Case Report

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Hereditary spherocytosis in a young female in Eastern Nepal: a case report

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Introduction and importance: Hereditary spherocytosis (HS), a rare familial extravascular haemolytic disorder, typically follows an autosomal dominant inheritance pattern with variable expressivity. Despite its classical presentation of anaemia, jaundice, and splenomegaly, HS is infrequently reported among individuals of Asian descent, contributing to its under diagnosis or delayed diagnosis. The primary objective of this case report is to underscore the pivotal role of the osmotic fragility test in diagnosing HS, emphasizing the importance of accurate and timely identification for effective clinical management and improved patient outcomes.

Case presentation: The patient, without known prior co-morbidities, presented with recurrent abdominal distension, early satiety, and easy fatigability persisting for 6 years. Physical examination revealed icterus, gnathopathy, left hypochondrium tenderness, and palpable splenomegaly. The osmotic fragility of red cells was significantly elevated. The patient underwent optimization before splenectomy, receiving immunization against encapsulated bacteria. Packed red blood cell transfusions were administered to achieve optimal haemoglobin levels. Follow-up showed symptom relief, significantly improving the patient's quality of life.

Clinical discussion: This case underscores the challenges of delayed HS diagnosis, with the patient enduring symptoms for years before seeking appropriate medical attention. Overlooking the simplicity and cost-effectiveness of an osmotic fragility test prolonged the diagnostic journey, emphasizing the impact on overall well-being.

Conclusion: HS remains underdiagnosed, especially in our regions. The osmotic fragility test emerges as an economical diagnostic tool in resource-limited settings, particularly when spherocytosis is absent in the peripheral blood smears. Its inclusion in diagnostic protocols can expedite accurate HS identification and enhance patient outcomes.

Keywords: Anaemia, case report, haemolytic, osmotic fragility, spherocytosis

Introduction

Hereditary spherocytosis (HS) is a familial extravascular haemolytic disorder. It is the most common cause of inherited haemolysis in Northern Europe and America with a reported incidence of 1 in every 5000 births[1]. It has an autosomal dominant inheritance pattern with variable expressivity, rarely reported in people of Asian descent. There has been a few case of HS reported from our country[2,3]. However, the incidence hasn't been well explored in our population. Though, the classical features of HS are anaemia, jaundice, and splenomegaly. These symptoms can vary in individuals ranging from asymptomatic to severe neonatal forms.

HIGHLIGHTS

- Hereditary spherocytosis is a haemolytic disorder rarely reported among Asians.
- The diagnosis was based on clinical profile and raised osmotic fragility test.
- Osmotic fragility test is an economical diagnostic tool in resource-limited settings.

The general therapeutic approach to HS involves both conservative and surgical measures. These approaches are based on the severity of the condition. Conservative measures include prescription of folic acid supplementations and blood transfusions in the milder forms of HS (Hb levels: 11–15 mg/dl, reticulocyte count: 3–6%, bilirubin levels: 17–34 μmol/l). The moderate forms of HS (Hb levels: 8–12 mg/dl, reticulocyte count: >6%, bilirubin levels: >34 μmol/l) can be optimizied through blood transfusions to manage anaemia and can be indicated the surgical approach on a case by case basis. The surgical approach involves splenectomy in the severe forms (Hb levels: <8 mg/dl, reticulocyte count: >10%, bilirubin levels: >51 μmol/l), especially in transfusion dependent cases. Immunization against encapsulated bacteria, such as Neisseria meningitidis, Streptococcus pneumoniae, and Hemophilus influenzae type B should be provided to prevent infections in case a patient undergoes splenectomy[4].

In this case report, we present a case of a 28 years' female with a delayed diagnosis of HS. The primary purpose of this case report is to shed light on the challenges associated with diagnosing HS and underscore the critical importance of utilizing the

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osmotic fragility test as a diagnostic tool. Through the detailed examination of this case, we aim to emphasize the significance of accurate and timely diagnosis in facilitating appropriate clinical management and improving patient outcomes. By highlighting the complexities and diagnostic hurdles encountered in this particular case, we seek to contribute valuable insights that underscore the relevance of the osmotic fragility test as an essential diagnostic tool in the identification and management of HS.

This case report has been reported in line with the SCARE Criteria 2023 guidelines[5].

Case presentation

A 28 years, female, non-smoker, non-alcohol consumer, with no known prior co-morbidities presented with complaints of generalized abdominal pain and easy fatigability for a week. According to her, she had recurrent episodes of abdominal distension, early satiety, and easy fatigability in the past 6 years. She had recurrent episodes of jaundice and had undergone multiple transfusions since her childhood. There was no any family history of haemolytic disorders. She had visited multiple primary level care centres with inconsistent follow-ups in the past resulting in a delay of diagnosis for her condition. She was usually treated for her low haemoglobin levels with folic acid medications in the past.

