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CASE REPORT

Late recurrence of Kawasaki disease

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Abstract

Report of a rare case of recurrence of Kawasaki Disease (KD) and, thus, draw the attention to the possibility of recurrence of the disease after the first episode and thee risk of coronary complications. Recorrence of KD is rare, occurs in only 3-5% of case described in Japan, and is even less frequent in other populations. The inscidence of recurrence in KD is highest in the first two years after the first diagnosis, being more frequent in male patients aged two years or less. Cardiac complications are more frequent in the recurrence of KD, and death can occur from coronary thrombosis or rupture of coronary aneurysm.

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INTRODUCTION

The etiology of Kawasaki Disease (KD), a self-limiting systemic vasculitis, is not fully understood. It predominantly affects medium-caliber vessels and has a predilection for coronary arteries[1,2]. It affects individuals within the entire pediatric age range, but most cases occur in children up to five years of age. Cases are rare in individuals aged eight years or older. Incidence is higher in males and children of Asian ethnicity[3]. The progression of KD occurs in three stages: acute, subacute, and convalescent[1,2]. Although the etiology is still undetermined, theories suggest the existence of unidentified infection that triggers abnormal immune response in genetically susceptible individuals[4]. KD is the most common cause of acquired heart disease in children in developed countries[5,6]. It can cause coronary artery abnormalities including coronary artery aneurysms and stenosis in up to 25% of untreated children[3,4]. These coronary artery abnormalities can cause myocardial ischemia, infarction, and even death[6].

Diagnostic criteria are based on clinical findings, since there is no specific diagnostic test or pathognomonic clinical finding for KD.[3] According to the guidelines of the American Heart Association (AHA) and the European League Against Rheumatism/Pediatric Rheumatology European Society (EULAR/PReS), the diagnosis of classic KD is defined by fever lasting five days or longer, accompanied by at least four of the following five clinical criteria[1,3,5,7,8]:

- Extremity changes, such as edema of the dorsum of the hands and feet and/or palmar or plantar erythema in the acute phase and/or periungual or perineal desquamation in the subacute phase.
- Changes in the lips and oral cavity, such erythema and fissuring of the lips and/or diffuse hyperemia of the oropharyngeal mucosa and/or "raspberry or strawberry tongue".
- Cervical lymphadenopathy ≥ 1.5cm, usually unilateral.
- Polymorphous rash.
- Bilateral non-exudative bulbar conjunctival hyperemia.

However, 20% to 30% of patients do not meet all the criteria for classic KD and are diagnosed with incomplete or atypical KD. In these cases, laboratory tests and echocardiography are recommended to evaluate coronary implications. The most commonly found alterations are: ESR >40mm/ 1st hour; CRP > 3mg/dL; platelets > 450,000/mm3 (after 7 days of disease); anemia; leukocytosis > 15,000/mm3; GPT > 50U/L; albumin < 3g/dL; sterile pyuria; hyponatremia; and z-score of the internal coronary artery diameter > 2.5 on echocardiography[8].

Incomplete or atypical KD must be considered when prolonged fever occurs in association with:

- Presence of four diagnostic criteria.
- Elevated ESR or CRP.
- Infants with unexplained irritability or aseptic meningitis.
- Rash and elevated inflammatory markers.
- Echocardiogram with signs of coronary heart disease.
- Cervical adenitis unresponsive to antibiotic therapy.
- Unexplained or culture-negative shock.
- Presence of typical clinical criteria, even in patients with documented infection[8].

Recurrence (or relapse) is defined as a repeated episode of complete or incomplete KD, after the complete resolution of a previous episode. Recurrence of KD has been reported in only 3-5% of cases of the disease in Japan and is even less frequent in other populations[3,4]. A Brazilian study found that 8.3% of the included patients had recurrence of KD during the first three years of follow-up, a proportion greater than the ones observed in previous studies conducted in other countries such as the United States, Japan, and China[9].

The incidence of recurrence in KD is highest in the first two years, although it may occur up to eight years after the first episode. Recurrence is more frequent in male patients aged two years or younger. Cardiac complications are more frequent in recurrent KD, and death may occur due to coronary thrombosis or a ruptured coronary aneurysm[10,11].

Regarding the risk factors associated with recurrent KD, some authors have pointed out factors present in the first episode of the disease that are more often related to recurrence, which included male gender, fever of longer duration, significant increases in transaminase and C-reactive protein levels, low hemoglobin levels, coronary changes, and disease refractory to intravenous immunoglobulin. However, information on the subject is still limited[12,13].

