

**Nellowe Candelario, MD**

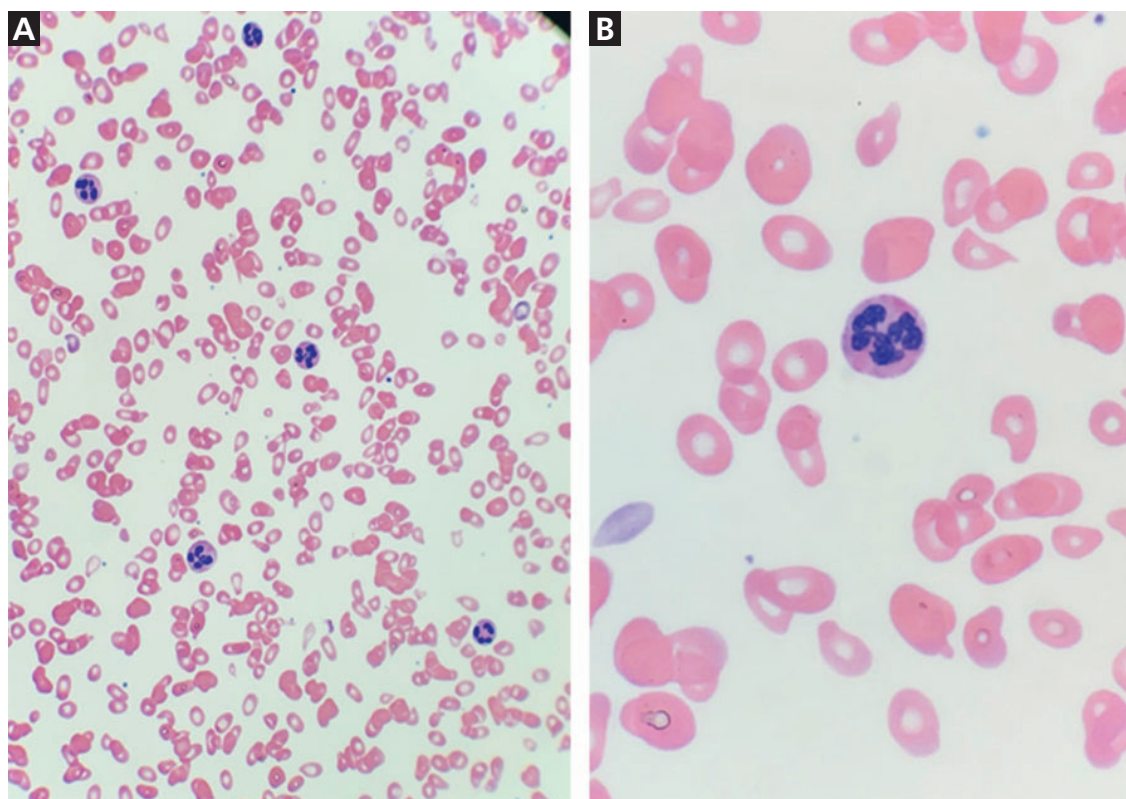
Department of Hematology and Oncology,  
University of Colorado Cancer Center,  
Anschutz Medical Campus, Aurora, CO

**Catherine Klein, MD**

Department of Hematology and Oncology,  
University of Colorado Cancer Center, Anschutz  
Medical Campus, Aurora, CO; Rocky Mountain  
Regional VA Medical Center, Aurora, CO

## Megaloblastic anemia due to severe vitamin B<sub>12</sub> deficiency

**Megaloblastic anemia is commonly related to vitamin B<sub>12</sub> or folate deficiency**



**Figure 1.** Peripheral blood smears show hypersegmented neutrophils consistent with megaloblastic anemia. Panel A (hematoxylin and eosin, magnification  $\times 40$ ) shows neutrophils with hypersegmented multilobed nuclei (more than 5 lobes, dark blue stain) in a background of anisocytosis with macrocytes, ovalocytes, and thrombocytopenia. Panel B (hematoxylin and eosin, magnification  $\times 100$ ) shows a neutrophil (stained dark blue) with multilobed nuclei.

**A** 75-YEAR-OLD MAN PRESENTED to the hospital with altered mental status and pancytopenia. He had a history of schizophrenia and gastrointestinal bleeding due to peptic ulcer disease, for which he had undergone subtotal gastrectomy.

