WISKOTT-ALDRICH SYNDROME (WAS)

X– linked

A rare, **X-linked genetic disorder** caused by mutations in the gene encoding the **Wiskott-Aldrich Syndrome protein (WASp)**. This mutation results in **combined T-cell and B-cell immunodeficiency**, impairing the body's ability to fight infections. WAS primarily affects **males** and is characterized by a classic triad of symptoms: **thrombocytopenia**, **eczema**, and **recurrent infections**.

CLINICAL FEATURES

Classic Triad:

1. **IMMUNODEFICIENCY**

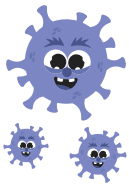
Combined T-cell and B-cell immunodeficiency

2. **ECZEMA**

3. **MICROTHROMBOCYTOPENIA**

Petechiae *(a distinguishing feature of WAS)*

- **Recurrent infections**
  - Sinopulmonary infections
  - Severe viral infections such as varicella



- **Risk for malignancy**
  - Leukemia
  - Lymphoma

PATHOGENESIS

WASp is a protein found exclusively in **hematopoietic cells**.

Lack of WASp → **Defective function** of multiple hematopoietic cell lineages → Global **dysregulation of immune function** → Abnormal **inflammatory responses** **Autoimmunity** **Susceptibility to malignancy**

In addition, WASp deficiency leads to **platelet defects**, causing **destruction** and **bleeding**.

DIAGNOSIS

Identification of **key clinical features**

- **Microthrombocytopenia** (low platelets and small in size)
- **Eosinophilia**
- **Antibody pattern**: low IgM, low/normal IgG, **high IgA/IgE** *(opposite to ataxia telangiectasia)*
- Low CD8+
- **Poor vaccine responses**

MANAGEMENT

- **Immunoglobulin replacement**.
- **Hematopoietic stem cell transplant**.
- **Prophylactic antibiotics** to prevent infections.
- **Gene therapy**: uses modified cells to correct the WASp deficiency.
- **Platelet transfusions** for severe bleeding.
- **Splenectomy**

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Dr. Katharine V. Jensen (Pediatric Resident, University of Alberta) and Dr. Karen Forbes (Professor of Pediatrics, University of Alberta) for www.pedscases.com