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CONTINUING MEDICAL EDUCATION
ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

Hematology Quiz – Case 74

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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2026, 43(3):428–430

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A previously well 33-year-old man was referred to the hematology clinic because of macrocytosis (MCV 103.9 fL) found in laboratory tests performed because of diarrhea and weight loss (12 kg) since his return from a trip to India two months earlier. There was no fever, rigors, or night sweats. A course of ciprofloxacin and metronidazole did not improve his symptoms. Laboratory examinations showed a hemoglobin concentration of 13 g/dL, white-cell count 6×10^9/L, platelets 290×10^9/L, albumin 3.6 g/dL, ferritin 200 ng/mL (normal 17–165), vitamin B_{12} 322 pg/mL (normal 170–590), folic acid 2.2 ng/mL (normal 1.5–5.5), normal urea and electrolytes, C-reactive protein (CRP) and liver function tests. Tests for HIV, HBV, HCV, and syphilis were negative, as well fecal cultures. A stool sample was negative for ova and parasites. A quantitative fecal fat test was performed and was compatible with steatorrhea. The patient's blood film is shown in figure 1. The bone-marrow aspirate smear is shown in figures 2–7 (fig. 7 is an iron stain).

Comment

The white cell differential in the peripheral blood was: neutrophils 64% with a right shift (5-lobed neutrophils 23%), lymphocytes 31%, monocytes 3%, and eosinophils 2%. The red blood cells showed mild macrocytosis without any other specific alterations. The platelets were normal in count and morphology. No intracellular or extracellular microorganisms were found.

Important clues from the patient's history include his recent trip to India and subsequent diarrhea. These should raise suspicion for an infectious disease acquired in the tropics including diarrhea caused by E. coli, Shigella spp, Salmonella spp, Campylobacter spp, Vibrio

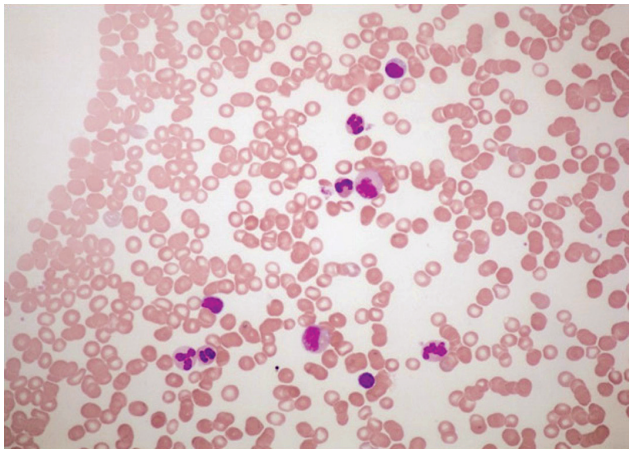

Figure 1.

