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POSTER ABSTRACTS

904.OUTCOMES RESEARCH-NON-MALIGNANT CONDITIONS

Patients with Non-Transfusion-Dependent Thalassemia May Evolve to Transfusion-Dependent Thalassemia in Adulthood

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Introduction: Non-transfusion-dependent thalassemia (NTDT) describes a prevalent and clinically heterogeneous group of patients in the United States. Adults with significant forms of NTDT display progressive age-related complications due to chronic anemia and ineffective erythropoiesis. While the importance of early diagnosis and close monitoring in pediatric patients with NTDT is well-established, the characteristics and complications of adults with NTDT in the United States is poorly described. Many adult patients with NTDT are managed by community providers who often have limited experience with this condition.This single-center observational study describes the clinical characteristics of patients with NTDT during their initial presentation to an adult thalassemia treatment center and identifies intervenable complications related to NTDT.
Methods: We evaluated patients referred to the Penn Comprehensive Adult Thalassemia Program between 2013 and 2023 who carried a diagnosis of NTDT (defined as alpha or beta thalassemia and requiring fewer than 8 units of red cells in the 12 months preceding their initial visit). Data was collected via manual chart review. Clinical complications were defined as symptoms at presentation, history of splenectomy, hepatosplenomegaly, paraspinal masses, pulmonary hypertension, cardiac arrhythmia, endocrine complications (hypothyroidism, hypogonadism, diabetes, decreased bone mineral density), thrombotic events, and iron overload requiring chelation. Laboratory markers of disease severity included hemoglobin (Hgb), markers of hemolysis, nucleated red blood cells, serum ferritin and MRI quantitation of liver and cardiac iron.
Results: Of the 94 patients with thalassemia referred to the Penn Comprehensive Adult Thalassemia Program, 34 carried a diagnosis of NTDT. Of these, 13 had α- thalassemia (deletional and non-deletional HbH), 19 had β-thalassemia variants (homozygous or double heterozygous β-globin gene mutations), and 2 had hemoglobin E/β-thalassemia. The median age at referral was 37.5 years (range 20-74); 71% were female. In general, patients with β-thalassemia had a larger number of significant complications than those with α-thalassemia. Overall, 11 patients (32%, all with β-thalassemia) had a history of splenectomy, 21 (62%) had evidence of extramedullary hematopoiesis with hepatosplenomegaly, and 7 (21%) had paraspinal masses. Pulmonary hypertension was seen in 5 of 21 patients with β-thalassemia and hemoglobin E/β-thalassemia (24%) while 4 patients overall (11%) had a history of thrombosis. The most common endocrinopathy was decreased bone mineral density (32%). Mean Hgb was 9.1 g/dL, however, 53% had a Hgb $<$ 9 g/dL. Seven patients had an increase in nucleated red blood cells (range 161-1522 %) as a marker of ineffective erythropoiesis. Serum ferritin exceeded international NTDT guidelines for tissue evaluation ($>$ 800 ng/mL) in 32% of patients; the mean ferritin for all patients was 897 ng/mL (range 45-7601 ng/mL). A liver MRI was obtained in 56% of patients with mean iron content of 25 mg/g dry weight (range 1.5 - 41.2 mg/g dry weight). No patients had evidence of cardiac iron overload.
Of the 34 patients referred for NTDT, 14 (41%) met criteria to initiate a chronic transfusion regimen to maintain a pre-transfusion Hgb $>$ 9.5 g/dL per established guidelines. Criteria included fatigue (all patients), extramedullary hematopoiesis (32%), Hgb $<$ 7 g/dL (8%), and pulmonary hypertension (15%). Several patients had more than one indication for chronic transfusion.
Conclusions: This is the first report of patients with NTDT in the United States that highlights clinically significant complications that accumulate in adults. Our results demonstrate a previously unknown high prevalence of conditions that warrant close monitoring, screening and intervention. Clinically, 41% of adult NTDT patients referred to our comprehensive adult thalassemia program met criteria to initiate a chronic transfusion program, a number that is significantly higher than previously

published rates outside of the USA. These findings indicate a critical need for thalassemia education of adult providers that emphasizes the importance of monitoring for early complications of NTDT, as well as criteria for initiating a chronic transfusion program to mitigate complications and provide meaningful impacts in clinical outcomes.

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