CASE REPORT

Copper deficiency mimicking myelodysplastic syndrome

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Key Clinical Message
Copper deficiency is a rare cause of pancytopenia that may be mistaken for myelodysplastic syndrome. Cytoplasmic vacuolization in erythroid and myeloid precursors is found on bone marrow examination. Patients with a history of abdominal surgery who present with anemia and neutropenia with dysplastic changes should have copper levels checked.

Keywords
Copper deficiency, dysplasia, gastric bypass, myelodysplastic syndrome, pancytopenia.

Case Presentation
A 74-year-old man was presented with a new normocytic anemia and neutropenia. Initial laboratory values were: WBC 2900/μL, ANC 900/μL, hemoglobin 12.0 g/dL, MCV 95 fl, and platelet count of 156,000/μL. Creatinine, AST, ALT, bilirubin, TSH, iron, total iron binding capacity, ferritin, and vitamin B12 levels were normal. Past medical history was significant for coronary artery disease, ulcerative colitis, and stage II esophageal adenocarcinoma treated with neoadjuvant concomitant radiation plus carboplatin and paclitaxel followed by Ivor-Lewis esophagectomy. Postoperative esophagocutaneous fistula formation led to long-term reliance on jejunal feeding for all caloric intake. His medications were Lorazepam, Aspirin, Amiodarone, Lisinopril, Balsalazide, Metoprolol, and Vitamin B12. He had no significant family history for blood disorders. Amiodarone was discontinued. A repeat CBC after 1 month showed WBC 2600/μL, ANC 200/μL, hemoglobin 12.7 g/dL, MCV 107 fl, and platelet count of 174,000/μL. A second repeat CBC after 2 months following discontinuation of amiodarone showed: WBC 2900/μL, ANC 300/μL, hemoglobin 11.0 g/dL, MCV 114 fl, and platelets 193,000/μL. Folate, vitamin B12, and homocysteine levels were normal. Methylmalonic acid was slightly elevated at 0.62 μmol/L (0.08–0.56). Examination of a bone marrow aspirate and biopsy specimen revealed normocellular bone marrow with progressive trilineage hematopoiesis, mild erythroid hyperplasia, with megaloblastoid features, and vacuolated erythroid cells, highly suspicious for myelodysplastic syndrome (Figs 1 and 2). Flow cytometric and cytoge-

Figure 1. Megaloblastoid erythroid hyperplasia and one dysplastic megakaryocyte.
netic analyses were normal. Additional laboratory evaluation included rheumatoid factor 12, ESR 30, CRP 0.4, serum zinc level 86 μg/dL (60–130) and serum copper <10 μg/dL (70–140). Copper (2 mg) orally daily was begun. A CBC after 1 month revealed WBC 7600/μL, ANC 5400/μL, hemoglobin 12.2 g/dL, MCV 120 fL, and platelet count 246,000/μL. Repeat serum copper was 97 μg/dL (Table 1).

Discussion

Copper is a micronutrient essential to hematopoietic function [3]. Ceruloplasmin and cytochrome oxidase are both copper-containing enzymes essential for heme synthesis [3]. The role of copper in neutrophil and platelet synthesis is unclear. Anemia due to copper deficiency can be microcytic, normocytic, or macrocytic [5]. Neutropenia and thrombocytopenia are less common [5]. Typical morphological findings in peripheral blood and bone marrow aspirate in copper deficiency can mimic myelodysplastic syndrome [1]. Bone marrow aspirate in both conditions may show dysplasia in the erythroid precursors such as large size, nuclear multilobulation, and nuclear budding as well as the presence of ring sideroblasts. Unlike myelodysplastic syndrome, the bone marrow aspirate in copper deficiency characteristically shows cytoplasmic vacuoles within erythroid and myeloid precursors [2]. Furthermore, karyotyping in cases of copper deficiency does not reveal cytogenetic features characteristic of myelodysplastic syndrome.

Copper is present in common foods including meat, fish, nuts, seeds, and legumes, and therefore deficiency from dietary inadequacy is rare [4]. Most copper absorption occurs in the stomach and proximal duodenum, although the more distal small intestine can also absorb copper. Problems with copper absorption leading to deficiency should be considered in patients who have history of gastric bypass or gastrectomy, are receiving chronic parenteral nutrition or tube feeding, or on zinc supplementation and develop pancytopenia and/or myeloneuropathy.

The daily required dose of micronutrients such as copper is unknown. Moreover, there are no standard recommended dietary allowances (RDA) for copper. However, per the Mayo Clinic the daily recommended intake for adults is 1.5–2.5 mg/day. Copper is available in both intravenous (cupric chloride) and tablet forms.

In this patient, we hypothesize that the long-term use of jejunal feeding led to a nutritional deficiency of copper and consequent pancytopenia. Treatment of copper deficiency is typically intravenous [1]. Currently, there is a national shortage of intravenous copper; therefore we elected to attempt correction of his copper deficiency with higher doses of oral copper. We were able to correct his copper levels rapidly. His cytopenias quickly resolved coincident with return of serum copper levels to normal.

Copper deficiency represents a rare but treatable cause of anemia and neutropenia that may be mistaken for myelodysplastic syndrome. Therefore, patients with a history of abdominal surgery who present with new found anemia and neutropenia with bone marrow biopsy showing dysplastic changes with no cytogenetic abnormalities should have copper levels checked. Recognition of copper deficiency as the cause of these blood abnormalities is critical to appropriately treat this disorder.

Table 1. Laboratory values.

| Date     | WBC (K/μL) | Hg (g/dL) | MCV (fL) | Platelet (K/μL) | ANC (K/μL) | Copper (μg/dL) |
|----------|------------|-----------|----------|----------------|------------|----------------|
| 5/26/12  | 2.9        | 12.0      | 95.0     | 156            | 900        | <10            |
| 6/5/12   | 2.7        | 12.1      | 98.2     | 169            | 600        | 97             |
| 7/3/12   | 2.6        | 12.7      | 107.4    | 174            | 200        | 134            |
| 8/7/12   | 2.7        | 11.6      | 113.8    | 187            | 300        |                |
| 8/14/12  | 2.4        | 11.2      | 113.3    | 203            | 600        |                |
| 10/9/12  | 2.6        | 10.3      | 121.8    | 187            | 200        |                |
| 10/16/12 | 1.9        | 10.3      | 123.0    | 212            | 300        |                |
| 11/6/12  | 7.6        | 12.2      | 120.1    | 246            | 5400       |                |
| 12/5/12  | 8.4        | 14.6      | 108.8    | 184            | 5700       |                |
Conflict of Interest
None declared.

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