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CASE REPORT

Case Report: Wiskott – Aldrich Syndrome in Patients with Normal Platelet Size in Bahrain

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Abstract

Regardless of ethnicity or geographical distribution, Wiskott-Aldrich syndrome affects 1 in every 100,000 live male births. It has been established that Wiskott-Aldrich syndrome may potentially be a source of autoimmune illnesses and reticuloendothelial malignancies, even though most patients present with the traditional triad of thrombocytopenia, eczema, and recurrent bacterial infections. This case report introduces a 4-year-old boy born with hematemesis, thrombocytopenia, eczema, recurring infections, and, most surprisingly, normal platelet size. Genetic testing confirmed the diagnosis, primarily based on clinical suspicion. Thus the case study attempts to increase awareness among doctors in Bahrain and globally in considering the diagnosis of Wiskott-Aldrich syndrome in any patient with eczema, recurrent infections and thrombocytopenia regardless of having a normal mean platelet volume .

Keywords: Genetic testing, Immunity disorder, Primary immuno deficiency disorder, Thrombocytopenia, Wiskott-Aldrich syndrome

Introduction

Wiskott-Aldrich syndrome (WAS), a rare X-linked hereditary primary immunodeficiency illness was first disclosed to medical professionals in 1937. This illness is caused by mutations in the gene that produces the WAS protein (WASP).[1] The gene is only expressed in cells of non-erythroid hematopoietic lineage and is found on the short arm of chromosome X, p11.22-p11.23.[2] Numerous hematological and immunological cell processes depend on the WASP, an essential regulator of the actin cytoskeleton.[3]

One in every 100,000 live male births is the stated WAS incidence worldwide.[4,5] However, any article with precise data on diagnosis in Bahrain is rare. The average age of WAS diagnosis is two years.[6] Wide-ranging clinical manifestations of WAS are correlated with the WAS gene mutation. It can range in severity from a mild form like X-linked thrombocytopenia (XLT), which low platelet count characterizes with the absence of or mild eczema., Like the classic WAS triad, more severe forms are characterized by severe immunodeficiency, macrothrombocytopenia, and eczema, with an increased risk of developing autoimmune diseases and tumors affecting the reticuloendothelial system. There is also the X-linked neutropenia (XLN) phenotype, which is linked to varying degrees of neutropenia.[7,8]

The diagnosis of WAS is difficult. The gold standard for confirming a WAS diagnosis is genetic sequencing. However, because it is uncommon in hospitals, clinical suspicion plays a crucial role in diagnosis. Patients with WAS who receive early diagnosis and therapy have better prognoses and outcomes.[7]

Hematopoietic stem cell transplantation is the only effective treatment for WAS, while gene therapy offers a hopeful outlook for treatment possibilities and has produced some encouraging outcomes.[6,9] In this case report, a 4-year-old male from Bahrain is presented. His initial symptoms included hematemesis, dermatitis, and decreased activity. The purpose of presenting this instance is to demonstrate the importance of identifying a rare disease within the community and initiating prompt treatment.

Case presentation

The case presented here concerns a 4-year-old Bahraini child whose complications started at birth. The patient is a product of full-term uneventful spontaneous vaginal delivery with a birth weight (BWT) of 2.8 kg from nonconsanguineous parents, with no maternal or neonatal infections. A few hours after birth, the baby had coffee grounds-like vomitus, which was dealt with by two episodes of gastric lavage. At the age of 1 month, this patient presented to the Emergency Department complaining of vomiting with streaks of blood and coffee-ground vomitus for 3 days. Intravenous fluids were administered, no investigations were done at that time and the parents were reassured. At the age of 4 months, patient presented to the Emergency Department complained of vomiting that contained streaks of blood (sometimes fresh blood) for a 1-month duration along with eczematous skin over the cheeks. To add, he had a history of reduced activity after vomiting but no history of reduced feeding, fever, cough, shortness of breath, trauma change in color of urine, melena, epistaxis or bleeding per rectal. Patient had a positive family history for G6PD enzyme deficiency, Immunization was up to date, and developmental milestones were appropriate for his age. The patient has no siblings. His mother received prenatal care, and follow-up visits were unremarkable. On examination, he was active, alert, and not in distress or tachypneic; he had hypopigmented patches with an eczematous rash on the cheeks. Abdominal examination showed a small umbilical hernia. Cardiovascular, respiratory, nervous, and ENT systems examinations were unremarkable. Blood was taken for complete blood count (CBC), and the results showed microcytic hypochromic anemia, low platelet count, and normal mean platelet volume (MPV) (Table 1). Immunoglobulin assay revealed normal immunoglobulin E (IgE), significantly low immunoglobulin A (IgA), low immunoglobulin G (IgG), and low immunoglobulin M (IgM) (Table 2). Given the patient's clinical presentation, lab findings, and biological gender, a high index of suspicion of WAS was developed. The blood sample was considered for testing for WAS gene, and a mutation was identified in the WAS gene. Regarding the patient's management, he was transfused with 252 ml of Platelets and 90 ml of Packed RBCs, after which hematemesis stopped, and patient Hb rose to 10 g/L. The patient's eczematous skin lesions were treated with topical Tacrolimus 0.03 % and topical steroids 0.05 %, after which the eczematous lesions improved and were less inflamed. The patient was discharged after ten days. In the meantime, live vaccines were deferred for the patient. The patient had multiple recurrent infections throughout his life. Moreover, the patient was admitted to the hospital four times, twice for a platelets transfusion in 2018 and 2019, once for umbilical hernia repair in 2022, and for adenotonsillectomy in 2022.

