemolytic anemia in children.

8d Prognosis (such as staging in oncology) where applicable The patient had a good postoperative prognosis following splenectomy, with marked clinical and hematological improvement, resolution of recurrent epistaxis, stabilization of hemoglobin levels, and improved functional status during follow-up. However, long-term monitoring was recommended because of the lifelong risk of post-splenectomy infections and potential complications associated with hereditary spherocytosis.

9a Types of therapeutic intervention (such as pharmacologic, surgical, preventive, self-care) . Therapeutic interventions included pharmacologic treatment with intravenous artesunate followed by artemether/lumefantrine for malaria, paracetamol for pain and fever control, folic acid supplementation, blood transfusions for severe anemia, and preventive pneumococcal vaccination prior to surgery. Definitive surgical management was performed through elective splenectomy to treat hypersplenism and recurrent transfusion-dependent hemolytic anemia.

8c Diagnosis (including other diagnoses considered) The final diagnosis was hereditary spherocytosis with hypersplenism and probable coexisting hyperreactive malarial splenomegaly causing severe chronic hemolytic anemia. Other differential diagnoses considered included

9b Administration of therapeutic intervention (such as dosage, strength, duration) The patient was initially treated with intravenous artesunate 60 mg, followed by oral artemether/lumefantrine for malaria treatment. Paracetamol 250 mg three times daily was administered for symptomatic relief of fever and pain. Folic acid supplementation was started at half a tablet daily to support erythropoiesis. Because of persistent severe anemia, the patient received packed red blood cell transfusions, including 100 mL of O-negative blood and later 200 mL of O-positive blood after compatible cross-matching. Pneumococcal vaccine (PCV23, 0.5 mL) was given before surgery. Following stabilization, the patient underwent elective splenectomy as definitive management for hypersplenism secondary to hereditary spherocytosis.

9c Changes in therapeutic intervention (with rationale) Despite initial antimalarial therapy, the patient continued to have worsening anemia, persistent splenomegaly, and recurrent epistaxis, indicating that malaria alone did not fully explain the clinical condition. Following peripheral blood smear findings suggestive of hereditary spherocytosis and ongoing transfusion dependence, management was modified to include folic acid supplementation, repeated blood transfusions, surgical consultation, and preparation for splenectomy. Elective splenectomy was ultimately performed because of severe hypersplenism, progressive splenomegaly, and persistent hemolytic anemia requiring recurrent transfusions.

10a Clinician and patient-assessed outcomes (if available) .....

10b Important follow-up diagnostic and other test results .....

10c Intervention adherence and tolerability (How was this assessed?) .....

10d Adverse and unanticipated events .....

Discussion

11a A scientific discussion of the strengths AND limitations associated with this case report This case report highlights a rare coexistence of hereditary spherocytosis and probable hyperreactive malarial splenomegaly in a child from a malaria-endemic region, emphasizing the diagnostic challenges posed by overlapping clinical features of chronic hemolytic anemia and malaria-related splenomegaly. A major strength of this report is the detailed clinical documentation demonstrating how persistent anemia, family history, peripheral blood smear findings, and failure to improve fully with antimalarial therapy contributed to identification of an underlying inherited hemolytic disorder. The case also illustrates the importance of considering dual pathology in children with massive splenomegaly in low-resource settings and demonstrates successful clinical improvement following splenectomy.

However, the report has several limitations. Specialized confirmatory investigations for hereditary spherocytosis, including eosin-5-maleimide binding assay, direct antiglobulin testing, reticulocyte count, and osmotic fragility testing, were unavailable because of resource limitations. Similarly, immunological investigations supporting hyperreactive malarial splenomegaly, such as serum IgM levels and malaria antibody titers, were not performed. Therefore, the diagnosis of hyperreactive malarial splenomegaly remained presumptive rather than definitive. In addition, long-term postoperative follow-up was limited, restricting assessment of long-term outcomes and complications.

