CASE REPORT

Kawasaki disease with G6PD deficiency: A case report and literature review

Hao Hu, Yan Pan*

Department of Pediatrics, The First Affiliated Hospital of Yangtze University, Jingzhou, Hubei Province, China

Received: January 12, 2025 **Accepted:** April 8, 2025 **Online Published:** April 22, 2025
DOI: 10.5430/dcc.v11n1p21 **URL:** https://doi.org/10.5430/dcc.v11n1p21

ABSTRACT

Objective: Kawasaki disease (KD) is the leading cause of acquired heart disease in children. Aspirin is widely used in KD management, but its use in glucose-6-phosphate dehydrogenase (G6PD) deficiency is challenging due to the risk of hemolysis. This report discusses the management of KD in a child with G6PD deficiency.

Case presentation: A 2-year-7-month-old girl presented with fever, jaundice, and rash. She developed classic KD symptoms, including conjunctival injection, strawberry tongue, and limb edema, with laboratory findings of elevated inflammatory markers, anemia, and thrombocytosis. Diagnosed with KD, she was treated with IVIG, dipyridamole, and low-dose aspirin to mitigate hemolysis risk. The patient recovered without complications, and follow-up revealed no coronary artery abnormalities.

Conclusions: Low-dose aspirin combined with other antiplatelet agents, such as dipyridamole, may have been safely used in this patient with G6PD deficiency. Individualized treatment strategies are essential, and further research is needed to optimize aspirin use in this population.

Key Words: Kawasaki disease, Early diagnosis

1. INTRODUCTION

Kawasaki disease (KD), also known as mucocutaneous lymph node syndrome, was first reported by Dr. Kawasaki from Japan in 1967. Over the past 50 years, it has become recognized as the leading cause of acquired heart disease in children. According to the Guidelines for Evidence-Based Diagnosis and Treatment of Kawasaki Disease in Children, the recommended treatment protocol includes intravenous infusion of high-dose immunoglobulin (single dose of 2 g/kg) within 12–14 hours, along with early administration of high-dose aspirin. After fever subsides (48–72 hours) or 14 days into the disease course, the dosage is reduced to a low-dose regimen (3–5 mg/kg/day, taken once daily) for 6–8 weeks. Aspirin is discontinued if the coronary arteries return to normal.[1]

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an X-linked, partially dominant hereditary disease. It results from mutations in the G6PD gene that cause reduced enzyme activity or changes in enzyme properties, leading to hemolysis and other related disorders. G6PD deficiency is the most common enzymatic disorder globally, with China being a high-prevalence region. It is predominantly distributed in areas south of the Yangtze River, with high incidences reported in provinces such as Guangdong, Guangxi, Yunnan, Hainan, Sichuan, and Guizhou. Studies have shown that aspirin may

*Correspondence: Yan Pan; Email: woshipanyan@126.com; Address: Department of Pediatrics, The First Affiliated Hospital of Yangtze University, Jingzhou 434000, Hubei Province, China.

induce hemolysis in patients with G6PD deficiency.[2] We report a case of a child with Kawasaki disease complicated by G6PD deficiency and review the literature on KD, aspirin, and G6PD deficiency.

2. CASE PRESENTATION

A 2-year-7-month-old female patient was admitted to the hospital on August 4, 2024, with complaints of "fever for 3 days and jaundice with rash for 1 day." The patient first developed a fever on August 1, with a peak temperature of 39.2°, occurring 2-3 times daily. The fever was managed with antipyretics, temporarily reducing the temperature to normal. On August 4, jaundice of the skin and sclera was observed. During the illness, the patient experienced one episode of non-projectile vomiting with yellow watery material, without coffee-ground appearance or blood streaks. Oral administration of amoxicillin and cephalosporin antibiotics outside the hospital resulted in no improvement. The patient subsequently developed polymorphic rash, primarily on the trunk, which partially coalesced into patches and caused itching. The patient was then brought to our hospital for further evaluation. The patient had a known history of a ventricular septal defect and G6PD deficiency. No other significant past medical history was reported.

A physical examination revealed generalized jaundice of the skin and sclera, without palmar erythema or spider angiomas. Scattered red petechial rashes were observed on the trunk, partially coalesced into patches, with associated itching. Several enlarged lymph nodes were palpable on the right side of the neck. The throat was congested, without lip fissures or strawberry tongue. The bilateral tonsils were Grade I enlarged, without exudates. No other abnormalities were observed during the examination. Initial laboratory tests showed elevated inflammatory markers, liver enzymes, and bilirubin levels. C-reactive protein (CRP) was markedly elevated at 144.2 mg/L, and procalcitonin (PCT) was 2.12 ng/mL. Biochemical tests revealed total bilirubin of 101.8 μmol/L, direct bilirubin of 77.6 μmol/L, Alanine aminotransferase (ALT) of 263 U/L, and Aspartate aminotransferase (AST) of 162 U/L. Total bile acids were significantly elevated at 413.20 μmol/L. Urinalysis indicated pyuria, proteinuria, and elevated bilirubin. The Coombs test and tests for Epstein-Barr virus (EBV) antibodies were negative. Cardiac ultrasound and abdominal ultrasound findings were routine, while cervical lymph node ultrasound showed several enlarged lymph nodes bilaterally, with the largest measuring 20 mm $\times$ 7 mm on the right side. The patient was initially diagnosed with cholestatic hepatitis, acute pharyngitis, and rash. She was treated with hepatoprotective measures, intravenous meropenem for anti-infection, and medication to promote bile drainage.

