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CASE REPORT

Kawasaki and risk factors for worse prognosis

Thales Araujo de Oliveira[1], Luiz Carlos Bandoli Gomes Junior[2], Priscilla Aguiar Araujo[3], Beatriz Soffe[4], Cynthia Torres França da Silva[5]

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Abstract

Kawasaki disease is an acute systemic vasculitis of unknown etiology. Currently, it has been replacing rheumatic fever as the main cause of acquired childhood heart disease in developed countries. Its diagnosis is based on the presence of clinical criteria: fever for five days, non-exudative bilateral conjunctivitis, lip and oral mucosa alterations, polymorphic exanthema, cervical lymphadenopathy, erythema and edema of hands and feet with periungual scaling. It has as its main fear the formation of coronary aneurysms. The objective of the report of this case is to draw attention to the factors that may favor the formation of these aneurysms and even their resurgence.

[1] Physician - Resident Physician in Pediatrics at Piedade Municipal Hospital (HMP).
[2] Pediatrician - Resident Physician in Pediatric Allergy and Immunology of the Public Servant Hospital (HSE).
[3] Medica Pediatra - Resident Physician in Pediatric Pneumology of the Margtagão Gesteira Institute for Pediatrics and Childcare IPPMG-UFRJ.
[4] Pediatrician - Coordinator of the Medical Residency Program in Pediatrics at Piedade Municipal Hospital (HMP).
[5] Pediatric Rheumatologist.

Correspondence to:
Thales Araujo de Oliveira.
Hospital Municipal da Piedade. Rua da Capela, nº 96. Rio de Janeiro - RJ. Brazil. CEP: 20740-310.

INTRODUCTION

Kawasaki disease (DK) is an acute and multiorgan vasculitis that affects small- and medium-sized vessels in the lungs, brain, heart and other organs[1,2].

The disease was first reported in 1967 by pediatrician Tomisaku Kawasaki in Japan[1]. Since then, the number of diagnosed cases has been increasing. It is currently estimated that KD affects approximately 1-10 out of every 1000 people worldwide[1,2], and it has replaced rheumatic fever as the main cause of acquired heart disease in children in developed countries[1,3,4].

KD occurs primarily in children between six months and five years of age, with 80% of cases falling within this age group. It is slightly more predominant in males (1.5:1)[1,2]. Its etiology, however, remains unknown; it has been suggested that autoimmune factors, infectious agents, and genetic susceptibility are involved in its pathophysiology[1,3,4].

Because there is no conclusive evidence on the etiology of the disease, its diagnosis is made based on clinical criteria, namely fever > 39ºC for more than five days (mandatory criterion), in addition to at least four of the following five criteria: bilateral conjunctival hyperemia; changes in the oropharyngeal mucous membranes (lips with hyperemia and/or cracked or "strawberry tongue"); cutaneous manifestations, including palmoplantar erythema and/or edema of the hands and feet (in the acute phase) or periungual scaling (in the recovery phase); polymorphous exanthema (predominantly in the torso, but never vesicular exanthema); and cervical lymph node enlargement with at least one lymph node > 1.5 cm[5].

The main complication of the disease is the occurrence of coronary artery aneurysm.

KD treatment should be initiated promptly, preferably in the first 10 days after disease onset, to rapidly reduce inflammation and thereby decrease the risk of coronary sequelae. The two drugs used for this purpose are intravenous immunoglobulin (IVIG) at a dose of 2 g/kg, and acetylsalicylic acid (ASA) at the anti-inflammatory dosage (80-100 mg/kg/day), which is later reduced to 3-5 mg/kg/day to achieve a platelet antiaggregant effect[5].

The objective of this report is to describe a case of KD that progressed to aneurysm even after an early diagnosis and treatment within the recommended period in order to raise awareness of the prognostic factors that favor the occurrence of aneurysm.

CASE REPORT

M.A.S., 8-month-old male Caucasian patient, developed persistent high fever, emesis, and diarrhea. After 24 hours, the patient exhibited generalized maculopapular exanthema, predominantly in the palmar region. Medical assistance was sought on the third day of disease, and an upper respiratory tract infection was diagnosed. Oral amoxicillin was initiated. However, because the fever and other symptoms did not improve, he underwent medical reassessment on the fourth day of treatment (seventh day of disease). He was hospitalized with a diagnosis of acute gastroenteritis (AGE) and transferred to our department. Upon admission, he had high fever, acute pain facies, intense irritability, labial and conjunctival hyperemia, mild diffuse exanthema, and dorsal edema of the hands and feet (Figures 1 and 2). The laboratory tests showed anemia (hematocrit 22%), leukocytosis (leukocytes 14.700/uL), thrombocytosis (platelets > 1.000.000/uL), increased inflammatory markers (CRP 108 mg/dL), and hypoalbuminemia (albumin 3.1g/dL). Because the infant met five of the six diagnostic criteria for KD, immunoglobulin IV (2 g/kg) and ASA at the anti-inflammatory dosage (100mg/kg/day) were initiated on the first day of hospitalization. The patient exhibited significant clinical improvement and was afebrile after 24 hours of treatment. Around the fifteenth day of illness, the infant exhibited periungual scaling on the fingers of hands and feet.

