Clinical Case Reports

Open Access

CLINICAL IMAGE

Copper deficiency-related bone marrow changes secondary to long-term total parenteral nutrition

Thein Hlaing Oo & Shimin Hu

The University of Texas M.D. Anderson Cancer Center, Houston, Texas, USA

Correspondence
Thein Hlaing Oo, Section of Thrombosis & Benign Hematology, Unit 1464, The University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, USA. Tel: 713-563-4260; Fax: 713-563-4443; E-mail: thoo@mdanderson.org

Funding Information
No sources of funding were declared for this study.

Received: 7 March 2016; Revised: 23 May 2016; Accepted: 28 November 2016

Clinical Case Reports **2017; 5(2): 195–196**

doi: 10.1002/ccr3.789

Key Clinical Message

Total parenteral nutrition can be complicated by the marrow sea-blue histiocytes as well as copper deficiency-related bone marrow changes. Cytoplasmic vacuoles in the erythroid and myeloid precursors raise the possibility of copper deficiency anemia. If the diagnosis is delayed, the clinical course can be complicated by neurologic deficits.

Keywords

Copper deficiency, cytoplasmic vacuoles, sea-blue histiocytes, total parenteral nutrition.

Case

A 40-year-old woman who had received radiotherapy for cervical cancer 19 years ago developed rectovaginal and vesicovaginal fistulas and intermittent small bowel obstruction, requiring multiple surgeries. In 2013, total parenteral nutrition (TPN) was initiated. She also has chronic kidney disease and her baseline hemoglobin was around 8.0 g/dL with serum erythropoietin 11.3 mIU/mL (2.6–18.5) in May 2015. In November 2015, she developed bacteremia (*Raoultella planticola, Klebsiella pneumonia*, and *Pseudomonas aeruginosa*) for which intravenous broad-spectrum antibiotics were administered. She had no neuropathy symptoms. Physical examination was remarkable for conjunctival pallor, intact gastrostomy tube, colostomy, and urostomy. Liver, spleen, and lymph nodes were not palpable. A complete blood count (CBC) showed WBC 12,800/μL (98% neutrophils), hemoglobin 6.5 g/dL, MCV 91 fL, platelet 115,000/μL, and reticulocyte count 0.8%. Two units of red blood cells (RBC) were transfused, and hematology consultation was obtained. Blood smear revealed anisopoikilocytosis, occasional Döhle bodies, and mild neutrophil hypogranularity, but no nuclear hypersegmentation or hyposegmentation. Serum iron profile revealed the following: iron 140 μg/dL (37–170), TIBC 176.1 μg/dL (250–450), and ferritin 3601 ng/mL (13–150). Serum LDH was normal. Bone marrow [BM] biopsy revealed the following: cellularity 30–40%, myeloid: erythroid ratio 2.5:1, blasts 1%, myelocytes 9%, metamyelocytes 13%, granulocytes 41%, eosinophils 2%, lymphocytes 5%, plasma cells 1%, and erythroid cells 26%, progressively maturing trilineage hematopoiesis, many cytoplasmic vacuoles in the myeloid precursor [Panel A × 1000], erythroid precursor [Panel B × 1000], and basophil precursor [Panel C × 1000] (Fig. 1), consistent with copper deficiency-related BM changes. In some areas, sea-blue histiocytes with cytoplasm containing large blue lysosomal granules were seen [Panel D × 1000]. There were no ring sideroblasts on the iron stain. Bone marrow cytogenetics revealed 46, XX [20]. Both serum copper (0.35 mcg/mL, normal range, 0.75–1.45) and ceruloplasmin (9.7 mg/dL, normal range, 16.0–45.0) were subsequently found to be decreased. Serum zinc level was 0.33 mcg/mL (normal range, 0.66–1.10). Intravenous copper (2.5 mg) was given daily for 10 days followed by copper supplementation in the TPN. Zinc content in the TPN was also adjusted. Two more RBC units were transfused prior to hospital discharge

