Health Care Provider Hemoglobinopathy Fact Sheet

Hemoglobin Bart's & Alpha Thalassemia

Hemoglobin Bart's is a tetramer of gamma (fetal) globin chains seen during the newborn period. Its presence indicates that one or more of the four genes that produce alpha globin chains are dysfunctional, causing alpha thalassemia. The more alpha genes affected, the more significant the thalassemia and clinical symptoms. Alpha thalassemia occurs in individuals of all ethnic backgrounds and is one of the most common genetic diseases worldwide. However, the clinically significant forms (Hemoglobin H disease, Hemoglobin H Constant Spring, and Alpha Thalassemia Major) occur predominantly among Southeast Asians. Summarized below are the manifestations associated with the different levels of Hemoglobin Bart's detected on the newborn screen, and recommendations for follow-up. The number of dysfunctional genes is estimated by the percentage of Bart's seen on the newborn screen.

Silent Carrier- Low Bart's

If only one alpha gene is affected, the other three genes can compensate nearly completely and only a low level of Bart's is detected, unless hemoglobin Constant Spring is identified (see below). Levels of Bart's below a certain percentage are not generally reported by the State Newborn Screening Program as these individuals are likely to be clinically and hematologically normal. However, a small number of babies reported as having possible alpha thalassemia trait will be silent carriers.

Alpha Thalassemia or Hemoglobin Constant Spring Trait- Moderate Bart's

Alpha thalassemia trait produces a moderate level of Bart's and typically results from the dysfunction of two alpha genes-- either due to gene deletions or a specific change in the alpha gene that produces elongated alpha globin and has a thalassemia-like effect: hemoglobin Constant Spring. These conditions are usually benign although mild microcytic anemia is common. However, two copies of the Constant Spring mutation may cause a mild hemolytic anemia. Follow-up is for the benefit of avoiding misdiagnosis of iron deficiency, or diagnostic dilemmas of non-responsive anemia. It is also for the benefit of determining reproductive risks for the family, which will differ depending on whether the individual has the dysfunctional genes on the same chromosome or different chromosomes.

Hemoglobin H Disease- High Bart's

A high level of Bart's is most often the result of three dysfunctional alpha genes due to deletions and generally manifests in a moderate hemolytic anemia. This usually occurs when one parent is a silent carrier (one dysfunctional alpha gene), and the other has alpha thalassemia trait (two dysfunctional alpha genes on the same chromosome). The clinical manifestations of this disorder are variable but most patients are anemic and develop some degree of splenomegaly. Hemoglobin H is unstable and patients with hemoglobin H disease have chronic hemolysis in addition to alpha thalassemia. They are susceptible to accelerated hemolysis when exposed to the same drugs that cause hemolysis in individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency. A list of these drugs can be furnished upon request.

Hemoglobin H Constant Spring Disease- High Bart's

Hemoglobin H Constant Spring disease is often a more severe phenotype than the more common form of Hemoglobin H Disease. This occurs when there is a high level of Bart's in combination with at least one Constant Spring mutation, typically resulting in only one functional alpha gene. Clinical manifestations of a compound heterozygote include moderate anemia, splenomegaly, and possible transfusion dependence.

Alpha Thalassemia Major (Fetal Hydrops Syndrome)

If none of the alpha genes are functional, a very severe hemolytic anemia begins in utero. The anemia is so severe that the disorder is lethal with fetal demise usually occurring in the third trimester. Also, pregnant women carrying an infant with fetal hydrops syndrome have a high rate of severe toxemia of pregnancy. This usually occurs when both parents have alpha thalassemia trait (two dysfunctional alpha genes on the same chromosome). Prospective parent screening and prenatal diagnosis is available if the potential for fetal hydrops syndrome is suspected.

Genetic counseling is advisable for families affected by these conditions to promote understanding of the significance for themselves and future offspring. A list of genetic counselors and hemoglobin consultants was included with this fact sheet ***(additional copies are available from our office; see reverse side of this page).***

Follow-up of Newborns with Hemoglobin Bart's

The following recommendations were developed with the help of the Newborn Screening Program's Hematology Consultants.

At Two to Three Months

Monitor growth and examine baby for splenomegaly.

- If baby is growing normally and no other hemoglobin abnormality other than Hemoglobin Bart's was present at birth, Hemoglobin H disease is unlikely and no further work-up is necessary until 9 to 12 months.

- If splenomegaly is present, the infant could be at risk of developing Hemoglobin H disease. Consultation with a pediatric hematologist in the assessment of these abnormalities is recommended.

Between Nine and Twelve Months

Do a CBC and reticulocytes.

- If results are normal, the child most likely is a silent carrier and the family is not at risk for Fetal Hydrops Syndrome in future pregnancies. No further work-up is necessary.

- If microcytic, do iron studies:

  If iron-deficient, treat for 3 to 6 months and then repeat the CBC. If microcytosis is corrected, the child most likely is a silent carrier and the family is not at risk for Fetal Hydrops Syndrome in a future pregnancy. No further work-up is necessary.

  If not iron deficient, (or if microcytosis persists after iron deficiency has been corrected), do a hemoglobin electrophoresis or HPLC (including quantitation of hemoglobins A2 and F). The work-up should include a stain for hemoglobin H inclusion bodies using brilliant cresyl blue. High levels of hemoglobin H inclusion bodies and unresolved microcytic anemia indicate that the child has Hemoglobin H disease. Lower levels of inclusion bodies are found with alpha thalassemia trait. Consultation with a pediatric hematologist in the assessment of these abnormalities is recommended.

The parents of a child with Hemoglobin Bart's, especially if at least one parent is Asian, should also have a CBC. If either parent is microcytic, further evaluation of the parents for alpha thalassemia may be warranted due to the risk of Hemoglobin H Disease or Alpha Thalassemia Major in future children.

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