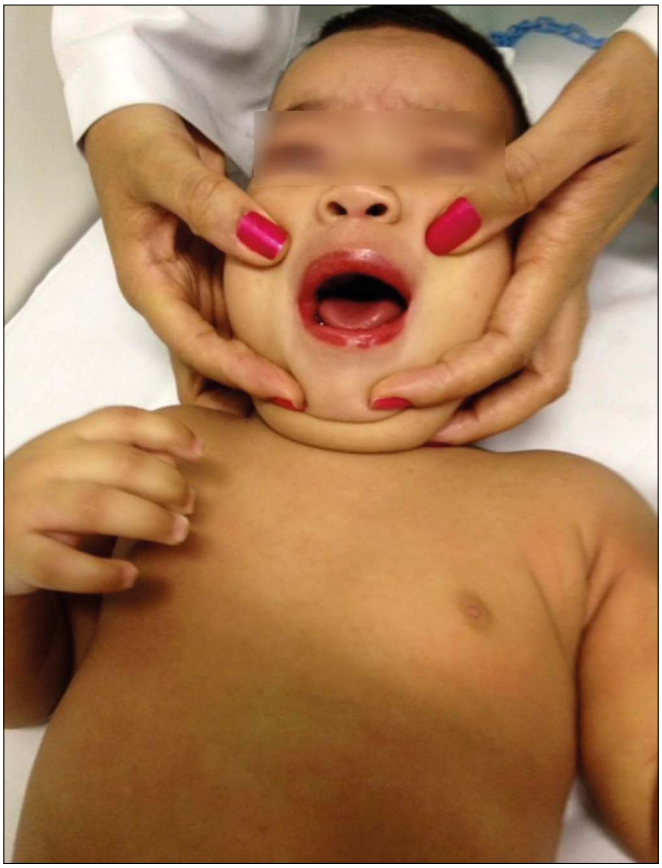

Figure 1. Labial and conjunctival hyperemia and mild diffuse exanthema.

Echocardiography performed on admission was normal; however, echocardiography performed one week after admission showed dilatation of the left coronary artery ostium (4 mm). He was discharged nine days after admission and was maintained on ASA (3-5 mg/kg/day), and outpatient follow-up by a pediatric rheumatologist and cardiologist was scheduled.

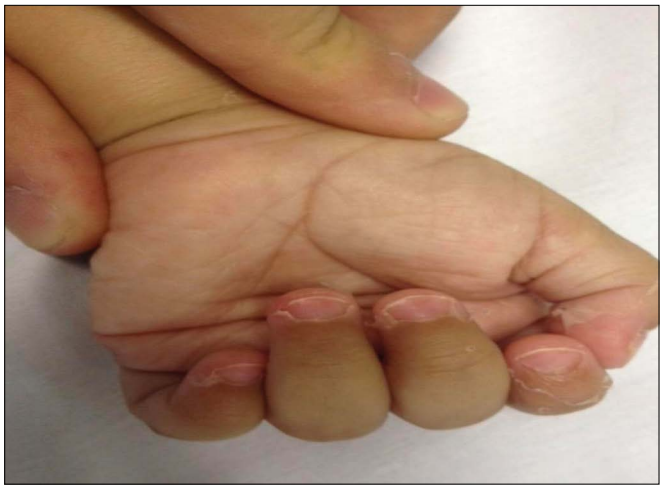

Figure 2. Dorsal edema of the hands.

Echocardiography and other follow-up exams performed nine months after treatment did not show any abnormalities.

DISCUSSION

In the case reported herein, the patient exhibited the typical manifestations of KD, meaning he met the criteria required for its diagnosis. There is no specific exam for the diagnosis of KD; it is established by the presence of the clinical signs and symptoms described previously. We emphasize that the diagnostic criteria are not usually concomitant, which often hinders diagnosis[1-3]. Upon admission, the patient was still in the acute phase of the disease, and IVIG was administered that same day. Several studies suggest that when IVIG is initiated in the acute phase, it is effective in reducing the risk of aneurysm of the coronary arteries in up to 20%, as well as in altering the three-stage progression of the disease, and reducing illness duration. However, coronary involvement occurs in 4% to 5% of patients, even with adequate treatment.