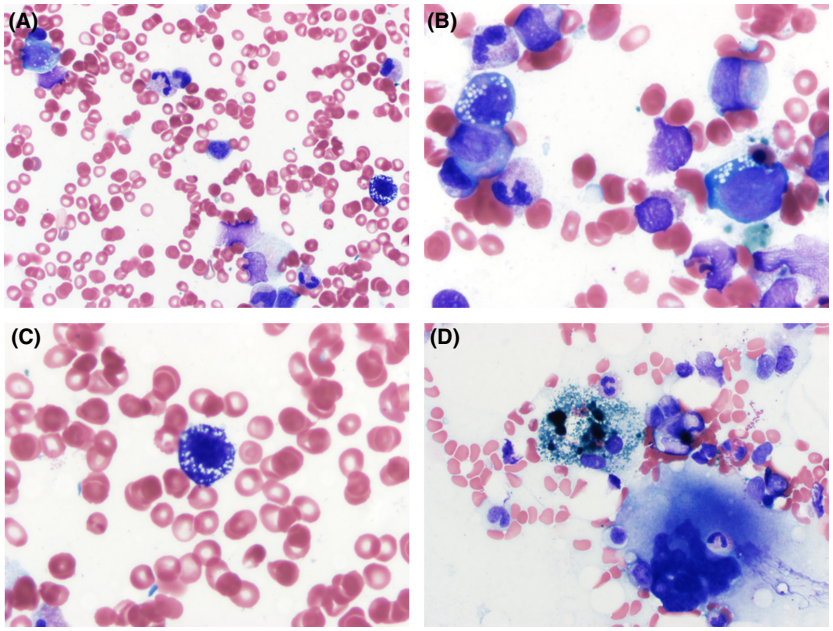

Figure 1. Panel A: cytoplasmic vacuoles in the myeloid precursors; Panel B: cytoplasmic vacuoles in the myeloid precursor (left) and erythroid precursor (right); Panel C: cytoplasmic vacuoles in the basophil precursor; Panel D: sea-blue histiocyte.

(hemoglobin 8.1 g/dL at discharge). Two months later, the CBC showed WBC 4800/μL, hemoglobin 11.3 g/dL, and platelet 246/μL. Her anemia was felt to be a combination of copper deficiency anemia, anemia of inflammation (from sepsis), and anemia of chronic kidney disease. Cytoplasmic vacuoles in the erythroid and myeloid precursors are well-recognized BM changes secondary to copper deficiency [1]. Sea-blue histiocytes are recognized findings in long-term TPN patients [2]. Copper deficiency is also a recognized complication of long-term TPN [3]. Hematologic findings such as neutrophil hypogranularity and cytoplasmic vacuoles can often be seen in myelodysplastic syndromes (MDS) and those cases may be misdiagnosed as such. However, it is to be noted that myeloid lineage vacuolation is not a recognized finding in MDS. Copper deficiency should be considered in the differential diagnosis of clinical and morphological features suggesting MDS. It is important to timely diagnose copper deficiency as one of its recognized complications includes the development of neurologic deficits manifested as subacute combined degeneration of the spinal cord and peripheral neuropathies, if left untreated [4].

Authorship

THO: wrote the manuscript. SH: reviewed the pathology.

Conflict of Interest

None declared.

References

1. Kobayashi, Y., and Y. Hatta. 2014. Copper deficiency anemia. Br. J. Haematol. 164:161.
2. Bigorgne, C., A. Le Tourneau, K. Vahedi, B. Rio, B. Messing, T. Molina, et al. 1998. Sea-blue histiocyte syndrome in bone marrow secondary to total parenteral nutrition. Leuk. Lymphoma 28:523–529.
3. Karpel, J. T., and V. H. Peden. 1972. Copper deficiency in long-term parenteral nutrition. J. Pediatr. 80:32–36.
4. Lazarchick, J. 2012. Update on anemia and neutropenia in copper deficiency. Curr. Opin. Hematol. 19:58–60.