Case Report *Iran J Ped Hematol Oncol. 2020, Vol 10, No 3, 200-202*

Hemoglobin Daneshgah-Tehran (HBA1:c.218A>G p.His72Arg): a Rare α1-Globin Variant from Iran

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Received: 10 October 2017 **Accepted:** 28 December 2019

Abstract
There are more than 400 different variations on α-globin protein, and most of them are not associated with noticeable clinical manifestation. Hemoglobin (Hb) is an oxygen-transporting protein and Hb Daneshgah-Tehran is an α-globin variant that for the first time was reported from Iran in a case with normal haematological indices. The capillary electrophoresis of an 8-year- old-girl with normal hematological parameters showed a peak in the location of Hb S (19.2%) with small amount of Hb A2 variant. The sequencing analysis indicated that the patient was heterozygote for Hb Daneshgah- Tehran (HBA1:c.218A>G p.His72Arg). Alpha and beta thalassemia are common health problems in north of Iran, and about 15% of Mazandarani people are carriers for alpha globin gene deletions, hence premarital screening program can help diagnosis of common and rare hemoglobinopathies. This case was the first report on Hb Daneshgah- Tehran from Mazandaran and the second one from Iran. The presented case showed that Hb Daneshgah- Tehran had haematological indices in normal range, and for the detection of this Hb variant, electrophoresis and PCR sequencing methods should be applied.
Key words: Alpha-globin, Capillary electrophoresis, Hemoglobin

Introduction

To date, more than 400 different hemoglobin (Hb : An oxygen-transporting protein) variants causing structural alteration of α-globin protein have been identified, many of whom are created as a result of point mutations in either of the two α-globin genes (HBA2 or HBA1). These DNA alterations lead to corresponding amino acid residues substitutions (1). Many of the variants do not have any noticeable clinical symptoms; however, some can affect Hb function and lead to erythrocytosis, Hb instability, and haemolytic anemia (2). Hb Daneshgah-Tehran was reported for the first time in a 57-year- old- Iranian man by Rahbar et al., in 1973 (3) and since then this variant has not been reported from Iran. The presented case was the first report on Hb Daneshgah-Tehran from north of Iran and the second one from Iran.

Case Report

An-8-year-old-girl was referred to Fajr medical laboratory (Sari, Iran) for routine haematological analysis in September 2017. The haematological indices were in normal range, while Hb electrophoresis using capillary electrophoresis method (Sebia Capillarys 2, France) showed a peak in the location of Hb S variant associated with small amount of Hb A2 variant at zone 1(Figure1). The capillary software suggested several Hb variants for this case except for Hb Daneshgah-Tehran. The metabisulphite test showed that the patient did not carry Hb S variant. Family analysis of the patient showed that her father had the same electrophoresis pattern (Table I). In order to find the possible changes on α-globin genes, the entire regions of HBA1 and 2 genes were investigated using sequencing analysis. Sequencing results revealed that the case was heterozygote for c.218 A> G mutation on α1-globin gene that converted His at

position 72 of alpha globin chain to Arg. This variant of Hb is named Hb Daneshgah- Tehran (Codon 72 CAC>CGC p.His72→Arg).

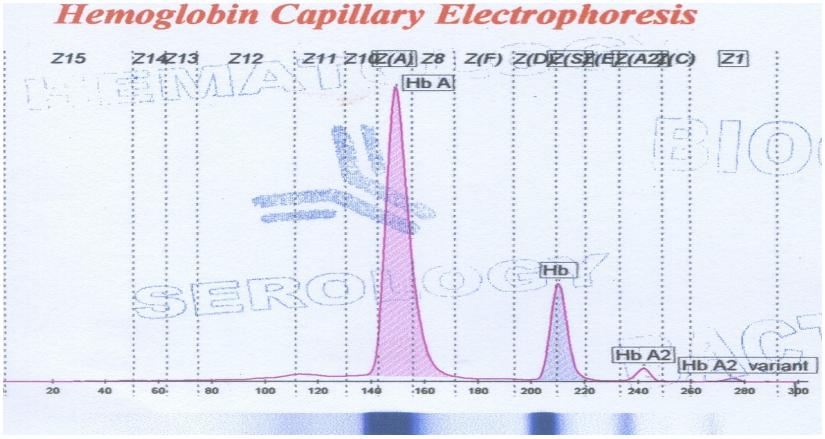

Figure 1. Capillary electrophoresis result of a patient with Hb Daneshgah- Tehran

Table I: Hematological indices of the patient and her parents

	Age (y)	RBC (x 10^6/µl)	Hb (g/dL)	Hct (%)	MCV (fl)	MCH (pg)	MCHC (g/dl)	Hb-A (%)	Hb-A2 (%)	Hb Daneshgah-Tehran	Hb A2Variant	Hb-F (%)
Case	8	8.4	12.2	36.2	76.4	25.7	33.7	78.1	2.2	19.2	0.5	**<0.5**
Father	35	5.45	16.2	47.7	87.5	29.7	34.0	79.3	1.9	18.4	0.4	**<0.5**
Mother	30	4.23	12.4	36.8	86.9	29.3	33.7	97.3	2.7	-	-	**<0.5**

Discusssion:

Thalassemia and hemoglobinopathies are the most common hereditary disorders worldwide. That regarding the number of defected genes and type of mutations wide spectrum of clinical manifestation ranging from an asymptomatic carrier to a very severe anemia incompatible with life is anticipated in affected subjects. There are two copies of α- globin gene on chromosome 16 at 16p13.3 position, and α- globin gene deletions are the most frequent type of mutations (4, 5). Alpha and beta thalassemia are common health problems in north of Iran, and about 15% of Mazandarani people are carriers for alpha globin gene deletions (6, 7). Besides, several cases with Hb D (8), Hb J-Toronto (9), and Hb Setif (10) were reported from that region. In the present report, the Hb Daneshgah-Tehran on α- globin gene for the first time was identified in north of Iran.

The first identified case with Hb Daneshgah-Tehran in 1973 had normal haematological indices expect hypochromia, while his affected child did not have that problem (3). Electrophoresis at alkaline pH on cellulose acetate showed a slow moving Hb like Hb S and small amount of Hb A2 variant. The presented case also showed a peak like Hb S in combination with small amount of Hb A2 variant (0.5) using capillary method. This variant of Hb for the second time was detected in an Argentinian-24- year- old- female in 1985 and like the presented case she had normal haematological indices(Hb 13.3 g/dl, red blood cell count(RBC) 4.7 x 106 /µl, Mean corpuscular volume (MCV) 89 fl, and Mean Corpuscular Hemoglobin (MCH) 27.9 pg) (11). Alpha-globin structural

variants analysis of 135,000 Brazilian individuals revealed that among the investigated cases 5 had α Daneshgah-Tehran α/αα genotype (12). Although the homozygote form of Hb Daneshgah-Tehran and its coinheritance with other heamoglobinophaties were not reported, the identified heterozygote subjects showed that Hb Daneshgah-Tehran was abnormal Hb variant without any significant haematological or clinical consequences. Moreover, for the detection of Hb Daneshgah-Tehran, DNA analysis is required.

Conclusion

This case was the first report on Hb Daneshgah- Tehran from Mazandaran and the second one from Iran. The presented case showed that Hb Daneshgah- Tehran had haematological indices in normal range, and for the detection of this Hb variant, electrophoresis and PCR sequencing methods should be applied.

Conflicts of Interest

There is no conflict of interest.

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