Iron-laden macrophage in autoimmune disease

14-year-old African American adolescent boy presented with a 20-lb weight loss, malaise, and arthralgia. Physical examination was unremarkable. CBC showed pancytopenia with a hemoglobin level of 7.9 g/dL, leukocytes 1.2 × 10⁹/L, and platelets 137 × 10⁹/L. Peripheral smear showed occasional dacrocyes and schistocytes. Other testing showed a creatinine level of 1.3 mg/dL, 1+ proteinuria, erythrocyte sedimentation rate of 99, iron level of 48 µg/dL, transferrin level of 114 mg/dL, and ferritin level of 1200 ng/mL. The bone marrow was mildly hypocellular, with erythroid hypoplasia, left-shifted granulopoiesis, and no evidence of malignancy. A bone marrow core biopsy was stained with (panel A) hematoxylin and eosin or (panel B) Prussian blue, indicating iron-laden macrophages. Titer of several autoantibodies were elevated, and a renal biopsy revealed nephritis. The final diagnosis was mixed connective tissue disease.

Macrophage iron accumulation occurs in numerous inflammatory states including autoimmune disease, cancer, and infection. Cytokines, including interleukins 6 and 22 and type I interferon, stimulate hepatic secretion of hepcidin, a peptide hormone that binds the iron exporter ferroportin and induces its degradation in macrophages and enterocytes (panel C, from Figure 1 in Andrews NC. Forging a field: the golden age of iron biology. Blood. 2008;112[2]:219-230). The net result is accumulation of iron in macrophages and impaired gut iron absorption. Consequently, iron availability for erythropoiesis is reduced, contributing to anemia of inflammation.
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