Case Report

Diagnosis and treatment of incomplete Kawasaki disease

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ABSTRACT

Kawasaki disease (KD) is a self-limiting systemic vascular condition predominantly affecting children under five, characterized by prolonged fever and specific clinical signs. Diagnosis is made through the presence of a fever lasting over 5 days and at least four of five criteria, which include oral mucosa changes, extremity alterations, rash, and absence of purulent conjunctivitis or lymphadenopathy. The disease presents significant risks, including coronary artery aneurysms, making timely diagnosis and treatment critical. This case report details a 3-year-old boy with incomplete KD, who manifested with fever, abdominal pain, and rash. Laboratory tests showed leucocytosis and elevated inflammatory markers, leading to an echocardiographic diagnosis of coronary artery dilation. Treatment with high-dose intravenous immunoglobulin and aspirin resulted in symptomatic improvement and stabilization of coronary artery dimension. KD remains the leading cause of acquired heart disease in children, underscoring the importance of recognizing its signs and initiating early treatment to prevent long-term complications.

Key words: Fever, Intravenous immunoglobulin, Kawasaki disease, Mucocutaneous lymph node syndrome, Vasculitis

Kawasaki disease (KD) also known as mucocutaneous lymph node syndrome is characterized as an acute systemic vascular disease, it is generally self-limited, and the highest incidence occurs in children under 5 years of age. A diagnosis of classical KD, also called complete KD (CKD), is usually made when the patient has a fever lasting >5 days and four of the following five manifestations: (a) changes to the oral mucosa, such as lip fissures, erythema, or strawberry tongue; (b) changes to the extremities, including edema, redness, or desquamation; (c) polymorphous rash; (d) no purulent bilateral eye injection; and (e) no purulent cervical lymphadenopathy (>15 mm) [1-4]. The incidence of KD remains the highest in Japan, followed by South Korea, and China. A study in Beijing indicated an increasing prevalence of incomplete KD (IKD). Seasonal correlations have been proposed by other researchers regarding the initiation of IKD, suggesting that seasonal differences in the onset of IKD may be associated with epidemiological changes in viral infections. The onset of IKD is also believed to be influenced by patient age. Children with IKD are younger than children with CKD, with a higher percentage of children aged ≤2 and ≥6 years [5].

KD presents challenges in diagnosis and management due to its diverse clinical manifestations and potentially serious complications. The authors report this case because of the limited data in Indonesia and the unusual manifestation of KD. Proper diagnosis based on clinical findings, proper investigations, and follow-ups are important to treat and prevent associated complications of the disease. Untreated cases are associated with coronary artery aneurysms (CAA) in approximately 25% of patients. It is the leading cause of acquired heart disease in developed nations and is slowly bypassing rheumatic heart disease in developing countries. Treatment with high-dose intravenous immunoglobulin (IVIG) significantly decreases the incidence of cardiac involvement [6,7].

Access this article online	
Received - 15 January 2025 Initial Review - 16 January 2025 Accepted - 03 April 2025	Quick Response code
DOI: 10.32677/ijcr.v11i5.5006	

CASE REPORT

A boy was brought to the emergency room with a complaint of high fever for 2 days. The fever was 39°C which was accompanied by tachycardia, pain and swelling in the neck area, colicky abdominal pain with reduced appetite, 5 times vomiting, and the appearance of a red rash on the facial area. The patient has been given antipyretic therapy and medication for nausea and vomiting with no improvement. Basic immunization status has been carried out according to age.

On physical examination, a reddish area on the face was found extending to the ears, hands, and feet, accompanied by itching. On the lips, canker sores appear in the oral cavity, accompanied by cracked skin. During the treatment period, it was found that the fever was still fluctuating, accompanied by colicky abdominal pain. On the 4th day of treatment, there was swelling in both hands and feet.

