CASE REPORT

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Acute myelofibrosis: multifocal bone marrow infiltration detected by scintigraphy and magnetic resonance imaging

Abstract Acute myelofibrosis is a rare, malignant hematological disorder of unknown etiology with an inevitably fatal outcome. Here we present the study of a 63-year-old Caucasian man with acute onset of pancytopenia. Repeated bone marrow biopsies showed dense fibrosis and hypoplastic hematopoiesis raising various differential diagnoses of malignant and nonmalignant conditions. Bone marrow scintigraphy and magnetic resonance imaging (MRI) showed areas suggesting neoplastic infiltration, mainly in both femurs and tibias. Histological examination of a surgical biopsy of the left tibia revealed acute megakaryoblastic leukemia. As the patient refused polychemotherapy, therapy with interferon gamma was initiated but discontinued prematurely because of intolerable side effects. The presented case therefore suggests that the combination of bone marrow scintigraphy and MRI is a valuable diagnostic tool in patients presenting with myelofibrosis of unknown origin.

Key words Acute myelofibrosis · Acute megakaryoblastic leukemia · Scintigraphy · Magnetic resonance imaging · Interferon gamma

Introduction

Acute myelofibrosis (acute myelodysplasia with myelofibrosis, acute myelosclerosis, malignant myelosclerosis) is a rapidly fatal disease of mostly elderly patients, with a median survival of 6 months after diagnosis. The patients’ symptoms are often nonspecific and splenomegaly is usually absent. The peripheral blood is characterized by pancytopenia, with occasional appearance of blast cells; the bone marrow is fibrotic, showing hypoplasia and immaturity of all three cell lines [4, 19]. However, in some cases, the fibrotic bone marrow may be mostly hypoplastic with only some focal areas of hyperplastic immature hematopoiesis [8, 12]. Bone marrow fibrosis in acute myelofibrosis as well as agnogenic myeloid metaplasia is a reactive process due to stimulation of nonclonal fibroblasts by growth factors shed from clonal megakaryocytes [17, 18]. The major cytokines involved are platelet-derived growth factor (PDGF) and transforming growth factor (TGF) beta. While PDGF stimulates fibroblasts to proliferate and secrete collagen, TGF beta enhances the production and secretion of extracellular matrix proteins [1, 17, 18]. To date, no curative treatment for acute myelofibrosis exists and, for many patients, only supportive care including red cell and platelet transfusions is indicated. Here we present a case of acute myelofibrosis with multifocal infiltration of megakaryoblastic clusters detected by bone marrow scintigraphy and magnetic resonance imaging (MRI). This patient was treated with interferon (IFN) gamma, a potent inhibitor of PDGF and TGF beta, and, as far as we know, this treatment has never before been reported for acute myelofibrosis.

Case report

A 63-year-old Caucasian man was admitted to a peripheral hospital because of increasing weakness and severe epistaxis. His blood counts showed marked anemia and thrombocytopenia, and he was treated with red cell and platelet transfusions.
row biopsy revealed dense fibrosis and hypoplastic hematopoiesis; however, a definite diagnosis could not be made and the patient was therefore referred to the university hospital. He presented with slight pallor but neither lymphadenopathy nor hepatosplenomegaly. His blood counts were: red blood cells (RBC), 2.3 \times 10^{12}/l; hemoglobin (Hb), 68 g/l; mean corpuscular volume (MCV), 91 fl; mean corpuscular hemoglobin (MCH), 30 pg; platelets (PLT), 21 \times 10^9/l and white blood cells (WBC), 3.7 \times 10^9/l (with a differential count of neutrophils, 69%; bands, 2%; pro-myelocytes, 1%; lymphocytes, 24% and monocytes, 4%). Further laboratory investigations revealed normal liver and kidney function and a serum C-reactive protein of 9.9 mg/dl (range 0–1 mg/dl). Another bone marrow biopsy confirmed the initial findings, raising various differential diagnoses of malignant and nonmalignant conditions. A chest X-ray, ultrasound of the abdomen, and a cerebral, abdominal and pelvic computed tomography (CT) scan were normal, as were upper and lower gastrointestinal endoscopy. The serum levels of parathyroid hormone and calcitonine were within normal limits excluding hyper- or hypoparathyroidism as a possible cause of bone marrow fibrosis. A chronic infectious disease like tuberculosis or a fungal infection as well as a toxic process, which may occasionally lead to bone marrow fibrosis, could also be excluded.

The diagnostic work-up included whole-body bone marrow scintigraphy with technetium-99m-nanocolloid. It revealed peripheral bone marrow expansion in the upper and lower limbs but significantly less tracer uptake in the proximal parts of the tibias (Fig. 1). This lack of tracer deposition was suggestive of either fatty marrow or a malignant bone marrow infiltration. To further differentiate these findings, MRI of the left tibia was performed, revealing a mostly fatty marrow with scattered foci of hematopoietic reconversion in the proximal part. T1-weighted images showed these foci as hypointense lesions within the fatty bone marrow (Fig. 2). On fat-saturated T2-weighted images, these focal lesions were not conspicuous, most likely due to a dense fibrosis. Histological examination of a surgical biopsy taken from these foci revealed dense fibrosis and infiltration of undifferentiated blast cells. Immunohistochemical staining showed a variable number of blasts positive for CD61, CD43, and factor VIII-rAg; acute myelofibrosis due to acute megakaryoblastic leukemia was therefore diagnosed (Fig. 3). Supportive therapy with red cell and platelet transfusions was continued. In addition, recombinant human erythropoietin at a dose of 10,000 U was administered daily for 8 weeks. As the patient refused polychemotherapy, therapy with IFN gamma at 0.1 mg s.c. three times weekly was initiated. However, 4 weeks later, the patient chose to discontinue IFN gamma treatment because of intolerable side effects, such as fever and bone pain. A reduction in red cell and platelet transfusions during that time could not be achieved. The patient died 6 weeks thereafter, 7 months after presentation, of bone marrow failure.

**Fig. 1** Bone marrow scintigraphy of the knee joints, the distal parts of the femurs and the proximal parts of the tibias: nearly absent technetium-99m-nanocolloid uptake in the proximal parts of both tibias and pathologically increased trace deposition in the distal part of the left femur and distal part of the left tibia.

**Fig. 2** T1-weighted MRI of the left tibia: several dark foci of neoplastic infiltration within the mostly fatty marrow in the proximal part of the tibia. From these areas a surgical biopsy was taken.

**Fig. 3** Acute myelofibrosis is an aggressive malignant hematological disorder of unknown etiology with an inevitably fatal outcome. Immunological staining shows a prominence of the megakaryocytic lineage and the blast cells...