Acta Scientific Women's Health (ISSN: 2582-3205)

Volume 6 Issue 8 August 2024

Case Report

Unlocking the Mystery: Hereditary Elliptocytosis Discovered Amidst Pancytopenia - A Case Report

Anubhuti Chaturvedi*, Sarika Singh, Lity Dhar and Rabish Kumar

Department of Pathology, Maulana Azad Medical College and Lok Nayak Hospital, New Delhi, India

***Corresponding Author:** Anubhuti Chaturvedi, Department of Pathology, Pathology Block, Maulana Azad Medical College and Lok Nayak Hospital, Bahadur Shah Zafar Marg, New Delhi, India.

DOI: 10.31080/ASWH.2024.06.0601

Received: June 28, 2024

Published: July 14, 2024

Abstract

We report a case of Hereditary Elliptocytosis (HE) diagnosed incidentally in a 24-year-old female with Pancytopenia, who had multiple underlying comorbidities like Mixed Connective Tissue Disorders (MCTD) and Tuberculosis.

HE is a heterogeneous group of disorders caused by gene mutations, which ultimately affects the red cell cytoskeleton and membrane protein integrity due to mutations in the α-spectrin, β-spectrin, or protein 4.1 genes. Therefore, it presents as a varied clinico-hematological picture.

In the literature reviewed, there have been no correlations between the presence of HE with MCTD or tuberculosis.

Finding a significant amount of elliptocytes on the peripheral smear examination, should raise an index of suspicion and further workup of the patient is warranted, to prevent complications arising out of any hemolytic episode that might occur later.

Keywords: Pancytopenia; Hereditary Elliptocytosis

Introduction

HE is an inherited heterogeneous red blood cells (RBC) disorder, first described by Dresbach in 1904, and later by Hunter, is characterized by elongated, oval, or elliptical-shaped RBCs on the peripheral blood smear [1].

Subtypes of HE include common hereditary elliptocytosis (HE), hereditary pyropoikilocytosis (HPP), Southeast Asian ovalocytosis (SAO), and spherocytic elliptocytosis (SE). These subtypes differ in RBC morphology and degree of hemolysis.

HE is most commonly seen in western and central Africans. Worldwide, the incidence is estimated to be 1/2000-4000 individuals [3]. The incidence of an elliptocytosis variant, SAO, is 5-25% in Melanesia, Philippines, Indonesia, and Southern Thailand. Most patients with heterozygous HE, are asymptomatic and require no treatment, although some may demonstrate mild hemolytic anemia and splenomegaly, which are managed by blood transfusions and splenectomy [2-4].

Mixed connective tissue disease (MCTD) is a rare systemic autoimmune disease with overlapping features of at least two connective tissue diseases (CTD), including systemic lupus erythematosus (SLE), systemic sclerosis (SSc), polymyositis (PM), dermatomyositis (DM) and rheumatoid arthritis (RA) with specific antibodies.

Clinical symptoms of MCTD are non-specific and include arthralgia, malaise, myalgia, and low-grade fever, and variable cytopenias.

Case Report

The present case is a 24-year-old female, known case of old treated tubercular lymphadenitis with Generalized Tonic-Clonic Seizure disorder (GTCS) and MCTD, who presented to the OPD with complaints of easy fatiguability, weight loss, loss of appetite, burning during micturition, and had subcentimetric cervical lymphadenopathy. Other systemic examinations were within normal limits.

Her USG-Abdomen was suggestive of abdominal lymphadenopathy and gall bladder calculi.

The peripheral blood EDTA sample revealed a hemoglobin of 9.1 gm%, RBC count of 3.71 million/microliter, TLC of 2160/mm^3, with Polymorphs 41%, Lymphocytes 46%, Monocytes 4%, Eosinophils 5%, Metamyelocytes 1% and Band forms 3% with a Platelet

Table 1: Investigations done.

Investigations	INDEX CASE	Reference Values
ESR	85mm/1st hr	0-20 mm/1st hr
S. Lactate Dehydrogenase (LDH)	307 U/L	140-280 U/L
D-Dimer	1641 ng/mL	<500 ng/mL
BNP	354.4 pg/mL	<100 pg/mL
Ferritin	366.3 ng/mL	11-306 ng/mL (women)

count of 1.27 lakhs/mm^3. The MCV, MCH, and MCHC were 84.9 fL, 24 pg, and 28.3 g/dL respectively. The Red Cell Distribution width (RDW) was 13.5%, Reticulocyte count was 0.7% and hematocrit was 31.5%.

The peripheral smear showed pancytopenia, with RBCs that were predominantly Normocytic Normochromic, with the presence of many Elliptical cells (20%), occasional spherocytes and very occasional pencil forms. TLC was markedly reduced and Platelets were marginally reduced. The impression given was Pancytopenia with features suggestive of HE (Figure 1,2).

In view of the presence of gallstones, >15% elliptocytes on peripheral blood smear, and a near normal reticulocyte count, a final diagnosis of asymptomatic HE was rendered.

