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## CASE REPORT

# Kawasaki disease with Glucose-6-Phosphate Dehydrogenase deficiency, case report



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## KEYWORDS

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**Abstract** Kawasaki disease (KD) is an acute, self-limited vasculitis of unknown etiology that occurs predominantly in infants and children younger than 5 years of age. Coronary artery abnormalities are the most serious complication.

Based on the literatures infusion of Intravenous Immunoglobulin of 2 g/kg and a high dose of oral aspirin up to 100 mg/kg/day are the standard treatment for Kawasaki disease in the acute stage, and should be followed by antiplatelet dose of aspirin for thrombocytosis. Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency is an inherited X-linked hereditary disorder, and aspirin can induce hemolysis in patients with G6PD deficiency. We report a case of a 5 year and 8 month old male with KD and G6PD deficiency.

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## 1. Introduction

Kawasaki disease was first described in 1967 by Tomisaku Kawasaki and has replaced acute rheumatic fever as the leading cause of acquired heart disease among children in developed countries (Taubert et al., 1991). KD is an acute, self-limited vasculitis of unknown etiology that occurs predominantly in infants and young children (Newburger et al., 2004). The exact etiology of KD remains unknown, although

genetic predisposition or infectious agents are likely to be the cause.

Recently, guidelines were published by the American Heart Association (AHA) to aid in the diagnosis and management of Kawasaki disease. Some children classified as atypical KD patients because they present with incomplete clinical features of KD instead of classical criteria. Typical KD diagnosed by clinical criteria include fever 39–40 °C for at least 5 days, however it could be lasting for 11 days if untreated with concurrent presence of four of other criteria or at least three if coronary artery aneurysms developed. Coronary artery aneurysms or ectasia develop in 15–25% of untreated children with the disease and may lead to myocardial infarction (MI), sudden death, or ischemic heart disease (Newburger et al., 2004). Other surrogate parameters can be elevated during acute phase include CRP and ESR however CRP test more accurate in case of patient recently treated with IVIG because IG can elevate ESR.

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Children with acute KD are treated according to the past AHA recommendation guideline with single dose of IVIG (2 g/kg) and a high dose aspirin (80–100 mg/kg/d, divided into four doses). Aspirin continued indefinitely in patient with coronary artery abnormalities or until six to eight weeks in normal finding. Repeat IVIG in patients who failed to initial therapy those with persistent or recurrent fever >36 h after completion of initial IVIG infusion.

The new data shows that it is unnecessary to expose children to high- or medium-dose aspirin therapy in acute KD when the available data show no appreciable benefit in preventing the failure of IVIG therapy or CAL formation or in shortening fever duration (Weng and Ou, 2011). Long term management of KD differs according to the risk level of coronary artery abnormalities.

G6PD deficiency is an inherited X-linked disorder. It causes a spectrum of disease including neonatal hyperbilirubinemia, acute hemolysis, and chronic hemolysis. Different gene mutations cause different levels of enzyme deficiency, with classes assigned to various degrees of deficiency and disease manifestation. The levels of enzyme deficiency categorized from severe, moderate, and mild to none (Frank, 2005).

We report a case of KD with G6PD compare it with established knowledge available based on guidelines and review articles.

## 2. Case report

5 years and 8 months old Saudi boy, 18 kg weight was admitted to the pediatric department. Patient was healthy until 2 weeks prior to admission, when he started to have gastroenteritis with fever and received treatment in another hospital for which diarrhea improved but fever persisted. Two days prior to admission, he was seen in pediatric clinic and diagnosed as case of tonsillitis with adenoid hypertrophy and treated with amoxicillin–clavulanate and planned for surgery, however his fever persisted and there was swelling of dorsum of both feet with inability to walk due to pain, so he came back for follow up and was advised to be admitted for query Kawasaki.

On admission his vital signs were: temperature 39 °C, blood pressure 100/50 mmHg, heart rate 104 beats/minute, oxygen saturation 98% on room air with no distress. He has enlarged congested kissing tonsils, bulbar conjunctivitis, cracked lips, bilateral cervical lymphadenopathy, Bilateral swollen and tender dorsum of the foot, tender calf muscles, swollen and tender left dorsum of the hand, and skin peeling in the fingers.

Blood investigations on the first day of admission were: WBC  $9.22 \times 10^3/\mu\text{L}$  with 45.5% Neutrophil 39.6% Lymphocyte, Hemoglobin 8.4 g/dl, Hematocrit 27.6%, MCV 62.3 fl, RDW 41.1%, platelet count  $486 \times 10^3/\mu\text{L}$ . Blood film showed microcytic hypochromic anemia with marked anisopoikilocytosis and picture of hereditary Elliptocytosis with reticulocyte of 7.7%. Blood chemistry showed sodium 132 mmol/l, potassium 4.4 mmol/kg, chloride 101 mmol/l, carbon dioxide 23 mmol/l, ionized calcium 1.16 mmol/l, serum creatinine 43  $\mu\text{mol/l}$ , urea nitrogen 2.3 mmol/l, Aspartate aminotransferase 25 IU/l, Alanine aminotransferase 26 IU/l, C-Reactive Protein 18.5 mg/l and Erythrocyte Sedimentation Rate 60 mm/h. G6PD was 4 mIU, Rheumatoid factor was negative < 10.0 IU/ml, C3, C4, Antinuclear Antibody and urine analysis were normal too.

