

β 121 Mutation with Coexisting Pernicious Anemia (A Case Report)

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In this report, the latest articles related to β 121 mutations have been reviewed and the association between β 121 mutation and pernicious anemia are first presented.

Key words: β 121 mutations, pernicious anemia

β 121 mutasyon ve pernisiyöz anemi birlikteliđi (Olgu sunumu)

Bu olgu sunumunda bir vaka nedeniyle β 121 mutasyonlar ile ilgili son literatür gözden geçirilmiř ve β 121 mutasyon ve pernisiyöz anemi birlikteliđi ilk kez bildirilmiřtir.

Anahtar kelimeler: β 121 mutasyonları, pernisiyöz anemi

Hb D Los Angeles, Hb O Arab, Hb St. Francis and Hb Beograd are formed by a single base substitution at the 121st codon of the third exon of the Beta globin gene. Hb D Los Angeles and Hb O Arab are the most common abnormal hemoglobins in Türkiye (1).

In previously reported β 121 mutation, there was no pernicious anemia. Therefore in this report, we present a β 121 mutation with pernicious anemia for the first time.

CASE REPORT

A 51 year-old-female from Erzurum. She was admitted to our clinic with complaints of pallor and fatigability.

Physical examination revealed a splenomegaly and hepatomegaly 6 cms below the right costal margin. The findings in neurologic examination were bilateral Hoffman's reflex positive and deep tendon reflexes hyperactive.

Laboratory examination revealed hemoglobin 5.9 g/dl, hematocrit 19.4 %, reticulocyte less than 1%, white blood cells 4800/mm³, thrombocyte 72000/mm³, ESR 25 mm/1st hour. On peripheral smear, a few target cells, hypersegmente neutrophils were noted. On bone marrow imprint examination was erythroid hyperactivity and megaloblasts. Haptoglobine was 1.8 g/L (0.7-3.8), direct and indirect coombs were negative, vitamin B12 was 76 pg/ml (220-940), folic asit was 12 ng/ml (3-17), gastrin was 250 pg/ml (25-125). In endoscopic examination and biopsy were seen chronic atrophic gastritis. In Schilling's

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urinary excretion test. radioactivity was assayed in urine specimen collected 72 hours thereafter was 5% (7%). This value was corrected toward 17% by administering intrinsic factor with the orally vitamin after 24 hours. Reticulocyte increase was noted 5 days after Schilling's test. With Cellulose acetate electrophoresis the mobility of the abnormal hemoglobin was identical to Hb S. Agar gel electrophoresis indicated that it was not Hb S and sickling was negative, solubility was negative, osmotic fragility was increased. Abnormal hemoglobin was identified as Hb D 30.8 % and Hb A2 was 1.2 %, Hb F normal. Then the DNA was extracted from peripheral blood mononuclear cells and the third exon of β -globin gene was amplified by polymerase chain reaction (PCR) so as to include the codon 121 for mutation analysis, and PCR product was digested with Eco RI in Pediatric Hematology and Molecular Pathology Department (Medical Faculty of Ankara). Therefore PCR also suggested that the abnormal Hb is a β 121 mutation.

Patient improved with the treatment of 1000 μ g of B12 intramuscularly monthly. On the 6th month after initiation of vitamin B12 treatment, the hematocrit was increased 31 % and the findings in neurologic examination were within normal limits. Patient's family was not screened because she didn't agree.

DISCUSSION

Hb S, Hb D Los Angeles and Hb O Arab are the most common abnormal hemoglobins in Türkiye (1). Hb D Los Angeles, Hb O Arab, Hb St. Francis and Hb Beograd are β 121 mutation variants. These abnormal hemoglobins are formed by a single base substitution at the 121st codon of the third exon of the Beta globin gene.

Hemoglobin (Hb) D was originally described as a variant of Hb A which on electrophoresis behaved like Hb S but did not cause the sickling phenomenon (2). When it was found that the original Hb D described in Los Angeles was identical to Hb D Punjab, the term Hb D Los Angeles was introduced. Hb D was first described in a patient with atypical hemolytic anemia who was a double heterozygote (2). Biochemically Hb

D is heterogenous and so far it has been found to occur in 4 forms: Heterozygous Hb D trait, Hb S-D disease, Hb D thalassemia and homozygous Hb D disease. Simple heterozygous Hb D is more than others. Review of the Turkish literature as well as of our file indicated that heterozygous (3, 4, 5) and homozygous (6, 7, 8) Hb D have been detected in different families of various district of Türkiye. In addition four different families with structurally unknown Hb D are present (9).

Hb O Arab (10, 11, 12), and Hb Beograd (13) reported previously from Türkiye and North Cyprus. But Hb St. Francis haven't been reported from Türkiye yet.

The differential diagnosis between Hb O Arab and other β 121 mutations also can be made by PCR and Restriction Endonuclease Mapping methods. But they can not be used to differential diagnosis of Hb D Los Angeles from Hb Beograd

The latest articles on related with β 121 mutation have been reviewed and the association between β 121 mutations and vitamin B12 deficiency are first presented in our patient. This association may be purely coincidental but this case suggest the possibility of coexistence of hemoglobinopathies and other anemias.

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