The Hemoglobin E Syndromes. II.
Sickle-Cell—Hemoglobin E Disease

By Muzaffer Aksoy

The first case of sickle-cell—hemoglobin E disease in an Eti-Turk family in Kelahmed village whose members had hemoglobins S and E was found by Aksoy and confirmed by Lehmann.1 The propositus was married to a man who presumably had the sickle cell trait. One of their children, the second example of sickle-cell—hemoglobin E disease among Eti-Turks, was discussed elsewhere.2 Both patients with sickle-cell—hemoglobin E disease were asymptomatic. They possibly had a compensated mild hemolytic process.

The purpose of this paper is to present a new family with sickle-cell—hemoglobin E disease and to furnish new data about the transmission of the abnormal hemoglobins in the first family.1,3

Case Presentation

C. Y., a woman 63 years of age, originally from Samandag, a small town in the county of Hatay, was examined during an electrophoretic survey in Kelahmed village. She complained of physical exhaustion and vague abdominal discomfort. She was well developed, well nourished and moderately pale. The spleen was palpated two finger breadths below the right costal margin. Roentgenograms of the skull were interpreted as showing a striking fine osteoporosis and mild thickening of occipital bone. There was a coarse striaion around the elbow joints.

Laboratory data.—The urine was normal. RBC 3,200,000/cu.mm.; hemoglobin 8.4 Gm./100 ml.; WBC 9200/cu.mm. (59 per cent neutrophils, 3 per cent band forms, 2 per cent eosinophils, 4 per cent monocytcs and 32 per cent lymphocytes); reticulocytes 4 per cent, platelets 380,000 per cubic millimeter; hematocrit 31 per cent; MCV 97 cu.μ.; MCHb. 26 μg.; MCHb.C 27 per cent. Erythrocytes on the blood film were characterized by mild anisocytosis, polychromatophilia, numerous target cells and few sickle cells. The sickling test was positive. Total bilirubin was 1.3 mg./100 ml. The electrophoretic pattern was S + E with greater density of hemoglobin in the position of hemoglobin S. Fetal hemoglobin was found to be 0.8 per cent.

Family studies (fig. 1).—The propositus married twice. By the first husband she had three children. We investigated one of these children and found her to have the hemoglobin E trait. After the death of the first husband, the propositus married again to a normal man. They had two children. The one available for study was also a carrier of the hemoglobin E trait. The propositus had three siblings living in the county of Hatay.

Additional information about the transmission of the abnormal hemoglobins in the second case of sickle cell—hemoglobin E disease2 was also collected (fig. 2). This man, the son of the first patient described, married a normal woman. They had eight children. Six of them are alive; five are carriers of the hemoglobin E trait while the sixth, an infant studied at the age of eight months, has the sickle cell trait.

Discussion

As mentioned above, our first two patients with sickle-cell—hemoglobin E disease were asymptomatic.2 They showed a few hematologic and clinical
changes indicative of a hemolytic process. The hemoglobin values were comparatively low, but the red cell counts were normal. The red cell morphology was only mildly abnormal, and there were few target cells. Osmotic fragility was decreased, and hemoglobin F could not be demonstrated. There was a history of long-standing osteoarticular pain, and mild splenomegaly was noted in one. The electrophoretic pattern was $S + E$.

In contrast, the clinical and hematologic manifestations in the new patient with sickle-cell–hemoglobin E disease herein described were moderate in degree. She had a moderate normocytic anemia and splenomegaly. She complained of physical exhaustion and of gastric discomfort. Erythrocytes on the stained blood film were characterized by numerous target cells, few sickle cells, anisocytosis and polychromatophilia. Mild roentgenographic changes of the type found in association with hemoglobinopathies were observed. No jaundice was detected.

As in the other hemoglobinopathies, such as sickle-cell–hemoglobin C dis-
Hemoglobin A + E

Hemoglobin S + E (sickle cell-hemoglobin disease)

Fig. 2.—The distribution of hemoglobins S, E and A in the members of the family of the second case of sickle-cell-hemoglobin E disease. (Numbers refer to the age of the subjects.)

ease,\textsuperscript{4} sickle-cell-thalassemia disease\textsuperscript{2,5,6} and thalassemia–hemoglobin E disease,\textsuperscript{7} etc., the clinical manifestations and hematologic findings of sickle-cell–hemoglobin E disease may apparently vary greatly. All gradations between the completely asymptomatic state to a moderate or severe anemia, comparable to sickle cell anemia in severity, can probably be found.

Most of the abnormal hemoglobins are believed to be controlled by genes which are alleles of hemoglobin A. At present, we know definitely that only hemoglobins C and S are allelomorphs of hemoglobin A.\textsuperscript{8,9}

We believe the genetic data obtained by evaluation of the genealogies for the two families with sickle-cell–hemoglobin E disease are sufficient to indicate that the genes responsible for hemoglobins E, S and A are alleles or linked. In brief, in the first family, the second case of sickle-cell–hemoglobin E disease was a man who married a woman who had only hemoglobin A. Of their six children, five had the hemoglobin E trait and one the sickle cell trait. Studies on the second family with sickle-cell–hemoglobin E disease also indicated that there is a genetic relationship of hemoglobins S, E and A. The propositus married twice. From each marriage one child is known to be a carrier of hemoglobin E trait.

**SUMMARY**

1. A clinical and hematologic description is presented of a patient with sickle-cell–hemoglobin E disease in a new family. In contrast to the mild
hematologic and clinical changes observed in the patients described by the author previously, the clinical and hematologic manifestations in the new patient were moderate in degree. The anemia was normocytic in type. Variation in the clinical and hematologic picture of sickle cell-hemoglobin E disease has been noted.

2. Genetic studies of two families with sickle-cell–hemoglobin E disease have been presented. According to the genetic data obtained by evaluation of the genealogies of these two families, it is strongly suggested that the genes responsible for hemoglobins S, E, and A are allelomorphs or linked.

SUMMARIO IN INTERLINGUA

1. Es presentate un description clinic e hematologic de un patiente con morbo de cellulas falciforme e hemoglobina E in un familia altere que illo del caso previemente reportate per le autor. Durante que le alterationes hematologic e clinic observate in ille previe caso esseva leve, in le patiente del presente reporto lor grado debe esser designate como moderate. Le anemia in question representa le typo normocytic. Variationes del tableau clinic a hematologic in morbo de cellulas falciforme e hemoglobina E es notate.

2. Es presentate studios genetic in duo familias con morbo de cellulas falciforme e hemoglobina E. Super le base del datos genetic obtenite per le evaluacion del genealogias in le duo familias in question, il es sugerite con alte grados de probabilitate que le genes responsable pro le hemoglobinas S, E, e A es allelomorphic o interligate.

REFERENCES

The Hemoglobin E Syndromes. II. Sickle-Cell—Hemoglobin E Disease

MUZAFFER AKSOY