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Case Report

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Homozygous hemoglobin D with alpha thalassemia: case report

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ABSTRACT

Hb D is a clinically silent condition, but co-inheritance of Hb D with sickle cell or thalassemia produces clinically significant conditions like sickle cell anemia or thalassemia intermedia and chronic hemolytic anemia of moderate severity. Here we present a case of homozygous Hb D with alpha 3.7kb deletion and phenotypic effect on patients. Diagnosis of Hb D patient was performed by high performance liquid chromatography (HPLC) and complete blood count was measured by automated cell analyzer. Molecular study for common alpha deletions done by Gap-PCR. A homozygous Hb D patient with alpha thalassemia was present mild clinical manifestations with normal reticulocytes and red cell indices. Thus observed case conclude the co-existence of alpha 3.7 deletions with homozygous Hb D present mild clinical –hematological picture.

INTRODUCTION

There are several hemoglobin D variants, amongst them Hb D-Punjab (also known as Hb D-Los Angeles) is by far the commonest [1, 2]. Hemoglobin D disease is very rare and affects both sexes equally. The disease occurs most often in people whose ancestors come from Pakistan and Northwestern India and Iran. It also occurs in people from England, Ireland, Holland, Australia, China and the Middle East [3, 4]. Structural form of Hb D is β 121 Glu-Gln [5]. Subsequently, several hemoglobin's have been described that have the same electrophoresis pattern and solubility as Hb D, and each has a mutation within the β globin gene. These include (Hb D-Iran, β 22 Glu→Gln) Hb D-Bushman (β 16 Gly-Arg), Hb D-Ouled Rabah (β 19 Asn-Lys), Hb D-Granada (β 22 Glu-Val),Hb D-Iran (β 22 Glu-Gln), Hb D-Ibadan (β 87 Thr-Lys), Hb D-Los Angeles (β 121 Glu-Gln), and Hb D-Neath (β 121 Glu-Ala) [6-8]. Hemoglobin D-Punjab occurs with greatest prevalence (2%) in Sikhs in Punjab,

India, whereas Gujarat, the province in the west from where the case was reported, has a prevalence rate of 1%. Hb D occurs in four forms: heterozygous Hb D trait, Hb D-thalassemia, Hb S-D disease and the rare homozygous Hb D disease, which is usually associated with mild hemolytic anemia and mild to moderate splenomegaly [2, 9].

However in India, lack of data with co-existence of alpha thalassemia with hemoglobin D. Thus we presenting interaction of alpha thlassemia with HbD and phenotypic effect on patients.

CASE REPORT

Patient was a 15 year old boy from Indian State Uttar Pradesh. He presented anemia, jaundice with fever and none of any other significant complications. Parents of the patient were not available for their investigations. Patient had never blood transfusions. On physical examinations patients spleen was enlarged, none of any muscular and skeleton deformities seen.

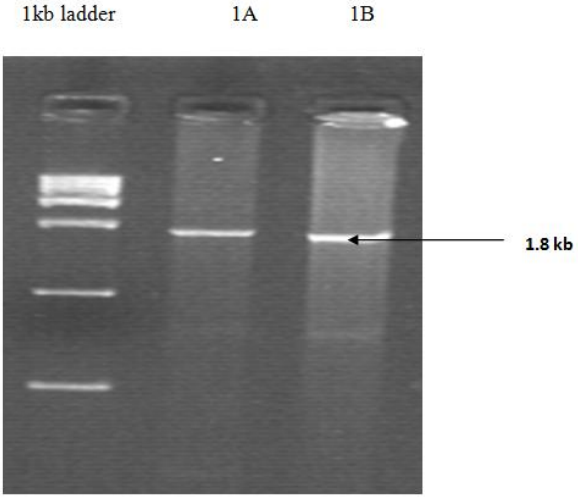

Figure-1. α3.7kb deletion in heterozygous condition(Primer A+ C (1A) normal and A+ B (1B) mutant are amplified in separate tubes because their product has the same size of 1.8kb)

MATERIALS AND METHODOLOGY

5 ml venous blood collected in an anticoagulant vial (3.2% sodium citrate). Complete blood count and red cell indices were measured by automated Analyzer (SYSMEX K-4500, Kobe Japan) Giemsa-stained peripheral blood smear were examined for red cell morphology. Quantitative assessment of hemoglobin, HbF, HbA, HbA2, HbD was performed by HPLC (Bio-Rad-VariantTM Bio Rad, CA, USA). Molecular study four common alpha deletions done according to published literature [10-12].

RESULT AND DISCUSSION

The patient's peripheral smears showed microcytic hypochromic red cells, decreased osmotic fragility and target cells with spherocytes. Hb D was 89.5% due to homozygous condition. Red cell indices; RBCs -3.16 millions/µl,HGB-8.8 g/dl,HCT-28.5%, MCV-90.2 fl,MCH-27.8 pg,MCHC-30.9 /dl were in normal ranges. Serum Iron was 53.2 µg/dL. HbA2 (1.5%), HbF (1.2%), were in normal ranges while Hb A was 3.3%. Alpha deletions (-α3.7.α4.2, SEA and SA) study done and patient was heterozygous for alpha 3.7kb deletions.(Gel picture shown in figure-1) Hemoglobin D is the fourth most common hemoglobin variant, which developed as a response to the selective pressure of malaria. It is most often found in people living in India, Pakistan, England, Ireland, Holland, Australia, China, Iran, Turkey and their descendants. Homozygous Hb DD is rare and a relatively mild disease. Heterozygous Hb D/β-thal is more common and more serious. Most people with hemoglobin D disease have mild anemia, which may be associated with a slightly enlarged spleen. Hemoglobin DD red blood cells look like a bull's eye target with a dark center [3]. Though Hemoglobin D is not very uncommon in India, its homozygous form is very rare [2, 4, 9] and very few case reports have been reported [9]. Heterozygous state of Hb D does not produce any clinical or hematological symptoms, but its association with Hb S produces clinically significant, but less severe condition mimicking sickle cell anemia [2, 13]. Even the different Hb D variants seem to produce different severity of disease with Hb S. Hb D-Punjab produces clinically significant condition like sickle cell disease, whereas Hb D Iran and Hb D Ibadan are non-interacting and produce benign conditions like sickle cell trait [14]. A Saudi family reported in the HbD trait with alpha thalassemia that showed mild phenotypic behaviour [15]. Hemoglobin D disease is usually clinically silent with no special treatment required. A mild hemolytic anemia usually develops in the first few months of life as the amount of fetal hemoglobin decreases [3]. The presented case of HbD disease showed mild

phenotypic nature. It assumed the homozygous conditions of HbD disease dose not produce serious complications to the patients. Co - existence of alpha thalassemia may affect the HbF and/or HbA2 level [16, 17]. Reticulocytes and red cell indices were normal and clinical symptoms were improved in presented case; this may be due to co-inheritance of alpha 3.7 kb deletions. Many literature report the co-existence of alpha thalassemia with hemoglobinopathies, improve the hematological as well as clinical manifestations [18-20]. It may be the possible factor that heterozygous forms of alpha 3.7 deletions alter the value of MCV in HbD patients. A previous report conclude the homozygous hemoglobin D present clinical manifestation from mild to moderate/severe microcytic anemia while chronic hemolytic state in compound heterozygous i.e. HbSD and HbDβ-thalassemia. However the study based on cation-exchange high performance liquid chromatography ant co-existence factors not described [21]. Observation of the case concludes the co-inheritance of alpha 3.7kb deletion present mild clinical – hematological picture in homozygous hemoglobin D patient.

CONFLICT OF INTEREST

The authors have no conflict of interest.

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