A Case With Wiskott-Aldrich Syndrome and Ascending Aorta Aneurysm

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Summary: Wiskott-Aldrich syndrome (WAS) is a rare X-linked primary immunodeficiency disorder that is characterized by a triad of microthrombocytopenia, severe immunodeficiency, and eczema. We report the case of a 7-year-old male patient with chronic thrombocytopenia that was diagnosed as WAS after dilatation of the ascending aorta was noticed. WAS is rare, and it is a disease that requires high suspicion for diagnosis. We recommend periodic echocardiography and magnetic resonance imaging examinations to evaluate aortic aneurysms in children with WAS and that surgical intervention should not be delayed when aneurysm is detected.

Key Words: aortic dilatation, immune thrombocytopenic purpura, resistant thrombocytopenia, Wiskott-Aldrich syndrome

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Wiskott-Aldrich syndrome (WAS) is a rare X-linked primary immunodeficiency disorder that is characterized by a triad of microthrombocytopenia, severe immunodeficiency, and eczema.[1] A few cases of aneurysmal formation or vasculitis have been reported in this syndrome in the literature, and the association has not been well established.[2–7] We report a case with chronic thrombocytopenia that was diagnosed as WAS after dilatation of the ascending aorta was noticed.

CASE REPORT

A 7-year-old male patient was admitted to the local hospital with cough at 38 days of age and the laboratory features were as follows: white blood cell: 3490/mm^3, hemoglobin: 9.2 g/dL, and platelets: 35,700/mm^3. He was hospitalized and treated with neonatal sepsis. It is learned that his platelet count returned to normal and that he was discharged when his symptoms improved. As regards his medical history, he was born via Cesarean section at 39 weeks of gestational age, and the parents are nonconsanguineous. There was no bleeding during the neonatal period or after circumcision. There was no similar family history.

The patient was admitted to the hospital after a head trauma at the age of 2 years. All physical examination findings were normal except for widespread petechial rash and an ecchymotic lesion on the head. Laboratory features revealed the following (and they are): white blood cell: 7400/mm^3, hemoglobin: 9.5 g/dL, and platelets: 21,000/mm^3. The mean platelet volumes (MPVs) of the patient were ranging from 7.1 to 7.7 fL (normal range: 7.2 to 11.1 fL), which is in subnormal ranges, and his peripheral blood smear showed borderline small platelet populations. Liver and renal function tests were normal. Antinuclear antibody, anti-DNA, anticardiolipin, antiphospholipid, and antimicrosomal antibodies were negative. Pürified protein derivative and human immunodeficiency virus tests were negative. Serum immunoglobulins were within normal limits for age. C3 and C4 levels were normal. Immunodeficiency cluster of differentiation panel evaluation for cellular immunity was normal according to his age. In the evaluation of bone marrow aspiration, immune thrombocytopenia could not be ruled out, and intravenous immunoglobulin (IVIG) treatments were started in the follow-up, although no satisfactory response was achieved.

When he was 6 years old, he was admitted with complaints of difficulty in walking, speech disorder. and headache. Cerebral computed tomography (CT) showed a hypodense lesion consistent with right cerebral infarction. It was reported as diffuse ischemia findings in the right frontoparietal and left anterior frontal region and occlusion of the distal section of the right internal carotid artery in the cerebral magnetic resonance imaging venography. The patient was followed-up in the intensive care unit. Transthoracic echocardiography showed mild aortic valve insufficiency and aortic root dilatation. Ejection fraction was 76%. Familial thrombosis risk factors were negative.

Thoracic CT was performed for the patient who was hospitalized with the diagnosis of pneumonia in January 2019 and whose treatment did not improve despite antibiotherapy. Aortic dilatation (38 mm at the aortic arch level), areas of pneumonic infiltration, and mediastinal lymphadenopathies were reported (Fig. 1). The patient whose general condition deteriorated was admitted to the intensive care unit. IVIG was administered at a dose of 1 g/kg. Plasmapheresis was performed 5 times every other day. In the imaging made for control purposes; aneurysmatic aorta (41 mm in width) was detected on thoracic CT and hepatosplenomegaly was detected on abdominal CT. Portal-hepatic veins, carotid arteries, and bilateral renal Doppler ultrasonographies were normal. Resistant thrombocytopenia with microthrombocytes (MPV = 5 to 7 fL) and aortic

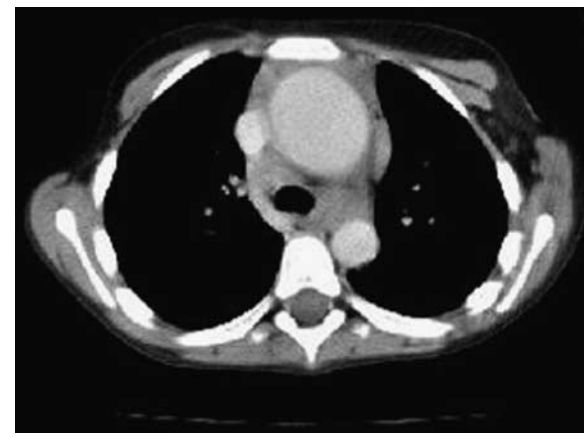


FIGURE 1. Dilatation of the ascending aorta in thorax CT. CT indicates computed tomography.