Examination revealed icterus and gnathopathy. Tenderness in the left hypochondrium and periumbilical region. The spleen was palpable 8 cm below the right costal margin. On ultrasonography of the abdomen, massive splenomegaly was detected. Peripheral blood smears revealed normal morphology of red, white blood cells, and platelets as shown in Fig. 1. The direct anti-human globulin (Coombs) test was negative. G6PD was normal. However, the osmotic fragility of the red cells was markedly raised.

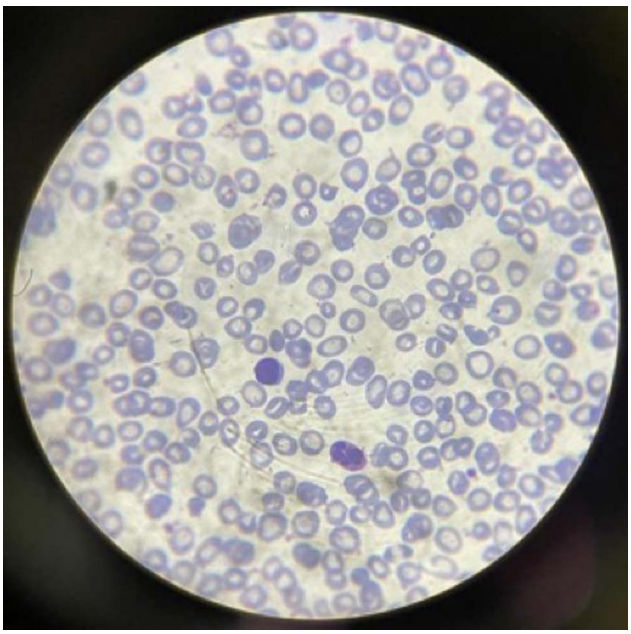

Figure 1. Peripheral blood smear showing normocytic normochromic red blood cells.

Based on the prolonged nature of the patient symptoms, enlarged tender spleen, blood transfusion history, haemoglobin levels in the range of 8–12 gm/dl, and raised bilirubin levels our patient was opted for splenomegaly. The patient was optimized before the surgery as shown in Table 1 and immunized for encapsulated bacteria Neisseria meningitiis, Streptococcus pneumoniae, and Hemophilus influenzae type B. Two units of packed red blood cells were transfused to raise the haemoglobin levels to an optimum level. The operative and postoperative period were uneventful. During her 1-week and 4-week follow-up, she gradually reported ease in her symptoms of abdominal distension, fatigability and improvement of icterus with normal laboratory parameters as shown in Table 1, leading to a better quality of life.

Discussion

HS occurs due to an intrinsic genetic defect caused by mutations in ANK1, EPB3, ELB42, SPTA1 and SPTB gene coding for ankyrin, band 3, protein 4.2, and spectrin. These membrane proteins are responsible for maintaining the integrity of the red blood cell (RBC) membrane[6]. This disease has a variable expressivity both in terms of its genetics and clinical presentation. This condition is inherited in an autosomal fashion; however, few cases may have sporadic mutations with no positive family history[7]. The severity of the disease depends on the extent of red cell membrane loss and ranges from asymptomatic to severe neonatal or prenatal forms[8]. Patients with HS may also remain undiagnosed for many years if they have milder forms and are well compensated[4].

HS can be diagnosed based on clinical history, positive family history, physical examination, complete blood counts, and reticulocyte count. Peripheral blood smears exhibiting spherocytes, elliptocytes, raised osmotic fragility of the RBCs can help make the diagnosis for HS. Specific tests include eosin-5-maleimide binding (EMA) test, acidified glycerol lysis time (AGLT), and genetic testing[4,9]. In our case, the patient had anaemia, jaundice, and massive splenomegaly. The PBS revealed normocytic, normochromic RBCs, and normal morphology of WBCs and platelets. So, the diagnosis was made based on clinical profile and raised osmotic fragility test.

In our case, the patient endured years of symptoms, including intermittent jaundice, abdominal distension, and easy fatigability, which progressively worsened over time. She sought

Table 1

Laboratory tests at the time of diagnosis, pre and post-splenectomy

Laboratory parameters	Diagnosis	Pre-splenectomy	Post-splenectomy
Haemoglobin (g/dl)	8.1	10.6	9.5
TLC (cells/mm^3)	4400	16 090	14 340
MCV (fl)	83.80	76.1	84.3
MCH (pg)	20.60	23.2	28.7
MCHC (g/dl)	29.30	30.5	34.2
Platelet (cells/mm^3)	132 000	107 000	153 000
Total bilirubin (mg/dl)	5.84	6.01	0.8
Conjugated bilirubin (mg/dl)	0.70	0.85	0.1
Unconjugated bilirubin (mg/dl)	5.14	5.16	0.7