Recurrence of KD must be recognized early on in order to prevent cardiovascular complications. Therefore, treatment should be initiated as soon as diagnosis has been confirmed[7].

The efficacy of treatment with intravenous immunoglobulin during the acute phase of KD to decrease the prevalence of coronary artery abnormalities is well established. Acetylsalicylic acid (ASA) has been used for years in the treatment of KD. However, despite its important anti-inflammatory and antiplatelet activity, ASA does not seem to decrease the occurrence of coronary abnormalities[10].

After about four to six weeks from the onset of KN, patients without coronary involvement after the acute phase of the disease may be discharged from cardiologic follow-up between four weeks and 12 months, provided that the recommended echocardiograms have been performed at the time of diagnosis, after one week, and four to six weeks after acute treatment. Post-discharge control echocardiograms must be considered to pick up possible late coronary changes[10].

This report presents a case of recurrent KD, in which the first manifestation was observed in the first year of life with recurrence occurring when the patient was aged six years. It also seeks to warn the medical community about the possibility of KD recurring after the first two years of the acute phase of the disease in patients over two years of age, which goes against the existing epidemiological data. The importance of this case report lies in the rarity of the event described in it, with few reports in the literature, and the relevance of early diagnosis, a key element in minimizing the risk of cardiac complications.

CASE DESCRIPTION

A one-year-old male infant born in Londrina-PR was brought to our service on July 4, 2014, with a history of fever lasting for five days (mean temperature 37.9ºC), which developed with diffuse skin rash, hyperemic hands and foot soles, and bilateral non-exudative conjunctival hyperemia. The patient's general condition was deteriorating and he was not eating well. Laboratory tests showed the following results: Hb 11.7; Ht 34.3; leukocytes 10 500; segmented 39%; eosinophils 9%; lymphocytes 41%; monocytes 10%; platelets 240 000; CRP 8.9 mg/dL (reference value < 3 mg/dL); negative serology for Dengue, Cytomegalovirus, Echovirus, Herpes 1 and 2, and Coxsackie virus. He was presumptively diagnosed with Kawasaki's disease and started on a single dose of intravenous immunoglobulin 2g/Kg associated with ASA 100mg/kg/day, with good clinical response, improvement of general condition, and return of appetite; he was afebrile 48 hours after immunoglobulin administration. After the patient was afebrile for 72 hours, the dose of ASA was decreased to 5mg/kg/day and maintained until late coronary anomalies were ruled out. An echocardiogram was performed in the acute phase, with no signs of coronary involvement. He was discharged on July 8 and placed on outpatient follow-up. His echocardiograms in the subacute and convalescent phases were normal and the patient was free from complications.

On December 25, 2019, at the age of six years, the patient's parents took him to a tertiary pediatric service in Londrina-PR, after he had spent a week with fever and painful cervical adenomegaly. Two days after admission, he developed conjunctival hyperemia, edema of the hands, and rash in the neck area and anterior thorax. On physical examination, the patient was in good general condition, with a heart rate of 103 bpm, a respiratory rate of 25 bpm, a blood pressure of 100/60 mmHg, normal rhythmic heart sounds with two clicks without murmurs, normal lung auscultation, and no abdominal findings. He had a strawberry tongue, bilateral conjunctival hyperemia without secretion, bilateral cervical adenomegaly measuring 2.5 cm, mild cervical and anterior thorax skin rash, mild edema and blushing of hands. Complementary serum tests on this day showed Hb 12%, Ht 36%, leukocytes 15 600/mm³, segmented 93%, lymphocytes 6%, monocytes 1%, platelets 541 000/mm³, CRP 23. 6 mg/dL (reference value < 0.5), GPT 617 U/L, GOT 605 U/L, CK-MB 19 U/L, CK 29 U/L, normal troponin levels, and negative serology tests for toxoplasmosis, cytomegalovirus, Epstein Barr virus, and dengue (NS1). The patient was diagnosed with Kawasaki disease. His echocardiogram did not show alterations. He was started on immunoglobulin 2g/kg and ASA 100mg/kg/day.

