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INTERACTIVE CLINICAL CASE

Incomplete Kawasaki disease with presentation of fever of unknown origin

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Abstract

Introduction: Kawasaki disease (KD) is a systemic vasculitis that mainly affects small and medium-sized vessels. **Objectives:** To present the case of a child with incomplete KD describing the investigation process until diagnosis. **Case Report:** A 2-year and 4-month-old female patient with daily two-week persistent fever associated with right unilateral cervical adenomegaly initially treated as bacterial adenitis. Due to the persistence of fever, she returned to the emergency unit with edema in both feet and periungual desquamation in the right hand. After investigation, the diagnosis of incomplete KD was confirmed late. **Discussion:** KD is one of the differential diagnoses of unknown origin fever. The incomplete form of the disease evolves with the absence of classic clinical signs. Given the severity of the disease and its possible complications, an early treatment it is essential. **Conclusion:** It is necessary to consider Kawasaki disease as a differential diagnosis of fever of unknown origin in children.

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INTRODUCTION

Kawasaki disease (KD), first reported in Japan by pediatrician Tomisaku Kawasaki in 1967, is a multisystem vasculitis that affects small and medium-sized vessels in various tissues during the acute febrile phase, mainly lung, brain and heart[1,2]. In the current context, considering the increase in the number of diagnosed cases, KD affects 1/1000 children in the world, being in developed countries the main cause of heart disease acquired in childhood, replacing the position previously occupied by rheumatic fever[2].

The diagnosis of KD is made through persistent fever associated with classic clinical criteria, however, a portion of patients has an atypical presentation, requiring a high level of suspension for the diagnosis to be made early. Laboratory and imaging tests may be necessary during the investigation. [3] Thus, the objective of this study is to report the case of a child with incomplete KD, addressing aspects that can help in the diagnosis of the pathology.

CASE REPORT

Female patient, brown, 2 years and 4 months old, previously healthy, presented with persistent fever, daily, on average twice a day, for two weeks, with a maximum temperature of 39.5ºC. In addition, adenomegaly was reported in the right unilateral cervical region, mobile, with fibroelastic consistency , around five centimeters. She denies coryza, cough or odynophagia in the period. Negative epidemiological history of contact with sick animals or people.

He sought the pediatric emergency unit on two occasions, being prescribed amoxicillin and cephalexin at different times, with no improvement. Hospitalization was chosen due to suspected bacterial adenitis, receiving intravenous antibiotic therapy for 4 days, with reduction of the cervical nodule and fever episodes. He was discharged to continue the treatment at home, but he was treated again with daily fever, in addition to symmetrical edema in the feet.

Returning to the emergency room, it was observed that she was active, with no signs of hemodynamic compromise. No skin, neurological, ophthalmological, oropharyngeal, cardiopulmonary or abdominal changes were observed. Examination of the cervical region was normal. Discrete edema in the feet, bilaterally, with the presence of Locker sign up to the ankle level, without the presence of heat, redness, pain or limitation of movements, called attention. In addition, discreet periungual desquamation was identified in the fingers of the right hand.

Laboratory tests requested at the emergency room showed hemoglobin: 9.5g/ dL , leukocytes: 6,460/mm³ (neutrophils: 41%, rods: 1%, segmented: 42%, lymphocytes: 52%, monocytes: 4%), platelets : 734,000/mm³, C-reactive protein (CRP): 37mg/ dL , erythrocyte sedimentation rate (ESR): 98mm/h, aspartate aminotransferase (AST): 88U/L, alanine aminotransferase (ALT): 35U/L, ferritin 120 μg /L , antibody antistreptolysin O (ASLO) < 100U/ml and creatinine: 0.2mg/ dL . Urinalysis showed only microscopic pyuria .

The patient was admitted to the pediatric ward of the institution with suspected Kawasaki disease. Viral serologies showed negative results. In addition, there was no growth of microorganisms in urine or blood cultures. Chest radiography was normal. Rheumatoid factor, antinuclear factor, anti- double-stranded DNA and anti-Smith were negative. The echocardiogram showed preserved cardiac function, without valvular changes, but with several saccular dilatations of coronary arteries. Cranial computed tomography angiography and Doppler ultrasound of renal, iliac, hepatic and aortic artery vessels were normal. In view of the findings, treatment with acetylsalicylic acid (ASA) and intravenous immunoglobulin (IVIG) was performed, in addition to follow-up with a pediatric cardiology and rheumatology team.

