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ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

Hematology Quiz – Case 61

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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2021, 38(5):716–717

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A 44-year-old man presented to our clinic for evaluation of splenomegaly and thrombocytopenia. Five days earlier, he was evaluated at the emergency department after a motorcycle accident. A routine trauma X-ray series showed no fractures. On abdominal ultrasonography, however, he was found to have splenomegaly (16.5 cm) and hepatomegaly (16.0 cm). His past medical history was unremarkable. He did not smoke, drank alcohol rarely, and took no medications. His family history was unremarkable.

On presentation, he reported having intermittent left-knee pain over the past four months, which had worsened after his accident. His knee was not red, hot, or swollen. There was no fever, weight loss, or pain elsewhere. On examination, he had palpable splenomegaly 2 to 3 cm below the left costal margin. There was no lymphadenopathy or stigmata of liver disease. The hemoglobin level was 12.7 g/dL, white-cell count 6.2×10^9/L (75% neutrophils), and platelet count 90×10^9/L. Urea and electrolytes, liver function tests, folic acid, and vitamin B12 were normal. Serum ferritin was 1,203 μg/L (normal: 30–400). An evaluation for hepatosplenomegaly was initiated, including bone-marrow examination. Figures 1 to 4 are representative fields of the bone-marrow aspirate smears. Figure 4 is a Perl's stain for iron. Magnetic resonance imaging (MRI) of the left knee revealed grade II avascular necrosis of the left lateral tibial condyle.

Comment

The bone marrow aspirate revealed that much of the marrow had been replaced by large macrophages with fibrillar or striated cytoplasm consistent with Gaucher's cells. The fine, scroll-like pattern in the cytoplasm like that of crinkled tissue paper or balled yarn is a characteristic feature. As seen in figure 5, the cells stained positive for iron. Gaucher's disease is an autosomal-recessive lysosomal storage disorder caused by a deficiency of β-glucocerebrosidase (glucosyl-