Echocardiography done at the day of admission and showed Right Coronary Artery diameter of 3.2 mm at its main stem and 3 mm at its distal part. Left Coronary Artery diameter was 3.1 at its origin and normal 2.2 mm at its end. No effusion or chamber dilatation.

Patient with persistent fever with four clinical features of KD with abnormal coronary artery and elevation of inflammatory markers diagnosed as case of Kawasaki disease, G6PD and microcytic hypochromic anemia. Patient was treated with single dose of Intravenous Immunoglobulin 2gm/kg over 12 h with no anti-inflammatory dose of aspirin.

On the second day, fever subsided, feet and hands swelling improved.

Echocardiogram was done on the fourth day of admission which revealed normalization of the coronary arteries lesions with normal myocardial function, and Dipyridamole was started as an anti-platelet at a dose of 4 mg/kg. In the next day the patient developed bloody diarrhea, Dipyridamole was stopped as it could be the cause and investigations were done: stool analysis was done twice over 2 days and it was normal except for positive occult blood stool, clostridium difficile negative. The third Stool analysis showed entameba histolytica which was treated successfully with metronidazole.

Blood indices were: iron 7  $\mu\text{mol/l}$ , total iron binding capacity of 30  $\mu\text{mol/l}$ , ferritin of 123.3 ng/ml, so iron supplementation was started.

Patient came for follow up after two weeks of discharge. Echocardiogram showed normal coronary arteries both right and left with good myocardial function. Electrocardiogram was normal. Complete Blood Count showed improvement of anemia as Hb 9.0 g/dl, Hct 27.5%, MCV 55.7 fl, and RDW 35.4%. platelet was  $486 \times 10^3/\mu\text{L}$ , so the patient was started on a low dose aspirin of 81 mg once daily.

CBC was repeated later and revealed hemoglobin of 10.5 g/dl and platelet of  $406 \times 10^3/\mu\text{L}$ , so aspirin was stopped. And echocardiogram was done 6 months after the initial presentation as a follow-up and was normal.

## 3. Discussion

According to the AHA guideline, acute management of KD include single infusion of 2 g/kg IVIG (level of evidence C) in combination with a high dose aspirin (80–100 mg/kg/day in 4 divided doses) that appear to possess additive anti-inflammatory effects (Kuo et al., 2011). High dose aspirin is discontinued after child has been afebrile for 48–72 h then begin low dose aspirin (3–5 mg/kg/day) for 6–8 weeks if patient showed no further abnormalities of coronary artery (level of evidence C) or indefinitely for children developed coronary artery abnormalities (level of evidence B) (Newburger et al., 2004). Children are at risk of developing Reye's Syndrome when taking aspirin while experiencing active influenza or Varicella infection. Children who take aspirin for long term should receive annual influenza vaccine. Patients with G6PD deficiency most likely have hemolytic anemia that caused by infection, ingestion of fava beans, or exposure to an oxidative drug (Frank, 2005).

However, this patient treated successfully with a single dose of IVIG alone without aspirin confirming the new available data that show it is unnecessary to expose children

to high- or medium-dose aspirin therapy in acute KD when the data show no appreciable benefit in preventing the failure of IVIG therapy or Coronary Artery Lesion formation or in shortening fever duration (Weng and Ou, 2011).

In the Andrew C. Lau, 1 study, she examined the efficacy of IVIG and salicylate (the active metabolite of aspirin) in inhibiting the 3 critical steps in disease pathogenesis of KD: T cell activation, TNF production, and TNF-mediated MMP-9 expression. Basically the TNF induced MMP-9 activity in smooth muscle cells is key to the development of coronary artery disease. In other hand, T cell activation leading to TNF-mediated MMP-9 activity is therefore a critical pathway in the development of coronary artery elastin breakdown in KD. IVIG was capable of inhibiting this mechanism even at subtherapeutic concentrations. However, Salicylate at therapeutic concentration cannot inhibit any of the 3 processes examined, and IVIG was not able to overcome the undesirable effects of salicylate-induced TNF expression. This implies that the usefulness of aspirin may be limited to its antiplatelet and antipyretic actions, which can be achieved at much lower doses (Lau, 2009).

As a result treatment of KD with IVIG only without aspirin in acute-stage had no effect on the response rate of IVIG therapy, duration of fever, or Coronary Artery Lesion incidence.

#### 4. Conclusion

KD is successfully treated with single dose IVIG without high or moderate doses of aspirin with good improvement of coronary artery disease and fever that promisingly giving good treatment option especially for G6PD deficiency patient.

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