After 24 hours of immunoglobulin administration, the patient became afebrile and started eating better. His skin rash improved along with conjunctival hyperemia, and he developed desquamation of the lips. Two days later, he developed febrile peaks and bilateral joint pain and edema in the ankles and knees. On December 29, he was started on corticosteroid therapy with methylprednisolone 30 mg/kg/day for three days and administered another infusion of immunoglobulin 2g/kg. He improved from the fever and joint pain. On January 3, he developed desquamation of the extremities. Laboratory test results were as follows: Hb 10.2; Ht 30.7; leukocytes 13 600; segmented 82%; lymphocytes 14%; monocytes 4%; platelets 855 000 (high platelet count); GPT 90; GOT 67; rheumatoid factor negative; CRP 7.7 mg/dL (< 0.5). The patient was discharged on January 6 with a prescription of ASA 100 mg/kg/day for 14 days. A high dose was kept due to the need for adjuvant therapy for remission of fever and the high platelet count presented in this second episode, after which it was reduced to 5mg/kg/day until the end of outpatient follow-up. The patient progressed without echocardiographic alterations in the control exams performed in the subacute and convalescent phases of the disease and his platelet count became normal in four weeks.

DISCUSSION

Although recurrent KD is uncommon, the number of children affected by this condition is not negligible. There are few detailed conclusive studies about recurrent KD and associated factors[12].

Medical personnel must consider the possibility of finding cases of recurrent KD in their patient populations. It is a rare condition with few cases reported in the literature. Patients may develop recurrent KD as long as five years after the first episode. The only risk factors associated with recurrence are male sex and having elevated CRP levels in the first episode of disease. Our patient did not develop coronary complications in any of the episodes of KD, which stresses the importance of early diagnosis and treatment as a way to minimize cardiovascular complications[7,10]. In both episodes of disease, KD was quickly recognized and treatment with immunoglobulin started. These factors contributed to the absence of coronary involvement in the echocardiographic examinations performed during follow-up (acute, subacute and convalescent phases).

Medical professionals must be able to recognize the classic clinical signs of the disease, as well as its incomplete or atypical form. Our patient was diagnosed based on clinical criteria, laboratory tests, and exclusion of other causes. Although

the clinical diagnosis of KD is still challenging, especially in cases of incomplete disease, it is essential that KD be considered in the differential diagnosis of febrile syndrome, and that recurrence may occur as long as two years after the acute phase of the disease, as in the case described in this report[1,14].

Recurrent KD may occur years after the patient first developed the disease. Since the risk of cardiovascular complications is higher in recurrent KD, early diagnosis and treatment are essential to minimize cardiac involvement, which is the main goal of the management of patients with the condition.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

REFERENCES

1. Singh S, Jindal AK, Pilania RK. Diagnosis of Kawasaki disease. Int J Rheum Dis. 2018;21(1):36-44.
2. Coelho NH, Barreto P, Martins V, Nogueira C, Campos J, Sousa P, et al. Systemic artery aneurysms in Kawasaki Disease a Comprehensive Review. Angiol e Cir Vasc. 2019;15(2):71-5.
3. De Castro PA, Urbano LMF, Costa IMC. Doença de Kawasaki. Anais Brasileiro Dermatologia. 2009;84(4):317-29.
4. Yim D, Curtis N, Cheung M, Burgner D. Update on Kawasaki disease: epidemiology, etiology, and pathogenesis. J Paediatr Child Health. 2013;49(9):704-8.
5. Roh DE, Kwon JE, Kim YH. Diagnosis and management of Kawasaki disease. J Korean Med Assoc. 2020;63(7):37481.
6. Shulman ST, Rowley AH. Kawasaki disease: insights into pathogenesis and approaches to treatment. Nat Rev Rheumatol. 2015;11(8):475-82.
7. Rodrigues M, Oliveira JC, Carvalho F, Silva H. Doença de Kawasaki e complicações cardiovasculares em pediatria. Nascer Crescer. 2018;27(1):54-8.
8. McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. Circulation. 2017;135(17):e927-e999.
9. Almeida FC. Avaliação das manifestações clínicas e achados laboratoriais em 301 pacientes com doença de Kawasaki: acompanhamento de dez anos. [Tese]. Brasília: Universidade de Brasília; 2018.
10. McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. Circulation. 2017;135:927-99.
11. Magalhães CMR, Melo RCS. Recidiva da doença de Kawasaki/ Relapse on Kawasaki disease. J Pediatr (Rio de Janeiro). 1999;75:204-6.
12. Gomes MC, de Melo MFB, Moreira NC, de Magalhães CM. Doença de Kawasaki recidivante/ Recurrent Kawasaki disease. Com Ciências Saúde. 2019;30(1):59-64.
13. Yang HM, Du ZD, Fu PP. Clinical features of recurrent Kawasaki disease and its risk factors. Eur J Pediatr. 2013;172:1641-7.
14. Gonçalves R, Silva S. Kawasaki disease: the importance of early recognition. Residência Pediátrica. 2019;9(3):222-7.