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aneurysmatic dilatation caused suspicion of WAS, and genetic studies were performed. Eltrombopag treatment was started in February 2019 for the patient who did not benefit from plasmapheresis and did not respond to IVIG treatments. WAS gene mutation analysis NM_0011107921.1c.1439_1444delCCATCCinsGAGTGGAT (p.A480Gfs) (p.Ala480Glyfs) (Hemizigot positive) was reported as highly pathogenic. The final diagnosis of the patient was made after gene mutation analysis, and the patient is currently in the preparation phase for bone marrow transplantation and is being followed-up.

DISCUSSION

WAS is a congenital X-linked recessive disorder that occurs in 4 of a million live male babies. Thrombocytopenia, small platelets, eczema, and immunodeficiency are characteristics of this disease.[4,8] Complete blood counts often support the diagnosis of WAS. MPV is a routine component of the automated complete blood count. In WAS patients, usually in laboratory findings, platelets are <70,000/ mm^3, and the MPV is <5 fL.[9] WAS may present with various clinical findings such as bloody diarrhea, epistaxis, hematuria, hematemesis, intracranial hemorrhage, petechial rash on the skin and oral mucosa, usually due to thrombocytopenia starting from the first weeks or months of life. Later, recurrent bacterial infections such as otitis media, pneumonia, sepsis, and meningitis develop. Suppression of cell-mediated immunity increases the risk of viral and opportunistic infection.[10–13]

Vasculitis and aortic aneurysm formation in WAS is a rare but life-threatening complication. The pathogenesis of aortic aneurysms remains unclear. Increased immunoglobulin A and IgE deposit in the vessel wall, and it is thought that vasculitis occurs as a result of abnormal immune reactions due to predisposition. Although rare, heart, liver, kidney, gallbladder, stomach, coronary, and cerebral middle and small diameter arteries may be affected. Involvement of the aorta is very rare.[4,5] To the best of our knowledge, a few adult patients[2–5] and children[6,7] have been previously reported in the literature. Aneurysms could be found in any part of the aorta, such as only in the ascending aorta, or both in the ascending and descending aorta. In our case, aneurysm was severe and widespread through the ascending and arcus of the aorta. The risk of death from aneurismal rupture seemed to be higher in that patient because of thrombocytopenia and impaired platelet function. Although surgical management of these patients is considered more complex than the general population, surgical intervention should not be delayed. Recently, Pellier et al,[7] reported that they had identified aortic aneurysms in 5 of 38 patients with WAS (13%) detected during childhood at the age of 10 to 16 years during childhood. WAS patients with aortic aneurysms in different case reports in the literature are compiled in Table 1. We think that aneurysm formation and vasculitis may be more common in WAS than reported.

TABLE 1. Description of WAS Patients With Aortic Aneurysm in Different Case Reports

References	Diagnosis Age of WAS (y)	Description of Aneurysm	Aid in Diagnosis	Aneurysm Detection Age (y)	Other Findings	Treatment	Prognosis
Narayan et al[5]	6	Aortic root and ascending aorta	Dyspnea	21	Calcification of aneurysm	Two surgeries	Alive
Ono et al[6]	5	Ascending and descending aorta	X-ray of chest	7	Acute lymphocytic leukemia, cytomegalovirus	Surgery and HSCT	Alive
Pellier et al[7]	NA	Descending thoracic aorta	X-ray of chest	10	Progression in aortic aneurysm	HSCT	Alive
	NA	Thoracic aorta	X-ray of chest	13	Insufficiency of aortic valve, left ventricle dilatation	HSCT	Death due to viral encephalitis after HSCT
	NA	Abdominal aorta	Abdominal ultrasound	13	Right iliac artery dilatation	NA	Death by lymphoma
	NA	Descending thoracic aorta	X-ray of chest	11	None	NA	Alive
	NA	Ascending aorta	Chest pain	16	Aortic dissection, valvular insufficiency	Surgery, methotrexate, steroids	NA
Onalan et al[14]	NA	Descending aorta	Chest pain and dyspnea	12	Left ventricle dilatation	Surgery	Alive
Wood et al[15]	NA	Descending aorta	Chest pain	29	Aortic valvular stenosis	Two surgeries	Alive
Van Son et al[16]	NA	Ascending aorta and descending thoracic aorta	X-ray of chest	23	Progression of aortic aneurysm and valvular insufficiency	Surgery	Alive

HSCT indicates hematopoietic stem cell transplantation; NA, information not available; WAS, Wiskott-Aldrich syndrome.

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In conclusion, WAS is rare; it is a disease that requires high suspicion for diagnosis, recurrent infections, eczema, and thrombocytopenia. We recommend periodic echocardiography and magnetic resonance imaging examinations to evaluate aortic aneurysms in children with WAS and that surgical intervention should not be delayed when aneurysm is detected.

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