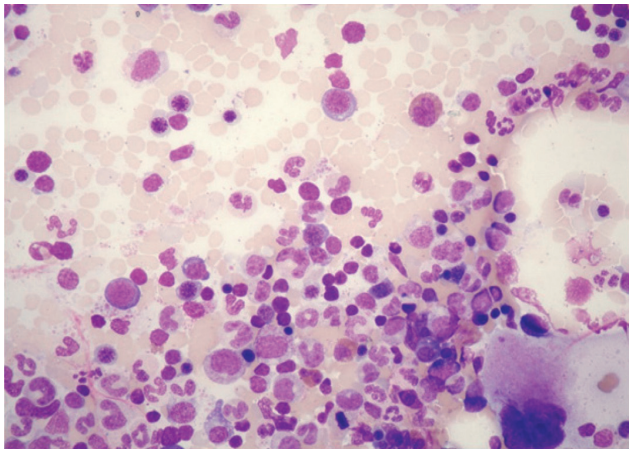

Figure 2

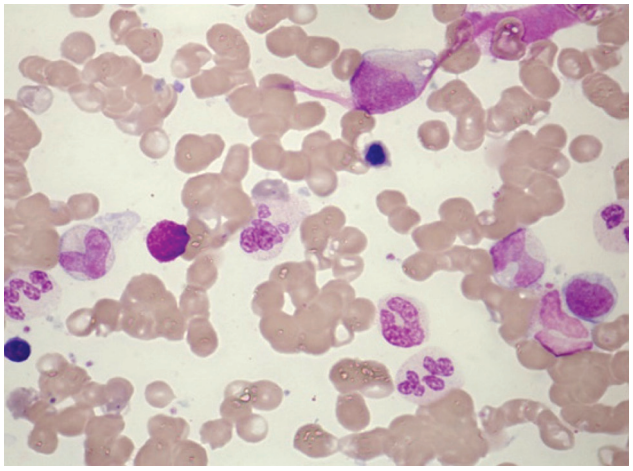

Figure 3

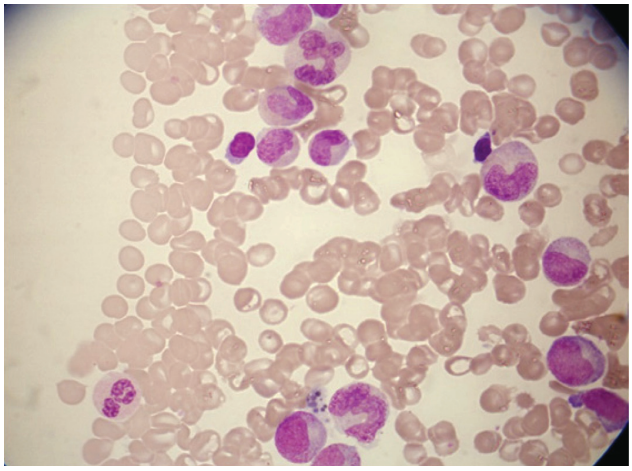

Figure 6

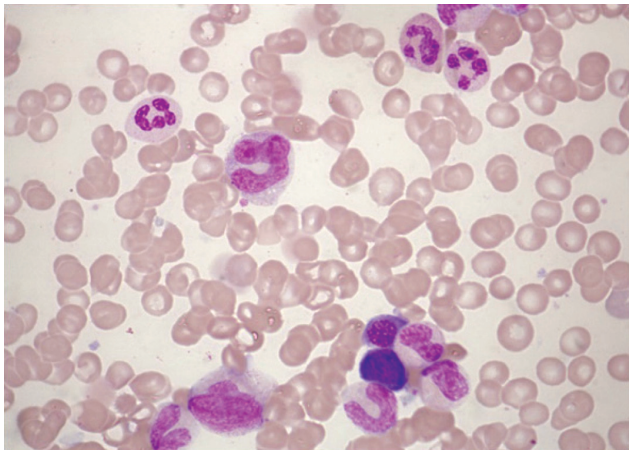

Figure 4

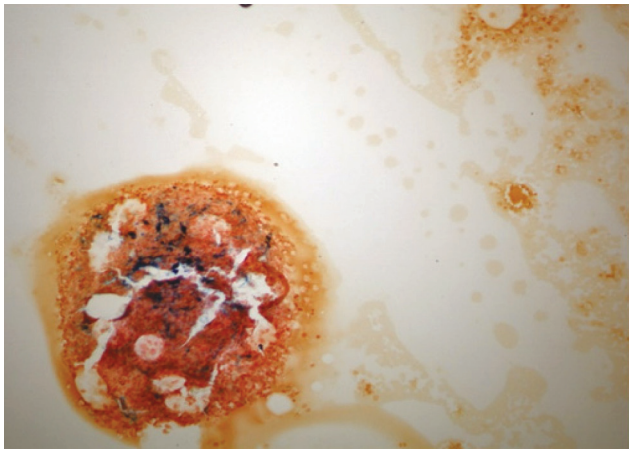

Figure 7

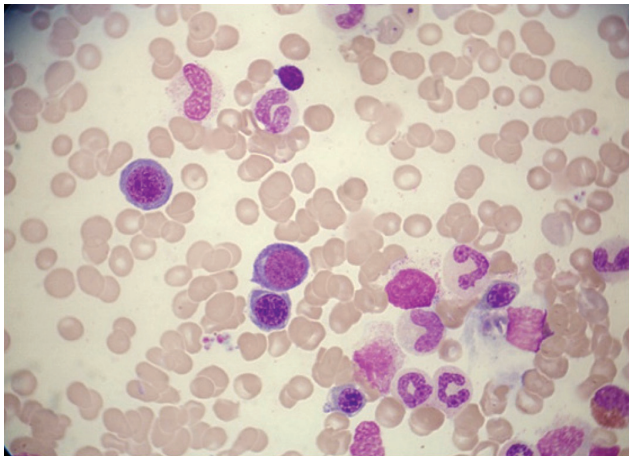

Figure 5

parahaemolyticus, Giardia, and Strongyloides. However, the results of stool cultures were negative. Despite the low-normal serum folate levels, the aspirate smears show clear-cut megaloblastic change in the granulocytic series with numerous giant metamyelocytes and hypersegmented mature forms. Erythropoiesis is less megaloblastic although some nuclear/cytoplasmic asynchrony was noted (fig. 5). Iron stores are adequate. One of the main causes of megaloblastic anemia in patients who live, or have travelled to tropical countries such as India or South America is folic acid deficiency caused by tropical sprue (post-infective tropical malabsorption) which is due to inefficient intestinal absorption of nutrients after a small intestinal (jejenum) infection with aerobic enterobacteria (Escherichia coli, Klebsiella spp, and Enterobacter spp), causing partial villous atrophy.

Tropical sprue presents with diarrhea, anorexia, weight loss, and megaloblastic anemia due to folic acid deficiency. The partial villous atrophy has been a constant finding. The differential diag-

nosis includes infections with Giardia and Strongyloides (parasitic malabsorption), pellagra (niacin [vitamin B3] deficiency), Whipple's disease, coeliac disease, idiopathic inflammatory bowel disease, common variable immunodeficiency, lymphoma (immunoproliferative small bowel disease [IPSID]), and opportunistic infections in immunocompromised individuals (e.g., CMV, Cryptosporidium, microsporidiosis, cyclospora, and Mycobacterium avium-intracellulare complex).The response to treatment to tetracycline and folic acid has been uniformly successful.

Folic acid deficiency causes similar hematological manifestations to vitamin B_{12} deficiency though neuropsychiatric manifestations are less common. The ability of nerve tissue to concentrate folate to levels five times greater than those in the plasma has been suggested as a reason for the absence of neuropathy in folate deficiency. Folic acid deficiency is associated with fetal neural tube defects, and possibly with an increase in atherosclerosis and arteriovenous thrombosis, dementia and colonic cancer. Dietary folic acid is present in the form of polyglutamates, which are converted to folate monoglutamates by the enzyme folate conjugase in the intestinal brush border, prior to absorption. The monoglutamates function as a carbon transporter (CH3) and are essential for DNA biosynthesis.

