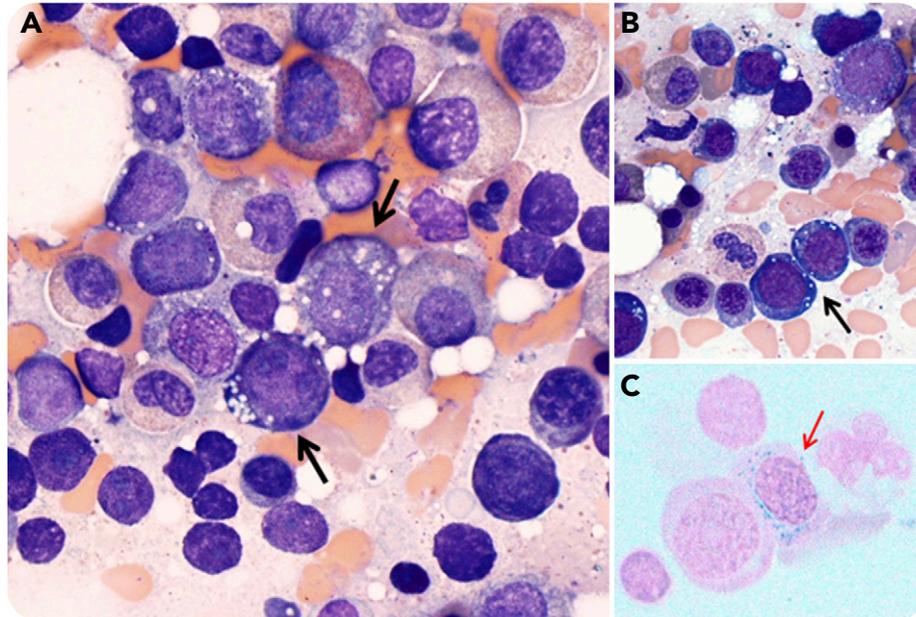


“Myelodysplasia” from copper deficiency

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A 45-year-old woman presented with pancytopenia (hemoglobin, 4.8 g/dL; mean corpuscular volume, 96; leukocytes, $0.9 \times 10^9/L$; platelets, $157 \times 10^9/L$; absolute reticulocytes, $34 \times 10^9/L$). Staining of the bone marrow aspirate showed rare ringed sideroblasts (panel C, red arrow; Prussian blue stain, original magnification $\times 1000$), mild dyserythropoiesis with nuclear to cytoplasmic dyssynchrony, and prominent cytoplasmic vacuolization (panels A-B, black arrows; Wright-Giemsa stain, original magnification $\times 1000$). Cytogenetics and sequencing for 97 myeloid genes were unrevealing. Laboratory studies documented a low serum copper (4 $\mu\text{g/dL}$) (normal, 75-175 $\mu\text{g/dL}$) and an elevated serum zinc (191 $\mu\text{g/dL}$; normal, 60-130 $\mu\text{g/dL}$). Additional history revealed frequent use of a zinc-containing denture adhesive. After 1 month without further zinc exposure and daily oral copper

supplementation, serum levels normalized and pancytopenia resolved.

Zinc and copper normally exist in a dynamic equilibrium. Excess zinc, however, induces metal-binding metallothioneins in intestinal enterocytes, which bind copper; the bound copper is then lost by enterocyte shedding. Hypocupremia is also associated with gastric surgery, malabsorption, and excess copper chelation. The resulting hypocupremia impairs iron absorption and insertion into the protoporphyrin ring, causing iron accumulation with ringed sideroblasts, dysplastic changes, and vacuolization. Similar to cobalamin deficiency, an irreversible myeloneuropathy has also been reported with hypocupremia. Copper deficiency is a rare nutritional cause of reversible pancytopenia with dysplastic changes and should be considered in the differential diagnosis of pancytopenia.