

First Observation of Hemoglobin G-Waimanalo and Hemoglobin Fontainebleau Cases in the Turkish Population

Türk Toplumunda Gözlenen ilk Hemoglobin G-Waimanalo ve Hemoglobin Fontainebleau Olguları

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To the Editor,

Deletional alpha thalassemia mutations can be detected by various methods such as reverse dot blot, gap-polymerase chain reaction (gap-PCR), and multiplex ligation-dependent probe amplification. Point mutations leading to abnormal hemoglobins (Hb) are also observed in common populations. When a point mutation is suspected, resequencing of the alpha genes has become a routine procedure [1]. Hb G-Waimanalo is a silent mutation characterized by a substitution to aspartic acid from asparagine at codon 64 [A64(A2), Asp>Asn] [2]. Hb Fontainebleau is a slightly unstable mutation characterized by a substitution to alanine from proline at codon 21 [A21(A2), Ala>Pro] [3]. To date, they have not been reported from Turkey [4]. Here we present two cases with abnormal Hbs.

Case 1: NB, a 33-year-old female, was admitted to the hemoglobinopathy diagnostic center for premarital thalassemia testing. Her complete blood count (CBC) was found to be normal with 24.2% abnormal bands in high-performance liquid chromatography (HPLC) (Table 1). A blood sample was studied further at the genetic diagnostic center. Following DNA extraction with a commercial kit (Roche, Mannheim, Germany) and amplification of the whole beta globin gene by standard protocols of PCR and DNA sequencing (Applied Biosystems, USA), mutation was not found in the beta globin gene. Sequence analyses of alpha genes A1 and A2 were performed and an abnormal Hb in the HbA2: c.193G>A change was detected. This change in the HbA2 gene was at codon 64 GAC>AAC (Asp>Asn), known as Hb G-Waimanalo.

Case 2: ND, a 37-year-old, female, was also admitted to the hemoglobinopathy diagnostic center for premarital testing. She had normocytic anemia in CBC and abnormal bands detected at 16.2% in HPLC. This band result was found to be lower because it may have been fragmented with results of slightly unstable mutation (Table 1). Her blood was studied by the same method at the genetic diagnostic center. Mutation was not found in the beta globin gene. The HbA2 and HbA2 genes were then selectively amplified by standard protocols of PCR. DNA sequencing revealed a G to C change at nucleotide position 21 in the HbA2 gene. This mutation at codon 21 GCT>CCT (Ala>Pro) in the HbA2 gene is known as Hb Fontainebleau.

Hb G-Waimanalo is an abnormal Hb and asymptomatic. It was reported in association with alpha and/or beta thalassemia [5,6]. There were no hematological findings in our case; the beta gene was found to be normal. Hb G-Waimanalo was identified in five cases in a study in China [7].

Hb Fontainebleau was described as a silent mutation for the first time in a family of Italian origin [8]. Two cases with mild microcytosis were reported in New Zealand [3]. Our patient had normocytic anemia based on CBC and lower abnormal bands by reason of a slightly unstable mutation in HPLC. Beta gene analysis was normal. So far, a total of 22 cases including 1 homozygous case without clinical findings and 11 heterozygous cases have been reported from premarital screening in the United Arab Emirates [9].

In conclusion, abnormal bands, especially in HPLC, should be investigated with sequence analysis to corroborate alpha and/or beta globin gene mutations.

Table 1. The results of complete blood count and high-performance liquid chromatography in the presented cases.

Case	Hb (g/dL)	Hct (%)	RBC (10 ¹² /L)	MCV (fL)	MCH (pg)	HbA1 (%)	HbA2 (%)	HbF (%)	Abnormal bands (%)
Case 1	13.3	39.4	4.31	89.1	34.6	73.5	1.6	0.3	24.6
Case 2	11.1	37.8	4.66	83.1	24.4	72.0	1.2	0.6	16.2

Hb: Hemoglobin, Hct: hematocrit, RBC: red blood cell, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin.

Keywords: Abnormal hemoglobins, Hemoglobin G-Waimanalo, Hemoglobin Fontainebleau

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Authorship Contributions

Concept: Duran Canatan, Design: Duran Canatan, Data Collection or Processing: Serpil Delibaş, Gülsüm Yazıcı, Vildan Çiftçi, Analysis or Interpretation: Türker Bilgen, İbrahim Keser, Gülsüm Yazıcı, Vildan Çiftçi, Literature Search: Duran Canatan, Türker Bilgen, Writing: Duran Canatan.

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Serum Lipids in Turkish Patients with β -Thalassemia Major and β -Thalassemia Minor

Türk β -Talasemi Majör ve β -Talasemi Minör Hastalarının Serum Lipidleri

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To the Editor,

It is well-known that β -thalassemia is associated with changes in plasma lipids and lipoproteins [1,2,3]. To our knowledge, no data are available on lipid profiles in Turkish β -thalassemia major (TM) and β -thalassemia trait (TT) patients together. The aim of this study was to evaluate lipid profiles in two groups of patients with β -TM and β -TT and to compare them with healthy controls. The study included a total of 311 subjects. Group 1 included 131 β -TM patients (mean age: 16.3 \pm 7.58 years). Group 2 included 68 β -TT patients (mean age: 7.25 \pm 4.43 years). Group 3 consisted of 112 age- and sex-matched healthy controls (mean age: 9 \pm 4.7 years). Serum ferritin level was 2487 \pm 1103 (range: 661-5745) ng/mL in Group 1. In comparing the correlation between ferritin and lipid parameters, while a significantly negative relationship was detected between ferritin and high-density lipoprotein cholesterol (HDL-C) ($p=0.000$, $r=-0.602$), a

significantly positive relationship was detected between ferritin and triglyceride (TG) levels ($p=0.02$) in TM patients. Serum lipid profiles of the 3 groups are shown in Table 1.

Previous studies have shown total serum cholesterol, HDL-C, lower low-density lipoprotein cholesterol (LDL-C), and higher TG in β -TM patients compared to healthy controls [1,2,3]. In our study, we found lower serum total cholesterol, lower HDL-C, LDL-C, and higher TG in β -TM patients compared to healthy controls. The pathophysiology of hypocholesterolemia in thalassemia remains obscure, although several mechanisms have been proposed; plasma dilution due to anemia, increased cholesterol requirement associated with erythroid hyperplasia, macrophage system activation with cytokine release, and increased cholesterol uptake by the reticuloendothelial system [4,5]. Previous studies reported different variations in lipid profiles of β -TT patients [6,7]. In our study, we demonstrated