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Sickle cell hemoglobin D disease
First reported case in IRAN

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Introduction: Hemoglobin in man is normally F variant in fetal life and 63-91% in early infancy, A and A2 variant there after. Hb A accounts for 97-98%, Hb A2 1.5-3. 5% of normal adult hemoglobin. Each of these Hbs has specific genetic sequences and chemical characteristics. There are several other types of abnormal Hb other than these three normal variants. Some of the important ones are: C,E,S, D,I,J,K, H,P,N,M, and L. The existence of each of these abnormal Hbs, when in a homozygote state, causes hemolytic anemia in man, usually has no abnormal sign as heterozygotes. It is necessary to ascertain the type of Hb for diagnosis of hemolytic diseases and heredity.

In this report two types of abnormal Hbs, D and S, were detected in the patient: each of which is inherited from one of the parents. This is genetically known as mixed heterozygous.

Hb S which was first described by Horrick in 1910

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causes a hereditary familial form of chronic hemolytic anemia essentially particular to negroes (2). This was nominated sickle cell anemia by Masson in 1922.

Hb D was first detected in four families and one unrelated individual(5). Hemoglobinopathy D is a rare disease. The disease Hb SD was first reported in a white American family in 1934(5).

In Hb S the α chain is normal but the β chain is abnormal where glutamic acid is replaced by valin.

Case report: Mr. F.K is an Iranian white young man 24 years old who came to the clinic with paleness, weakness, and swollen joints.

Past history: jaundice, right after birth, which lasted 10 days. At two months of age fever, anemia, and enlarged liver recovered by treatment. At the age of 11 months swollen and painful fingers also treated with no exact diagnosis. At the age of 14 months rheumatoid manifestation episodes. He had measles at the age of three, meningitis at seven and tonsillectomy at eight.

Familly history: parents were not related by blood. Both were clinically healthy. He has one sister and one brother both alive and normal but had a dead brother and a dead sister, the cause of death being an unknown infectious disease.

Observation, march 1, 1962: He was very pale with jaundice in the eyes and pain in the left omoplate. Oral temperature 38.5.c. Pulse rate 130/min. Blood pressure 120/70 Spleno-hepatomegaly.

Paraclinical findings: R.B.C. 2,300,000. W.B.C. 7,000

Identification of the abnormal hemoglobins have been carried out by Dr S. Rahbar. University of Teheran.

Segments 75%. Monocytes 16%. Lymphocytes 8%. Hb 7gr. Per 100 ml. A lot of sickle celles. Erythroblaste 8%. Reticulocyte 20%. Sedimentation rate 35 mm after 1 hour, 70 mm after 2 hours. Fibrinogen 740 mg/ 100ml. C.R.P. negative. A.S.T.O. 120 Todd units. Diret Vandenbergh: negative. Indirect Vandenbergh: positive. Thymol test 6 units of Maclagan. Cephalin cholesterol : negative . Protein electrophoresis: decreased albumin, increased γ globulin (albumin 45.7%, α_1 globulin 6.1%, α_2 globulin 9.2%, β globulin 15%, γ globulin 24%.). Total protein 6.4 gr/100 ml.

Hb electrophoresis of the patient performed on cellulose acetate led to the formation of a single band on the SD region. But in agar gel electrophoresis at H6 Hb. S and Hb. D were separated.

The same test on the patient's father resulted in two bands. one on the A region and one on the S region (AS). Hb electrophoresis of the mother also resulted to the formation of two bands, on the A and D regions (AD). (F.1). These were confirmed by agar gel electrophoresis.

Solubility test of the Hb from the patient in 2.24M. phosphate buffer was 31%, representing the existence of heterozygous SD.

The percentage solubility of Hb from the father and mother were 50 and 95 respectively, which correlated with heterozygous AS and AD.

Bone marrow puncture showed erythroid hyperplasia.

Falciformation tests of the patient and his father were positive after 3 hours but negative for the rest of the family. (F2,F3).

Increased resistance of the red corpuscles in isotonic saline solution: hemolysis started at 6% and completed in 2%.

Father
patient
Mother
Control

F: 1

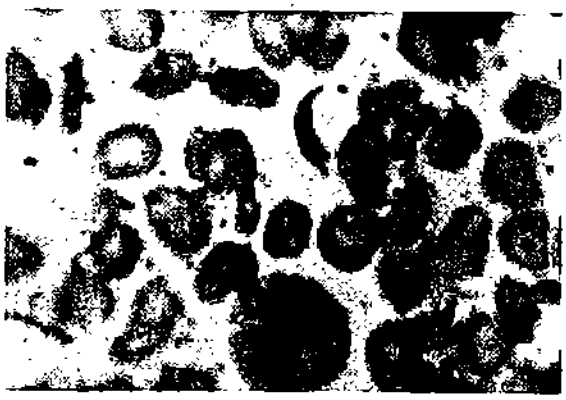

Fig. 2

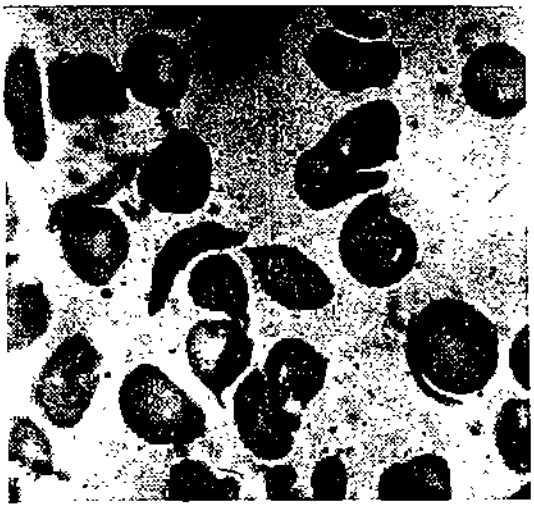

Fig. 3

Presence of bile pigments in urine.

