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CONTINUING MEDICAL EDUCATION
ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

Hematology Quiz – Case 54

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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2017, 34(4):570–573

**J.V. Asimakopoulos,
L. Papageorgiou,
V. Telonis,
A. Zannou,
P.M. Arapaki,
T. Giannikos,
M. Belia,
E.F. Triantafyllou,
E. Konstantinou,
M. Efstathopoulou,
C. Chatzidimitriou,
G. Gainarou,
E. Sinni,
P. Tsaftaridis,
E. Plata,
T.P. Vassilakopoulos,
M.K. Angelopoulou,
K. Konstantopoulos,
J. Meletis**

Hematology Department and Bone Marrow Transplantation Unit, National and Kapodistrian University of Athens, School of Medicine, "Laiko" General Hospital, Athens, Greece

A 72-year-old Greek woman was admitted to our Department because of fever and pancytopenia. The patient had fever up to 38.4 °C, which was not responding satisfactorily to non-steroid anti-inflammatory drugs, for the last five days. She was also complaining for progressive fatigue, weakness, dizziness and exercise intolerance for the last three months. Her past medical history included diabetes mellitus and a mild heart failure.

On admission, the patient's temperature was 38.0 °C and she had chills; her blood pressure was 125/80 mmHg, the pulse rate was 122/min, and the respiratory rate was 21/min. The physical examination revealed distinct pallor of the skin and the mucous membranes, and a mild splenomegaly (2 cm under the costal margin). The liver and the peripheral lymph nodes were not palpable. There was no pupruric rash or other signs of a bleeding diathesis. No signs of infection could be found.

The patient's hematological profile was as follows: WBC 2.4×10^9/L (differential count: neutrophils 48%, lymphocytes 36%, monocytes 5%, blasts 1%; erythroblasts 2/100 nucleated cells), Hb 8 g/dL, Ht 25.6% and platelets 72×10^9/L. The reticulocyte count was 0.3% and the erythrocyte sedimentation rate was 36 mm. The peripheral blood smears morphology is shown in figures 1 and 2. The serum biochemical tests revealed increased LDH (562 IU/L) and uric acid (8.1 g/dL), and a small monoclonal IgGκ-band in the immunoelectrophoresis of serum proteins, without any quantitative disturbance of the γ-globulins. Serum B_{12}, folate and ferritin levels were normal as were the osmotic fragility and the autohemolysis tests. The direct antiglobulin test was positive and antiplatelet antibodies were also detected. The blood and urine cultures yielded no bacteria or fungi. The bone marrow aspiration showed a hypercellular marrow with megalo-