During hospitalization, the patient developed conjunctival congestion in both eyes, a strawberry tongue, and hard edema of the hands and feet. The fever persisted for 5 days. A repeat blood test showed further elevated CRP (161.33 mg/L), anemia (hemoglobin 99 g/L), hypoalbuminemia (29.4 g/L), and an Erythrocyte Sedimentation Rate (ESR) of 44 mm/h. Abnormal urinalysis findings persisted, with elevated white blood cells (21.92/HPF), proteinuria, and ketones. Based on the clinical presentation of prolonged fever, rash, cervical lymphadenopathy, conjunctival congestion, strawberry tongue, and limb edema, along with laboratory findings of elevated inflammatory markers, anemia, hypoalbuminemia, and pyuria, a diagnosis of Kawasaki disease was made. Intravenous immunoglobulin (IVIG) at 2 g/kg was administered on August 7, 2024. Oral dipyridamole was initiated for antiplatelet therapy. Considering the patient's G6PD deficiency, which is a relative contraindication for aspirin due to the potential risk of hemolysis, low-dose aspirin therapy was started with parental consent. Following treatment, the patient's fever resolved, and clinical symptoms, including rash, jaundice, and limb edema, gradually improved. Laboratory tests showed normalization of inflammatory markers, liver function, and urinalysis findings.The G6PD variant information for this patient is not available in detail. G6PD is an important enzyme in red blood cells, and its variants can lead to enzyme deficiency, potentially causing hemolytic anemia. The World Health Organization (WHO) classifies G6PD variants based on the severity of enzyme deficiency and the extent of hemolysis, but without specific data, we cannot determine the severity of enzyme deficiency in this case.Regarding the cardiac ultrasound findings, the initial echocardiogram on August 10, 2024, revealed the following: the left main coronary artery (LMCA) diameter was 1.6 mm, the left anterior descending artery (LAD) was 1.1 mm, the left circumflex artery (LCX) was 1.2 mm, and the right main coronary artery (RCA) was 1.7 mm. No abnormalities were noted in the pericardial cavity. Doppler examination showed mild tricuspid regurgitation, and TDI (tissue Doppler imaging) demonstrated that the mitral annulus e' wave was greater than the a' wave. The overall left ventricular function was normal. The calculated Z-values for coronary artery diameters were as follows: RCA 0.21, LMCA -0.99, LAD -2.07, and LCX -0.70. Cardiac ultrasound follow-up revealed no significant coronary artery abnormalities, with Z-scores within normal ranges. The patient was discharged with recommendations for regular follow-up. Discharge medication instructions: Aspirin enteric coated tablets (50 mg/time); Once a day); Dipyridamole tablets (25 mg/time, 2 times/day).

3. DISCUSSION

Globally, G6PD deficiency is prevalent in populations with historical exposure to malaria, particularly in Africa, the Mediterranean, and Southeast Asia, making it a significant public health consideration in diverse clinical settings. KD is characterized by systemic vasculitis and immune dysregulation, with its pathophysiology involving complex interactions between genetic predisposition, environmental triggers, and immune responses. Aspirin, as one of the first-line treatments for KD, plays a critical role in the acute phase of the disease. During this phase, hemodynamic changes in the body activate platelets, and aspirin helps reduce fever, alleviate pain, regulate body temperature, and inhibit platelet aggregation. Aspirin has significant anti-inflammatory effects at high doses and antiplatelet effects at low doses. High-dose aspirin, in combination with intravenous immunoglobulin (IVIG), provides additional anti-inflammatory benefits. However, a meta-analysis[3] has shown no statistically significant differences between low-dose and high-dose aspirin in terms of coronary artery lesion rates, fever duration, and length of hospital stay. For certain patients, high-dose aspirin treatment should be avoided due to the risk of severe complications, such as the development of Reye syndrome in children infected with varicella virus or influenza. In this case, the patient has G6PD deficiency, where high-dose aspirin use could trigger hemolysis. Studies have indicated that dipyridamole and aspirin may have synergistic effects.[4] In this case, the patient exhibited progressive thrombocytosis early on, prompting the use of combined dipyridamole therapy.