11b Discussion of the relevant medical literature **with references** Hereditary spherocytosis is an inherited red blood cell membrane disorder caused by defects in membrane proteins such as spectrin, ankyrin, band 3, or protein 4.2, leading to chronic hemolysis, anemia, jaundice, and splenomegaly (Bolton-Maggs et al., 2012). Diagnosis is supported by family history, peripheral blood smear findings of spherocytes, elevated mean corpuscular hemoglobin concentration, reticulocytosis, and confirmatory laboratory testing such as eosin-5-maleimide binding or osmotic fragility testing (Ciepiela, 2018). In severe or transfusion-dependent cases, splenectomy remains an important therapeutic option after appropriate vaccination and infection prevention measures (Bolton-Maggs et al., 2012).

Hyperreactive malarial splenomegaly is a chronic immune-mediated complication associated with repeated malaria exposure in endemic regions and is characterized by persistent massive splenomegaly, elevated antimalarial antibodies, increased serum IgM, and clinical response to prolonged antimalarial therapy (Leoni et al., 2015). In malaria-endemic settings, massive splenomegaly is frequently attributed to malaria alone, which may delay recognition of underlying inherited hematological disorders. Previous reports from African settings have shown that hereditary spherocytosis may remain undiagnosed for years because symptoms overlap with more common infectious causes of anemia and splenomegaly (Steward et al., 2014).

This case demonstrates the diagnostic challenge created by the coexistence of hereditary spherocytosis and probable hyperreactive malarial splenomegaly in a child from a malaria-endemic region. Persistent anemia despite antimalarial treatment, positive family history, recurrent transfusion requirements, and peripheral blood smear findings were important clues supporting an inherited hemolytic disorder. The case highlights the importance of considering dual pathology in children presenting with chronic hemolysis and massive splenomegaly in low-resource settings.

11c The scientific rationale for any conclusions (including assessment of possible causes) The conclusions in this case were based on the combination of persistent hemolytic anemia, massive splenomegaly, family history of similar illness, and peripheral blood smear findings demonstrating spherocytes, all of which strongly supported hereditary spherocytosis as the underlying hematological disorder. The persistence of severe anemia and progressive splenomegaly despite appropriate antimalarial therapy suggested that malaria alone could not fully explain the clinical presentation. In addition, the patient originated from a malaria-endemic region and had clinical features compatible with hyperreactive malarial splenomegaly, making coexistence of both conditions likely. The marked clinical and hematological improvement following splenectomy further supported hypersplenism secondary to hereditary spherocytosis as a major contributor to the patient's condition.

11d The primary "take-away" lessons of this case report (without references) in a one paragraph conclusion This case highlights the importance of considering inherited hemolytic disorders such as hereditary spherocytosis in children presenting with persistent anemia and massive splenomegaly in malaria-endemic regions. Reliance on malaria alone as an explanation for chronic splenomegaly may delay diagnosis and appropriate management. Careful clinical assessment, family history, and peripheral blood smear evaluation are essential for identifying underlying hematological disorders in resource-limited settings. Early recognition and timely intervention, including splenectomy when indicated, can significantly improve clinical outcomes.

12 Patient Perspective The patient's caregiver reported that the child had experienced progressive abdominal swelling, repeated illness episodes, and generalized weakness for several years, which significantly affected her daily activities and quality of life. The family initially believed the condition was related only to recurrent malaria because they lived in a malaria-endemic area and had sought treatment multiple times without lasting improvement. The repeated hospital admissions and blood transfusions caused emotional and financial stress to the family.

Following admission, investigations, blood transfusions, and eventual splenectomy, the caregiver observed marked improvement in the child's condition. The abdominal swelling reduced, the child became more active, appetite improved, and there were no further episodes of severe weakness or nose bleeding. The caregiver expressed gratitude for the treatment received and acknowledged the importance of follow-up care and infection prevention after splenectomy.

Informed Consent **13** Did the patient give informed consent? Please provide if requested ..... **Yes** ☑ **No** ☐