

# **BONE MARROW FAILURE ASSOCIATED WITH CD8 T-CELL EXPANSION IN A PATIENT WITH TRICHORHINOPHALANGEAL SYNDROME AND COMMON VARIABLE IMMUNODEFICIENCY**

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**Objective:** To report a case of trichorhinophalangeal syndrome coexistent with common variable immunodeficiency (CVID)-like phenotype with a polyclonal expansion of CD8 T-cells

**Case:** A 34-year-old white woman with multiple congenital abnormalities, autoimmune endocrinopathies, and chronic neutropenia with splenomegaly presented with daily low-grade fever. Laboratory examination showed pancytopenia and persistent neutropenia now unresponsive to G-CSF. A bone marrow biopsy revealed 95% cellularity, myelofibrosis, increased histiocytes and eosinophils, and extensive lymphoid infiltration all interpreted to represent a T-cell proliferative disease, possibly malignant or as secondary to either long-term G-CSF treatment or CVID. To better understand her problems, her full history was reviewed, the literature was searched, and a T-cell receptor gene rearrangement analysis was performed.

**Discussion:** CVID is clinically diverse: several potential genetic and immunopathogenic mechanisms may account for these heterogeneous and poorly defined clinical phenotypes<sup>1</sup>. Polyclonal expansion of large granular lymphocytes with neutropenia has been reported in a substantial proportion of CVID patients and is associated with elevated levels of soluble Fas ligand<sup>2</sup>. Molecular genetic analysis of the marrow showed that the T cells were polyclonal, ruling out malignancy. Although this patient's congenital abnormalities are likely unrelated, we hypothesize at least some of her endocrinopathies and all of her hematologic abnormalities are a manifestation of immunodysregulation due to CVID. This stresses the need to more precisely define distinct clinical phenotypes and to develop guidelines for diagnosis and treatment of a very heterogeneous syndrome, CVID.

1: Chapel H et al. Common variable immunodeficiency disorders: division into distinct clinical phenotypes. *Blood*. 2008 Jul 15;112(2):277-86.

2: Holms et al. Polyclonal expansion of large granular lymphocytes in common variable immunodeficiency - association with neutropenia. *Clin Exp Immunol*. 2006 Jun;144(3):418-24.