Case report

Citation: Fernando N, Jayamanna C & Fernando K, 2021. An incidental finding of a Southeast Asian ovalocytosis patient in Sri Lanka: Case report and review of the literature. Sri Lanka Journal of Medicine, 30(1), pp 38-41
DOI: <http://doi.org/10.4038/sljm.v30i1.215>

An incidental finding of a Southeast Asian ovalocytosis patient in Sri Lanka: A case report and review of the literature

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Abstract

Southeast Asian ovalocytosis (SAO) is an autosomal dominant, red cell membrane defect due to mutation in SLC4A1 gene which code for band 3 protein. Though this condition is common among Southeast Asia, the prevalence is very low in Sri Lanka. We report a case of asymptomatic SAO in western province, Sri Lanka who was found incidentally. She was treated for pyelonephritis and while investigating, the peripheral blood film reveals, the presence of numerous ovalocytes (knizocytes) and elliptocytes compatible with SAO. Diagnosis is done by finding many ovalocytes in the blood film supported by genetic analysis and knizocytes are also seen in the blood film. Treatment is unnecessary. Good prognosis has observed in heterozygous form.

Keywords: *Southeast Asian ovalocytosis, Knizocytes*

INTRODUCTION

Southeast Asian ovalocytosis (SAO) is an autosomal dominant red cell membrane defect, which is common in Southeast Asian and Melanesian population [1],[2]. Though this is very common among certain ethnic groups of Malaysia, Papua New Guinea, the Philippines and Indonesia [3], this is rare among Sri Lankans [2]. It is caused by a heterozygous 27 nucleotide deletion in SLC4A1 gene, which is located on Chromosome 17. This gene SLC4A1 codes for a band 3 protein (anion transport protein), which is the bicarbonate/chloride exchanger in red blood cell membrane. Abnormal band 3 proteins bind tightly to ankyrin, thus leading to increased rigidity of red cells [3].

This condition also known as stomatocytic hereditary elliptocytosis [4], because red cells in this condition are oval, which are often macrocytes and have a longitudinal slit in the middle. This ovalocytic erythrocytes are highly resistant to invasion by malaria parasite (both *Plasmodium knowlesi* and *Plasmodium falciparum* in vitro), and this is the only human red cell variant known to be resistant to both [5]. Hence this can be taken as an example, where a mutation of a structural protein of the red cell that endows the bearer with a selective advantage [4].

CASE REPORT

A 54-year-old woman presented to our hospital with a history of fever with shaking chills and dysuria for two weeks. Her past medical history was significant for type 2 diabetes mellitus, for which she was on metformin 500mg twice daily. She had no family history of haemolytic disease. On examination she was alert; febrile with a temperature of 39.0° Celsius, her blood pressure was 129/88 mmHg and pulse rate was 110 beats per minute. On physical examination, she was not pale nor icteric, but revealed right side costovertebral angle tenderness. There were no other specific findings in her physical examination.

Her capillary blood sugar was 229 mg/dL and she was started on soluble insulin 8 IU, thrice a day together with oral metformin. A routine haematological examination revealed a white blood cell count of 28,000/ μ L, with 73% of neutrophils and 17.6% lymphocytes. Her haemoglobin level was 13.6g/dL, MCV was 78.3fL, MCH was 27.4pg, HCT was 39.3%, and her platelet count was 622,000/ μ L. Her C reactive protein level was 205mg/L. Her urinalysis results were 2+ for albumin, 8-10 pus cells per high-power field with no erythrocytes. Her urine culture was negative. At this point she underwent ultrasound scan of the abdomen and KUB to evaluate the possibility of

pyelonephritis. It showed mildly echogenic and oedematous right kidney which is suggestive of right-side acute pyelonephritis. This patient was treated with cefotaxime as an intravenous antibiotic for 7 days. She recovered well and laboratory values normalized.

