Beta-thalassemia minor due to HBB deletions with increased HbA2 and HbF

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Introduction

Beta-thalassemia is an inherited blood disorder which is characterized by reduced synthesis of the hemoglobin beta chain that results in microcytic hypochromic anemia(1). It is usually caused by different mutations in beta-globin gene. Large deletions account for a small fraction of cases. Deletions in HBB and HBD, cause increased serum HbF and normal HbA2.

Case Presentation

Two Iranian patients who were suspected to be carrier of beta-thalassemia with hypochromic, microcytic anemia referred to our laboratory.

	RBC	MCV	MCH	Hb	HbA2	HbA1	HbF
Patient A	5.8	61.6	20.5	12.1	7.2	88.2	4.6
Patient B	6.62	65.6	22.1	14.6	7.9	83.3	8.8

Methods

✓ ARMS-PCR and direct sequencing methods were performed to detect point mutation in the beta-globin.

✓ Multiplex gap-PCR and multiplex ligation-dependent probe amplification (MLPA) technique was used to detect deletions in beta-globin gene cluster.

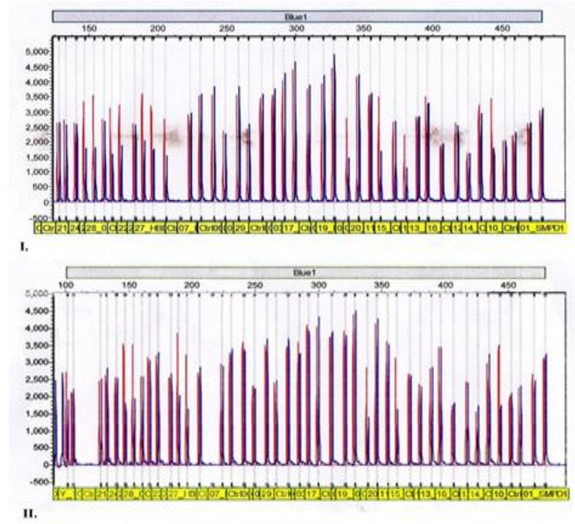
Results

✓ No point mutation or deletion were found using ARMS-PCR, gap-PCR and direct sequencing methods.

✓ Investigation by MLPA method revealed two different deletions which both of them were started from downstream of HBD-exon 3.

I. In patient A, deletion was extended to the HBB region covering all 3 exons as well as 800 bps downstream of the gene.

II. In patient B, deletion was extended to the 2nd intron of HBB and the 3rd exon was intact.



Conclusion

High HbA2 would be due to deletions in β-globin gene and its promoter in addition to intact HBD gene(2).

References

1. Weatherall DJ, Clegg JB. The Thalassemia Syndromes. 4th ed. Oxford, England: Blackwell Science Ltd; 2001.

2. A novel deletion of β-globin promoter causing high HbA2 in an Indian population -letter to editor- hematological 97(9) 2012.