

## 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 autoimmune 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-itp.net>) may further elucidate the frequency of the rare combination of ITP and ES.

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