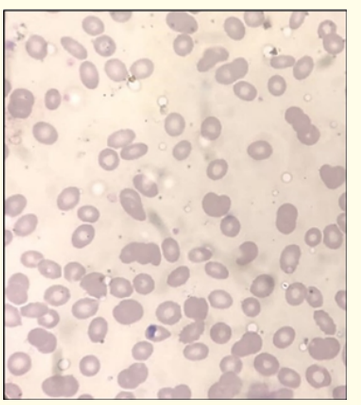

Figure 1: Elliptocytes on Peripheral smear (Giemsa, Oil Immersion, 100X).

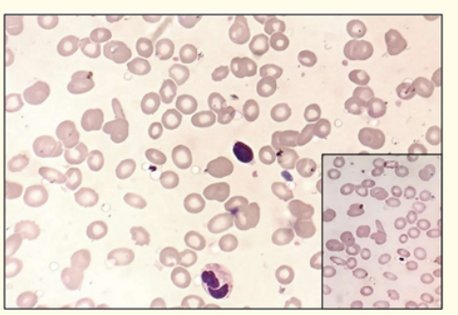

Figure 2: Elliptocytes on Peripheral blood smear with neutrophil and lymphocyte in the field (Giemsa, 400X); Inset- oil Immersion (1000X).

Discussion

The HE syndromes are a family of genetically determined erythrocyte disorders characterized by elliptical RBCs on the peripheral blood smear.

	Common HE	Hemolytic HE	Hereditary Pyropoikilocytosis	Spherocytic Elliptocytosis	South East Asian Ovalocytosis	INDEX CASE
Anemia	None	Moderate to Severe	Severe	Mild to Moderate	None	Mild
Hemolysis	None to mild	Moderate to severe	Severe	Mild to Moderate	None	None
Peripheral Blood Smear	Elliptocytes	Elliptocytes; poikilocytes; fragments	Poikilocytes; RBC budding with fragments; Elliptocytes; Microspherocytes	Rounded Elliptocytes; Spherocytes	Rounded Elliptocytes	Elliptocytosis
Inheritance	AD	AR	AR	AD	AD	Could not be assessed
MCV	Normal to Increased	Decreased	Decreased	Increased	Normal to Increased	Normal
RDW	Normal to Increased	Increased	Increased	Increased	Normal to Increased	Normal
Retic %	Normal to Increased	Increased	Increased	Increased	Normal to increased	Normal
% Elliptical cells	15-90%	Usually > 20%	Variable >20%	Variable	30%	>15%
OFT	Normal	Increased	Increased	Increased	Normal	Could not be assessed
Thermal Stability	Normal	Normal	Increased	Normal	Normal/Increased	Could not be assessed

Table 2: Classification of Hereditary Elliptocytosis Syndromes.

Abbreviations: HE-Hereditary Elliptocytosis; AD-Autosomal Dominant; AR-Autosomal Recessive; OFT-Osmotic Fragility Test.

The HE disorders are caused by intrinsic membrane protein abnormalities, which alter RBC membrane function, change RBC shape, and, in some cases, cause hemolysis. Studies have shown the principal defect in HE is fragility of the RBC membrane skeleton, due to qualitative and/or quantitative defects in several membrane skeleton proteins, α-and β-spectrin, protein 4.1R, or GPC [5,6].

Some HE syndromes are associated with symptomatic hemolytic disease, although most are clinically silent and are discovered incidentally when a blood smear is reviewed. The clinical severity of common HE is extremely variable, ranging from most commonly observed incidental asymptomatic condition, to mild-to-moderate hemolytic anemia.

There is much overlap when these disorders are classified on a clinical, biochemical, or molecular basis [6].

Initial laboratory studies in a patient with a suspected HE syndrome should assess whether the patient is anemic, with compensation (reticulocyte count), or with excessive RBC destruction (increased serum LDH and bilirubin). MCV is important because some hemolytic HE and HPP variants with RBC fragmentation often demonstrate severe microcytosis as a result of RBC fragmentation, producing a marked decrease in MCV.

Careful evaluation of the blood smear is essential both for diagnosing HE and classifying the disorder into major subtypes. The diagnostic criteria include the presence of at least 15-20% elliptocytes or similar family history [1]. Osmotic Fragility is normal in nonhemolytic HE but is increased in hemolytic HE variants with poikilocytosis, HPP, and SE.

Once the diagnosis of HE is established, it is possible to further characterize the specific membrane lesion by using biochemical and molecular studies to identify specific protein defects [7].

In view of the benign nature of HE, therapeutic intervention is not indicated. Patients with HE variants associated with severe hemolytic anemia are provided supportive care like supplemental folic acid, periodic screening for cholelithiasis, transfusion during a hemolytic or aplastic crisis, and splenectomy if indicated, which has a good prognosis [1].

The complications include megaloblastic anemia, pigment gallstone/s leading to cholangitis, cholecystitis, or pancreatitis, splenomegaly, renal tubular acidosis (associated with SAO) and skeletal abnormalities due to marrow expansion [1].

Conclusion

In the index case, diagnosis of HE was an incidental finding with moderate severity, as the patient had no underlying predisposing condition or symptoms to suggest otherwise. The presented case could not be assessed for molecular and family studies as she succumbed to her other comorbidities. There have been no correlations between the presence of HE with MCTD or tuberculosis in published data yet. A high index of suspicion should arise on sighting elliptical cells and a complete workup should be undertaken to avoid complications.

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