Results of a complete blood cell count at presentation showed the following:

- Hemoglobin 5.5 g/dL (reference range 14.5–18.1)
- Hematocrit 17.5% (42.0–54.0)
- Mean corpuscular volume 108.7 fL (80–100)
- White blood cell count  $3.5 \times 10^9/L$  (4.41–10.05)
- Platelet count  $54 \times 10^9/L$  (150–400)
- Lactate dehydrogenase 3,320 U/L (90–285)

doi:10.3949/ccjm.89a.21041

- Haptoglobin < 10 mg/dL (33–171)
- Total bilirubin 2.6 mg/dL (< 1.2)
- Indirect bilirubin 1.8 mg/dL (< 1.2).

Results of an iron panel study were consistent with anemia of chronic inflammation with serum iron 177 µg/dL (40–150), total iron binding capacity 179 µg/dL (280–500), iron saturation 98.89%, and ferritin 408 ng/mL (40–400). The reticulocyte percentage was 1% with a reticulocyte index of 0.17%, indicating a hypoproliferative type of anemia.

In addition, the vitamin B<sub>12</sub> level was low at 93 pg/mL (220–600), serum folate was normal at 8.2 ng/mL (> 3), homocysteine was elevated at 138 µmol/L (0.0–19.2), and methylmalonic acid was elevated at 25,024 nmol/L (0.0–378). A peripheral blood smear (Figure 1) showed the presence of macrocytosis, thrombocytopenia, and hypersegmented neutrophils (ie, with multiple lobes in nuclei). These findings, consistent with megaloblastic anemia, confirmed the diagnosis of megaloblastic anemia due to vitamin B<sub>12</sub> deficiency.

### MEGALOBlastic ANEMIA: DIAGNOSTIC CLUES

Macrocytic and megaloblastic anemia from vitamin B<sub>12</sub> deficiency leads to defective DNA synthesis in hematopoietic precursors manifesting as pancytopenia and hemolysis owing

to ineffective hematopoiesis. Megaloblastic anemia is commonly related to vitamin B<sub>12</sub> or folate deficiency.<sup>1–4</sup> Important differential diagnoses to consider include medication side effects (eg, methotrexate, chemotherapy, or antibiotics such as trimethoprim), and malabsorption due to an anatomic or autoimmune cause (pernicious anemia), as well as a primary bone marrow pathology such as myelodysplastic syndrome.

In this patient, megaloblastic anemia was diagnosed based on clinical and laboratory findings of severe vitamin B<sub>12</sub> deficiency, for which subtotal gastrectomy is a known predisposing factor.

### CASE CONCLUSION

The patient was immediately started on vitamin B<sub>12</sub> 1,000 µg weekly by intramuscular injection. Several days after the start of treatment, repeat testing showed improving bone marrow recovery, with an increase in reticulocyte count and normalization of lactate dehydrogenase. At 2 weeks, the patient experienced significant improvement in complete blood cell count and mental status.

### DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

gastrectomy anemia: evaluation of 72 cases with post-gastrectomy anemia. *Hematology* 2007; 12(1):81–84. doi:10.1080/10245330600938554

4. Green R, Datta Mitra A. Megaloblastic anemias: nutritional and other causes. *Med Clin North Am* 2017; 101(2):297–317. doi:10.1016/j.mcna.2016.09.013

Address: Nellowe Candelario, MD, Department of Hematology and Oncology, University of Colorado Cancer Center, MS 8117, 12801 East 17th Avenue, Aurora, CO 80045; nellowe.candelario@cuanschutz.edu

### REFERENCES

1. Stabler SP. Clinical practice. Vitamin B12 deficiency. *N Engl J Med* 2013; 368(2):149–160. doi:10.1056/NEJMc1113996
2. Socha DS, DeSouza SI, Flagg A, Sekeres M, Rogers HJ. Severe megaloblastic anemia: vitamin deficiency and other causes. *Cleve Clin J Med* 2020;87(3):153–164. doi:10.3949/ccjm.87a.19072
3. Beyan C, Beyan E, Kaptan K, Ifran A, Uzar AI. Post-

**At 2 weeks, the patient experienced significant improvement in complete blood cell count and mental status**