An uncommon RBC membranopathy : two case reports

Ritika Khurana[1], Purva Kanvinde[1], Mukesh Desai[1], Nitin Shah[1], Archana Swami[1], Minnie Bodhanwala[1], and Sangeeta Mudaliar[1]

[1]Bai Jerbai Wadia Hospital for Children

March 07, 2024

Title page

Title - **An uncommon RBC membranopathy : two case reports**

Authors

R Khurana – Senior resident, Pediatric hematology – oncology, B.J. Wadia hospital for children, Mumbai, India

P Kanvinde - Consultant, Pediatric hematology – oncology, B.J. Wadia hospital for children, Mumbai, India

M Desai – Senior Consultant & head of Immunology, Pediatric hematology – oncology, B.J. Wadia hospital for children, Mumbai, India

N Shah - Senior Consultant, Pediatric hematology – oncology, B.J. Wadia hospital for children, Mumbai, India

A Swami - Senior Consultant, Pediatric hematology – oncology, B.J. Wadia hospital for children, Mumbai, India

M Bodhanwala – CEO, B.J. Wadia hospital for children, Mumbai, India

S Mudaliar – Head of the department, Pediatric hematology – oncology, B.J. Wadia hospital for children, Mumbai, India

Corresponding author – Dr Sangeeta Mudaliar

Address – B. J. Wadia hospital for children, Acharya Donde Marg, Parel, Mumbai

Phone no – +91967307272

Email id - mudaliarsangi@rediffmail.com

Word count – 733

Figures – 1

Tables – 1

Key words – sitosterolemia, Phytosterolemia, stomatocytes, macrothrombocytopenia, sterols, hemolytic anemia

Abbreviations

Abbreviations	Full form
MCV	Mean Corpuscular Volume

Abbreviations	Full form
WBC	White blood cell
LDH	Lactate Dehydrogenase
EMA	Eosin 5' Maleimide
PS	Peripheral smear
NGS	Next Generation Sequencing
GC-MS	Gas Chromatography – Mass spectroscopy

Main text

An uncommon RBC membranopathy : two case reports

R Khurana, P Kanvinde, M Desai, N Shah, A Swami, M Bodhanwala, S Mudaliar

Sitosterolemia is a rare autosomal recessive disease of plant sterol metabolism. Bhattacharyya and Connor first described this disease in 1974 (1). To date, there are only about 100 known cases worldwide (2).

We describe two patients diagnosed with Sitosterolemia at our centre. Patient A is a 12 year old male, presented with complaints of short stature, abdominal distension & gradually progressive paleness since 2 months. He had pallor, hemolytic facies and both weight (25kg) & height (130cm) were less than 3rd centile and had spleno-hepatomegaly.

His investigations (table1) were suggestive of a chronic hemolytic anemia. Since the child did not have spherocytes on peripheral smear & had giant platelets, diagnosis of hereditary spherocytosis seemed unconvincing. So genetic work up by next generation sequencing was done which revealed mutation in ABCG8 gene, suggestive of Sitosterolemia. On review, his peripheral smear showed some stomatocytes (figure1).

Patient B is a 12 year old child who was referred to us for splenectomy. Child had splenomegaly bicytopenia, diagnosed during work up for a short febrile illness. There were stomatocytes in his smear too & sterol levels were borderline high, hence genetic studies were sent, which revealed compound heterozygous variants in the ABCG5 gene, suggestive of Sitosterolemia type 2.

Both the patients are under regular follow up for monitoring diet, counts & changes of early atherosclerosis. If dietary changes are not adequate, we will consider ezitimibe for them.

Discussion

Patients with Sitosterolemia can have a variety of presentations like short stature, chronic abdominal discomfort, splenomegaly etc indicating a chronic hemolytic disease. Some may present with tendinous and cutaneous xanthomas, arthritis, and arthralgias. They have a strong propensity towards premature coronary atherosclerosis (3).

Laboratory features are suggestive of chronic hemolysis with presence of stomatocytic red cells and macrothrombocytopenia on blood films. Eosin 5' maleimide test by flow cytometry (EMA) is usually abnormal. Plasma levels of plant sterols (sitosterol, cholestanol, and stigmasterol) measured by GC-MS (gas chromatography-mass spectrometry) are elevated. The identified homozygous or compound heterozygous mutations in ABCG5 and ABCG8 genes further confirm the diagnosis.

Treatment predominantly involves dietary changes & pharmacological adjuncts. All sources of vegetable fats like vegetable oils, nuts, seeds, olives, avocados etc. should be eliminated. Food derived from animal sources with cholesterol as the dominant source should be allowed (4). Bile acid resins like cholestyramine may be useful, statins have no role (5). Ezetimibe was US FDA approved in 2002 for use in patients with sitosterolemia. Ezetimibe alone or in combination with cholestyramine effectively reduces plant sterol levels by around 50%(6). Some patients may require surgical interventions like ileal bypass to effectively reduce sterol levels.

We feel that this condition is under reported as many may remain misdiagnosed as hereditary spherocytosis or hyperlipidemias. Measures as simple as dietary modification can control this condition & prevent a splenectomy(which will be detrimental in patients with Sitosterolemia). Hence, stomatocytes should be actively searched for in patients with large platelets and unexplained mild hemolysis. Consider early NGS to determine diagnosis.

References

1. Bhattacharyya AK, Connor WE. Beta-sitosterolemia and xanthomatosis. A newly described lipid storage disease in two sisters. J Clin Invest. 1974;53(4):1033-1043.
2. Kidambi S, Patel SB. Sitosterolaemia: pathophysiology, clinical presentation and laboratory diagnosis. J Clin Pathol. 2008; 61(5):588-594.
3. Merkens LS, Myrie SB, Steiner RD, Mymin D. *Sitosterolemia. GeneReviews [Internet]* Seattle (WA): University of Washington; 2016. [updated 2013 Apr 4].
4. EscolaGil JC, Quesada H, Julve J, MartinCampos JM, Cedo L, BlancoVaca F. Sitosterolemia: diagnosis, investigation, and management. Curr Atheroscler Rep 2014;16:424.
5. Parsons HG, Jamal R, Baylis B, Dias VC, Roncari D. A marked and sustained reduction in LDL sterols by diet and cholestyramine in betasitosterolemia. Clin Invest Med 1995;18:389400.
6. Lutjohann D, von Bergmann K, Sirah W, Macdonell G, JohnsonLevonas AO, Shah A, et al. Longterm efficacy and safety of ezetimibe 10 mg in patients with homozygous sitosterolemia: a 2year, openlabel extension study. Int J Clin Pract 2008;62:1499510.

Hosted file

`TABLE 1.docx` available at https://authorea.com/users/728533/articles/709570-an-uncommon-rbc-membranopathy-two-case-reports