Myelofibrosis with myeloid metaplasia with fatty bone marrow: report of a new case

Myelofibrosis with myeloid metaplasia with fatty bone marrow is a very rare variant characterized by severe myeloid hypoplasia at bone marrow biopsy and dislocation of hematopoiesis in extramedullary sites. We report a new case in which the finding of an unusually high number of circulating CD34+ cells confirms the hyperproliferative nature of the disease and the high potential for extramedullary hematopoiesis.

The histologic feature of fatty bone marrow is an unusual finding in subjects suffering from myelofibrosis with myeloid metaplasia (MMM). In 1986, Polino *et al.*[1] reported four cases of this anatomic-functional variant, in which myeloid hypoplasia at iliac spine bone marrow biopsy was associated with the ferrokinetic feature of expanded erythropoiesis and dislocation of erythropoietic activity to extramedullary sites. No other cases have since been reported in the literature. We now report a new case of MMM with fatty bone marrow with the aim of better characterization of the pattern of hematopoiesis and of describing the response to cytoreductive therapy.

This report deals with a 74-year old man who presented with a two-month history of abdominal fullness, early satiety, weakness, weight loss and pain in the left upper abdomen. On admission, physical examination revealed increased abdominal volume caused by visible spleen enlargement. The size of the spleen, as measured by ultrasonography, was more than 25 cm in length and 675 cm^2 using the spleen index calculated by multiplying the length of the longitudinal axis by that of the transverse axis.[2] The liver was 4 cm below the right costal margin. Laboratory data showed moderate normocytic anemia (Hb = 8.4 g/dL), leukocytosis (WBC = 14×10^9/L), thrombocytosis (Plt = 660×10^9/L) and leukoerythroblastosis with teardrop red cells in the peripheral blood smear.

At flow cytometric analysis the number of circulating CD34+ cells resulted as 432×10^6/L, with respect to 0.5×10^6/L in normal subjects. This value was the highest of 84 recently examined consecutive MMM patients, in whom the median number of circulating CD34+ cells measured at diagnosis and out of therapy was 81.9 $\times 10^6$/L with a range from 2.04 to 349.4.[3] When cells were double-stained with anti-CD34 and anti-CD38, 31% of the cells were $CD34^+$ /$CD38^-$, thus showing a high degree of immaturity. The ferrokinetic study revealed reduced ^{59}Fe plasma clearance ($T_{1/2}$ = 23'; n.v.= 60-120), while the plasma iron turnover (21.8 mg/L/d; n.v. 4-8) and red cell iron utilization (8 mg/L/d; n.v. 5) were increased. Radioactivity was detectable over the spleen but not over the sacral area. The bone marrow histologic pattern and immunohistochemistry for anti-CD34 antibody (QB-END/10)[4] are shown in Figure 1 and Figure 2. The liver biopsy revealed extramedullary hematopoiesis. Cytogenetic analysis evidenced a 46, XY karyotype and polymerase chain reaction for Bcr-Abl rearrangement on peripheral blood was negative.

After 6 months of therapy with hydroxyurea (1g/per day) a consistent reduction of the spleen volume was recorded. The spleen length reduced to 18 cm, and the spleen index to 294 cm^2, i.e. 56.4% reduction. The CD34+ cells in peripheral blood dropped to a value of 68 $\times 10^6$/L, i.e. 94% reduction. These modifications were associated with improvement of well-being, but not of anemia that was constantly severe and necessitated transfusions.

This case confirms that fatty bone marrow with severe myeloid hypoplasia is the distinctive marker of an anatomic-functional variant of MMM. The high number of circulating hematopoietic stem cells in association with a bone marrow depleted of progenitor cells suggests either dislocation of hematopoiesis in distal bone marrow sites or pure extramedullary hematopoiesis or both. There are insufficient data to draw a conclusion about this issue; nevertheless, this variant seems to be an informative model for the study of hematopoiesis in MMM.

