Case Report

Intracranial myeloid metaplasia in idiopathic myelofibrosis

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ABSTRACT

Extramedullary hematopoiesis is a common finding in idiopathic myelofibrosis and is generally found in the liver, spleen and lymph nodes, but meningeal extramedullary hematopoiesis is very rare. Some diseases may be causes of intracranial masses and diagnosis is difficult. We present a case diagnosed as intracranial and meningeal extramedullary hematopoiesis with idiopathic myelofibrosis inducing serious headache.

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Extramedullary hematopoiesis (EMH) may occur in various types of hemodyscrasia and dyshematopoiesis, and is generally seen in the spleen, liver and lymph nodes, but rarely within other sites.[1] Intracranial and meningeal extramedullary hematopoiesis have very rarely been reported in the literature in patients with idiopathic myelofibrosis.[2-4] We present an 18-year-old man with refractory serious headache with idiopathic myelofibrosis, which has intracranial and meningeal diffuse mass due to EMH.

Case Report. An 18-year-old man was admitted to our hematology clinic with refractory headache, dyspnea, fatigue, and anemia. He had been experiencing frequent headaches for the past 3 weeks. There was no history of trauma or primary malignancy. Six years prior to the admission he had been diagnosed with myelofibrosis. On physical examination, his blood pressure was 110/70 mm Hg, pulse 94 beats per minute, and respiratory rate 18 breaths per minute; the abdomen was distended and the liver enlarged. Splenectomy was carried out for thrombocytopenia and painful splenomegaly 2 months previous. The hematologic examination before splenectomy revealed a hemoglobin (Hb) of 8 gr/dl, white blood cell (WBC) count of 37,900/mm^3, and platelets of 38,000/mm^3. In clinical follow up, headache was not responding to non-narcotic and narcotic analgesics. Hemoglobin level was 9.2 g/dL, WBC count 4,500/mm^3, platelet count 65,000/mm^3 and a peripheral blood smear revealed anisocytosis, poikilocytosis, teardrop cells, and leukoerythroblastic changes. Bone marrow aspiration revealed a focal hypercellular marrow with megakaryocytic hyperplasia and biopsy revealed fibrosis and focal hypercellular marrow and megakaryocytic hyperplasia. The results of the biochemical parameters were as follows: alkaline phosphatase, 404 IU/L (53-41); lactate dehydrogenase, 235 IU/L (135-225); uric acid, 8.8 mg/dl (3.5-6.4); alanine aminotranspherase,10 IU/L (0-41); aspartate aminotransferase, 9 IU/L (0-37); total protein, 5.7 g/dl (6.4-8.3); albumin, 2.4 g/dl (3.5-5.0); total bilirubin, 1.2 mg/dl (0-1.0); and unconjugated bilirubin, 0.8 mg/dl (0.2-0.7). Chest roentgenography and echocardiographic examination were normal. Magnetic resonance imaging (MRI) showed diffuse signal enhancement surrounding the brain (**Figure 1**). Bone morrow of whole body and cranium SPECT studies were obtained using 10 mCi ^{99m}Tc nanocolloid. Cross

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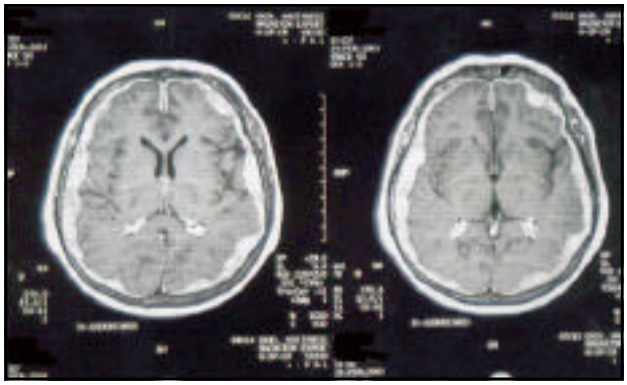

Figure 1 - Cranial magnetic resonance imaging with intravenous gadolinium showing meningeal diffuse mass surrounding the brain.

