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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2008, 25(4):548–549

Clinical Immunology Quiz – Case 5

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Peripheral blood from a 10-year old female was referred to the Immunology Lab for immunophenotyping. The patient complained for recurrent upper respiratory tract infections and otitis media during the last year while a history of frequent infections was recorded since infancy. Although, the absolute number of lymphocyte subsets was into normal ranges (fig. 1 and tab. 1), the patient displayed a mild hypogammaglobulinemia (tab. 1). Although the patient did not fulfill the diagnostic criteria for the diagnosis of common variable immunodeficiency (CVID), a molecular analysis of *TNFRSF13B* gene (encoding TACI) was performed.

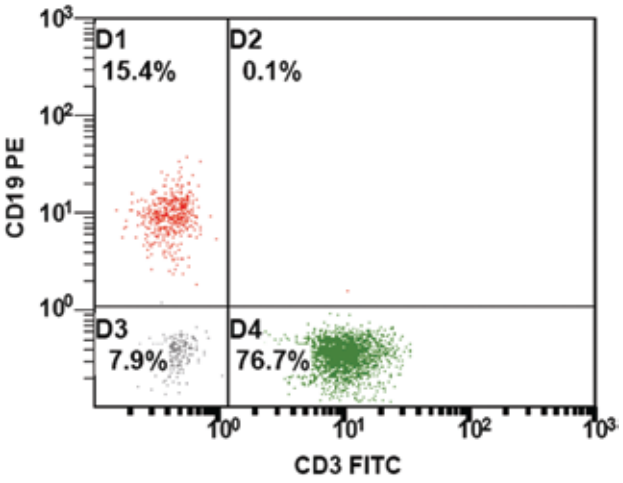

Figure 1. Flow cytometry analysis showing normal lymphocyte subsets.

Table 1. Lymphocyte subsets and serum immunoglobulins of the patient.

Blood lymphocyte subpopulations (×10⁹/L)		
Total lymphocyte count	4.217	(2.9–5.1)
T lymphocytes		
CD3	3.163	(1.8–3.2)
CD4	1.718	(1.0–1.8)
CD8	1.242	(0.3–0.6)
B lymphocytes		
CD19	0.577	(0.3–0.6)
Quantitative serum immunoglobulins (mg/dL)		
IgG	919	(934–1640)
IgA	51	(85–242)
IgM	47	(100–252)

Interestingly, the patient was double heterozygous in *TNFRSF13B*, carrying the mutations V220A and P251L (fig. 2). Further analysis demonstrated that her parents were *TNFRSF13B* heterozygotes but did not display hypogammaglobulinemia.

Comment

TACI (Transmembrane Activator, calcium modulator and Cyclophilin ligand Interactor) is a transmembrane receptor, which mediates isotype switching in B cells. Recently, 6 mutations (in homozygous or heterozygous state) in TNFRSF13B gene were found to be present in 10% to 20% of patients with CVID, implying the contribution of this gene in the disease pathogenesis and/or phenotype. However, TNFRSF13B mutations were reported in normal

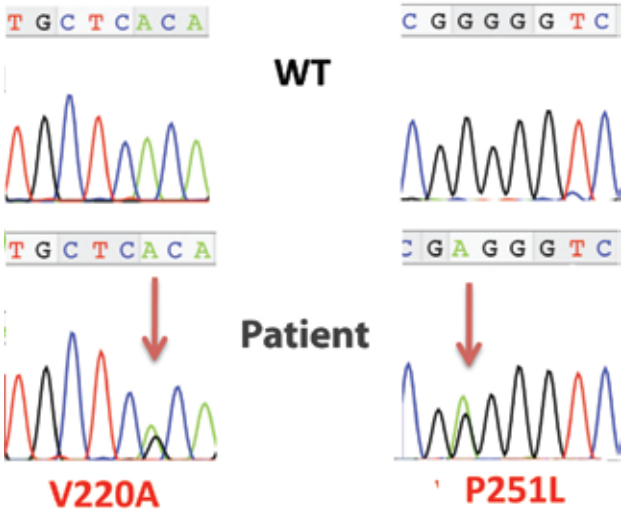

Figure 2. Molecular analysis of *TNFRSF13B* gene, showing the presence of the V220A and P251L mutations.

individuals, indicating possibly that when alone do not necessarily predispose to CVID pathogenesis. Nevertheless, their presence could be considered as an early indicator of CVID emergence, considering that in several CVID patients the diagnosis is underestimated and a delayed diagnosis can lead to increased morbidity and mortality. Thus, in our patient, persistent hypogammaglobulinemia and recurrent infections are followed-up for Ig replacement to be considered.

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