MCH, Mean Corpuscular Hemoglobin; MCHC, Mean Corpuscular Hemoglobin Concentration; MCV, Mean Corpuscular Volume; TLC, Total Leukocyte Count.

medical attention at primary care centres near her residence, initially being evaluated for anaemia and managed with folic acid medications. However, a lack of adequate follow-up, combined with limited resources, contributed to a delayed diagnosis. The healthcare providers at the primary care level, recognizing the triad of anaemia, jaundice, and splenomegaly had initially considered haemolytic anaemia in their differential diagnosis. Unfortunately, the absence of appropriate laboratory settings, including the unavailability of a straightforward and cost-effective osmotic fragility test, hindered a conclusive diagnosis at that stage. The patient and her family faced financial constraints, and the limited resources and time further complicated the pursuit of a definitive diagnosis. This situation, unfortunately, led to a prolonged period of seeking medical opinions, contributing to a noticeable impact on the overall well-being of the patient.

The oversight of not including a cost-effective diagnostic test in the initial evaluations and the patient's inability to pursue further assessments due to financial limitations collectively underscore the need for affordable and widely available diagnostic tools. This case emphasizes the importance of the challenges faced by both healthcare providers and patients in resource-constrained settings, urging for increased accessibility to crucial diagnostic resources for rare diseases like HS to improve patient outcomes.

In the context of managing HS over the long term, splenectomy is considered a standard surgical intervention. Splenectomy is typically recommended for individuals with haemoglobin levels below 8 g/dl or a reticulocyte count exceeding 10% or are dependent on blood transfusion[4]. In our case, the patient had consistently low haemoglobin levels, was transfusion dependent and had massive splenomegaly. These combined factors prompted us to pursue splenomegaly. Post-splenectomy, the patient is doing well with gradually improving symptoms and has a better quality of life.

Post-splenectomy, about 10% of the patient have the highest risk of developing thrombotic complications within a week which may range from portal vein thrombosis to deep vein thrombosis and pulmonary embolism. However, this risk of venous thromboembolism (VTE) due to thrombocytosis remains elevated during the first 6–10 months[10]. So, patients who have undergone splenectomy should be followed 1 week and every 4 weeks for thrombotic complications in the first six months. However, due to lack of definite recommendations regarding post-splenectomy anti-coagulation, we did not prescribe any anti-coagulation medication for our patient. Additionally, patients are also at risk of overwhelming post-splenectomy infections (OPSI) caused by encapsulated bacteria like Neisseria meningitidis, Streptococcus pneumoniae, and Hemophilus influenzae type B throughout their life[11]. Hence, they need to be immunized for Pneumococcal and Meningococcal at a regular interval, 2 weeks' pre-splenectomy and every 5 years. The booster dose of Hemophilus spp is not currently recommended[12]. In our case, we followed up our patient after one week to screen for any thrombotic complications of splenectomy and every four weeks afterwards to screen for both VTE and OPSI. Currently, the patient is leading a better quality of life with improved symptoms.

HS is a rare haematological condition in our setting. While our country has documented a few cases[2,3], the presence of the classic triad of anaemia, jaundice, and splenomegaly should prompt the consideration of HS as a potential diagnosis. In situations where direct diagnostic tools are limited, osmotic fragility tests can be the most important and economic choice for diagnosing HS, especially in cases where there are no any pronounced spherocytes in the peripheral blood smear.

The limitations of our case report includes a singular presentation which could limit generalizability, and a retrospective nature may introduce recall bias. The lack of limited socioeconomic exploration is an additional challenge which is limited by the scope of the case report.

Conclusion

In summary, this case report underscores the challenges associated with diagnosing HS due to its rarity and overlapping symptoms with other haematological disorders. The delayed diagnosis in the presented case highlights the need for heightened clinical suspicion and awareness among healthcare providers. The key findings emphasize the pivotal role of the osmotic fragility test in accurately identifying HS. Early diagnosis is crucial, as it enables timely initiation of appropriate treatment measures, such as splenectomy, leading to improved patient outcomes. This case underscores the importance of early recognition and intervention in managing HS, thereby preventing complications associated with chronic haemolysis and enhancing the overall quality of patient care.

Ethical approval

Ethical approval was not provided by our institution as it is a case report.

Consent

Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

A.R.: conceptualization, writing—original draft, writing—review and editing. M.S.: conceptualization, writing—original draft, writing—review and editing. P.K.C.: resources, data curation , writing—review and editing. R.M.: supervision, validation, writing—review and editing.

Conflicts of interest disclosure

Authors declare no competing interests.

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Guarantor

All authors confirm that the data supporting the case are available within the article. Raw data that support the findings of this study are available from the corresponding author upon reasonable request.

Data availability statement

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