DISCUSSION

The case addressed directs the clinical reasoning to a patient with a syndromic diagnosis of fever of undetermined origin (FUO), which is characterized by the maintenance of body temperature greater than or equal to 38°C for a period greater than 1-2 weeks, after investigation. negative initial. [4] Among the most prevalent causes of FUO, infectious diseases, rheumatology and malignancies (Table 1). [4-6]

Table 1. Differential diagnosis of Fever of Undetermined Origin.

Differential diagnosis of Fever of Undetermined Origin (FUO)	
Infectious diseases viral	Epstein-Bar Virus, Adenovirus , Enterovirus , Arbovirus, Measles, Cytomegalovirus, Human Immunodeficiency Virus, Herpes Simplex, Hepatitis
Bacterial infectious diseases	Brucellosis, Urinary tract infections, Pyelonephritis, Mycoplasma , Tuberculosis, Typhoid fever, Abscess, Septicemia, Osteomyelitis, Meningitis, Endocarditis, Rheumatic fever, Leptospirosis, Bacterial adenitis, Rickettsiosis, Lyme disease , Scarlet fever, Streptococcal or Staphylococcal Toxic Shock Syndrome
Fungal infectious diseases	Blastomycoses , Histoplasmosis, Paracoccidioidomycosis, Cat Scratch Disease
Parasitic infectious diseases	Leishmaniasis, Malaria, Toxoplasmosis
Rheumatological diseases	Kawasaki disease, Polyarteritis nodosa, Juvenile idiopathic arthritis, Reactive arthritis, Systemic lupus erythematosus, Pediatric multisystem inflammatory syndrome (P-SIM), Inflammatory bowel disease
Malignancies	Lymphoma, Neuroblastoma , Lymphohistiocytosis hemophagocytic

In this sense, the clinical suspicion of the reported patient was supported by the presence of fever, adenomegaly of fibroelastic consistency in the cervical region and edema of the extremities with periungual desquamation , which suggest Kawasaki Disease (KD) as the main diagnostic hypothesis. It

is a disease whose pathogenesis is not yet fully elucidated, however, it is believed to be due to an unknown stimulus that triggers an immune- mediated inflammatory cascade in genetically susceptible children. [7] It is the second most frequent vasculitis in the pediatric population. [2] It affects more males (2:1) and children of Japanese descent, mainly between 6 months and 5 years of age. [8]

The diagnosis of KD is made in the presence of fever ≥ 5 days associated with at least 4 of 5 clinical criteria: non--purulent conjunctivitis, alteration of the oral mucosa or raspberry tongue, cervical adenomegaly, polymorphous erythema, edema or scaling of the hands . [9] It can be classified completely, when it meets the diagnostic criteria, or incompletely, in the presence of at least 2 criteria after ruling out other possible causes. [10]

Despite the diagnostic criteria, Gonçalves et al. in a descriptive study with 12 children diagnosed with KD, they identified that skin rash was the most prevalent sign among those analyzed, being observed in all patients, followed by periungual desquamation (83%), oral cavity alteration (66%), conjunctivitis non-purulent (58%) and lymph node enlargement (50%). In addition, the frequency of signs depends on the stage of the disease, so that the least observed in the initial stage is swelling of the extremities and periungual desquamation. [1]

As demonstrated in the study by Rife et al., several diseases share signs and symptoms similar to those of KD, and a differential diagnosis with other pathologies should be performed. It is important to consider the characteristics of each disease, seasonality, local epidemiology and immunoprotection through vaccines already offered. [7] Our patient was initially treated with antibiotic therapy due to suspected bacterial adenitis. Rossi et al. also reported the case of a 7-year-old patient with cervical adenomegaly who received cefadroxil , followed by venous ceftriaxone and oxacillin , but evolved with labral alteration, non-exudative conjunctival hyperemia and skin rash on the fourth, new and tenth days of fever, respectively, with a late diagnosis of KD. [11]

