CASE REPORTS

A RARE PRESENTATION OF WISKOTT - ALDRICH SYNDROME WITH MACROTHROMBOCYTOPENIA

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Abstract

We report a one and half year old male child diagnosed with Wiskott - Aldrich syndrome (WAS). He had persistent thrombocytopenia which on bone marrow biopsy was found to be macrothrombocytopenia. He did not exhibit any characteristic clinical and laboratory findings indicating the syndrome. A test for WASp gene was done which showed reduced expression. Thus it is essential to test for mutations of the WAS gene in all unexplained cases of infantile thrombocytopenia even in the absence of characteristic feature of microthrombocytopenia.

Keywords

Wiskott Aldrich syndrome, Wiskott Aldrich syndrome protein (WASp), macrothrombocytopenia, primary immunodeficiency

Introduction

Wiskott–Aldrich syndrome (WAS) is a rare X-linked recessive disease characterized by eczema, thrombocytopenia (low platelet count), immune deficiency, and bloody diarrhea (secondary to the thrombocytopenia). It is also sometimes called the eczema-thrombocytopenia-immunodeficiency syndrome in keeping with Aldrich's original description in 1954. (1) The reason we are reporting this case is due to a rare presentation of WAS where Wiskott Aldrich Syndrome protein (WASp) deficiency was documented but his immunoglobulin levels were within normal limits and instead of the characteristic feature of microthrombocytopenia the patient presented with macrothrombocytopenia.

Case Report

A one and a half year old male child was admitted to the hospital with fever for 5-7 days and one episode of vomiting. The NS1 report for dengue done in a private hospital was positive. He had been admitted at the age of 7 months for thrombocytopenia and had received platelet transfusion. Birth history was normal and family history was not contributory. The developmental history was normal. Immunization history was complete till age as per the expanded programme of immunization (EPI) schedule. On clinical examination, he had pallor and a petechial rash over the abdomen and the face. The right side of forehead along with the face and neck showed a few hypopigmented patches. Hepatosplenomegaly was observed as well. Complete blood count showed hemoglobin 8.4 g/dl with haematocrit of 26.8%, white blood cell (WBC) count 5090 cells/cumm and platelet count of 15,000/cumm. Mean Platelet volume (MPV) was 14.8FL (Normal: 5-7 fl). The child was referred to us from Hingoli district, a place on the outskirts of Maharashtra where he had already received platelet transfusion due to the diagnosis of dengue and per rectal bleeding. Peripheral smear showed mild anisocytosis, hypochromasia, poikilocytosis of the red blood cells (RBC) with reduced WBC count and there was presence of plasmacytoid lymphocytes. Platelets were reduced on smear. Bone marrow aspiration showed normocellular bone marrow with mild erythroid hyperplasia. Lymphocytes were 30%, monocytes were 2%. Blast cells were 2% and marrow iron was absent. Megakaryocytes were reduced. Immunoglobulin titres were normal (IgG was 11.6 g/L, IgA was1.08g/ L, IgM was 1.41g/L and IgE was 18.9 IU/ml). Anti-WASp flow cytometric assay was done which showed MFI = 3701 (Control MFI 19,149, Travel control MFI 7975) thus suggestive of reduced expression. Hence a diagnosis of Wiskott Aldrich syndrome with macrothrombocytopenia was made.

Discussion

The incidence of this rare X-linked primary immunodeficiency disorder is approximately one to four cases per 1,00,000 live male births, with an average age at diagnosis of 24 months in families without a previously affected family member. (2) The abnormal gene is located on the short arm of the X chromosome at Xp11.22–p11.23 near the centromere and encodes the WAS protein (WASp), which is a 501-amino acid cytoplasmic protein that manifests in lymphocyte and megakaryocyte cell lines. (3) The mutations usually have three different phenotypes: a) The classic clinical WAS triad of microthrombocytopenia, eczema, recurrent infections; b) the milder X-Linked Thrombocytopenia (XLT) variant, characterized predominantly by platelets reduced in size and number; and c) congenital neutropenia without the clinical findings characteristic for WAS/XLT. (3,4) Our patient had macrothrombocytopenia as demonstrated by an increased mean platelet volume. This finding is not seen in WAS as a literature search on PubMed with the words WAS and thrombocytopenia showed only one article. (5)

