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Case Report

Exploring the atypical: a case of atypical Kawasaki disease in a 9-year-old Filipino male with Down syndrome

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ABSTRACT
Kawasaki disease (KD) is an acute systemic vasculitis of the small- and medium-sized arteries. Due to its predilection for the coronary arteries, there is a potential for the development of coronary artery aneurysms and subsequent risk of sudden death. Down syndrome is a less-frequently occurring comorbidity in KD, as reported in a Japanese nationwide survey in 2017. A 9-year-old Filipino male with Down syndrome was referred to dermatology service due to generalized erythematous plaques and oral mucosal changes, accompanied with intermittent high-grade fever, and not responding to cefuroxime IV at 64mg/kg/day, paracetamol IV at 10mg/kg, and cetirizine 10mg/day. Further workup revealed dilated right coronary artery on two-dimensional echocardiography. Patient was then managed as a case of atypical Kawasaki disease, and was started on aspirin 80mg/tab ½ tab once daily. It is essential to consider atypical Kawasaki disease in patients having features of KD and yet not meeting the criteria for classic KD and to promptly start proper treatment in order to avoid development of coronary artery aneurysms and subsequent risks. Despite being a less-frequently occurring comorbidity in KD, patients with Down syndrome may also present with incomplete or atypical KD with coronary artery abnormalities.

1. Introduction

Kawasaki disease (KD), also known as mucocutaneous lymph node syndrome, is an acute systemic vasculitis of the small- and medium-sized arteries (1). It is most often seen in children between 6 months and 5 years of age, regardless of ethnicity (2). Given its predilection for the coronary arteries, there is a potential for the development of coronary artery aneurysms and subsequent risk of sudden death (3). According to the registry of the Philippine Pediatric Society, there have been 2,897 reported cases of KD from 2017 to 2020 in the Philippines.

A patient is classified to have atypical or incomplete KD if he or she did not fulfill the clinical diagnostic criteria for classic KD, presenting with symptoms suggestive of KD. Incomplete KD is associated with delayed diagnosis and treatment, which in turn can lead to the development of coronary artery lesions (4). In a 10-year review done in a tertiary hospital in the Philippines, 21% of KD cases presented as atypical or incomplete (5).

Down syndrome, in addition to being the most common chromosomal condition associated with intellectual disability, is characterized by a variety of clinical signs and symptoms (6). In a study determining the prevalence of birth defects at a tertiary level hospital in the Philippines from 2011 to 2014, there were 30 out of 574 neonates born with Down syndrome, with an occurrence of 14.33 per 10,000 births (7).

A Japanese nationwide survey in 2017 reported that Down syndrome is less-frequently occurring comorbidity in KD. According to the survey, in 94,233 patients with KD from 2005 to 2012, only 16 children (0.017%) had Down syndrome, half of which presented with incomplete KD (8). All 16 children with Down syndrome had no coronary artery abnormalities. As Down syndrome is a rare co-morbidity in patients with KD, no studies regarding the incidence of KD among patients with Down syndrome have been published yet.

This report describes a 9-year-old Filipino male with Down syndrome who was managed as a case of Atypical Kawasaki disease, presenting with generalized erythematous plaques, intermittent high-grade fever, and dilated right coronary artery on two-dimensional echocardiography.

2. Clinical case

A 9-year-old Filipino male with Down syndrome was referred to our service due to plaques and pustules on trunk, groin, bilateral upper and lower extremities.

Five days prior to admission, patient had erythematous patches over the groin accompanied with minimal pruritus. No other symptoms were noted. No consult was done and no medications were given.

Four days prior to admission, there was noted spreading of lesions to trunk, and bilateral upper and lower extremities. This was associated with fever (Tmax 39^{o}C), which was intermittently relieved by paracetamol.

Three days prior to admission, patient was brought to a clinic where complete blood count was requested revealing leukocytosis (16.85x10^9/L) with predominance of neutrophils (84%). Patient was given cefuroxime, zinc, and vitamins, which did not provide relief of symptoms. One day prior to admission, there was eruption of pustules over abdomen and groin, and cough, which prompted consult and subsequent admission.

