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Case Report

Wiskott-Aldrich Syndrome: Case Report- Characteristics, Diagnosis, and Treatment Approaches for a Challenging Disease

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Abstract

Wiskott-Aldrich syndrome (WAS) is a rare X-linked immunodeficiency disorder characterized by thrombocytopenia (low platelet count), eczema, recurrent infections, and an increased risk of autoimmune disorders and malignancies. This case report discusses a 4-month-old infant suspected of having WAS, detailing the clinical features, diagnostic evaluation, and genetic testing performed.

The patient had a history of bloody diarrhea along with thrombocytopenia and peripheral ecchymosis (bruising). Genetic testing confirmed a pathogenic variant in the Wiskott-Aldrich syndrome gene. Despite receiving supportive treatments, including immunoglobulin transfusions, the patient's condition worsened, leading to a massive cerebral hemorrhage that did not respond to symptomatic treatments.

Managing WAS requires a multidisciplinary approach involving supportive care, immunoglobulin replacement therapy, and allogeneic hematopoietic stem cell transplantation, which is considered a curative option. Additionally, novel targeted therapies, such as gene therapy, are being investigated.

This case highlights the challenges in diagnosing and managing WAS and underscores the importance of specialized medical care for patients with primary immunodeficiency disorders. Heral ecchymosis spots. Genetic testing confirmed a pathogenic variant in the Wiskott-Aldrich syndrome gene. Despite supportive treatment, including immunoglobulin transfusion, the patient's condition worsened, and a massive cerebral hemorrhage occurred, which did not respond to symptomatic treatments. The management of WAS involves a multidisciplinary approach, including supportive care, immunoglobulin replacement therapy, and allogeneic hematopoietic stem cell transplantation as a curative option. Novel targeted therapies, such as gene therapy, are also being explored. The case highlights the challenges in diagnosing and managing WAS and emphasizes the importance of specialized medical care for patients with primary immunodeficiency disorders.

Keywords: *Wiskott-Aldrich Syndrome; X-Linked Immunodeficiency; Thrombocytopenia; The WAS Gene; Immunoglobulin Transfusion*

Introduction

Wiskott-Aldrich Syndrome (WAS) is an X-linked immunodeficiency disorder characterized by thrombocytopenia (a low platelet count with small platelets), eczema, recurrent infections due to immune system deficiencies, as well as an increased risk of autoimmune diseases and cancers.

The syndrome was first described in 1973 by a Bavarian pediatrician, Alfred Wiskott. In 1954, Robert Aldrich observed a similar clinical phenotype in a study of sixteen males from a single family over six generations, noting that the condition did not appear in females. This observation provided clear evidence of its X-linked mode of inheritance. Wiskott-Aldrich Syndrome (WAS) is named after both physicians who contributed to its identification.

Case Report

We present the case of a 4-month-old infant with a history of bloody diarrhea and thrombocytopenia diagnosed at 15 days of age, alongside a familial history suggestive of gestational thrombocytopenia during the second trimester of pregnancy. The family investigation did not reveal any specific bleeding disorders.

The infant was admitted due to the presence of ecchymotic purpura on both lower limbs. Clinical examination revealed widespread ecchymotic spots on the feet, accompanied by peripheral eczematous lesions.

A peripheral blood cell count indicated a white blood cell (WBC) count of 17 × 10^9/L (normal range: 3.5 - 9.5 × 10^9/L), hemoglobin of 13.9 g/L, and a platelet count of 13 × 10^6/L. Peripheral blood smears showed the presence of small platelets.

Measurement of immunoglobulin levels demonstrated significantly low levels of IgM and IgG. Lymphocyte subtyping revealed an increase in T lymphocytes, but no other significant immunological abnormalities were noted. Bone marrow examination and platelet antibody levels did not exhibit any specific findings.

The patient received an immunoglobulin transfusion, but this did not improve. The hemorrhagic symptoms worsened, leading to the emergence of conjunctival hemorrhages, hematuria, and rectal bleeding. Consequently, a hereditary platelet disorder was diagnosed.

Genetic testing identified the patient as hemizygous for a pathogenic variant in the Wiskott-Aldrich syndrome gene (NM_000377.2:c.403C>T). Management included conservative supportive treatment, including prophylactic antibiotics to prevent infections and platelet transfusions. Unfortunately, the patient passed away four months later due to a massive cerebral hemorrhage that did not respond to symptomatic treatments.

Discussion

Wiskott-Aldrich syndrome (WAS) is a rare X-linked primary immunodeficiency disorder that primarily affects males. Its estimated incidence ranges from 1 in 100,000 to 1 in 250,000 live births. WAS is more commonly observed in individuals of Caucasian or Ashkenazi Jewish descent, but it can occur in individuals from any ethnic background.

