LETTER TO THE EDITOR
Evans Syndrome and Idiopathic Thrombocytopenic Purpura in Families: Consider Autoimmune Lymphoproliferative Disease

To the Editor: We read with interest the Letter by Naithani et al., [1] describing two siblings, one with idiopathic thrombocytopenic purpura (ITP) and the other with Evans syndrome (ES), defined as the combination of ITP plus autoimmune hemolytic anemia (AIHA). ITP is defined as a bleeding disorder with the hallmark of autoimmuned mediated thrombocytopenia. The incidence is between 2 and 5/100,000 children [2]. Autoimmune lymphoproliferative syndrome (ALPS) was first clinically described as the combination of lymphadenopathy, splenomegaly, AIHA and ITP by Canale and Smith [3], and can operationally be defined as a chronic, nonmalignant lymphoproliferation in patients with increased double negative T cells (CD3+/CD4−/CD8−), and defective lymphocyte apoptosis [4]. Most cases are inherited in an autosomal dominant pattern. ITP, AIHA, and combined cytopenias have been described to be part of clinical and immunological features in affected patients. Mutations causing ALPS in the genes coding for FAS, FASL and caspase 8 and 10 have been identified, somatic mosaicism has been described, and further genetic causes are suspected [5–9]. On the other hand, in one ES cohort, 6 out of 12 patients fulfilled the diagnostic criteria for ALPS [10]. Therefore, if ITP and combined cytopenias co-occur in different members of one family, underlying ALPS has to be considered as a possible cause. In a cohort of 28 consecutively recruited ITP patients in our institution diagnosed based on published guidelines [11] we detected one family with several cases of ITP and AIHA; however, the diagnostic criteria of ALPS were neither fulfilled at initial diagnosis nor during a 6-year follow-up of the index case. We therefore conclude that familial cases with co-occurrence of ITP, AIHA, and combined cytopenias without ALPS do exist, and speculate, that a mechanism may be present, which causes a milder phenotype than the patients described to have ALPS. Interference with apoptotic signaling in activated B and T cell clones might be involved in the pathomechanism of familial ITP in co-occurrence with combined cytopenias as ES.

In the future, ongoing Pediatric and Adult Registry on Chronic ITP (PARC-ITP, contact https://www.parc-tp.net) may further elucidate the frequency of the rare combination of ITP and ES.

ACKNOWLEDGMENT

We thank all patients for their participation. This work was financially supported in part by the ITP foundation, by an unrestricted grant from Jan Devay, CSL Behring (Schweiz) AG, Zurich, and by the authors’ institution.

Johannes R Rischewski, MD
Thomas Kühne, MD
Paul Imbach, MD
Pediatric Oncology/Hematology
University Children’s Hospital Basel
PO Box 4005, Basel, Switzerland

Stephan Ehl, MD
Department of Pediatrics and Adolescent Medicine
University of Freiburg
Freiburg, Germany

REFERENCES


© 2008 Wiley-Liss, Inc.
DOI 10.1002/pbc.21501

© 2008 Wiley-Liss, Inc.
DOI 10.1002/pbc.21501