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ARCHIVES OF HELLENIC MEDICINE: ISSN 11-05-3992

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ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

ARCHIVES OF HELLENIC MEDICINE 2007, 24(6):633
ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2007, 24(6):633

Clinical Immunology Quiz- Case 3

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Peripheral blood from a 54-year old female was referred to the Immunology Lab for immunophenotyping. The patient was admitted to the hospital three days ago, because of stroke and right hemiparesis. During the three months preceding her illness the patient complained only for fatigue. She had no history of thrombosis; she was not taking oral contraceptives and was not using alcohol or tobacco. She had had two pregnancies with normal vaginal deliveries and no spontaneous miscarriages. She reported appendectomy and tonsillectomy at childhood. On clinical examination there was no hepatomegaly, splenomegaly and lymphadenopathy. Laboratory data revealed a WBC of 9.3×10^9/L, with 61% neutrophils, 28% lymphocytes, and 11% monocytes. The hematocrit was 43.3%, the hemoglobin was 13.9 g/dL, but the platelet count showed mild thrombocytosis (570×10^9/L). Serological exams, urinalysis and chest X-ray were normal, while antinuclear and anti-ds-DNA antibodies were undetectable. Laboratory tests for both inherited and acquired thrombophilia were negative. Considering the immunophenotyping, the absolute number of lymphocyte subsets was into normal ranges but the neutrophils displayed two distinct populations in terms of the expression of CD16 and CD66c (Korsa) (fig. 1). Further study revealed the absence of eosinophils and of a PNH clone (normal expression of CD55 and CD59).

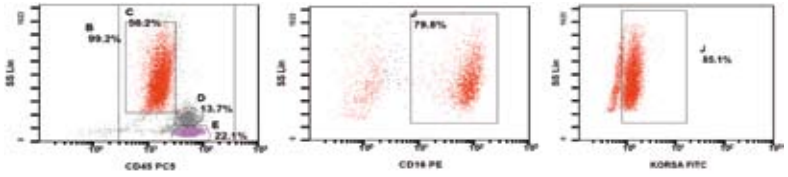

Figure 1. CD16 and CD66c expression on neutrophils.

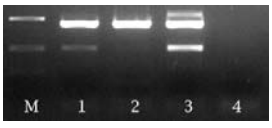

Figure 2. JAK2–V617T mutation established by allele-specific PCR. M: 100bp ladder molecular weight marker (Invitrogen, UK).
Lane 1: patient's sample positive for JAK2–V617F mutation
Lane 2: negative control (patient with MGUS)
Lane 3: positive control (patient with polycythemia vera)
Lane 4: negative PCR control. The PCR products were analyzed in 2% TBE agarose gel.

Which is the next laboratory step?

CD16 and CD66c are GPI-anchored proteins and their expression may be affected in clonal disorders of myeloid cells (as myelodysplastic or myeloproliferative disorders). Considering that the patient displayed only mild thrombocytosis and stroke, the possibility of an underlying myeloproliferative disorder had to be taken account. Although bone marrow aspiration and trephine biopsy were not diagnostic, the molecular analysis for the detection of JAK2–V617F mutation revealed its presence in the patient's peripheral blood (fig. 2).

Comment

Myeloproliferaive disorders (MPD) arise from a multipotent hematopoietic progenitor cell and result in overproduction of one or more hematopoietic cells. The diagnosis of MPD is currently based on a combination of clinical and pathological criteria, the most important of which is the presence of abnormally high levels of peripheral blood leukocytes, granulocytes, hemoglobin and platelets. MPD display a high tendency for thrombotic complications, both at diagnosis and the follow-up period, although several studies have shown that the thrombotic events may precede even 1–2 years before MPD diagnosis. Thus, some patients with thrombosis may have a latent or subclinical MPD, without elevated blood counts. Recently, a mutation in the JAK2 gene, which is associated with several types of MPD (polycythemia vera, essential thrombocythemia and idiopathic myelofibrosis), has been detected in a proportion of patients with unexplained thrombosis or thrombosis in unexpected sites (as Budd-Chiari syndrome), providing further evidence that these patients have a latent MPD. Thus, testing for JAK2 mutation in patients with hypercoagulable state and mild elevation of blood counts is a reasonable approach. In our patient, the clinical and hematologic findings did not fulfill the criteria for diagnosis of either essential thrombocythemia or polycythemia vera. However, the combination of a mild thrombocytosis, the abnormal expression of CD16 and CD66c on neutrophils and the presence of a major thrombotic event (without thrombophilia), imply the presence of an underlying MPD. The diagnosis was confirmed after the detection of the JAK2–V617F mutation indicating that such analysis is useful in differentiating MPD from reactive thrombocythemia or erythrocytosis.

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