

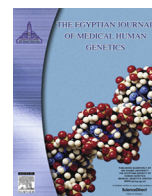
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Case Report

A novel MYH9 mutation in a beta thalassemia major patient with thrombocytopenia

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ABSTRACT

Macrothrombocytopenia is a congenital autosomal dominant blood disorder characterized by increased platelet size and decreased number of circulating platelets (Althaus and Greinacher, 2009). Here, we report a 32 year old beta thalassemia major patient admitted to the hospital for the evaluation of low thrombocyte count. In this study, we aimed to analyze mutations in MYH9 gene in our patient, we found a T to G nucleotide change at 3814 in exon 25, resulting in a transition of Serine to Alanine (p.S1195A) in MYH9 gene (Fig. 1) This mutation is reported for the first time in our population and not defined at Human Gene Mutation Database (HGMD) previously.

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1. Introduction

Macrothrombocytopenia is a congenital autosomal dominant blood disorder characterized by increased platelet size and decreased number of circulating platelets [1]. Macrothrombocytopenia is classified within the genetically heterogeneous group of rare disorders, which are related to several genes involving the MYH9 (*Myosin Heavy Chain-9*), ACTN1, TUBB1, Gp1B, Gp13A. The most frequent forms of these disorders, such as May Hegglin anomaly and Bernard Soulier syndrome, are associated with mutations in MYH9, which forms a dominant negative protein inhibiting the function of wild type heavy chain protein. The MYH9 gene encodes the non-muscle myosin heavy chain IIA (NMMHC-IIA), a cytoskeletal contractile protein. According to the research results the relation between MYH9 and macrothrombocytopenia was determined from the observations of occurrence hematological signs and inhibition of wild type heavy chain function by the dominantly active mutated heavy chain. This is resulted from the degradation of MYH9 gene by the one of the unstable heavy chain within NHMCHIIA class of non-muscle heavy myosin chain's one of the isoforms, where MYH9 gene is involved [2,3] Several mutations in the MYH9 gene lead to premature release of platelets from the

bone marrow, macrothrombocytopenia and cytoplasmic inclusion bodies within leukocytes.

2. Case report

Here, we report a 32 year old beta thalassemia major patient admitted to the hospital for the evaluation of low platelet count. She said that she had also low platelet counts and she was splenectomised previously. Her blood count is shown in Table 1. Her peripheral blood sampling showed that she had platelet clumping and some macrothrombocytes. This finding revealed the possibility of macrothrombocytopenia. Further; her beta thalassemia gene mutation analysis revealed IVS-1 nt 110 G-A mutation in homozygous state.

So we aimed to analyze mutations in MYH9 gene in our patient. A written informed consent for genetic analysis was obtained. Peripheral blood was collected and DNA was isolated by proteinase K and phenol/chloroform extraction. MYH9 gene was screened by polymerase chain reaction (PCR) and was sequenced, using a DNA sequencer (Beckman Coulter DNA Sequencer, USA). When the sequence analyzed (primers for F: 5' GCAAATCTGCTCCTTGAG 3', R: 5' AGCCAGGTCCTCAACAGAC3'), we found a T to G nucleotide change at 3814 in exon 25, resulting in a transition of Serine to Alanine (p.S1195A) in MYH9 gene (Fig. 1) This mutation is reported for the first time in our population and not defined at Human Gene Mutation Database (HGMD) previously. And we evaluated 40 control samples for this case, when selecting control samples, the ones with hematological disease were omitted.

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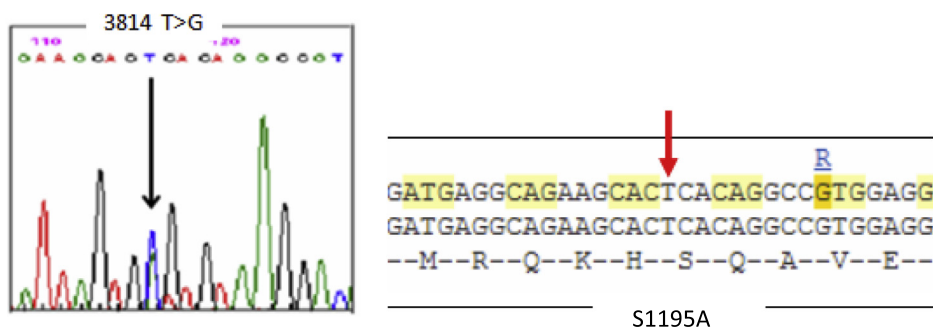
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Table 1

Laboratory data of the patient.

Hb (g/dl)	RBC ul	Hct %	MCV fl	MCHC g/dl	MCH pg	RDW %	Plt	Ferritin (ng/ml)
10.0	3.9	29	90.0	34.3	32.6	13.4	19000	5900

Hb: Hemoglobine, MCHC: Mean Corpuscular Haemoglobin Concentrate, RBC: Red Blood Cell, Hct: Hematocrit, MCV: Mean Corpuscular Volume, MCH: Mean Corpuscular Hemoglobin, RDW: Red Cell Distribution Width, Plt: Platelets.

**Fig. 1.** Sequence analysis of the patient.

3. Discussion & conclusion

The most important point in this case, it should be remembered that beta thalassemia patients develops hypersplenism and low platelet count occurs during this period. So every patient with low platelet count, should be evaluated for underlying macrothrombocytopenia and if possible gene analysis also performed.

References

- [1] Althaus K, Greinacher A. MYH9-related platelet disorders. *Semin Thromb Hemost* 2009;35:189–203.
- [2] Epstein CJ, Sahud MA, Piel CF. Hereditary macrothrombocytopenia, nephritis and deafness. *Am J Med* 1972;1972:299–310.
- [3] Kelley MJ, Jawien W, Ortel TL, Korczak JF. Mutation of MYH9, encoding non-muscle myosin heavy chain A, in May-Hegglin anomaly. *Nat Genet* 2000;26:106–8. doi: <http://dx.doi.org/10.1038/79069>.