Patients usually come with prolonged bleeding in the form of purpura, hematemesis, melena, epistaxis or hematuria, which can be life-threatening. (6) Our patient presented with per rectal bleeding as well. Atopic dermatitis and recurrent infections are usually present in first year of life. Infections initially are caused by bacteria having a polysaccharide capsule as the response to this antigen is poor so it leads to pneumococcal infections like otitis media, pneumonia etc. Later infections with Pneumocystis carinii and herpes simplex occur. (7) Biochemical investigations reveal normal or slightly low IgG levels, high IgA and IgE levels and low levels of IgM that are secondary to accelerated synthesis and catabolism. Antibody responses are inconsistent and may show adequate response to some antigens and an abnormal response to others, including polysaccharide antigens and bacteriophage ΦX174. (3,6) Our patient presented with near normal levels of immunoglobulins. The reason for this is not known as no literature is available for the same. In lieu of the WASp deficiency, skin lesion and recurrent infections it was diagnosed to be a case of

Wiskott Aldrich Syndrome. However another interesting thing that we noted was that our patient did not have a florid skin infection like a full-fledged eczema which could be attributed to the near normal immunoglobulin levels which led us to believe that this could be a mutation of the WASp gene leading to a milder variant of the disease. The patient did not agree for genetic testing due to financial constraints. Screening for WASp mutations is performed by flow cytometry; however, this does not identify carriers or those patients with X-linked thrombocytopenia. Sequence analysis of the WAS gene is essential to confirm the diagnosis. (3)

Traditional management includes antibiotic therapy to prevent infections and platelet transfusions, to treat major bleeding episodes. Immunosuppressive treatments may be required for autoimmune manifestations. Splenectomy in patients with WAS increases the risk of septicemia and, if performed, requires lifelong antibiotic prophylaxis. To avoid splenectomy, autoimmune cytopenias can be treated with the monoclonal antibody targeting CD20 (rituximab). Patients with significant antibody deficiency may receive replacement IgG either intravenously or subcutaneously. (6) Survival beyond teens is rare and death is usually due to bleeding, infection and Epstein Barr virus induced cancers. (3) Curative therapy for Wiskott Aldrich Syndrome is hematopoietic cell transplantation. (3) While optimal results can be obtained with hematopoietic stem cell transplantation (HSCT) from HLA-identical family donors, experience with matched unrelated donors (MUD) has shown good response provided the transplant is done within the first 5 years of life, once again stressing the need for accurate prediction of the clinical phenotype. (7)

Conclusion

This case emphasizes the need for multidisciplinary assessment of patients with unexplained persistent infantile thrombocytopenia including testing for mutations in WAS gene even in the absence of micro thrombocytopenia and immunoglobulin deficiencies.

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References :

1. Aldrich RA, Steinberg AG, Campbell DC. Pedigree demonstrating a sex-linked recessive condition characterized by draining ears, eczematoid dermatitis and bloody diarrhea. Pediatrics. 1954;13: 133–139.
2. Buchbinder D, Nugent DJ, Fillipovich AH. Wiskott–Aldrich syndrome: diagnosis, current management, and emerging treatments. Appl Clin Genet. 2014; 7: 55–66.
3. Behrman RE. Primary combined antibody and cellularimmunodeficiencies. In: Behrman RE, Kliegman R, Jenson HB (eds). Nelson's textbook of Pediatrics. 16th edn. Saunders. 2000; 588-590
4. Park SK, Kim CS, Song DK, Kim JY, Choi IJ, Kim DK. A Familial Case of Wiskott-Aldrich Syndrome with a Hotspot Mutation in Exon 2 of the WAS Gene. J Korean Med Sci. 2007;22:998-1001.
5. Skoric D, Dimitrijevic A, Cuturilo G, Ivanovski P. Wiskott-Aldrich syndrome with macrothrombocytopenia. Indian Pediatr. 2014;51:1015-1016
6. Agarwal S, Mayer L. Diagnosis and Treatment of Gastrointestinal Disorders in Patients With Primary Immunodeficiency. Clin Gastroenterol Hepatol. 2013;11:1050-1063.
7. Notarangelo LD, Mori L. Wiskott–Aldrich syndrome: another piece in the puzzle. Clin Exp Immunol. 2005; 139:173–175.

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