Unusual Anemias

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KEYWORDS

• Thalassemia • Aplastic anemia • Paroxysmal nocturnal hemoglobinuria
• Spur cell anemia • Burns • Drug induced

KEY POINTS

- Thalassemia can have a variable presentation ranging from mild microcytosis to transfusion-dependent anemia.
- Paroxysmal nocturnal hemoglobinuria should be considered in any patient with hemolysis, especially if complicated by thrombosis.
- Diverse processes can lead to acquired hemolytic anemias.

A variety of processes lead to anemia, and this review discusses causes beyond the classic conditions often considered (**Box 1**). This report reviews thalassemia, rare nutritional anemias, paroxysmal nocturnal hemoglobinuria, bone marrow failure syndromes, and unusual types of hemolysis.

THALASSEMIA

Although not frequently seen in North America, thalassemias are the most common hemoglobin defect in the world.[1] Thalassemias are diseases of hemoglobin synthesis and are subclassified by the hemoglobin chain involved—most often the α or β chain. Each chromosome 16 carries 2 copies of the gene encoding the α globin chain ($\alpha\alpha/\alpha\alpha$). When any of these genes is mutated, the result is α thalassemia, of which, 4 varieties exist: α thalassemia minor-1 (1 gene affected; α-/$\alpha\alpha$), α thalassemia minor-2 (2 genes affected; α-/α- or $\alpha\alpha$/-), hemoglobin H disease (3 genes affected; α-/–) and hemoglobin Bart's (4 genes affected; –/–). Patients with 1 mutation are considered *silent carriers*, whereas those with 2 mutations are considered to have the α thalassemia trait, which typically manifests with mild microcytosis without anemia. Hemoglobin H disease is

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Box 1
Less common anemias

Thalassemia
Clinical clues to diagnosis: microcytosis with normal iron stores, positive family history
Diagnostic tests: hemoglobin electrophoresis, DNA sequencing
Treatment: Severe, stem cell transplant, transfusions, iron chelation

Copper deficiency
Clinical clues to diagnosis: neutropenia, normal platelet counts, sensory neurologic defects
Diagnostic tests: copper level, ceruloplasmin
Treatment: copper supplementation

Paroxysmal nocturnal hemoglobinuria
Clinical clues to diagnosis: Coombs negative hemolysis, thrombosis, pancytopenia
Diagnostic tests: high-sensitivity flow cytometry
Treatment: complement C5 inhibitor eculizumab

Aplastic anemia
Clinical clues to diagnosis: pancytopenia
Diagnostic tests: bone marrow biopsy and aspirate
Treatment: stem cell transplant or immunosuppression

Pure red cell aplasia
Clinical clues to diagnosis: severe anemia with markedly reduce reticulocyte count
Diagnostic tests: bone marrow biopsy and aspirate
Treatment: CSA

Microangiopathic hemolytic anemias
Clinical clues to diagnosis: schistocytes, high low-density lipoprotein level, thrombocytopenia
Diagnostic tests: blood smear, review of history/examination for severe hypertension, recent mitral valve repair, presence of VAD
Treatment: treatment of primary cause (eg, reducing blood pressure)

Clostridium sepsis
Clinical clues to diagnosis: fevers, severe hemolysis
Diagnostic tests: spherocytes and ghost cells on blood smear
Treatment: treatment of infection

Spur cell anemia
Clinical clues to diagnosis: severe hemolysis in the setting of ESLD
Diagnostic tests: blood smear showing spur cells
Treatment: liver transplant

Wilson disease
Clinical clues to diagnosis: Coomb negative hemolysis in the setting of liver disease
Diagnostic tests: serum copper and ceruloplasmin level, presence of bite cells, and spherocytes in blood smear
Treatment: copper chelation, liver transplant

Burns
Clinical clues to diagnosis: history
Diagnostic tests: spherocytes, fragmented red cells
Treatment: supportive care

characterized by pronounced hemolytic anemia, splenomegaly, and complications related to iron overload. Hemoglobin Bart's is the complete failure to produce an α globin chain, resulting in hydrops fetalis and death in utero or soon after birth.

The geographic locations in which α thalassemias are most common are Africa, the Mediterranean, and Southeast Asia.[2] Interestingly, the more severe phenotypes (hemoglobin H disease and hemoglobin Bart's) are typically seen only in the