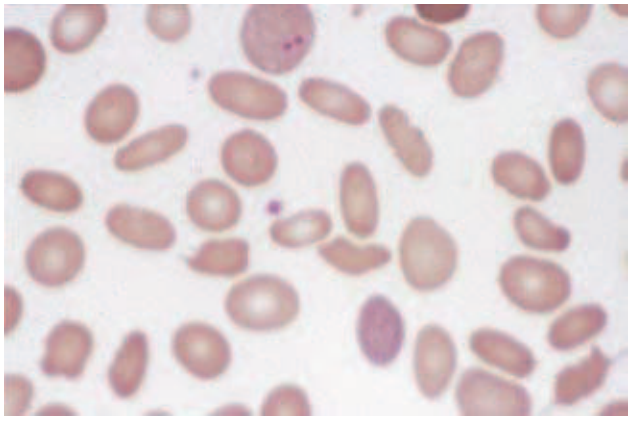

Figure 1

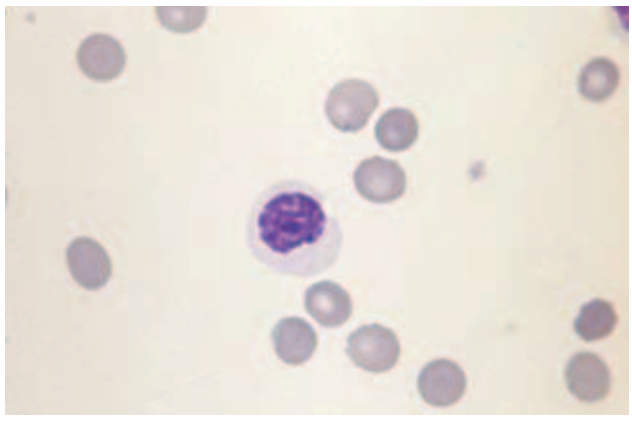

Figure 2

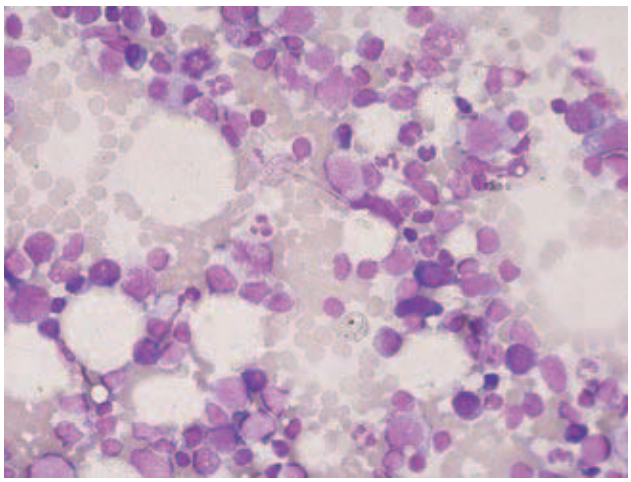

Figure 3

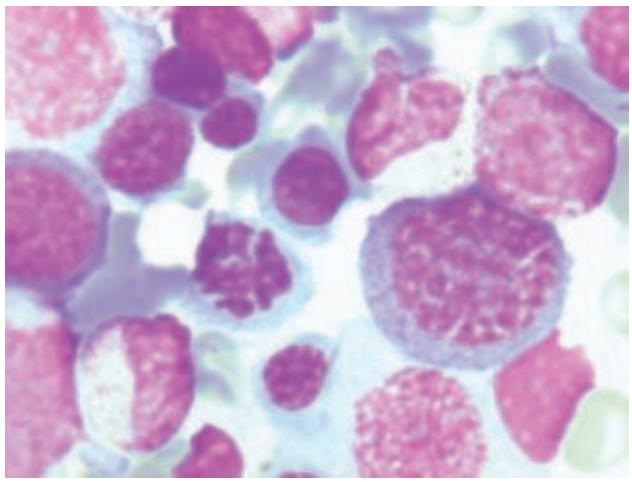

Figure 6

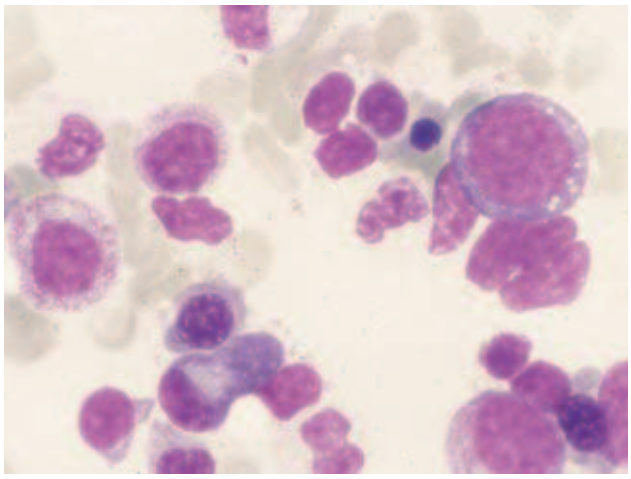

Figure 4

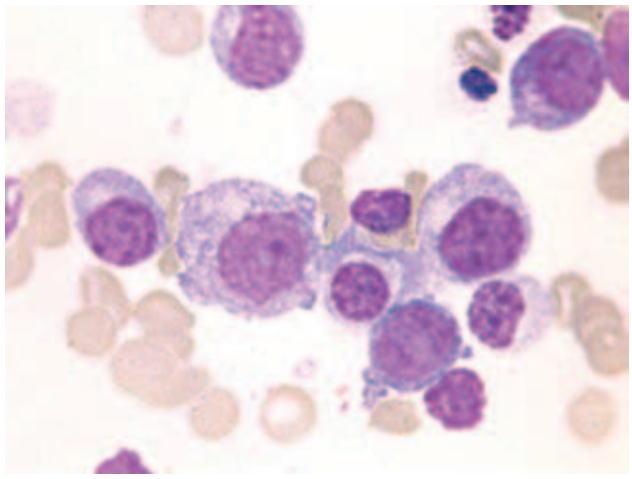

Figure 7

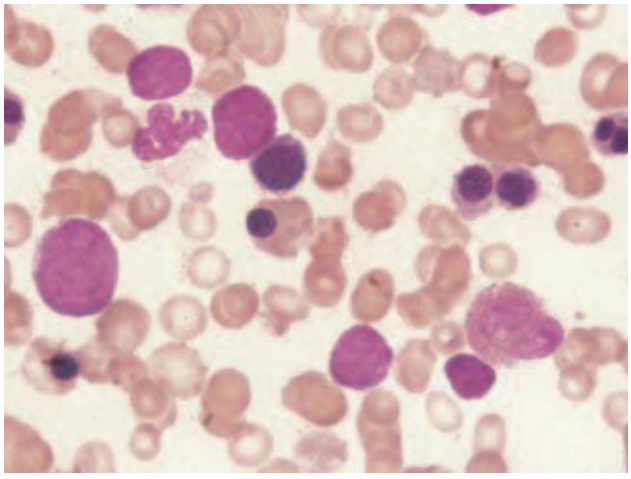

Figure 5

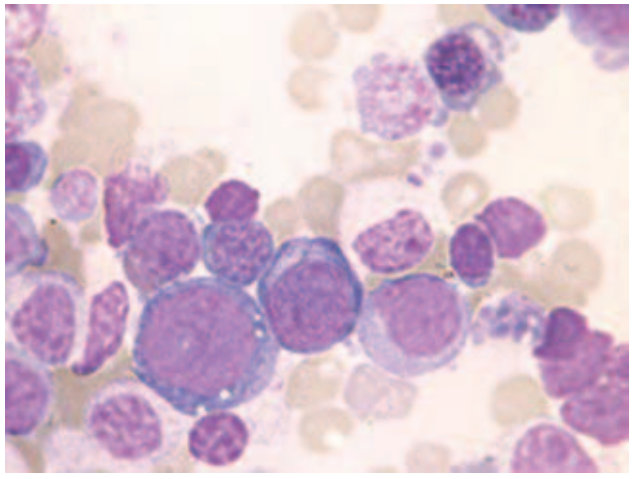

Figure 8

blastic features, reduced granulation, micromegakaryocytes and blasts in a percentage of 17%. The bone marrow morphology is given in figures 3 to 8. The cytogenetic analysis revealed a monosomy 7 in 60% of the analyzed metaphases. The sephacryl gel microtyping system for the detection of CD55 and or CD59 deficient red cell population in the peripheral blood, revealed no PNH phenotype.

The fever subsided after one week of treatment with a combination of penicillin-G with amikacin. The patient was also treated appropriately for her primary disease.

Comment

In all entities of the myelodysplastic syndromes there are several alterations of all cellular series characterized as dyserythropoiesis, dysgranulopoiesis and or dysmegakaryopoiesis.

Findings characteristic of dyserythropoiesis

Bone marrow: Hyperplasia or hypoplasia of the erythroid series, maturation arrest, megaloblastoid changes, irregular lobated erythroblasts (trifoil-like appearance, nucleus-cytoplasmic maturation asynchrony, erythroblasts with one or more nuclei, presence of giant erythroblasts, hemoglobinization disturbances, abnormal sideroblasts [ring forms]).

Peripheral blood: Ovaloid macrocytes, hypochromic microcytes, double population morphology, poikilocytosis-acanthocytosis, siderocytes, basophilic stippling.

Findings characteristic of dysgranulopoiesis

Bone marrow: Hyperplasia or hypoplasia of the granulocytic series, monocytic cells hyperplasia, nucleus-cytoplasmic maturation arrest, presence of pseudo-Pelger neutrophils, hypersegmented nuclei, presence of pseudonucleoli (intranuclear inclusions), absent or irregular granulation, presence of pseudo-Chediak-Higashi neutrophils, increase of blast percentage, increase of abnormal promyelocytes, increase of promonocytes/monocytes, monocytoid appearance of the granulocytic series cells, in large clusters colony growth in in vitro cultures.

