Wiskott-Aldrich Syndrome (WAS): A Case Report of Mauritius and Review

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Abstract:

Wiskott-Aldrich is an X-lined recessive disorder typically characterized by thrombocytopenia, eczema and recurrent infections. We report the four- year treatment progress of a six- year old boy, who initially presented with vesicular lesions over the trunk, upper and lower extremities and face and blood tinged stools at the age of 2 weeks. From the family pedigree, there were two suspected cases that were never successfully diagnosed with similar symptoms. The patient was diagnosed with Wiskott-Aldrich syndrome and underwent symptomatic treatment and treatment with prednisolone for the last four years. The platelet count over these four years was also studied.

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. The rapid destruction of abnormally shaped platelets is the main cause for severe thrombocytopenia in Wiskott - Aldrich syndrome patients (1). T-lymphocyte and B-lymphocyte dysfunction in WAS patients leads to immunodeficiency. The protein encoded by the WAS gene codes for the protein (WASp) is a hematopoietic specific regulator of actin nucleation in response to signals arising at the cell membrane (2).

The aim of reporting this case and the family history of this case is to increase the awareness of pediatricians of developing countries regarding any suspicion of WAS in a patient and understand the effect of symptomatic treatment and use of steroids on a long term plan for regulating platelet counts in patients not having any splenectomy or bone marrow transplantation.

Case report

In 2008, a two weeks old boy, born by normal vaginal delivery of a non-consanguineous marriage, presented with vesicular lesions and a complaint of five episodes of bloody stools. The rash initially started on the head and progressively moved to all over the body. The patient was given broad spectrum antibiotics as prophylactic treatment and the symptoms subsided over the next few days.

At the time of the admission there was no recent immunization done and the patient was apyrexial. Prenatal and postnatal history was uneventful. Possible auto-immune reaction leading to the symptoms was mooted.

In 2010 the same patient presented to the Emergency Room (ER) with epistaxis, malena and fever. On examination several ecchymosis spots were observed over the body with bruises found on lips and buccal cavity. The platelet count on admission was 22,000/cmm. The patient started having coffee brown vomitus and platelet concentrate was transfused. The mother of the patient had a brother who died with similar symptoms at the age of four and no clear diagnosis was made at that time. Idiopathic thrombocytopenia, sickle cell anemia and thalassemia were highly suspected at that time due to the maternal family history.

A bone marrow biopsy was conducted. No sickling was found and the Hemoglobin (Hb) electrophoresis ruled out sickle cell anemia and thalassemia. Blood urea, creatinine and urine were normal on routine examination and microscopy and urine culture was sterile. Immunoglobulin profile showed high Immunoglobulin A (IgA), low Immunoglobulin M (IgM), high Immunoglobulin E (IgE) and normal Immunoglobulin G (IgG).

The diagnosis of Wiskott-Aldrich syndrome was made. The option of splenectomy was discussed, but rejected by the parents. During the four- year treatment plan, he has been using prednisolone, immune replacement therapy and symptomatic therapy. His platelet count prior to any transfusion was plotted in (Figure.1).

The patient has encountered delays in his developmental milestones. There are no other major clinically relevant abnormal findings. A pedigree diagram was made during our research and any possible cases of Wiskott-Aldrich syndrome were added.