Folate is found in green vegetables and fruits and deficiency can result from decreased intake, impaired absorption and increased utilization, although the commonest cause is dietary insufficiency. Other causes include alcoholism, excessive cooking of vegetables, and malabsorption, as in this patient. Increased demand for folic acid occurs in pregnancy because the growing fetus has a high avidity for folate. For this reason, folate supplementation has been widely recognized as an essential part of routine antenatal care to reduce the risks of neural tube defects. High folate utilization also occurs in hemolytic anemias such as sickle cell disease due to high red cell turnover and exfoliative dermatitis. Several drugs, including sulfasalazine, trimethoprim, methotrexate, pyrimethamine and phenytoin, can also interfere with folate metabolism.

Folate-deficient individuals develop a macrocytic anemia with peripheral blood and bone marrow findings similar to that found in vitamin B_{12} deficiency. Diagnosis of folate deficiency is confirmed by the presence of low serum folate. Red cell folate levels decrease more slowly than serum levels during the 120-day turnover of the red cells. Red cell folate levels may be a better indicator of tissue folate levels than serum folate, although red cell folate can be more expensive and falsely low in case of vitamin B_{12} deficiency. It should also be remembered that folate deficiency may be associated with falsely low serum vitamin B_{12} levels.

The patient was found to have a low red cell folate level (113 ng/L; normal >150 ng/L); thus confirming the diagnosis of folate deficiency. He received antibiotic therapy with tetracycline 250 mg×4 per os and high-dose folic acid supplementation 5 mg×4 per os for one month, resulting in remission of the diarrhea, followed by tetracycline 250 mg×2 and folic acid 5 mg×2 for 5 months. Revaluation after three months showed normal laboratory tests and clinical condition.

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