

CONTINUING MEDICAL EDUCATION ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

Hematology Quiz – Case 4

A 67-year-old woman was admitted to our department due to intense dyspnoea, fatigue, dizziness and leg cramps. Her past medical history included hypertension and diabetes mellitus, while her family history was unremarkable. The physical examination revealed pale skin, increased heart rate (110/min) and rapid breathing (22/min).

The full blood count revealed severe macrocytic anemia (Hb 7.8 g/dL, hematocrit 24.2%, MCV 106 fL, MCH 32 pg), with normal white blood cell counts $4.6 \times 10^9/L$ (differential counts: neutrophils $2.6 \times 10^9/L$, lymphocytes $1.2 \times 10^9/L$, and monocytes $0.8 \times 10^9/L$) and increased platelet count of $672 \times 10^9/L$. The evaluation of peripheral blood smear revealed macrocytosis, and dysgranulopoiesis of neutrophils with Pelger-Huët-like hyposegmentation. No blast was observed. The reticulocyte counts were 0.8% (fig. 1). Serum concentrations of vitamin B₁₂, and folate acid as well as iron tests were normal. Serum erythropoietin concentration was 32 mU/mL (the upper normal limit in our laboratory is 20 mU/mL). The direct Coomb's test was IgG positive (2+) without evidence of clinical or laboratory hemolysis. The biochemistry profile of the patient including lactate dehydrogenase, bilirubin and electrolytes was within normal limits. Chest X-rays and ultrasound of the abdomen revealed no pathology.

The bone marrow aspiration was normocellular (figures 2, 3). Erythroid lineage was normocellular with megaloblastoid changes, while myeloid series showed dysgranulopoiesis. No ringed sideroblasts were observed. In trephine biopsy dysplasia of all series was accompanied by grade I fibrosis. Bone marrow karyotype showed 46,XY,del(5)(q15q33)[5]/46,XX[15]. The diagnosis was established and the patient was given red blood cell transfusions along with erythropoietin administration. There was no erythroid response to erythropoietin and the patient received lenalidomide achieving major erythroid response but not cytogenetic response after 6 months of therapy.

Comment

5q- syndrome is classified as a subtype of myelodysplastic syndromes (MDS) according to WHO classification of myeloid malignancies, and is generally associated with a good prognosis showing a median survival of >5 years in the majority of cases. This MDS subtype is characterized by refractory

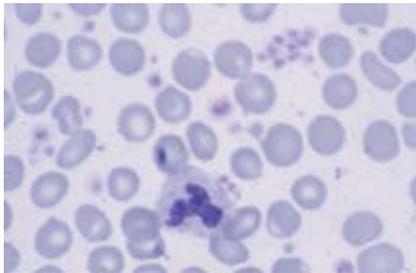


Figure 1

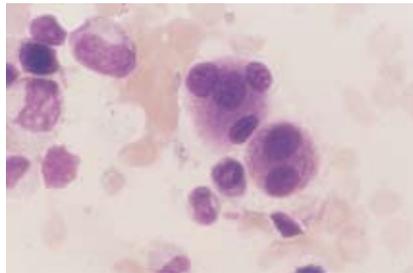


Figure 2

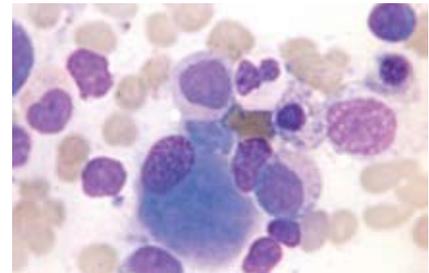


Figure 3

anemia with or without multilineage dysplasia and chromosome 5q deletion as the sole karyotypic abnormality in conventional cytogenetics. The 5q-syndrome is found predominantly in elderly women and consists of macrocytic anemia, thrombocytosis, and megakaryocyte hyperplasia with nuclear hypolobation. Patients have often a stable clinical course but sometimes are transfusion dependent. Very few of these patients transform to an acute myeloblastic leukemia; the cumulative risk of AML evolution 2 years after diagnosis is approximately 8% in 5q-. Although the specific molecular abnormalities in 5q-myeloid disorders are unknown, inactivation of one or more genes in the 5q31q33 segment is critical. This 5q31q33 region includes the genes for the macrophage colony-stimulating factor-1 receptor (CSF-1R), secreted protein, acidic, cysteine-rich (SPARC), and glutamate receptor (GR1A1). This region, critical to the 5q-syndrome, appears to be distinct from the other 5q regions associated with other MDS subtypes and myeloid leukemia. Anemia of 5q-syndrome responds very rarely to erythropoietin. Lenalidomide is an immunomodulatory

agent with biological activity in several hematologic malignancies, including 5q-syndrome. Lenalidomide induces a direct cytotoxic effect against 5q-clones in leukemia cell lines and enhances ligand-induced erythropoietin receptor signaling in erythroid progenitors. Clinical trials with lenalidomide in MDS have demonstrated a high frequency of cytogenetic and pathologic responses in patients with MDS and deletion of chromosome 5q-. Therefore, lenalidomide was approved for the treatment of transfusion-dependent patients with low to intermediate risk MDS and chromosome 5q deletion.

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ARCHIVES OF HELLENIC MEDICINE 2008, 25(1):123
ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2008, 25(1):123

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