

Molecular identification of a rare hemoglobin variant, Hb J-Iran [beta77(EF1)His->Asp], in Denizli province of Turkey

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ABSTRACT

Hb J-Iran [beta77(EF1)His-Asp], a rare hemoglobin variant that does not present health problems, was reported for the first time in the Turkish population in 1986. Our case is the fourth case reported in Turkey and the first case from the Denizli province.

Key Words: Hb J-Iran, abnormal hemoglobin

ÖZET

Hb J-Iran [beta77(EF1)His-Asp] herhangi bir sağlık sorunu yaratmayan nadir hemoglobin türlerinden olup Türkiye'de ilk kez 1986 yılında bildirilmiştir. Bu çalışmada sunulan heterozigot olgu ülkemizde bildirilen dördüncü, Denizli yöresinde ise ilk olgu olma özelliğini taşımaktadır.

Anahtar Sözcükler: Hb J-Iran, anormal hemoglobin

INTRODUCTION

There has been enormous effort to identify abnormal hemoglobin in Turkey since the first reported Hb S case by Aksoy *et al.* To date, 42 hemoglobin variants have been identified in the Turkish population [1]. The Denizli province is located in the Aegean region of Turkey. Premarital screening has been conducted by the Turkish Ministry of Health Hemoglobinopathy Center in Denizli since 1995. The most prevalent abnormal variant in the Denizli province is Hb D-Los Angeles, with a frequency of 57.8%; Hb S is the second most frequent anomaly (21.9%). Hb G-Coushatta, Hb E-Saskatoon and Hb C are also observed at frequencies of 15.6%, 3.1% and 1.6%, respectively [2]. Hb J-Iran [beta77(EF1)His-Asp] was reported by Rahbar *et al.* [3] in 1967 from Iran. In Turkey, the first Hb J-Iran [beta77(EF1)His-Asp] case was reported by Arcasoy *et al.* [4]. There have been three reported cases from the Turkish population, from Ankara, Antalya and Muğla [4-6]. Here we report the fourth heterozygous case of Hb J-Iran [beta77(EF1)His-Asp] detected during a premarital screening program in the Denizli province of Turkey.

CASE REPORT

This study reports observation of the heterozygous Hb J-Iran [beta77(EF1)His-Asp] in a 25-year-old male living in Denizli city located in the Aegean region of Turkey. This variant was observed during a premarital screening program, which is being routinely conducted in the Denizli Hemoglobinopathy Center of the Turkish Ministry of Health. Written informed consent was obtained for laboratory tests and DNA analysis from the propositus. Total blood count values were normal and there were no clinical findings. There was one fast moving band ahead of Hb A on both alkaline and acid electrophoresis done by agarose based gels (Figure 1). Hb A₂ and Hb X values were 1.8% and 45.0%, respectively, as determined by DE-52 microcolumn chromatography. DNA was isolated with the standard phenol-chloroform extraction method. Non-radioactive fluorescence dye-based DNA sequencing was performed by BECKMAN Coulter CEQ8000 genetic analysis system. For the sequencing template preparation, beta globin gene exon 1 and exon 2 were amplified by the forward primer PAM604 (5'-GGTTGGCCAATCTACTCCCAGGAG-3') and reverse primer PAM607 (5'-CCCTCCTATGACATGAACCTAACCAT-3') resulting in 652 bp

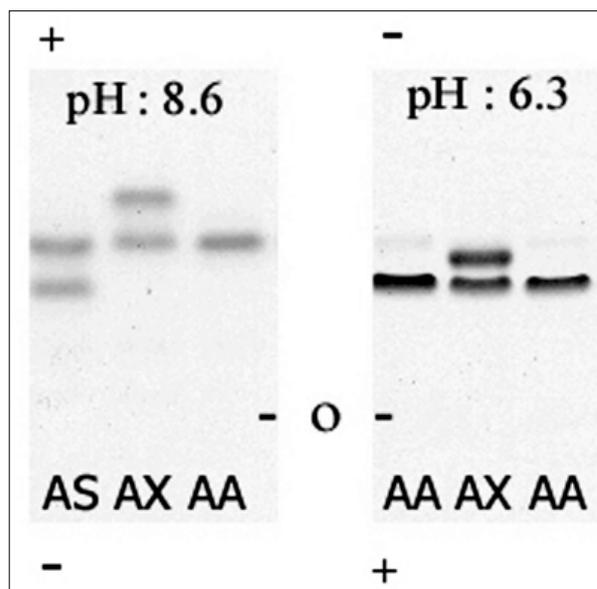


Figure 1. Hemoglobin electrophoresis of Hb AX. (O: Origin of application)