The three-stage progression of KD consists of: a) the acute stage, with signs and symptoms characteristic of the disease lasting for 1-2 weeks; b) the subacute stage: defervescence phase lasting 2-4 weeks, with higher thrombocytosis and higher risk for coronary complications such as aneurysm; and c) the chronic stage, 6-8 weeks (it may even last months), with an increase in signs and symptoms and normalization of the laboratory markers of inflammation and of thrombocytosis[5].

Our patient developed one of the main complications of KD: aneurysm of the coronary artery. Harada suggested some factors that are potentially associated with a higher risk for the occurrence of coronary artery aneurysm and established a scoring system (the Harada Score) that may aid in predicting the occurrence of coronary artery aneurysm, although it is not widely accepted in the literature. According to this score, the presence of four of the following five criteria indicates a high risk of coronary involvement: age < 1 year; male; leukocytosis > 12,000; platelets > 350,000; hematocrit < 35%; albumin < 3.5 g/dl; and CRP > 3 mg/dl[6] (Table 1).

Table 1. Fatores de riscos para formação de aneurisma observados no caso.

Risk factors for aneurisma	Reference	Values of the present case
Leucogram	> 12,000/mm^3	14,700/mm^3
Platelets	350,000/mm^3	1,194.000/mm^3
PCR (protein C reaction)	> 3	108
Albumin	< 3.5 g/dl	3.1 g/dl
Hematrocrit	< 35%	22%
Age	< 12 months	9 months
Sex	male	male

The patient met all of the criteria of this score, which may explain the progression of the disease in this case: although treatment was initiated on the seventh day of illness (in the acute phase), the infant developed coronary artery aneurysm. It has been established that 4% of these patients have coronary aneurysms even when adequate treatment has been administered in the first 10 days of the disease (the acute phase)[7].

In the case reported herein, aneurysm regression occurred after nine months of disease. The literature shows that young age, mildly dilated coronary arteries, and prompt initiation of IVIG therapy are factors that affect the prognosis of coronary lesion progression, which may explain aneurysm regression in our patient. The literature describes that coronary aneurysms regress in up to 50% to 70% of cases in the first two years after disease onset[7].

Factors such as young age, female sex, and fusiform and/or distal aneurysms favor regression. When regression does not occur after this period, the lesions may develop stenosis or thrombi, with a high risk of ischemic heart disease. Therefore, it is recommended that all patients with KD be monitored by a pediatric cardiologist and rheumatologist for a period of three to five years and that echocardiography and electrocardiography be performed.

Another pillar of KD treatment is the administration of ASA. First, aspirin is administered at anti-inflammatory doses (80-100 mg/kg/day) for approximately 48-72 hours until the patient becomes afebrile or for 14 days after the onset of symptoms. After the fever subsides, the medication the dose of is reduced to platelet antiaggregant levels (3-5 mg/kg/day) and maintained for at least 6-8 weeks (patients without aneurysms) or for a longer period, depending on coronary involvement[1-3,5,8]. They may be administered for the rest of the patient's life if the aneurysm persists, or for approximately two years after echocardiographic normalization of the coronary lesions to prevent the formation of thrombi.

Approximately 10% to 20% of patients with KD are refractory to the first dosage of IVIG. Repetition of the IVIG dose is recommended in these cases, in the same dosage. Systemic corticosteroids may be combined with the second dose of IVIG, because research has shown that they provide a more effective reduction in inflammatory markers and fever. Recent studies indicate that the use of immunosuppressant agents, such infliximab and plasmapheresis, is effective[9,10].

CONCLUSION

KD is a self-limiting acute vasculitis of unknown etiology. It is currently the main cause of acquired heart disease in children in developed countries, which makes early diagnosis and adequate treatment essential for the prevention of coronary aneurysms, a feared complication of the disease.

Even when adequate treatment is performed, there is still a 4% risk of patients exhibiting cardiac involvement. This risk increases in younger patients, especially those who are less than one year old. The occurrence of coronary complications is more significant and echocardiographic screening for early detection and appropriate treatment is always required in these cases. Although it is a feared complication, coronary involvement in children with KD is transient in many cases, with approximately 50% to 70% of children exhibiting regression in the first two years of illness, mainly as a result of using IVIG and/or other drugs. This fact does not exclude the need for long-term follow-up, since there is a risk of developing coronary disease in the future[5].

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