Peripheral blood: Neutropenia, neutrophilia, monocytosis, presence of pseudo-Pelger neutrophils, hypersegmented neutrophils, agranular neutrophils, neutrophils with Döhle bodies, presence of pseudo-Chediak-Higashi neutrophils, eosinophils with decreased granulation or containing vacuoles.

Findings characteristic of dysmegakaryopoiesis

Bone marrow: Hyperplasia or hypoplasia of the megakaryocyte series, mononuclear or binuclear megakaryocytes, increase of micromegakaryocytes, megakaryocytes containing cytoplasmic vacuoles, growth in large clusters in in vitro cultures.

Peripheral blood: Thrombocytopenia or thrombocythemia, decreased platelet granulation, platelets with abnormal granules, giant platelets, megakaryocyte fragments in the peripheral blood, persistence of microtubuli (ring-like forms), dilatation of the microtubuli system (Swiss cheese type appearance), absence of platelet aggregation in the blood smear, abnormal functional platelet tests (abnormal aggregation, in collagen etc.).

In the hematology examination, presence of a normochromic normocytic or mild macrocytic anemia with red cell morphology like a "double population" (existence of a hypochromic normocytic and a normochromic macrocytic red cell population) with or without contemporary reticulocytosis. Sometimes, there is leukopenia and or thrombocytopenia. The bone marrow is hypercellular (mainly the erythroid series) with abnormal maturation, resulting in intramyeloid erythroblast destruction and maturation arrest of other myeloid series. The image is compatible with that of peripheral blood pancytopenia, with a rich bone marrow (picture of ineffective hemopoiesis). The mature cells of all three myeloid series which are produced have many qualitative abnormalities (morphologic, functional and biochemical). Many signs of ineffective erythropoiesis are present such as increased marrow iron stores, increased siderophyline saturation, ferritin levels usually increased.

^{59}Fe kinetics: Plasma clearance is normal, normal bone marrow uptake but there is a retardation and insufficient iron incorporation to erythroblasts.

Findings of high cellular turnover (hyperuricemia, increased LDH).

In refractory anemia with excess of blasts (RAEB) the characteristic findings are: Cytopenia usually of two or more myeloid series with the presence of trilineage abnormalities.

Blasts in the peripheral blood less than 5%.

The bone marrow is hypercellular with erythroid and granulocytic series hyperplasia, existence of dyserythropoiesis, dysgranulopoiesis and dysmegakaryopoiesis, as well as the presence or not of ring sideroblasts and dysplastic features in all myeloid series.

Blasts in the bone marrow from 5 to 20% (or type I and II with few granules)

Anemia is more severe and less macrocytic, while leukopenia and or thrombocytopenia are usually present (existence of characteristic findings of dysgranulopoiesis and dysmegakaryopoiesis and often myeloperoxidase deficiency).

Blasts in the bone marrow are from 5 to 20%, giving an image of acute leukemia in the beginning of its evolution.

The differential diagnosis from acute myelogenous leukemia is based on the absence of Auer bodies in blasts, the absence of severe thrombocytopenia, at the age of presentation and in the future progression of the disease.

The existence of ringed sideroblasts is possible (less than 15%) and monocytosis (differential diagnosis from myelomonocytic leukemia is based on the absence of splenomegaly, in low leukocyte numbers and in the absence of increased serum and urine lysozyme levels).

The disease outcome is fatal (median survival about one year) because of bone marrow insufficiency aggravation or the evolution to acute myeloblastic leukemia.

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Corresponding author:

J. Meletis, Hematology Department and Bone Marrow Transplantation Unit, National and Kapodistrian University of Athens, School of Medicine, "Laiko" General Hospital, Athens, Greece, tel.: +30 210 74 66 902, fax: +30 210 7456698
e-mail: imeletis@med.uoa.gr

Diagnosis: *Myelodysplastic syndrome, refractory anemia with excess of blasts (RAEB)*