Upon admission, patient was still febrile at 38.6^{o}C. Cardiac examination was unremarkable. Complete blood count was requested showing leukocytosis (17.1x10^9/L) with predominance of neutrophils (75.6%), and lymphocytopenia (18.2%). Patient was started by the main service on cefuroxime IV at 64mg/kg/day, paracetamol IV at 10mg/kg as needed for fever, and cetirizine 10mg/day. Persistence of lesions prompted referral to dermatology service.

Past medical history showed Down syndrome with unrecalled heart disease. He has no known allergies and no prior history of bronchial asthma, pulmonary tuberculosis, and diabetes mellitus. Family, personal, and social history were unremarkable.

On general physical examination, the patient was awake, alert, and afebrile. Examination of the oral mucosa revealed dry lips, and red fissured tongue with prominent papillae (Fig. 1A). No palpable lymphadenopathy was appreciated. Dermatologic examination revealed multiple, generalized, ill-defined, erythematous plaques, some topped with scattered pustules, over the trunk, groin, bilateral upper and lower extremities (Fig. 1B-D). Dermatologic working impression was to consider Kawasaki disease vs. Scarlet fever. Erythrocyte sedimentation rate was normal at 2.0 mm/Hr, C-reactive protein was positive by latex agglutination, and Antistreptolysin O was negative by latex agglutination. Patient was also started on emollient twice daily for the beginning desquamation on the abdomen.

On the seventh day of referral, two-dimensional echocardiography was requested, which showed Congenital heart disease, Tetralogy of Fallot, major aortopulmonary collateral artery, and dilated right coronary artery of 3.0mm (Z score 3.18). Patient was then managed as a case of atypical Kawasaki disease, and was started on aspirin 80mg/tab ½ tab OD. Repeat complete blood count showed normal leukocytes (WBC 7.0 x 10^9/L, neutrophil 47.9%, and lymphocyte 41.0%). He was then discharged stable and improved.

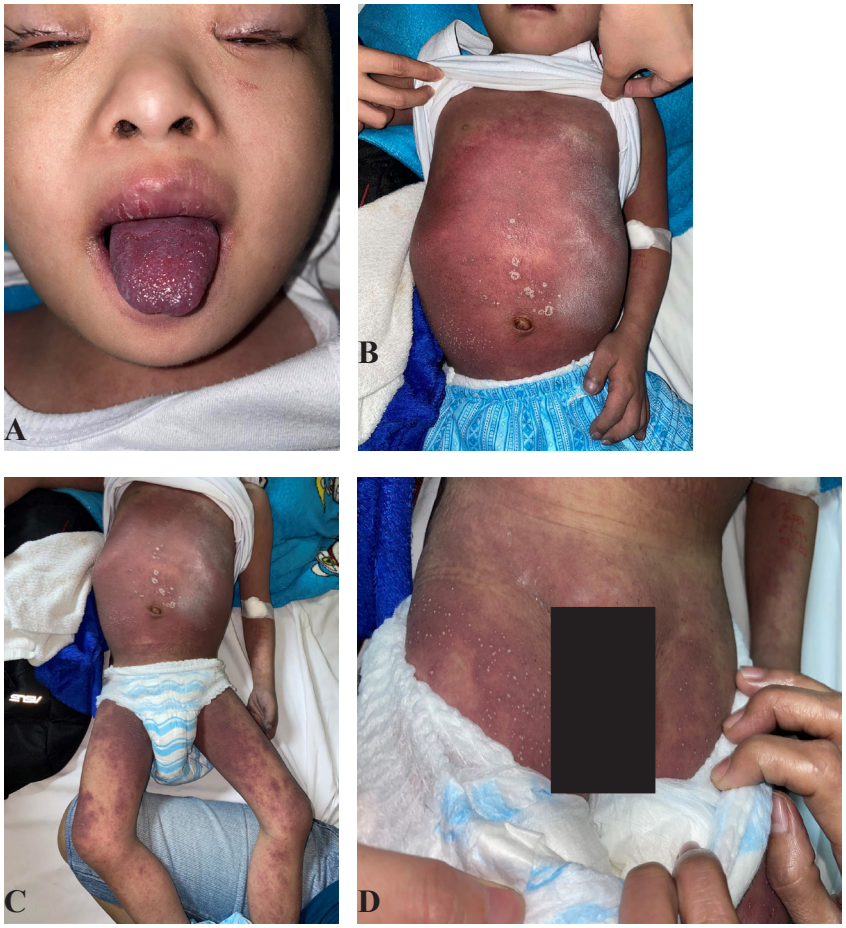

Fig. 1. *(A): Examination of the oral mucosa revealed red fissured tongue with prominent papillae. (B-D): On dermatological examination, there were noted multiple plaques, some topped with scattered pustules, over the trunk, groin, bilateral upper and lower extremities.*

