Case Report

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Wiskott Aldrich Syndrome in an Infant – A Case Report

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Abstract

Background: Wiskott-Aldrich is an X-lined recessive disorder typically characterized by thrombocytopenia, eczema and recurrent infections. We present a 11 month old male child with classical symptoms of thrombocytopenic purpura, eczema and recurrent infections. The diagnosis of Wiskott-Aldrich syndrome was made based on history, physical examination and preliminary laboratory investigations. He was managed with antibiotics, platelet transfusion and symptomatic skin care.

Conclusion: Need for lifelong monitoring and higher levels of therapy as needed was informed to the parents.

Keywords: Atopic dermatitis; eczema; recurrent bacterial infection; Thrombocytopenic purpura

Introduction

Wiskott - Aldrich syndrome (WAS) is an X-linked recessive disorder originally described with a clinical triad of eczema, thrombocytopenia with small platelets and immunodeficiency.[1] It was first reported by Wiskott in 1937, and then in 1954 Aldrich et. al. reported that in 6 generations of a family, 16 of 40 males, but no females, died of a disease similar to that Wiskott's report, and they proposed an X-linked mode of inheritance. Wiskott-Aldrich syndrome protein (WASP) with 502 amino acids. WASP is majorly expressed by non-erythroid hematopoietic cells.[2] This protein is involved in actin polymerization, signaling pathways, and cytoskeletal rearrangement; and it is crucial for the monocytes and macrophages migration. WASP deficiency (either complete or partial) may cause malfunctioning of tissue macrophages, neutropenia, and small platelet sizes, resulting in chronic and repeated infections.

Case Report

An 11 month old male child second born to non consanguineous parents presented with complaints of bleeding per rectum of one day duration. The child had 2 episodes of epistaxis. The blood volume lost was approximately 5 to 10 ml. He had no fever, haematemesis, haematuria, abdominal pain, abdominal distension, incessant cry. He was diagnosed with atopic dermatitis at 4 months of age and was on antihistaminics. He had one episode of right sided purulent ear discharge around 5 months of age which subsided with oral antibiotics. He was born out of full term delivered by cesarean section with a birth weight of 2.5 Kg. He had achieved age appropriate developmental milestones. There was no family history of bleeding diathesis. Child was immunized for age.

On examination child was alert, afebrile; he had no anemia or lymphadenopathy. Examination of systems was normal. Physical examination was significant for extensive skin lesions with scabs over the trunk and face; purpuric spots on the back; dry scaly lesions on face and arms (Fig. 1). He fell

under moderate acute malnutrition with regards to his anthropometry. Investigations showed elevated total WBC count of 25400 cells per cu.mm of blood, hemoglobin 10.8g/dl, platelet count of 4000 cells per cu.mm of blood. Peripheral smear showed hypochromic, microcytic RBCs, WBCs of normal morphology, increased Eosinophils and a marked reduction in platelet count and distinctly smaller platelets. Absolute Eosinophil count was 680 cells per cu.mm (normal count 350-400 cells per cu.mm). Serum IgA and IgE levels were elevated with low normal levels of IgM and IgG. Platelet transfusion was done for clinical bleed with thrombocytopenia. A diagnosis of Wiskott-Aldrich syndrome was made based on the classical triad of thrombocytopenia, eczema and infection in a male child and smear showing decrease in size and number of platelets. The child's parents were explained about the chronic nature of the illness, need for periodic transfusions, immunoglobulin infusions, antibiotic prophylaxis and genetic diagnosis during follow up.

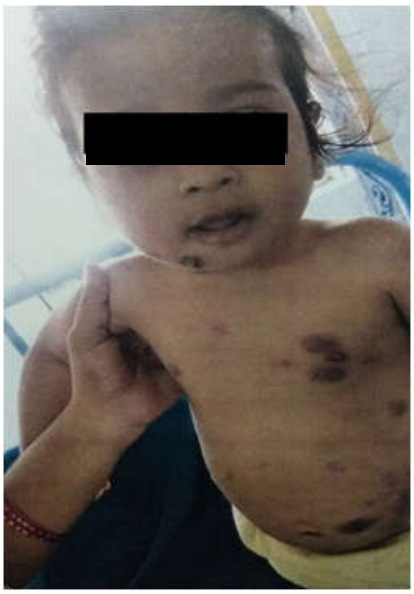

Fig 1: Purpuric Spots Over the Trunk and Face.

Discussion

Wiskott-Aldrich syndrome (WAS) is an X-linked recessive disorder with wide clinical manifestations.[3] Incidence of WAS is 1 to 10 of every million male newborns. Patients may have mild thrombocytopenia or suffer more severe disorders from the spectrum. Autoimmune disorders are frequent, in upto 40% of cases. Malignant tumors can also occur more frequently in adolescents and young adults with the classic form of disorder. Thus diagnosis can be difficult and is supported by detecting WAS gene mutations. The life expectancy varies and is approximately 15 years. The main cause of death is hemorrhage which can be non-life threatening such as epistaxis, purpura, and petechiae to severe intestinal and intra cranial bleeding.[4] Thrombocytopenia in WAS occurs irrespective of the degree of gene mutation. The megakaryocyte level is usually normal in WAS patients. The exact cause of the thrombocytopenia is not yet clear; megakaryocytes may or may not be present in bone marrow aspirates, platelet agglutinins are absent and donor platelets have a normal survival time, all suggesting defective synthesis rather than increased destruction.

WAS patients develop a rash resembling acute or chronic eczema which is seen in 80% of patients.[5] The cause of the eczema has not been fully understood. The high levels of IgE in WAS patients strongly suggests an atopic origin. WAS patients can present with several autoimmune manifestation simultaneously and this carries a poor prognosis. Leukemia, myelodysplasia and lymphoma take up to 90% of the malignancies in WAS. These patients have a poor prognosis. There are two major aims of treatment: symptomatic and long-term. In many underdeveloped countries symptomatic management forms the mainstay of treatment. Bleeding is managed with regular transfusions of blood and platelets; infections are avoided with antibiotics and immunoglobulin replacement. Splenectomy improves the platelet number but increases the risk of sepsis and the patient should be kept on lifelong antibiotic prophylaxis.[6] Eczema is treated with steroids and may fail to subside despite long term therapy.

Long term treatment includes the Hematopoietic Stem Cell Transplantation (HSCT) with an 80% survival rate.[7] HSCT in a matched unrelated donor before 5 years of age and a mismatched related donor before 2 years of age has a better outcome.[8] Gene therapy currently shows a glimmer of hope for a possible "cure", but for developing countries, the treatment of choice remains symptomatic care.[9]

Conclusion

Due to the high propensity of association with auto-immune disorders and lympho-reticular malignancies besides the need for long term symptomatic care for the classical symptoms, patients with WAS have to be under meticulous medical vigilance. In resource limited settings,

stem cell transplant and gene therapy may not be immediate options.

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