Haemoglobin Lepore_{Boston} in a Turkish family

AYHAN O. ÇAVDAR and AYTEN ARCASOY

From the Haematology Division, Department of Pediatrics, Medical School of Ankara University, Ankara, Turkey

Summary. Haemoglobin Lepore was demonstrated in four members of a Turkish family. It was found in the heterozygote state and was associated with erythrocyte morphology similar to that observed in the β thalassaemia trait. The average concentration of haemoglobin Lepore was 8.1% of the total haemoglobin. Structural analysis showed that the Lepore haemoglobin was the Lepore_{Boston} type. This is the first reported instance of the occurrence of haemoglobin Lepore in Turkey.

Haemoglobin Lepore was first discovered in an Italian family by Gerald and Diamond in 1958. Several Lepore type haemoglobinopathies have been seen within the past 17 years (Ostertag and Smith, 1969; Pearson, Gerald, and Diamond, 1959; Pearson et al, 1962).

Haemoglobin Lepore is now accepted as an abnormal haemoglobin made up of two Lepore (δβ) chains and of two normal α chains (Ostertag and Smith, 1969). The Lepore chain is made up of the N-terminal end of part of the δ chain joined to a portion of the C-terminal end of the β chain (Ohta et al, 1971). Baglioni (1962) showed that Lepore haemoglobins were the fusion products of unequal crossing over between δ and β structural genes.

Three different types of haemoglobin Lepore have now been identified each resulting from genetic crossovers at different sites; namely haemoglobin Lepore_{Boston}, haemoglobin Lepore_{Hollandia} and haemoglobin Lepore_{Baltimore} (Ostertag and Smith, 1969; Williams et al, 1972). The fusion in haemoglobin Lepore_{Boston} has occurred somewhere between residue 87 of the δ chain and 116 of the β chain (Ostertag and Smith, 1969; Rahbar, Golbani-Moghadam, and Saso, 1974). The crossing over in haemoglobin Lepore_{Hollandia} is between the nucleotides coding for δ_{22} Ala and β_{80} Thr (Barnabas and Müller, 1962). In haemoglobin Lepore_{Baltimore} the crossover is between residue 50 of the δ chain and residue 86 of the β chain (Ostertag and Smith, 1969).

It is of considerable interest that the Lepore haemoglobins have been found almost exclusively in Mediterranean, Papuan, and Negro populations (Barnabas and Müller, 1962; Beaven et al, 1964; Fessas, Stamotoyannapoulos, and Kerakis, 1962; Jonxis, 1962; Ostertag and Smith, 1969; Quattrin et al, 1967; Ranney and Jacobs, 1964). However, no case of haemoglobin Lepore has yet been shown in Turkey. A description of haemoglobin Lepore occurring in a Turkish family forms the basis of this report.

Subject and methods

Blood counts, haemoglobin, and packed cell volume were measured by conventional methods. Starch block and starch-gel electrophoreses and the determination of haemoglobin F were performed by previously described techniques (Çavdar and Arcasoy, 1971). A solubility test was carried out according to Itano's method (Lehmann, Huntsman, and Young, 1966) and sodium metabisulfite was used for a sickling preparation (Pearson et al, 1959).

The structural identification of the abnormal haemoglobin was performed at the MRC Abnormal Haemoglobin Unit, Cambridge, by previously described methods (Arcasoy et al, 1974).

Case report

The propositus was a 10-year-old boy who was first brought to our attention about a year ago because of fever and a swollen neck. Physical examination showed a slight pallor, marked bilateral cervical lymphadenopathy, and tonsillitis. A differential white cell count suggested the diagnosis of infectious mononucleosis. The blood counts were repeated after the patient recovered from the infection, because of an alteration in red cell morphology noticed on the initial blood film.

The haematological findings were as follows: Hb,
11.2 g/dl; RBC, $4.3 \times 10^{12}$/l; PCV, 31%; WBC, 6.52 × $10^{9}$/l; platelets, $350 \times 10^{9}$/l; MCV, 74 fl; MCH, 26 pg; MCHC, 28%. The blood film again showed hypochromia, anisopoikilocytosis, elliptocytosis and a few target cells and basophilic stippling. These findings were considered to be compatible with heterozygous β thalassaemia and further haematological studies were performed. On starch block electrophoresis at pH 8.6, an abnormal fraction was observed in the position of haemoglobin S (Fig. 1). Starch gel electrophoresis also confirmed this finding. However, sickling and solubility tests were both negative. Furthermore the abnormal haemoglobin accounted for 8% of the total haemoglobin of the patient. The haemoglobin A₂ level was 2.1% (normal: 2.4 ± 0.4%) and the haemoglobin F was slightly raised at 4.7%. The serum iron level was a little raised to 175 μg/dl, and TIBC was decreased to 220 μg/dl. These findings were similar to those found in previously described haemoglobin Lepore heterozygotes.