Table 1: Results from the CBC examination

Hb	MCV	MCH	RDW	PLT	WBC	Neutrophils	MPV	Lymphocytes
7.1	70.4	21.9	15.1 %	20*109/L	13.5	12.9 %	10.7	63.6 %
g/L	fL	pg			*109/L		fL	

Hb, hemoglobin; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; RDW, red cell distribution width; PLAT, platelets; WBC, white blood cell count; MPV, mean platelet volume

Table 2 : Immunoglobulin assay

IgG	IgE	IgA	IgM
4.97 g/L	57.51 IU/ml	0.24 g/L	0.25 g/L

Discussion

Immune Thrombocytopenia is frequently the first diagnosis for children with WAS,[13] which results in both inappropriate treatment and delay in the most effective life-saving medication. However, emphasis on the disease's characteristic presentation will aid in a more accurate diagnosis.[15]

The case discussed above demonstrated the Wiskott-Aldrich syndrome's diagnostic clinical triad (thrombocytopenia, eczema, and recurrent bacterial infections), which puts patients at risk for a reduced life span.

The underlying cause of each symptom in the triad, beginning with recurrent infection, is that individuals with WAS eventually experience impaired T cell activities, predisposing them to opportunistic infections, as was the case with this 4-year-old male.

There are few reported cases of WAS with normal platelets size. One similar case was regarding a 9-month-old Malayan boy who presented with thrombocytopenia at birth. After investigations and genetic testing, the patient was diagnosed to have WAS with normal platelet size. Genetic analysis in this patient revealed a C.1264G mutation in exon 10 of the WAS gene. [14] Similarly, the patient discussed in the present study had the same mutation on exon 10 of the WAS gene, and both cases turned out to have WAS with normal MPV.

WAS is a challenging and X-linked severe condition, where the average life expectancy varies and is 15 years. Hemorrhages are the primary cause of death in 21% of cases, and the patients might manifest mild epistaxis, purpura, petechiae, or severe intestinal and cerebral bleeding. Because of a reduced platelet size brought on by a WASP mutation in platelets, severe thrombocytopenia can cause bleeding.[16] Thrombocytopenia develops in WAS patients regardless of the WAS gene's level of mutation. In WAS patients, the megakaryocyte count is typically normal. The spleen's peripheral destruction of platelets is a significant contributor to the thrombocytopenia. Megakaryocytes may or may not be found in bone marrow aspirates, platelet agglutinins are absent, and donor platelets have a normal survival duration, all of which suggest faulty synthesis rather than excessive destruction.[17] The specific etiology of the thrombocytopenia is still unknown.

Patients with WAS frequently develop skin rash that resembles either acute or chronic eczema. The elevated IgE levels in WAS patients consistently point to an atopic etiology. Recent research has provided an explanation for the difference in Th2 cytokine production in WAS patients.[16]

Patients with WAS may exhibit multiple autoimmune symptoms simultaneously, worsening their prognosis. As mentioned before, the patient in this study experienced numerous recurring infections. This patient did not get cancer, which typically manifests in later life and has an average onset of about ten years. Up to 90% of cases develop either lymphoma, leukemia, or myelodysplasia. Less than 5% of these individuals survive past the 2-year mark, giving them a poor prognosis.

Patients are categorized based on the severity of their diseases using the WAS scoring system. A score of 1 indicates that the patient solely has thrombocytopenia. In contrast, a score of 2 indicates that the patient has moderate or transitory eczema or minor infections in addition to thrombocytopenia. Patients are deemed to have XLT if they score 1 or 2. After receiving the best care, patients with recurring infections and treatment-resistant eczema are given a score of 3 (mild WAS) or 4 (severe WAS). Regardless of the initial score, patients with autoimmune illness or malignancy receive a score of 5. Using this system, the patient had a score of 3, indicating the mild WAS variant.[19]

The detection of a mutation in the patient and evaluating the carrier status of the mother will enable family counseling in any future pregnancies. A prenatal diagnosis or blood tests performed in the first few days of life in families with affected children will allow for an early stem cell transplantation arrangement and prevent potentially harmful procedures from being given to infants with WAS, such as the administration of live vaccines

and intramuscular injections that may cause severe infection and bleeding tendencies.

Conclusion

In conclusion, although being a rare illness, Wiskott-Aldrich syndrome is a significant hereditary immunodeficiency disorder that must be taken into consideration. The case presented in this study highlights the importance of considering the diagnosis of WAS in any case presenting with eczema, recurrent infections and thrombocytopenia even if the MPV was normal. The condition can be, confirmed by performing genetic workup and screening family members in order to identify any carriers.

Declaration

Pictures could not be included as the parents agreed to write this case report but not to include any pictures.

Conflicts of Interest

Nil

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