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Laboratory examination on the 1st day of hospitalization showed leukocytosis of 16.8 × 103/μL with 88% neutrophilia and increased C-reactive protein (CRP) of 91.63 mg/L with normal urinalysis results. On the 4th day of hospitalization, a laboratory re-examination was carried out. The results showed that there was still leukocytosis of 14.6 × 10^3/μL with 75% neutrophils, an erythrocyte sedimentation rate (ESR) of 18 mm/h, an increase in CRP of 240.84 mg/L, and hypo albumin of 2.8 g/dL. The results of urine and creatinine examinations were within normal limits. On the 5th day, a re-examination is carried out, namely albumin and electrolytes to find out the cause of fever and swelling in the extremities. The albumin results showed hypo albumin of 3.1 g/dL and hyponatremia of 131 mmoL/L. On the 7th day of treatment, another laboratory examination was carried out. It was found that there was still leukocytosis of 16.4 × 103/mL, an increase in the sedimentation rate of 42 mm/h, thrombocytosis of 548 × 10^3/mL, and a high CRP concentration of 156.32 mg/dL.

Due to the patient clinical condition who still has a fever with swelling of the hands and feet, supported by the presence of leukocytosis, CRP, and thrombocytosis on the 8th day of treatment, an echocardiography examination was carried out to support the diagnosis of KD. Echocardiography results showed left main coronary artery (LMCA) dilatation with a diameter of 4.1 mm, mild mitral regurgitation of 27 mmHg, and mild tricuspid regurgitation of 25 mmHg. Systolic function is still within normal limits, namely 81% with Z score is 2–<2.5. These results support the diagnosis of KD.

Based on the existing signs and symptoms, the patient was given 2 g/kg IVIG therapy for 24 h and given had aspirin therapy 4 times 500 mg daily for 48 h. The patient underwent another laboratory examination and echocardiography on day 5 after IVIG and found an improvement in the LMCA diameter of 1.9 mm and there was no longer fever and swelling in the hands and feet. Treatment was then continued with administration of low-dose aspirin 50 mg once daily for 6–8 weeks. It is recommended to perform echocardiography again in another 2 weeks.

DISCUSSION

KD is one of the most common vasculitis in children with a predilection for coronary arteries. It is an acute, self-limiting medium vessel vasculitis of unknown origin. KD is characterized by fever, rash, conjunctival injection, oral mucositis, extremity changes, cervical lymphadenitis, and in several cases dilatation or aneurysm of coronary and other arteries. KD is recognized as the leading cause of acquired heart disease in children in developed countries replacing rheumatic fever as the most common cause in India and other Asian countries [2-6]. KD strikes predominantly infants and young children; 80% of patients are younger than 5 years of age [8].

The etiology of KD remains unknown, but there have been several hypotheses and postulations. Some of its epidemiological and clinical features suggest an infectious origin. It could be due to, immature immunity in childhood rather than in adulthood [9,10]. In addition, seasonality, geographical clustering, and occasional occurrence in families may suggest infectious and environmental origin. Based on data, it is estimated that there are around 5000 new cases every year in Indonesia, cases that can be diagnosed are recorded <200 cases/year (4%) so there are still around 96% of KD cases in Indonesia that have not been detected (underdiagnosis) resulting in poor diagnosis and treatment [5,8,11,12].

The pathological essence of IKD is the excessive activation of the body's immune system caused by systemic small- and medium-sized vasculitis. Because the clinical symptoms of IKD are incomplete, difficulties in diagnosis, treatment delays, and increased complications are common. The laboratory indicators are almost identical. Among numerous laboratory indicators, CRP and ESR are the most effective indicators of systemic inflammation in KD. IKD should be considered in any infant or child with prolonged unexplained fever, fewer than 4 of the principal clinical findings, and compatible laboratory or echocardiographic findings [2-5,13,14].

