

CONTINUING MEDICAL EDUCATION ΣΥΝΕΧΙΖΟΜΕΝΗ ΙΑΤΡΙΚΗ ΕΚΠΑΙΔΕΥΣΗ

Clinical Immunology Quiz - Case 1

Peripheral blood from a 44-year old female was referred to Immunology Lab for immunophenotyping. The patient complained for chronic abdominal pain during the last 2 years and the current clinical and laboratory evaluation revealed only increased levels of LDH (440 U/L, normal range: 120-220 U/L). The absolute number of lymphocyte subsets was into normal ranges but the immunophenotyping of neutrophils and monocytes revealed the presence of two distinct populations, in terms of the expression of CD16 and CD14, respectively (Figures 1 and 2).

Which is the next laboratory step?

CD14 and CD16 are GlycosylPhosphatidyInositol (GPI) anchored proteins and their expression is affected by the PhosphatidyInositol Glycan complementation group A (*PIG-A*) gene, which encodes a subunit of an enzyme involved in the synthesis of the GPI membrane anchor. *PIG-A* somatic mutations result in the emergence of paroxysmal nocturnal hemoglobinuria (PNH) clones, characterized by decreased expression of GPI-linked proteins, including CD14, CD15, CD16, CD55, CD58, CD59, etc. Therefore, we decided to proceed with the detection of CD55 (decay accelerating factor) and CD59 (membrane inhibitor of reactive lysis) which is the standard diagnostic test for the presence of PNH clones. Indeed, flow cytometric quantitation of these molecules revealed the absence of CD55 and CD59 expression in approximately 50% of neutrophils (Figure 3).

Comment

PNH is a rare disorder characterized by hemolysis due to the absence of CD55 and CD59 molecules (protecting erythrocytes from complement-mediated lysis), cytopenias and an increased incidence of venous thrombosis. Nocturnal hemoglobinuria is attributed to processes that enhance complement-mediated lysis, such as respiratory acidosis during sleep. Most patients, however, do not have a clear clinical presentation, while PNH clones are present in many other conditions, like aplastic anemia, myelodysplastic syndromes, large granular lymphocyte (LGL) leukemia, plasma cell dyscrasias, etc. In some cases, the emergence of PNH clones precedes the clinical presentation of the underlying disease.

Despite the presence of the PNH clone, our patient did not display any other clinical or laboratory finding able to establish the diagnosis of PNH. Perturbations, however, of microcirculation could justify her chronic abdominal pain. Thus, the patient received antiplatelet treatment and followed up by close clinical and laboratory monitoring.

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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2007, 24(4):398

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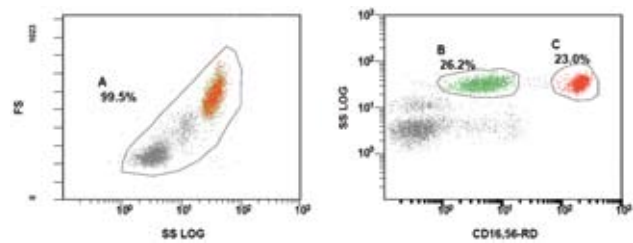


Figure 1. CD16/56 expression on neutrophils.

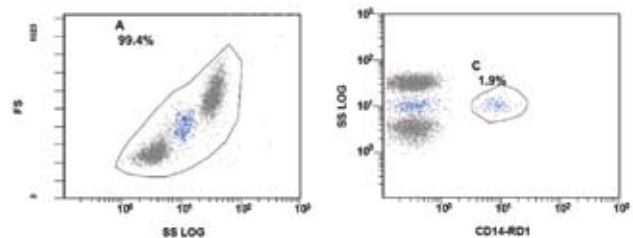


Figure 2. CD14 expression on monocytes.

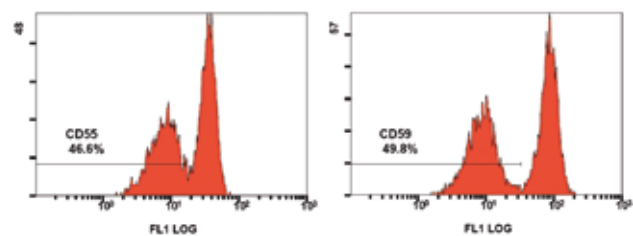


Figure 3. CD55 and CD59 expression on neutrophils revealed the presence of the PNH clone.

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Diagnosis: PNH clone in a patient with chronic abdominal pain