Revised diagnostic criteria for the autoimmune lymphoproliferative syndrome (ALPS) (Canale-Smith syndrome)

(Oliveira JB et al., Blood 2010, 116(14) :e35-e40)

Required

1. Chronic (> 6 months), nonmalignant, noninfectious lymphadenopathy or splenomegaly or both
2. Elevated $CD3^+TCR\alpha\beta^+CD4^-CD8^-$ DNT cells (≥ 1.5% of total lymphocytes or 2.5% of $CD3^+$ lymphocytes) in the setting of normal or elevated lymphocyte counts

Accessory

Primary

1. Defective lymphocyte apoptosis (in 2 separate assays)
2. Somatic or germline pathogenic mutation in *FAS*, *FASLG*, or *CASP10*

Secondary

1. Elevated plasma sFASL levels (>200 pg/mL) OR elevated plasma interleukin-10 levels (>20 pg/mL) OR elevated serum or plasma vitamin B12 levels (> 1500 ng/L) OR elevated plasma interleukin-18 levels > 500 pg/mL
2. Typical immunohistological findings as reviewed by an experienced hematopathologist
3. Autoimmune cytopenias (hemolytic anemia, thrombocytopenia, or neutropenia) AND elevated immunoglobulin G levels (polyclonal hypergammaglobulinemia)
4. Family history of a nonmalignant/noninfectious lymphoproliferation with or without autoimmunity

A definitive diagnosis is based on the presence of both required criteria plus one primary accessory criterion.

A probable diagnosis is based on the presence of both required criteria plus one secondary accessory criterion.

Abbreviations:

DNT: double negative T-lymphocytes

FAS: Fas cell surface death receptor (TNF receptor superfamily, member 6; apoptosis stimulating fragment)

FASGL: FAS ligand

CASP10: caspase 10, apoptosis-related cysteine protease

sFASL: soluble FAS ligand