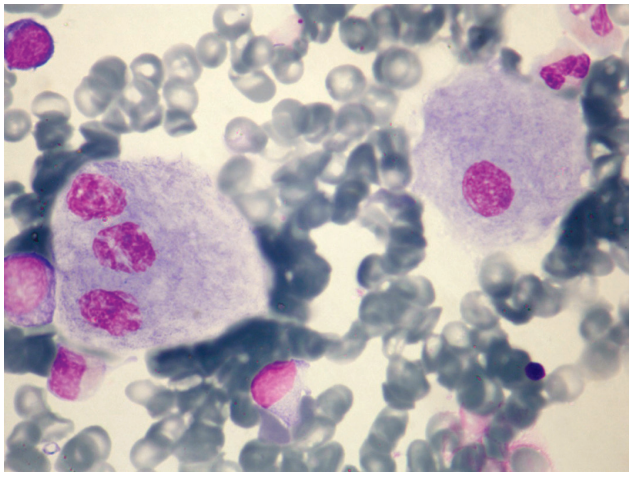

Figure 1

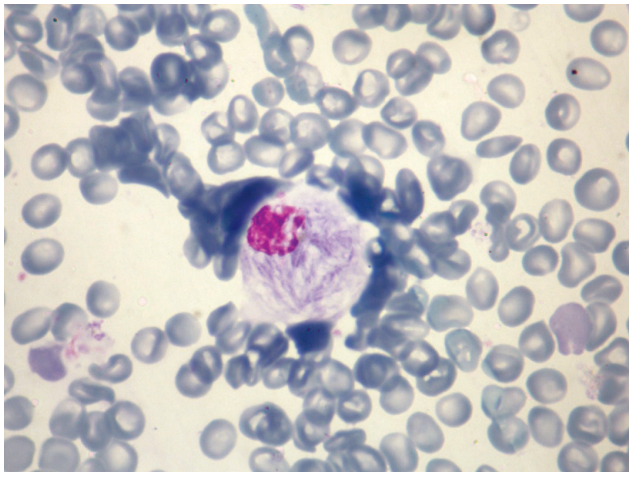

Figure 2

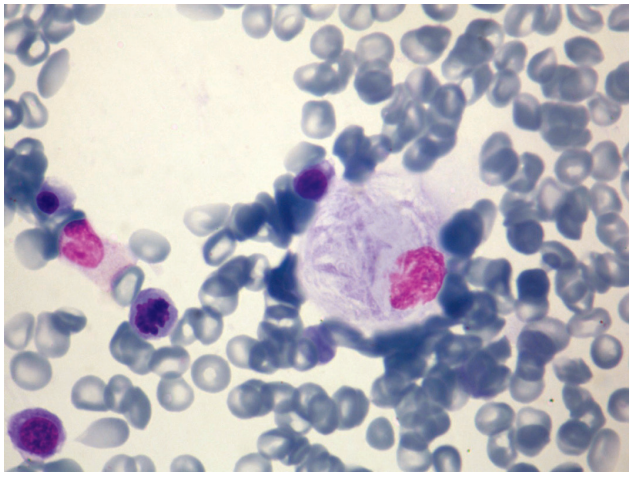

Figure 3

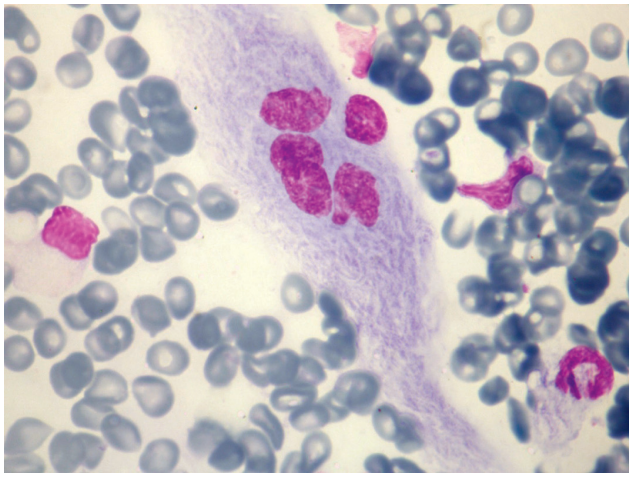

Figure 4

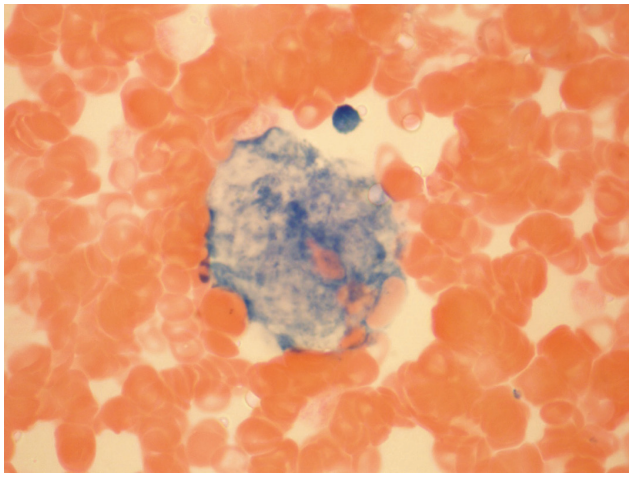

Figure 5

ceramidase), the enzyme required for the lysosomal degradation of glycolipids (i.e. lipids containing covalently bound sugars). The gene for β-glucocerebrosidase (GBA) is located on chromosome 1q21. In patients with Gaucher's disease, more than 200 different mutations have been identified in this chromosomal region. Three clinical subtypes have been recognized on the basis of the absence (type I) or presence (types II–III) of neurological manifestations. All forms are panethnic, however, type I is especially prevalent among Ashkenazi Jews. Severe forms of Gaucher's disease are quite rare, but milder forms are not uncommon. In mildly affected individuals, diagnosis may be made in middle or old age. The combination of bone pain and hepatosplenomegaly strongly suggests Gaucher's disease. The differential diagnosis includes other metabolic storage diseases such as Niemann-Pick disease and secondary accumulation of pseudo-Gaucher's cells in persons without β-glucocerebrosidase deficiency. Pseudo-Gaucher's cells may be found when there is a very high rate of cell turnover e.g. chronic myeloid leukemia, thalassemia, multiple myeloma, and myelodysplastic syndromes.

Gaucher's disease has two main treatment approaches: enzyme-replacement therapy and substrate-reduction therapy. Enzyme-replacement therapy with recombinant glucocerebrosidase e.g. imiglucerase, the current standard-of-care, improves hematological and biochemical indices, reverses organomegaly, decreases bone-related pain, and improves quality of life. Substrate-reduction therapy is an alternative strategy that uses glycosylceramide synthetase inhibitors e.g. miglustat to diminish glycolipid biosynthesis.

In our patient, white cell β-glucocerebrosidase activity was 2.7 nmoL/hour/mg protein (normal: 6.0–23.0), and DNA testing revealed the genotype N370S/D409H:H255Q. He is being treated with intravenous imiglucerase (60 IU/kg given fortnightly), with clinical improvement.

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Diagnosis: *Gaucher's disease, type I*