In addition to the classic signs, the incomplete form of KD can present atypical manifestations such as heart failure, aseptic meningitis, stroke, empyema, arthritis, hepatitis, pancreatitis, hydrocele and uveitis, which makes the diagnosis more difficult. [3,7,11] In this sense, during the investigation of KD, some laboratory alterations can help in the diagnostic reasoning, such as the presence of normocytic normochromic anemia , leukocytosis, thrombocytosis , ALT > 50UI/L, increased inflammatory tests, serum albumin < 3mg/ dL and urinalysis with more than 10 leukocytes/field. There is no specific marker for the pathology in question. [1,2,8,9,10] Furthermore, the change in the echocardiogram showing coronary aneurysms also helps in the diagnosis, which is the most feared complication of the disease, which can occur in up to 20% of untreated patients, with a higher risk from 7 to 10 days of fever. [1]

Thus, it is necessary that the diagnosis be made as early as possible, so that appropriate treatment can be instituted in a timely manner. This consists of the administration of IVIG, 2 grams/kg, with a single infusion for 10 to 12 hours, associated with ASA, 80 - 100mg/kg/day until fever resolution, usually 3 - 7 days, followed by dose reduction to 3 – 5mg/kg/day, to be used for a period of 6 - 8 weeks. [3] About 10 to 20% of patients do not respond to the recommended treatment and, therefore , are considered resistant to IVIG .

cyclophosphamide or plasmapheresis . [7,8,9,11]

Currently, an inflammatory condition associated with coronavirus-19 (COVID-19) with KD-like characteristics has been described, the so-called pediatric multisystem inflammatory syndrome (P-SIM). The main clinical manifestations of SIM-P are persistent fever, conjunctivitis, mucositis , lymphadenopathy and rash , which makes this syndrome differential diagnosis with classic KD, especially during the COVID-19 pandemic period. However, some epidemiological differences between SIM-P and DK were noted, such as the higher incidence of SIM-P in children over five years of age and in children of African descent. For the diagnosis of SIM-P, in addition to persistent fever, increased inflammatory tests (CRP, ESR, ferritin, or procalcitonin), and multisystem organ involvement , evidence of exposure to COVID-19 four weeks prior to the onset of symptoms is required. by serology or positive RT-PCR. [7]

CONCLUSION

It is important that there is a high degree of suspicion of Kawasaki Disease as a differential diagnosis of fever of undetermined origin in children, in order to identify the problem early and avoid its possible complications.

REFERENCES

1. Gonçalves RCB, Silva SD. Doença de Kawasaki: a importância do seu reconhecimento precoce. Resid Pediatr. 2019;9(3):1-6.
2. Oliveira TA, Gomes Junior LCB, Araujo PA, Soffe B, Silva CTF. Kawasaki e fatores de risco para pior prognóstico. Resid Pediatr. 2017;7(2):73-6.
3. Diniz LMO, Oliveira EC, Garcia DP, Teixeira S, Silva CFX, Gontijo NP. O desafio diagnóstico da doença de Kawasaki incompleto. Rev Med Minas Gerais. 2015;25(1):115-9. 4Residência Pediátrica; 2021: A h e a d o f P r i n t .
4. Chow A, Robinson JL. Fever of unknown origin in children: a systematic review. World J Pediatr. 2011 Fev;7(1):5-10.
5. Antoon JW, Peritz DC, Parsons MR, Skinner AC, Lohr JA. Etiology and resource use of fever of unknown origin in hospitalized children. Hosp Pediatr. 2018 Mar;8(3):135-40.
6. Kim YS, Kim KR, Kang JM, Kim JM, Kim YJ. Etiology and clinical characteristics of fever of unknown origin in children: a 15-year experience in a single center. Korean J Pediatr. 2017 Mar;60(3):77-85.
7. Rife E, Gedalia A. Kawasaki disease: an update. Curr Rheumatol Rep. 2020 Set;22(10):75.
8. Forsey J, Mertens L. Atypical Kawasaki disease - a clinical challenge. Eur J Pediatr. 2012;171(4):609-11.
9. 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 abr;135(17): e927-e99.

10. Giannouli G, Tzoumaka-Bakoula C, Kopsidas I, Papadogeorgou P, Chrousos GP, Michos A. Epidemiology and risk factors for coronary artery abnormalities in children with complete and incomplete Kawasaki disease during a 10-year period. Pediatr Cardiol. 2013 Ago;34(6):1476-81.

11. Rossi FS, Silva MFC, Kozu KT, Camargo LFA, Rossi FFP, Silva CA, et al. Extensa linfadenite cervical mimetizando adenite bacteriana como primeira manifestação da doença de Kawasaki. Einstein. 2015 Jun;13(3): 426-9.