The diagnosis is based on recognition of a constellation of clinical features and excluding other similar clinical conditions. The fever is usually high-grade lasts for more than 5 days and is usually associated with extreme irritability. The fever typically does not respond to antibiotics, for example, in this patient, antibiotics were given, and antibiotics were changed to assess the response to therapy, but there was no improvement. There are five principal clinical findings: First, there are changes in the extremities. Distinctive erythema and edema of palms and soles and induration of dorsum of hands and feet are seen in early stages which at times are painful. These changes follow desquamation starting from periungual regions. In this patient, there was swelling in both hands and feet but no signs of desquamation because the desquamation process started 2–3 weeks from the onset of fever. The second is swelling of the conjunctiva, non-purulent bilateral conjunctival injection is usually found in 93% of cases of children with KD, but in this patient, there were no signs of conjunctival injection. Third is an oral changes. Oral changes can include: (a) Erythema, dryness, fissuring and cracking, peeling, and bleeding of lips. (b) "Strawberry tongue" with erythema and prominent fungiform papillae; and (c) diffuse erythema of the oropharyngeal mucosa. In this patient, the results were more toward cracking, fissuring, and bleeding of lips. The fourth sign is exanthem or rash. The cutaneous manifestations of KD are protean and present in more than 90% of KD patients. The rash is erythematous, morbilliform, and non-pruritic. The rash is transient and fades away within a few days. In this patient, the results were more toward cracking, fissuring, and bleeding of lips. Fifth is cervical lymphadenopathy. Unilateral anterior cervical lymphadenopathy is the least common feature of KD, occurring in about 50–60% of patients. Children with KD initially present with fever and unilateral cervical lymphadenopathy [2-4,8,9].

Patients who do not fulfill the complete diagnostic criteria for KD are preferably diagnosed as IKD. IKD is more common in infants, and they are the patients who are at the highest risk of developing CAA. Echocardiography results in this patient showed

cardiovascular abnormalities. The initial echocardiography before IVIG was given showed LMCA dilatation of 4.1 mm, mild mitral regurgitation, and mild tricuspid regurgitation. The pathological changes in KD affect medium-sized, extra-parenchymal muscular arteries, most commonly the coronary arteries. The echocardiogram is the mainstay of cardiac imaging during the acute phase. The recently revised 2017 American Heart Association guideline updated the definition of coronary abnormalities and the aneurysm classification by the Z score system. Small aneurysms as those with a Z-score of ≥2.5–<5.0, medium aneurysms as those with a Z-score of ≥5–<10 and an absolute dimension <8 mm, and large or giant aneurysms as those with a Z score of ≥10 or absolute dimension ≥8 mm. Echocardiography should be repeated at 1–2 weeks and 4–6 weeks after treatment. Thrombocytosis is a characteristic feature of the subacute phase of KD. Mild hyperbilirubinemia occurred in about 10%. Hypoalbuminemia is associated with more severe acute disease [2,5-7,15].

The goal of therapy in the acute phase is to reduce inflammation and arterial damage and to prevent thrombosis in those with coronary artery abnormalities. The mainstay of initial treatment for both complete and IKD is a single high dose of IVIG together with acetylsalicylic acid (ASA). IVIG should be instituted as early as possible within the first 10 days of illness onset of fever. IVIG should also be administered to children presenting after the 10th day of illness if they have ongoing systemic inflammation as manifested by elevation of ESR or CRP (CRP >3.0 mg/dL) together with either persistent fever without other explanation or CAAs (luminal dimension Z score >2.5). Patients should be treated with IVIG 2 g/kg as a single infusion, usually given over 10–12 h, together with ASA. During the acute phase of illness, ASA is administered every 6 h, with a total daily dose of 80–100 mg/kg/day in the United States and 30–50 mg/kg/day in Japan and Western Europe. When high-dose ASA is discontinued, low-dose ASA (3–5 mg/kg/day) is begun and continued until the patient has no evidence of coronary changes by 6–8 weeks after onset of illness[6-7,11-13,15,16]. The patient underwent another laboratory examination and echocardiography on day 5 and found an improvement in the LMCA diameter of 1.9 mm and there was no longer fever or swelling in the hands and feet. The patient was then given a controlled dose of ASA for another 2 weeks for clinical evaluation and echocardiograph.

CONCLUSION

We report a case of IKD with a sudden onset of fever. KD is an important cause of fever in young children. It results in a high incidence of cardiovascular damage if not treated promptly. The diagnosis should always be considered in a young child with an unexplained and persistent fever, despite the absence of full diagnostic criteria.

ACKNOWLEDGMENTS

The authors received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Santoso SA, Wangunhardjo G, Santoso IA. Diagnosis and treatment of incomplete Kawasaki disease. Indian J Case Reports. 2025; 11(5):191-193.