WAS-related disorders

Genetics

-Gene: WAS (Wiskott-Aldrich syndrome protein, Xp11.23)

-XLR

Clinical findings/Dysmorphic features

-Spectrum of disorders of hematopoietic cells (defects of platelets and lymphocytes): Wiskott-Aldrich syndrome, X-linked thrombocytopenia (XLT), X-linked congenital neutropenia (XLN)

-Affected males: thrombocytopenia, intermittent mucosal bleeding, bloody diarrhea, intermittent/chronic petechiae; eczema; recurrent bacterial/viral infections (mainly ear)

-40% of those who survive early complications develop autoimmune conditions (hemolytic anemia, immune thrombocytopenic purpura, immune-mediated neutropenia, rheumatoid arthritis, vasculitis, immune-mediated damage to kidneys and liver)

-Males with XLT: thrombocytopenia with small platelets; eczema; immune dysfunction, are usually mild or absent

-Males with XLN: congenital neutropenia, myeloid dysplasia, lymphoid cell abnormalities

Etiology

-Prevalence: 1-4 per 1,000,000

Pathogenesis

-WASP in hematopoietic cells: signal transduction and actin cytoskeleton organization in response to external stimuli

-T and B lymphocytes, neutrophils, macrophages, DC of males with WAS-related disorders exhibit defects in migration, anchoring, localization

Genetic testing/diagnosis

-Male proband with both congenital thrombocytopenia (<70,000 platelets/mm3) and small platelets + at least one of the following: eczema, recurrent bacterial/viral infections, autoimmune disease(s), malignancy, reduced WASP expression in fresh blood sample

-Identification of hemizygous WAS pathogenic variant is necessary to confirm the diagnosis