G6PD deficiency is the most common hereditary red blood cell enzymopathy worldwide. Clinical manifestations can include miscarriage, preterm birth, stillbirth, and fetal hydrops during pregnancy. After birth, affected individuals may present with hemolysis, anemia, jaundice, or, in severe cases, bilirubin encephalopathy or death. Chronic manifestations include non-spherocytic hemolytic anemia. Due to reduced G6PD enzyme activity, red blood cells in affected individuals have diminished antioxidant capacity, leading to recurrent hemolysis. Substances with oxidative properties, such as compounds found in fava beans, can induce hemolysis after consumption. Similarly, certain oxidizing drugs can trigger acute hemolytic anemia in G6PD-deficient individuals. Common drugs associated with this reaction include antipyretic analgesics like acetylsalicylic acid (aspirin), antimalarials like primaquine and quinine, sulfonamides like sulfamethoxazole, and nitrofuran derivatives like furazolidone. However, the specific dose of aspirin that induces hemolysis remains unclear. Currently, the safety of low-dose aspirin in children with G6PD deficiency is not well-established. In this case, the patient did not experience hemolysis after the administration of low-dose aspirin.

Previous case reports of Kawasaki disease with G6PD deficiency have systematically avoided aspirin use due to theoretical hemolytic risks. Obeidat et al. described a G6PD-deficient child treated solely with IVIG and corticosteroids,[5] while Chen et al. reported a case managed with IVIG alone.[6] Our study represents the first documented use of low-dose aspirin (3-5 mg/kg/day) combined with dipyridamole in this population, expanding therapeutic options while maintaining safety. This contrasts with previous conservative approaches and suggests that individualized aspirin regimens, guided by close hemolytic monitoring and alternative antiplatelet adjuvants, may mitigate historical concerns.Based on the above, when a patient is diagnosed with KD, it is essential to assess whether they also have G6PD deficiency. For patients with G6PD deficiency, treatment may be considered with low-dose aspirin. Depending on the patient's condition, aspirin may be substituted or combined with other antiplatelet medications. High-dose aspirin treatment should be avoided whenever possible. However, the appropriate dosage of aspirin for KD patients with G6PD deficiency remains an area requiring further research.

ACKNOWLEDGEMENTS

We would like to extend our special thanks to the patients who participated in this study.

AUTHORS CONTRIBUTIONS

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

FUNDING

The Hubei Pediatric Alliance Medical Research Project, No. HPAMRP202117.

CONFLICTS OF INTEREST DISCLOSURE

The authors declare no conflicts of interest.

INFORMED CONSENT

Obtained.

ETHICS APPROVAL

The Publication Ethics Committee of the Sciedu Press. The journal's policies adhere to the Core Practices established by the Committee on Publication Ethics (COPE).

PROVENANCE AND PEER REVIEW

Not commissioned; externally double-blind peer reviewed.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

DATA SHARING STATEMENT

No additional data are available.

OPEN ACCESS

COPYRIGHTS

REFERENCES

[1] Jone PN, Tremoulet A, Choueiter N, et al. Update on Diagnosis and Management of Kawasaki Disease: A Scientific Statement From the American Heart Association. Circulation. 2024; 150(23): e481-e500. PMid:39534969. https://doi.org/10.1161/CIR.0000000000001295

[2] Luzzatto L, Nannelli C, Notaro R. Glucose-6-Phosphate Dehydrogenase Deficiency. Hematol Oncol Clin North Am. 2016; 30(2): 373-93. PMid:27040960. https://doi.org/10.1016/j.hoc.2015.11.006

[3] Safar FM, Kaabi WM, Aljudaibi RS, et al. The Effectiveness of No or Low-Dose versus High-Dose Aspirin in Treating Acute Kawasaki Disease: A Systematic Review and Meta-Analysis. Clin Pract. 2024; 14(4): 1296-1309. PMid:39051299. https://doi.org/10.3390/clinpract14040105

[4] Li J, Chen Y, Ou Z, et al. Aspirin Therapy in Cardiovascular Disease with Glucose-6-Phosphate Dehydrogenase Deficiency, Safe or Not? Am J Cardiovasc Drugs. 2021; 21(4): 377-382. PMid:33313989. https://doi.org/10.1007/s40256-020-00460-8

[5] Obeidat HR. Kawasaki disease in a child with glucose-6-phosphate dehydrogenase deficiency: A case report and management considerations. Saudi Pharm J. 2015; 23(4): 455-457. PMid:27134550. https://doi.org/10.1016/j.jsps.2014.11.003

[6] Obeidat HR, Al-Dossary S, Asseri A. Kawasaki disease complicated with glucose-6-phosphate dehydrogenase deficiency: A case report. J Microbiol Immunol Infect. 2014; 47(3): 261-263. PMid:22727889. https://doi.org/10.1016/j.jmii.2012.05.002