Extensive iron overload in bone marrow: A cause of pancytopenia in a thalassemia major patient – A case report

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Abstract:
Iron overload-associated organ damage in transfusion-dependent anemias is a well-known phenomenon. Here, we discuss a case of 28-year-old, poorly chelated thalassemia major patient, whose blood workup revealed pancytopenia and moderately raised serum ferritin levels. His bone marrow examination was performed which revealed massive iron overload. Aggressive iron chelation led to successful recovery of peripheral blood counts in his patient. This case focuses on the importance of early detection and timely management of reversible iron overload toxicities. Serum ferritin although is convenient marker to assess iron overload, but it should not be relied upon to assess the severity of iron overload. Hence, organ-specific diagnostic modalities must be used along with serum ferritin to assess the severity of iron overload to prevent long-term complications in patients with regular blood transfusions.

Keywords:
Bone marrow, iron overload, thalassemia major

Introduction
Thalassemia major is a transfusion-dependent globin chain disorder which requires frequent transfusions.[¹] One of the common complications is iron overload as a result of chronic transfusion which eventually leads to end-organ damage and high morbidity and mortality.[²,³] Serum ferritin is commonly used serum marker for the assessment of total body iron stores and has a role in both diagnosis and management of iron overload and iron deficiency.[⁴] Thalassemia is a common disorder in our part of the world due to consanguineous marriage and lack of awareness regarding premarital screening and prevention. Due to high economic burden and lack of health-care facilities, most of the thalassemics are poorly managed and remain under-chelated. Majority of these patients receive inadequate blood transfusion without regular monitoring of iron burden or iron-induced organ damage, and serum ferritin remains the investigation of choice to assess iron stores. It has been observed that, though serum ferritin gives some estimate about body iron burden, the correlation is not very strong to assess the degree of iron overload.[⁵,⁶] We report a case of thalassemia major who was transfusion dependent since 1 year of age whose bone marrow was received for reporting.

Case Report
A 28-year-old male known case of thalassemia major on regular transfusion presented with bone pains. He had no history of fever or any constitutional symptoms. On examination, there was...
pallor; abdomen was soft and nontender with no hepatosplenomegaly. On chest auscultation, he had loud second heart sound due to pulmonary hypertension. Rest of the systemic examination was normal apart from thalassemia-related bone deformities. His regular medication includes deferasirox (20 mg/kg) and calcium supplements. Clinical details were obtained after contacting the primary physician. Complete blood count showed hemoglobin (Hb) of 9.0 g/dL (posttransfusion), hematocrit 26.2%, mean corpuscular volume 85.6 fL, mean corpuscular Hb 29.4 pg, white cell count was 1.67 × 10 E9/L, absolute neutrophil count 0.78 × 10 E9/L, and platelet count of 59 × 10 E9/L. Peripheral blood film showed dimorphic blood picture, anisocytosis, poikilocytosis, moderate neutropenia, and low platelets. Reticulocyte count corrected for the Hb level was reported to be 0.1%. Direct antiglobulin test and antibody screening were performed and reported to be negative. His serum ferritin was 1064 ng/ml (28–365) which was in concordance with previous values ranged between 950 and 1100 mg/ml performed on random occasions. There was no clear pattern followed for testing and only a few results were available. Hepatitis B virus surface antigen, anti-HCV, and anti HIV I and II were negative. Bone marrow aspirate revealed tri-lineage hematopoiesis with erythroid hyperplasia. There was marked increase in macrophages and histiocytes containing siderotic granules as shown in Figure 1 (panel a). Perl’s iron stain revealed increased iron stores with nonringed sideroblasts [Figure 1, panel b]. Bone trephine section showed decreased cellularity for the age of around 50% with replacement of normal hematopoietic precursors by markedly increased hemosiderin-laden macrophages [Figure 1, panel c]. Perl’s iron stain was performed on trephine section as well which showed intense iron deposits [Figure 1, panel d]. Based on collective findings of bone marrow biopsy, he was given hyperchelation therapy containing desferrioxamine with a dose of 40 mg/kg IV infusion every 12 hourly to reduce the burden of iron overload in bone marrow. His overall clinical condition improved with improvement in peripheral blood counts with better tolerance of subsequent transfusions. His cardiac and endocrine evaluation was also planned but postponed due to financial constraints.

Discussion
Iron overload whether primary or secondary can induce toxicities which may affect various parts of the body such as heart, liver, endocrine organs, and joints. Bone marrow failure is one of the important manifestations of iron overload, resulting in peripheral blood cytopenias. Numerous clinical studies have shown improvement in hematological parameters with iron chelation, supporting iron overload-associated bone marrow suppression. There are various causes of cytopenias in transfusion-dependent thalassemia syndrome such as hypersplenism, transfusion-transmitted infection notably hepatitis C, and drugs, for example, interferon, etc., which were evaluated in this patient. The mechanism leading to bone marrow suppression in iron overload includes the generation of reactive iron species with bone marrow microenvironment injury that damages the hematopoietic stem cells and progenitor cells. Initially, it was studied that, in the presence of iron overload; bone marrow mesenchymal cells undergo unbalanced osteogenic/adipogenic differentiation as well along with decreased hematopoietic supporting functions of bone marrow mesenchymal cells secondary to generation of reactive oxygen species. Our patient was on inadequate iron chelation as it was assessed by serum ferritin only leading to iron overload-induced damage. Reports like this may act as an awareness tool for physicians to correctly identify and manage patients with iron overload-induced toxicities.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in...
the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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