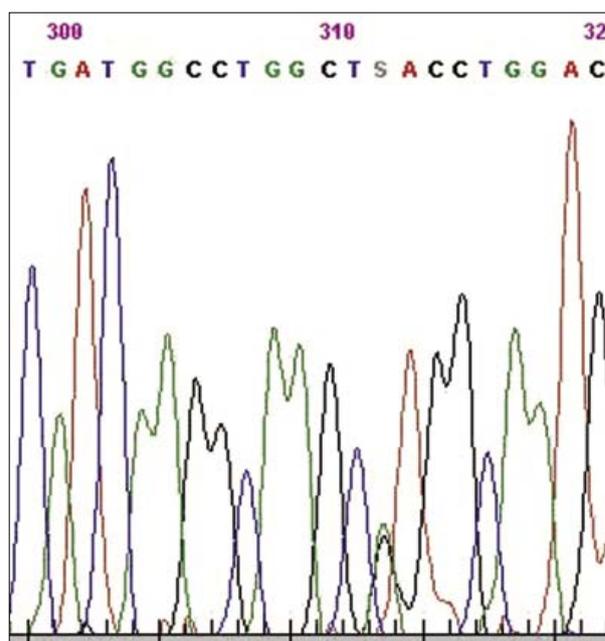


Figure 2. DNA sequencing of the Hb AX (SAC> C/G AC).

PCR product. PCR product was cleaned-up by Quiagen Clean-up kit before sequencing reaction. Forward primer PAM604 was used for sequencing reaction according to the manufacturer's instructions. Sequencing data showed the presence of CAC>GAC mutation as heterozygous form at codon 77 corresponding to the heterozygous Hb J-Iran [beta77(EF1)His-Asp] (Figure 2). The nucleotide sequence of Hb J-Iran was also submitted to NCBI GenBank [7].

DISCUSSION

Our heterozygous Hb J-Iran [beta77(EF1)His-Asp] propositus is the fourth case reported in the Turkish population. The other three cases were from Ankara, Antalya and Muğla^[4-6]. Since Muğla, Denizli and Antalya neighbor each other geographically, Hb J-Iran [beta77(EF1)His-Asp] cases are likely to be observed more frequently in this region during screening and/or premarital detection programs in the future. Therefore, we concur with Yenice *et al.*^[6] who suggested that Hb G-Coushatta [beta22(B4)Glu-Ala] and Hb J-Iran [beta77(EF1)His-Asp] seem to be sporadic and not rare for the Turkish population. Considering the increased number of well-equipped local university laboratories in different parts of Turkey, many different hemoglobin variants have been reported and the incidence will no doubt increase in the future. Hemoglobin variants, which do not present health problems even in homozygous cases, will be detected in increasing numbers in premarital screening programs in the coming years. These hemoglobin variants will contribute to basic hemoglobin research, as far as different globin gene interactions are concerned, and to protein structure-function studies as a well-

defined protein model system. On the other hand, a national hemoglobin registry should be established. Altay^[1] points to this problem, stating that the exact number of subjects having abnormal hemoglobins in Turkey is not known due to the absence of a national registry system for these conditions. The heterozygous Hb J-Iran [beta77(EF1)His-Asp] case reported here is the first case from Denizli and the fourth case in the Turkish population. Our results regarding abnormal hemoglobin research during the premarital screening program confirm that the number of hemoglobin variants that do not cause health problems will be identified more intensively in the Denizli province of Turkey.

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