**Family study**

We investigated the family over three generations and three additional cases were also found to be the carriers of haemoglobin Lepore, namely the father, the paternal uncle, and the paternal grandfather (Fig. 2). The father aged 42 years was not anaemic. His blood count was as follows: Hb 13.0 g/dl; RBC, $4.74 \times 10^{12}$/l; PCV, 40%; MCV, 85 fl; MCH, 27.5 pg; the red cells were hypochromic and there was anisopoikilocytosis, target cells, and ovalocytes on the film. The serum iron was 180 μg/dl and TIBC 330 μg/dl. The paternal grandfather aged 91 years was anaemic. His blood count was as follows: Hb, 10.2 g/dl; RBC, $3.58 \times 10^{12}$/l; PCV, 35%. His red cells showed anisopoikilocytosis, hypochromia, elliptocytosis, and target forms. The mother was not anaemic and had no abnormal haemoglobin. The electrophoretic analysis of the family is shown in Table I. The structural analysis of abnormal haemoglobin fraction showed the characteristic changes of haemoglobin Lepore in the family with the fusion of δ and β chains between residues 87 and 116.

**Discussion**

The family described here represents the first example of heterozygote haemoglobin Lepore in a Turkish family. This haemoglobinopathy was characterized by erythrocyte morphology similar to that observed in β thalassaemia trait and by the presence of an abnormal haemoglobin with the same mobility as haemoglobin S on starch block and starch gel electrophoresis. The Lepore haemoglobin occurred in a concentration of average 8.1% of the total haemoglobin in 4 members of this family. It is interesting to note that the oldest person carrying haemoglobin Lepore in the family was the paternal grandfather, aged 91, who appeared to be more anaemic than the other haemoglobin Lepore carriers. Old age could have contributed to the severity of his anaemia.

Haemoglobin Lepore in the family. This haemoglobinopathy has been observed among Italians, Rumanians, Yugoslavians, Greeks, Cypriots, and Iranians, since the original description

<table>
<thead>
<tr>
<th>Case</th>
<th>Hb Lepore (%)</th>
<th>A2 Hb (%)</th>
<th>F Hb (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propositus</td>
<td>8.0</td>
<td>2.1</td>
<td>4.7</td>
</tr>
<tr>
<td>Father</td>
<td>8.5</td>
<td>2.2</td>
<td>4.6</td>
</tr>
<tr>
<td>Grandfather</td>
<td>5.8</td>
<td>1.2</td>
<td>2.2</td>
</tr>
<tr>
<td>Uncle</td>
<td>10.2</td>
<td>2.2</td>
<td>2.2</td>
</tr>
<tr>
<td>Mother</td>
<td>Absent</td>
<td>2.8</td>
<td>1.5</td>
</tr>
</tbody>
</table>
in an Italian family in Boston (Beaven et al, 1964; Duma et al, 1968; Fessas et al, 1962; Gerald and Diamond, 1958; Quattrin et al, 1967; Rahbar et al, 1974; Ranney and Jacobs, 1964; Rawly et al, 1972). The interaction of haemoglobin Lepore and β thalassaemia to produce a disease resembling thalassaemia major has also been described (Beaven et al, 1964; Gerald and Diamond, 1958). The homozygous state of haemoglobin Lepore has been observed among Italians, Yugoslavian, and Iranian families (Rahbar, Azizi, and Nowzari, 1975; Weatherall and Clegg, 1972). Furthermore, the patients doubly heterozygous for one of the haemoglobin Lepore variants and haemoglobin C, S, and haemoglobin Peterbrough, have been seen in Afro-American, Greek, and Jamaican families (Ranney and Jacobs, 1964; Weatherall and Clegg, 1972).

Although the haemoglobin Lepore abnormality has been previously reported in Turkish Cypriots, this is the first observation of haemoglobin Lepore in a Turkish family living in the mainland of Turkey (Beaven et al, 1964).

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REFERENCES


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A O Cavdar and A Arcasoy

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