The diagnosis of Wiskott-Aldrich syndrome involves a combination of clinical evaluation, immunological assessment, and genetic testing. Key clinical features that may raise suspicion for WAS include recurrent infections-especially bacterial infections of the respiratory tract and ears-eczema or other skin-related issues, and thrombocytopenia, which leads to easy bruising, petechiae, and prolonged bleeding.

Several biological tests can be conducted to confirm the diagnosis of Wiskott-Aldrich syndrome:

1. Complete blood count (CBC): This test helps evaluate blood cell counts, including platelets. Thrombocytopenia is a characteristic feature of WAS, and a low platelet count is often observed.
2. Immunological assessment: This involves measuring immunoglobulin levels (IgG, IgA, and IgM) and assessing lymphocyte subsets (CD3, CD4, CD8, CD19, CD16/56, etc.) using flow cytometry. Patients with WAS typically show immunodeficiency characterized by decreased immunoglobulin levels and abnormal lymphocyte subsets.

3. Wiskott-Aldrich syndrome protein (WASP) expression: The deficiency or absence of WASP expression is a hallmark of the disease. Flow cytometry or Western blot analysis can be used to detect WASP protein expression in lymphocytes.
4. Genetic testing: DNA sequencing or targeted mutation analysis can identify mutations in the WAS gene located on the X chromosome, confirming the diagnosis of Wiskott-Aldrich syndrome.

Various methods can be employed to detect mutations in the WAS gene:

1. Sanger sequencing or next-generation sequencing (NGS): These approaches directly sequence the coding regions and intron-exon boundaries of the WAS gene, allowing for the detection of point mutations, small insertions or deletions, and other sequence variations.
2. Multiplex ligation-dependent probe amplification (MLPA): This technique is used to detect copy number variations (deletions or duplications) within the WAS gene. MLPA utilizes specific probes that target different regions of the gene, enabling the identification of structural abnormalities.
3. Targeted mutation analysis: This focuses on specific known mutations prevalent in certain populations or families with Wiskott-Aldrich syndrome. This method allows for rapid and cost-effective analysis of a limited set of specific mutations.
4. Whole exome sequencing (WES): WES is a powerful genomic technique that sequences all human genes' protein-coding regions (exons). It is a comprehensive approach to identifying genetic mutations in the WAS gene and other associated genes linked to immunodeficiency disorders. WES can be particularly useful when clinical presentations overlap with other conditions or when the underlying genetic cause is unknown [1-7].

The treatment of Wiskott-Aldrich Syndrome (WAS) requires a multidisciplinary approach that addresses the immunodeficiency, autoimmunity, and bleeding tendencies associated with the condition. Here are some commonly employed treatment strategies:

1. Supportive care: This focuses on managing the symptoms and complications of WAS. It includes regular monitoring of blood counts and immunoglobulin levels, administering prophylactic antibiotics to prevent infections, and providing prompt treatment for infections when they occur. Patients with WAS often have low immunoglobulin levels, which increases their susceptibility to infections. To counter this, immunoglobulin replacement therapy through regular infusions of intravenous immunoglobulin (IVIG) can help boost the immune system and reduce the risk of infections.
2. Allogeneic hematopoietic stem cell transplantation (HSCT): HSCT is the only curative treatment for WAS. This procedure replaces the patient's defective immune system with healthy stem cells from a matched donor. HSCT can restore immune function and correct the underlying genetic defect associated with WAS. However, the success of HSCT depends on factors such as the patient's age, donor availability, and overall health.
3. Novel targeted therapies: Approaches such as gene therapy or gene editing techniques are being explored as potential treatment options for WAS. These methods aim to correct the genetic defect in the patient's cells, potentially offering a more precise and durable solution for the disorder. Nonetheless, further research and clinical trials are necessary to establish the safety and efficacy of these therapies.
4. Management of bleeding tendencies: Given the increased bleeding risks associated with WAS, managing and preventing bleeding complications is essential. This may involve platelet transfusions, administering medications to promote platelet production and careful monitoring and control of bleeding episodes.

It is essential for patients with WAS to receive treatment from a specialized medical team with expertise in managing primary immunodeficiency disorders. Treatment plans should be tailored to each patient's specific needs and may require a combination of the approaches mentioned above [8,9].

Conclusion

In conclusion, Wiskott-Aldrich syndrome (WAS) is a rare X-linked immunodeficiency disorder. It is characterized by low platelet counts (thrombocytopenia), eczema, recurrent infections, and an increased risk of autoimmune disorders and cancers. Diagnosis typically involves a clinical evaluation, immunological testing, and genetic analysis.

Treatment options include supportive care, immunoglobulin replacement therapy, allogeneic hematopoietic stem cell transplantation (HSCT), and new targeted therapies that are being developed. It is crucial to manage bleeding complications effectively. Patients with WAS require specialized medical care and a tailored treatment plan to address their unique needs.

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