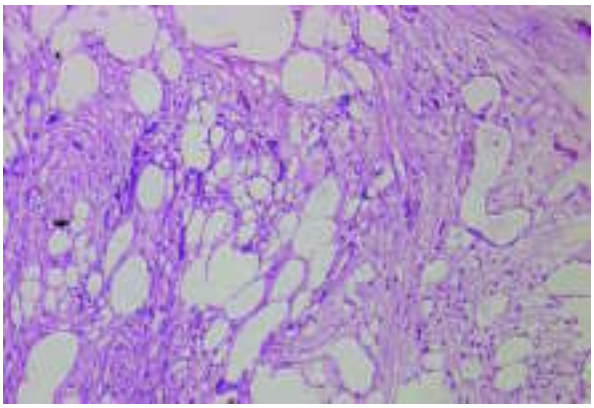

Figure 1. The bone marrow histologic pattern appears markedly hypocellular. Fatty replacement of hemopoietic elements and single or clustered megakaryocytes with markedly condensed and distorted nuclei are evident. Dilatation of the sinusoids and increased reticulin fibers are also observed (hematoxylin-eosin stain, ×40).

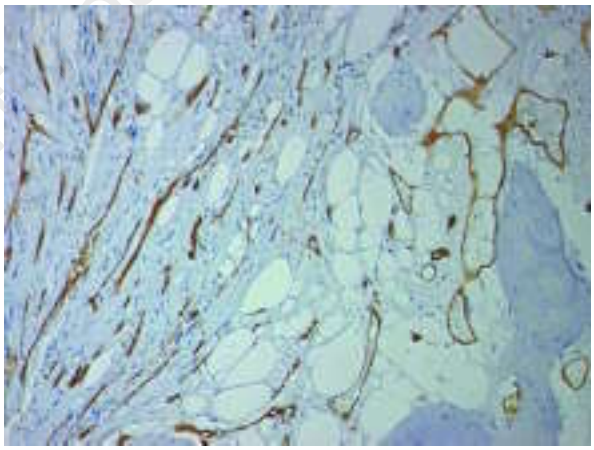

Figure 2. Immunohistochemistry shows marked increase of vasal density, especially in areas displaying collagen fibrosis (anti-CD34 antibody, ×40).

Gian Carla Gerli, Umberto Gianelli, Maria Cristina Carraro, Alberto Bestetti,° Monia Marchetti,^ Giovanni Barosi^*

*Dipartimento di Medicina, Chirurgia ed Odontoiatria; *Istituto di Anatomia Patologica; °Istituto di Scienze Radiologiche, Ospedale San Paolo, Universita' di Milano; ^ Laboratorio di Informatica Medica, IRCCS Policlinico San Matteo, Pavia*

Key words: Myelofibrosis with myeloid metaplasia, fatty bone marrow, CD34+ peripheral cells.

Correspondence: Gian Carla Gerli, M.D., Dipartimento di Medicina e Chirurgia, Odontoiatria, Ospedale San Paolo, Università di Milano, via di Rudinì 8, 20142 Milan, Italy. Phone: international +39.02.81844374 Fax: international +39.02.89123960. E-mail: giancarla.gerli@unimi.it

References

1. Polino G, Barosi G, Berzuini A, et al. Fatty bone marrow with severe myeloid hyploplasia in idiopathic myelofibrosis. Haematologica 1986; 71:117-21.
2. Goulis J, Chau TN, Jordan S, et al. Thrombopoietin concentrations are low in patients with cirrhosis and thrombocytopenia and are restored after orthotopic liver transplantation. Gut 1999; 44:754-8.
3. Barosi G, Viarengo G, Pecci A, et al. Diagnostic and clinical relevance of the number of circulating CD34-positive cells in myelofibrosis with myeloid metaplasia. Blood (in press)
4. Mesa RA, Hanson CA, Rajkumar SV, Schroeder G, Tefferi A. Evaluation and clinical correlations of bone marrow angiogenesis in myelofibrosis with myeloid metaplasia. Blood 2000; 96:3374-80.