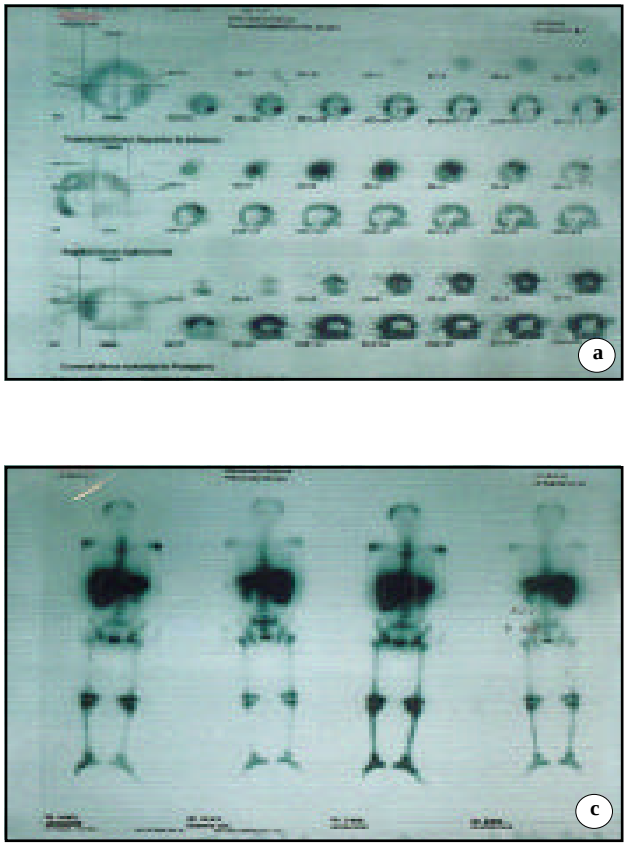

Figure 2 - Whole body bone and bone marrow 99mTc nanocolloid scintigraphy and cranium SPECT study of the patient. **a)** Cross section of trans-sagittal, transaxial and coronal images of brain, 99mTc nanocolloid scintigraphy showing multifocal radiotracer uptake. **b)** The image of enlarged liver with 99mTc nanocolloid scintigraphy. **c)** Whole body bone and bone marrow 99mTc nanocolloid scintigraphy showing multifocal radiotracer uptake.

sections of trans-sagittal, transaxial and coronal images of brain were obtained during the SPECT study (**Figure 2a**). Increased radiotracer involvement was observed in the left temporal and left occipital bone more clearly than in the frontal, parietal, and right temporal areas. In addition, increased radiotracer involvement was observed in lateral sulcus bilaterally, especially in cerebral longitudinal fissure. In planar images, liver was enlarged and radiotracer uptake was increased (**Figure 2b**). In addition, increased radiotracer involvement was observed in the femur and tibia. Bone scintigraphy with 20mCi Tc99m MDP showed increasing osteoblastic activity in the left frontal and lateral parietal bones and in shoulders, knee and ankle joints, and both metatarsal bones (**Figure 2c**). Bilateral parietal and left frontal bone involvement was detected on both bone marrow and whole body scintigraphy. A biopsy of the mass revealed extramedullary hematopoiesis composed of erythroblasts, promyelocyte, myelocyte, metamyelocyte, band form, mature cells and megakaryocytes. Blast cells were not found. We concluded that these represented foci of EMH due to idiopathic myelofibrosis. Headache was slightly decreased, and MR images were sustained after 18

GY (9 fr at 11 days) external cranial radiotherapy. A 5-month follow-up showed the symptoms had not resolved completely.

Discussion. Patients with extramedullary hematopoiesis may be divided into 2 main groups. The first group shows paraosseous foci that may result from herniation of medullary tissue from the underlying bone. This is seen in hemolytic disorders such as thalassemia and sickle cell anemia, where the marrow has tremendous activity. The second group shows extraosseous soft tissue foci, which may arise from multipotential stem cells. This occurs when the marrow activity is ineffective, as in idiopathic myelofibrosis or, rarely, with toxic or tumoral marrow destruction.[2] The liver, spleen, and lymph nodes are often involved, but involvement of other sites such as the intrathoracic cavity, kidney, and thyroid have been reported.[1,5-7] However, it is very rare in intracranial and meningeal areas.[3,4] As the spleen is a prime site of hemopoiesis in agnogenic myeloid metaplasia, its removal might have facilitated extramedullary hematopoiesis at different sites including intracranial location in attempt to compensate for myelophthisis. Accelerated hepatomegaly in 16.1% of patients, as has been in our case (**Figure 2b**) and blast transformation in 16.3% of patients is well described by Tefferi et al's report on 223 patients who were evaluated, cardiac EMH was reported only in one patient on the necropsy material and intracranial-meningeal EMH was not reported.[8] Increased radiotracer uptake in extramedullary hematopoietic tissue may be confused as tumor activity. Noninvasive imaging (CT, MRI and ^{99m}Tc-nanocolloid scintigraphy) can be used to help establish the diagnosis of EMH.[9] However, biopsy is needed to provide cytologic or histologic confirmation.[10]

Our case concerns a patient with intracranial EMH suspected on MRI and with ^{99m}Tc-nanocolloid bone and bone marrow scans subsequently confirmed with tissue biopsy. The first description of the cranial imaging findings in EMH was published by Lund and Aldridge.[2] Four patients with intracranial masses of hematopoietic tissue in the subdural space were reported. Landolfi et al reported the occurrence of meningeal masses causing exophthalmus and fever in a patient with myelofibrosis secondary to polycythemia vera. The patient subsequently developed a rapidly worsening tumor-like syndrome with hemiparesis, aphasia, and loss of sphincteric control. Radiotherapy produced a complete and stable regression of clinical symptoms, and a marked reduction of meningeal masses.[4] Kandel et al reported a patient with polycythemia vera and meningeal masses of 9 years' duration who developed increased intracranial pressure related to a mass obliterating the sagittal fissure. Although clinically and radiologically simulating a meningioma, biopsy revealed EMH involving the falx cerebri.[11]

This case illustrates that myeloproliferative disease can present with clinical symptoms and radiologic features similar to primary intracranial tumors. Intracranial EMH should be considered in the differential diagnosis of patients presenting with refractory headache, chronic anemia, and an extramedullary tumor-like appearance.

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