Presence of eggs of ankylostomia in feces.

X ray: osteoporosis in ribs, thickened skull and calcification of post part of the skull.

With the diagnosis of sickle cell Hb D disease the patient was under transfusion and other palliative treatment until 29, April 1975 the patient remained under ambulatory treatment.

Paraclinical findings in 29th April 1975: W.B.C. 14.200 Hb 8.8 gr/100 ml. Reticulocytes 11.6%. Platelets: normal. Hematocrite 30% Eosinophiles 4%. Segments 54%. Lymphocytes 6%.

Anisocytosis, poikilocytosis, polychromatophilia, sickle cells and cabot's ring were present in a number of red blood cells (10).

As the diagnosis was confirmed by electrophoresis and falciformation test there was no need of repetition so transfusion and paliative treatments were continued.

Discussion: Sickle cell anemia (SS) is characterised

clinically by symptoms of anemia, attacks of pain with rheumatoid manifestation in joints, leg ulcers and morphologically by the presence of sickle shape red corpuscles and S Hb in peripheral blood. (1.3.6).

Although some exceptions exist evidence supports the theory that when the gene for sickling is heterozygous(AS), only sickle cell trait is found, where as the homozygous (SS) state produces sickle cell anemia. (1,4,6,7). When Hb S is deoxygenated it has the power of combining with itself into long rigid rods which twists the red blood cells out of shape, and this leads to the recognition of Hb S disease. (5.6.7).

The condition which facilitates the formation of sickle cell is the increased Hb S in low H and stasis in blood vessels which leads to thrombosis and infarction which causes aseptic necrosis, leg ulcers, hematosele, respiratory and nervous disorders. (2,3,5).

It has been considered that sickling of red corpuscles is a phenomenon found exclusively in the negro race or in individuals who have negro blood, However a number of cases in white families from the mediteranean region (Greek, Italian) have been reported. Though not sex limited, it may be somewhat commoner in females, and has been observed particularly in young individuals. (2,5,7,8,9).

Normally, hemoglobinopathy AD has no clinical symptoms. However, Hb AD on electrophoresis gives two bands, one in the A region and one in the D region which have the same magnitude of migration as the Hb S.

Therefore for differentiation of the two (S and D) sickling and solubility test and agar gel electrophoresis can be performed.

On the contrary, hemoglobinopathy SD causes the revealance of the following clinical symptoms in the patients:

Anemia, splenomegaly, echimotic spots and abdominal pain which are comparatively mild with respect to the SS disease. In peripheral blood target cells , polychromatophilia and a few normoblasts can be observed. Since Hb S and Hb D have the same electrophoresis migration rate in alkalin buffer, they are differentiated by sickling and solubility tests and agar gel electrophoresis.

A sickling test for the Hb of patients with the SD disease is positive with a percent solubillity of 31.

Summary

A case of sickle cell Hb D disease is reported in a young Iranian male, the father of whom carried an AS sickle cell trait and the mother an AD trait . This disease was diagnosed by Hb electrophoresis, agar gel electrophoresis sickling and solubility tests.

This is the first case of sickle cell HB D disease reported in IRAN.

Bibliography

1- *Lehman, H. and Huntsman. R.G.*
"Man's Hemoglobin",
North Holland 1966, Page 99-126.

2- *Cecil-Loeb*
"Text book of Medicine"
Edited by: Paul B. Beeson, M.D.,
and Walsh McDermatt, M.D., Eleventh Edition 1963
Page 1099-1104.

3- *The "Merck Manual"*
Eleventh Edition 1967, Page 41-44.

4- *Davidson, S.*
"The Principles and Practice of Medicine"

Eleventh Edition 1965, Page 579-655.

5- *Maxwell M. Wintrobe, M.D. Ph. D.*
"Clinical Hematology"
Sixth Edition LEA and Febiger, Philadelphia
Page 688-707.

6- *Rahbar, S. Beale D. Isaaes, W. and Lehmann H.*
"Abnormal Hemoglobines in Iran Observation of
New Variant of Hemoglobine J. Iran."
Brit Med. J. 1967 (1) 674-677.

7- *Rahbar S. Kinderlerer, L. and Lehmann H.*
"Hemoglobine L. Persian Gulf"
Acta Hematologica 42: 169-175-, 1969.

8- *Lorkin, P.A. chastorworth D. Lehman H. Rahbar S.*
Lielngo L. Trichinda S. Two hemoglobin Q"
Brit. J. hematology (1970) 19-117.

9- *With by and Hitton C.J.C.*
Disorders of the blood, 9ed J. and A. Churchil Ltd;
London, 361-368.

10- *Medical file; Bahrami Hospital.*