We proceeded with peripheral blood smear due to leucocytosis and thrombocytosis, and in blood picture it revealed normocytic and normochromic red cells with numerous ovalocytes with knizocytes and elliptocytes (

Figure 1), occasional polychromatics and increased rouleaux and commented as appearance suggestive of Southeast Asian ovalocytosis (

Figure 1). White blood cell changes were: Neutrophil leucocytosis with toxic changes which is compatible with changes of a bacterial infection with reactive thrombocytosis. Serum electrolytes, renal function tests, liver function tests and family screening were also suggested.

Her liver function tests and renal function tests were within normal limits. Her serum sodium level was 144 meq/L and serum potassium was 3.9 meq/L. Her arterial blood gas analysis was normal.

She was diagnosed to have Southeast Asian Ovalocytosis and clinically asymptomatic-without haemolysis or acidosis.

Figure 1: The patient's peripheral blood smear. The black arrow shows a Knizocyte. The blue arrow shows a normal red blood cell

DISCUSSION

According to literature, only few cases of SAO had been reported in Sri Lanka. Most of the SAO patients are asymptomatic, but has been reported to be associated with signs of mild haemolysis such as intermittent jaundice, gallstones [4], and babies have been reported with neonatal hyperbilirubinemia [6].

Individuals who are homozygous for the SAO are not clearly identified and thought to be lethal. Anyhow, the study conducted by Liu S.C. observed, that none of the children were homozygous in families where both parents were heterozygous for SAO27bp deletion [3]. Those families had high rates of miscarriages [3]. However, Picard Veronique, recently reported a case of homozygous SAO where extremely severe dyserythropoietic anaemia associated with distal renal tubular acidosis. It was in a child born to asymptomatic Comorian parents. On 22 weeks of gestation, this male foetus presented with hydrops and severe anaemia (Hb of 2.9g/dL) and had to be treated with in-utero transfusions. Even after birth he needed monthly blood transfusions to keep the haemoglobin level between 7 and 10g/dL [7].

Diagnosis can be done by molecular genotyping where genetic analysis conducted to identify the mutation in SLC4A1 gene. Light microscopic diagnosis is also a possibility. Red blood cell morphology in the peripheral blood smear shows the presence of $\geq 25\%$ ovalocytes and some stomatocytes[8]. The red blood cells of SAO are often described as being stomatocytic elliptocytes with a slit-like area of central pallor. In a small proportion of these stomatocytes, 2 or less frequently 3 pale regions separated by a well haemoglobinated ridge are apparent, giving the appearance of double stomatocytes, known as “Knizocytes” [9]. This feature is not pathognomonic for SAO but this morphology is the key to accurate diagnosis of SAO by a stained peripheral blood smear [9]. In a study by O'Donnell, red cells with 2 or more linear or irregular shaped pale regions (knizocytes) were

also the most consistent feature of SAO in microscopy [10].

Most of cases of SAO are asymptomatic and treatment is not necessary. For the once who presents with uncompensated haemolytic anaemia, splenectomy can be considered, as some patients undergo remission with splenectomy [11].

Prognosis in heterozygous form is good and not life threatening. However, prognosis is uncertain in homozygous individuals [7].

Author declaration

Acknowledgements

We thank the patient for her interest and support, the staff of the medical unit for their valuable help in the management of this patient and all the members involved in hematology and chemical pathology laboratories in District General Hospital, Negombo for the technical skills.

Author Contributions

Nilshan Fernando was involved in the initial conception of the study and collected and interpreted clinical and biological data. Champa Jayamanna treated the patient. Kavindya Fernando was involved in data analysis, planning of the study and drafted the manuscript. All three authors revised the final manuscript.

Funding sources

No sources of funding were involved in this paper

Availability of data and materials

Pictures of the blood smears used in the study are freely available from the corresponding author.

Ethics approval and consent to participate

Informed written consent to publish the details of the patient was taken from the patient herself.

Competing interests

We declare no competing financial interests

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