

Hemoglobin E without Hemoglobin A

Establishing a Diagnosis is Important!

In the past 18 months, 4 newborns with hemoglobin E, E and no hemoglobin A have been identified through NY State Newborn Screening in our 9 county area. This represents 22% of the all the newborns with disease reported to us. Each of the parents of these newborns was Southeast Asian.

Hemoglobin E without hemoglobin A may be either:

- Homozygous hemoglobin E (E/E) or
- Hemoglobin E/ β^0 -thalassemia (E/ β^0 -thal).

A distinction between these is important because:

- E/E is a clinically benign condition
- E/ β^0 -thal results in a moderate to severe hemolytic anemia which may require regular transfusion and iron chelation therapy.

Measurement of HbA₂ to detect a β -thalassemia gene is not possible in the presence of HbE because A₂ and E migrate identically on electrophoresis. Also the appearance of small amounts of hemoglobin A after birth do not necessarily rule out β -thalassemia because some mutations of the β -thalassemia gene result in some hemoglobin A production.

Testing the parents of a child identified with hemoglobin E without hemoglobin A can distinguish between these 2 genotypes. However, in some cases both parents may not be available for testing, or as in the case cited below, DNA studies may be needed to define a diagnosis.

α -Thalassemia can ameliorate E/ β^0 -thalassemia

Krishnamurti¹ et al. report the case of a 31 month old child of Laotian descent who on newborn screening had hemoglobins F and E, but no A. An assumption was made that the child had homozygous hemoglobin E because the parents had no symptoms and were normal on physical examination. When the child failed to thrive and

became profoundly anemic, DNA analysis was done and revealed that the father and the child both had E/ β^0 -thal!

The dramatic clinical difference between the father and child was ascribed to the finding that the father had 2-gene-deletion-type alpha-thalassemia which the son did not inherit. (The mother had hemoglobin E trait and a full complement of α genes). The child underwent splenectomy and with regular transfusions is growing well.

Excess of α chains causes the problem.

Beta-thalassemia is due to a deficiency of β globin chains. The excess α chains precipitate in the red cell causing a hemolytic anemia. Alpha-thalassemia lowers the production of α chains. In the presence of β -thalassemia, α -thalassemia lessens the imbalance of globin chains thereby ameliorating the clinical effects.

Careful surveillance necessary to define E/ β^0 -thalassemia

Newborns identified with hemoglobin E without hemoglobin A should be followed closely during the first 2 years of life. A complete blood cell count with red cell indices and hemoglobin electrophoresis at 6 mos. of age is recommended. A pediatric hematologist should be consulted for any child manifesting significant signs of anemia. DNA analysis of the globin genes can be used to identify the genotype of the infant.

If it is determined that the child has E/ β^0 -thalassemia careful observation for

- significant anemia
- failure to thrive or
- hepatosplenomegaly

is important before initiating any transfusion program. Some children with this diagnosis may grow and develop well without transfusion.

References:

1. Krishnamurti L. et. al., *J Pediatr* 1998; 132:863-5
2. Weatherall D. *J Pediatr* 1998; 132:765-7
3. Glader BE, *Ped. Hematology* 1996; 43:665-79