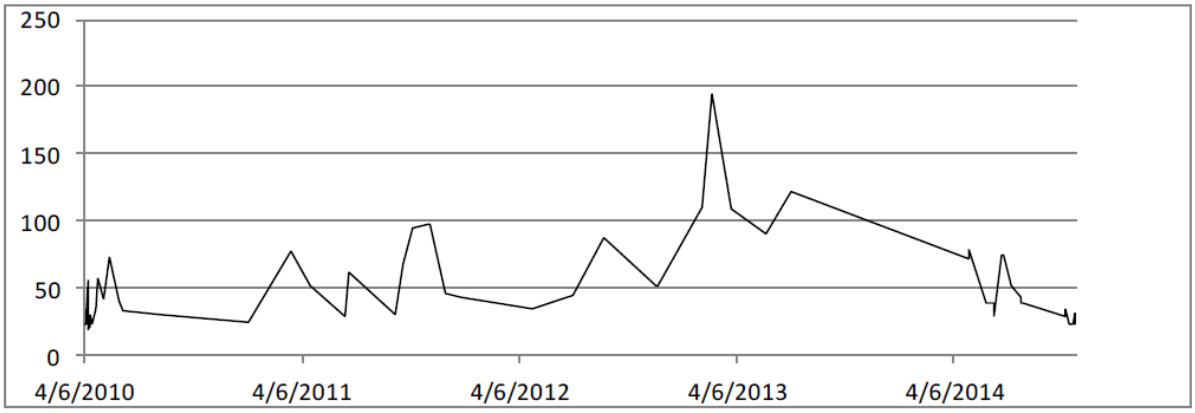


Fig.1: Platelet count plotted against time in Day/Month/Year format at which blood sample was collected

Discussion

The case presented above showed the characteristic clinical triad of Wiskott- Aldrich syndrome: thrombocytopenia, eczema and recurrent bacterial infections. Immunoglobulin profiles showed low IgA, IgM and high IgE with a normal IgG level. The small platelet size and low platelet count was also observed in the patient. In patients with WAS the T cell functions are eventually affected, predisposing them to opportunistic infections. WAS is a complex and severe X-linked disorder that affects 1 to 10 of

every 1 million male newborns. The life expectancy varies and is approximately 15 years. The main cause of death in 21% (3) of cases is by hemorrhages and can present as non-life threatening manifestations of epistasis purpura, petechiae to severe intestinal and cranial bleeding. Bleeding results from severe thromobocytopenia due to a reduced platelet size that result from mutation of WASp in platelets (4). Thrombocytopenia in WAS patients occurs irrespective of the degree of mutation of the WAS gene. The megakaryocyte level is usually normal in WAS patients. Peripheral destruction of platelets in spleen plays an important role in the thrombocytopenia. 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 (5). WAS patients typically experience a skin rash resembling acute or chronic eczema which is seen in 80% of patients (3). The cause of the eczema has not been fully understood. The high levels of IgE in WAS patients strongly suggests an atopic origin (6). An imbalance in cytokine production towards the 2 type in WAS patients has been described recently (7). WAS patients can present with several autoimmune manifestation at the same time and this contributes to a poor prognosis. Our patient developed generalized painless lymphadenopathy in 2013 that failed to subside with antibiotics and symptomatic treatment and biopsy ruled out any lymphoid malignancy. Two different surveys have shown a 13% (3) and 22% (6) incidence of tumors in WAS patients. Tumors in WAS patients generally arise in childhood but are also present in adolescents and young adults. Leukemia, myelodysplasia and lymphoma take up to 90% of the cases. These patients have a poor prognosis with less than 5% Wiskott-Aldrich Syndromemaking it past the 2 -year survival period (3).

There are two major aims of treatment: symptomatic and long-term. In many underdeveloped countries the physicians are considering the symptomatic approach. Bleeding is controlled through regular transfusions of blood and platelets and 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 (8). Antibiotics do not improve thrombocytopenia but helps to prevent any bacterial or viral infection. Eczema is treated with steroids and may fail to subside despite long term use in some patients. Long term treatment includes the Hematopoietic Stem Cell Transplantation (HSCT). There is an 80% survival rate with HSCT from a related donor. HSCT in a matched unrelated donor before 5 years of age and a mismatched related donor before 2years of age has a better outcome (9-14).

Recently a research team in Germany has initiated a gene therapy trial for WAS. The team used a murine Moloney leukemia virus derived retroviral vector encoding the full WASp cDNA. There are several genetic and immunological factors leading to the development of WAS in patients (15). Gene therapy currently shows a glimmer of hope for any possible “cure” (16, 17), but for developing countries such as Mauritius, the treatment of choice for WAS patients remain symptomatic care.

Conclusion

For physicians from developing countries, any patient presenting with bleeding manifestation along with history of recurrent sino-pulmonary infection and eczema especially should be ruled out for WAS while

considering possible causes of the symptoms. An early diagnosis might help the patient with a better prognosis.

Conflicts of interests: None.

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