3. Discussion

The etiology of KD is still ambiguous. It has been proposed that an immune response to an infectious organism in a genetically susceptible host is responsible. However, the causative infectious organism has not been identified (9).

The diagnostic criteria for classic KD include fever for at least 5 days accompanied by at least 4 of 5 criteria, as shown in Table I. In our case, the patient presented with 3 of 5 criteria namely: oral mucosal changes, strawberry tongue, erythema of the palms and soles, and scarlatiniform rash.

For patients who do not meet the criteria for classic KD but have no other diagnosis that fits their symptoms, incomplete and atypical forms of KD have been described. According to the 2017 American Heart Association (AHA) scientific statement, incomplete KD is suggested in a patient with at least 5 days of fever, 2 or 3 compatible clinical criteria, and abnormal laboratory values typical of KD or a positive echocardiogram (Z score of left anterior descending coronary artery or right coronary artery ≥2.5; coronary artery aneurysm is observed; or ≥3 other suggestive features exist, including decreased left ventricular function, mitral regurgitation, pericardial effusion, or Z scores in left anterior descending coronary artery or right coronary artery of 2 to 2.5) (10). In our case, the patient presented with

a dilated right coronary artery (Z score 3.16) and the following abnormal laboratory values: positive CRP by latex agglutination, albumin <3.0g/dL, and white blood cell count of >15,000/mm3, confirming the diagnosis of atypical KD.

Table I. Diagnostic criteria of classic Kawasaki disease (10)

Classic KD is diagnosed in the presence of fever for at least 5 d (the day of fever onset is taken to be the first day of fever) together with at least 4 of the 5 following principal clinical features:
1. Erythema and cracking of lips, strawberry tongue, and/or erythema of oral and pharyngeal mucosa
2. Bilateral bulbar conjunctival injection without exudate
3. Rash: maculopapular, diffuse erythroderma, or erythema multiforme-like
4. Erythema and edema of the hands and feet in acute phase and/or periungual desquamation in subacute phase
5. Cervical lymphadenopathy (≥1.5 cm diameter), usually unilateral

Dilated coronary arteries are uncommon as a clinical problem in the pediatric population, including children with Down syndrome. When found, they are usually associated as a sequelae or complication of KD. Tetralogy of Fallot (TOF) is comprised of pulmonary stenosis, overriding aorta, ventricular septal defect, and right ventricular hypertrophy (11). TOF mainly affects the chambers and main arteries, while KD is an acute vasculitis that predominantly affects the coronary arteries (12). In this patient, the coronary artery dilation may be attributed to atypical KD. Coronary arterial lesions have been observed in 5%-20% of patients with KD during the acute stage (13).

The administration of intravenous immunoglobulin (IVIG) and high-dose aspirin has been considered the most appropriate treatment option for patients with KD. These drugs can reduce the development of coronary artery complications when instituted by day 10 of the illness (14). Administration after 10 days of disease onset may help relieve symptoms in patients with active disease, but provides less benefit in reducing coronary artery changes (10). In our case, only aspirin was given to address the diagnosed coronary artery changes on echocardiography, since patient was already stable and asymptomatic.

4. Conclusion

A case of atypical Kawasaki disease with coronary artery abnormality in a 9-year-old filipino male with Down syndrome was presented. It is essential to consider atypical Kawasaki disease in patients presenting with features of KD but not meeting the criteria for classic KD, to promptly start proper treatment and to avoid the development of coronary artery aneurysms and subsequent risks, such as sudden death. Despite being a less-frequently occurring comorbidity in KD, patients with Down syndrome may also present with incomplete or atypical KD with coronary artery abnormalities.

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DISCLOSURE

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