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 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 cm² 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 × 10⁹/L), thrombocytosis (Plt = 660 × 10⁹/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 × 10⁹/L with respect to 0.5 × 10⁹/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 81.3 × 10⁹/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 ⁵⁹Fe plasma clearance (T₁/₂: n.v. = 60–120), while the plasma iron turnover (23.8 mg/L/d; n.v. = 8–13) and red cell iron utilization (8 mg/L/d; n.v. = 3) 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/10ª) 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 (1 g per day) a consistent reduction of the spleen volume was recorded. The spleen length reduced to 18 cm, and the spleen index to 294 cm², i.e. 56.4% reduction. The CD34+ cells in peripheral blood dropped to a value of 68 × 10⁹/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.

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