Wiskott-Aldrich syndrome and X-linked thrombocytopenia

GENERAL INFORMATION

Description:

Defects in WASP are the cause of Wiskott-Aldrich syndrome (WAS), an X-linked recessive immunodeficiency characterized by eczema, thrombocytopenia, recurrent infections, and bloody diarrhea. Death usually occurs before age 10. Two forms of WAS exist: a severe form culminating in early lymphoma, and a milder form compatible with survival to adult life. X-linked thrombocytopenia it is a mild variant with thrombocytopenia and without eczema and immune deficiency.

Alternative names:

- Aldrich-Dees syndrome
- Aldrich-Wiskott syndrome
- Wiskott's syndrome
- Wiskott-Aldrich-Huntley syndrome
- Wiskott-Aldrich-Dees syndrome
- Aldrich's syndrome
- Aldrich-Huntley syndrome
- Wiskott-Aldrich syndrome protein

Classification:

- Other well-defined immunodeficiency syndromes

Inheritance:

X-linked

OMIM:

- #301000 Wiskott-Aldrich syndrome; WAS
- #313900 Thrombocytopenia1; THC1
- 300392 WAS gene; WAS

Incidence:

1: 20,000 births/year

CLINICAL INFORMATION

Description:

The onset of disease is early in childhood with severe eczema, wich has an atypical distribution compared to atopic eczema. The clinical presentation of the Wiskott-Aldrich Syndrome (WAS) varies from patient to patient. Some patients present with all three classic manifestations, including low platelets and bleeding, immunodeficiency and infection, and eczema. Other patients present just with low platelet counts (thrombocytopenia) and bleeding. Patients have some characteristic hemorrhagic signs (purpura, petechiae, ecchymoses, epistaxis, bloody diarrhea). Infections develop gradually and affect the respiratory tract (bronchial, pulmonary, ENT) and are bacterial. Autoimmunity is presented by vasculitis and glomerulonephritis.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Wiskott-Aldrich syndrome, ORPHANET

Genetic:

- WAS, IDdiagnostics
- WAS-Related Disorders , GeneTest
- Department of Clinical Genetics - Rigshospitalet (Copenhagen), EDDNAL
- Ulleval University Hospital - Department of Medical Genetics (Oslo), EDDNAL
- North East Thames Regional Clinical Molecular Genetics Laboratory (London), EDDNAL
- Leiden University Medical Centre, EDDNAL
- Laboratorio di Genetica Pediatrica "Angelo Nocivelli" - University of Brescia, EDDNAL

Therapeutic options:

- Intravenous immunoglobulins should be used if recurrent bacterial infections are a problem. Good management of infections can lower the risk of complications of the disease like lymphoma and tumors. Splenectomy may be beneficial for thrombocytopenia. Bone-marrow transplant cures all the features of the disease.
- Wiskott-Aldrich syndrome, eMedicine

Research programs, clinical trials:

- European Initiative for Primary Immunodeficiencies

GENE INFORMATION

Names:

HUGO name: WAS
Alias(es): IMD2, THC, WASP, Wiskott-Aldrich syndrome protein

Localization:

Reference sequences:

DNA: AF196970 (EMBL) , **cDNA:** U12707 (EMBL) , **Protein:** P42768 (SWISSPROT)
Other Sequences

Chromosomal Location:

Xp11.4-p11.21

Maps:

WASP (Map View)

Other gene-based resources:

Ensembl: ENSG00000015285, GENATLAS: WAS, GeneCard: WAS, UniGene: 2157, Entrez Gene: 7454, euGenes: 7454, GDB: 120736

PROTEIN INFORMATION

Description:

Protein function:

Possible regulator of lymphocyte and platelet function. May be involved in signaling pathways with cytoskeletal function.

Subunit:

Binds to Cdc42, Rac, Nck, Fyn, Src kinase Fgr, BTK, Abl, Wip, and to the P85 subunit of Plc-gamma.

Other features:

Other related resourses:

InterPro: IPR000095; PAKbox/Rhobndng, InterPro: IPR000697; RanBP1_WASP, InterPro: IPR001960; WH1, InterPro: IPR003124; WH2, Pfam: PF00568; WH1, Pfam: PF00786; PBD, Pfam: PF02205; WH2, SMART: SM00285; PBD, SMART: SM00461; WH1, SMART: SM00246; WH2, PROSITE: PS50108; CRIB

Expression pattern for human:

Tissue	Exp. (%)	Clones
leukocyte	21.73	8:8982
T cells from T cell leukemia	10.18	1:2397
thymus, pooled	7.70	1:3169
lymph	7.58	20:64395
B-cells	7.38	5:16533
spleen	6.75	2:7229
placenta human 8 week	6.05	1:4035
lymph, T-cell	5.74	2:8503
colon, 2 pooled adenocarcinomas	5.53	2:8815
leukopheresis	5.35	1:4557

OTHER RESOURCES

Societies:

General:

- International Patient Organization for Primary Immunodeficiencies
- Immune Deficiency Foundation
- European Society for Immunodeficiencies
- NIH/National Institute of Allergy and Infectious Diseases