Initial manifestations of incomplete or atypical Kawasaki disease: case series report.

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Abstract

Introduction: Kawasaki disease (KD) is a multisystemic vasculitis that affects small and medium-sized vessels. It is considered the leading cause of acquired heart disease. Its presence at ages less than nine months or after five years is rare. Cases of incomplete or atypical KD may present symptoms of an infectious entity or unusual findings during a disease, making early detection difficult and causing growth retardation and increased risk of cardiac involvement.

Case series: Six clinical cases with a diagnosis of incomplete EK were presented at Dr. Roberto Gilbert Children's Hospital between January 2017 and April 2019; 83.4% were men, 66.8% were under one year of age, and the reason for consultation was fever > 5 days in all cases and rash in 66.6%. On admission, three patients (50%) met 1 of the five diagnostic criteria. Leukocytosis >16,000 u/µl was present in all cases; C-reactive protein (CRP) >15 mg/l was positive in 66.6%, and platelets less than 450 x mm3 in 66.6%. The associated manifestations were aseptic meningitis (33.4%), vesicular hydrops (16.6%), acute abdomen (16.6%), pneumonia (16.6%), and hip synovitis (16.6%).

Conclusions: It can be concluded that the cases described exemplify the variety of incomplete or atypical forms of presentation since the similarities with other infectious processes due to the initial clinical manifestations made diagnosis difficult, which delayed the start of a specific therapy.

Keywords:

MeSH: Systemic Vasculitis; Mucocutaneous Lymph Node Syndrome; Fever; Case Reports.

Abbreviations

KD: Kawasaki disease.

Supplementary information

No supplementary materials are declared.

Acknowledgments

Not declared.

Author contributions

Santiago Chavesta Aray: Conceptualization, data curation, formal analysis, fund-raising, research, writing - original draft.
Evelyn Ordóñez González: Conceptualization, data curation, formal analysis, data analysis, writing – corrections.
Juan Chang Asinc: Research, Methodology, Software, Writing – original draft.
All the authors have read and approved the final version of the manuscript.

Financing

The authors of this article financed the costs of this research. The treatment and procedures are a regular part of the pediatric service, so they do not constitute an additional cost for the patients.

Availability of data and materials

Not declared.

Pediatrics

Introduction

Kawasaki disease (KD) is a multisystemic vasculitis that affects small and medium-sized vessels. In most cases, 85% of patients are under five. Its presence at ages under nine months or over five years is rare. It predominantly affects children, with a male:female ratio of 1.5-2:1. In 1967, Dr. Tomisaku Kawasaki first reported approximately fifty (50) cases of the disease that bears his name; until 2017, in countries such as Japan, more than 300,000 patients with this pathology were reported [1]. It is considered the leading cause of acquired heart disease in countries where rheumatic fever is no longer prevalent. It has an annual incidence in children under five years of age as follows: worldwide 1-10/100,000; in Japan, 90/100,000 children; in the United States, 20-25/100,000 children; and in Latin America, 3/100,000. Ecuador has no active surveillance of this health problem [2]. It is a rare pathology in infants, especially before three months of age, which suggests that maternal transfer of antibodies protects infants from this disease. Despite multiple investigations, there is still no certainty about the etiology of KD, and the pathological changes are thought to result from an exaggerated immune response to a pathogen in patients with genetic susceptibility. Its clinical and epidemiological characteristics lead some authors to suggest an infectious cause since it presents seasonal peaks during winter and early summer. Infections could be a trigger for inflammation; it has been related to the following agents: S. Pyogenes, S. Aureus, M. Pneumoniae, adenovirus, Epstein–Barr virus, parvovirus B19, herpesvirus 6, parainfluenza virus type 3, HIV, measles, rotavirus, dengue, chikungunya, cytomegalovirus, coxsackie, respiratory syncytial virus, coronavirus, metapneumovirus, and enterovirus [3].

The classic diagnosis is based on the presence of 5 or more days of fever (generally higher than 38.5 °C) together with at least 4 of the five main clinical features: bulbar conjunctivitis without exudate, lesions of the oral cavity (cheilitis and raspberry tongue), edema - palmar-plantar erythema with subsequent peri-ungual desquamation, cervical adenopathy of > 1.5 cm, generally unilateral, and polymorphous rash. Some patients may present with other manifestations, such as irritability, diarrhea, vomiting, respiratory symptoms, myocarditis, pericarditis, aseptic meningitis, vesicular hydrops, symmetrical arthritis of small and large joints, urethritis, uveitis, myositis, abdominal pain, perineal erythema, and local reactions. in the BCG vaccine inoculation area, which has been described in incomplete or atypical cases [4]. Children with an unexplained fever of at least five days of evolution associated with 2 or 3 of the clinical criteria are considered "incomplete disease" [5]. "Atypical disease" is reserved for patients with symptoms or signs not typically seen in KD [6]. Applying these definitions, although it can lead to confusion, a patient with fever and suspicion of KD could present both forms: incomplete if they do not meet the four necessary criteria and atypical if they offer an unusual manifestation [7]. It is significant to make clear that the difference between complete and incomplete or atypical Kawasaki disease is clinical; the laboratory and echocardiographic findings are identical. Aneurysms appear in 30-40% in the unfinished or atypical form compared to 10% in complete cases, probably due to the delay in diagnosis and treatment [8]. Maintaining a high suspicion index to initiate specific therapy and prevent cardiac involvement [9].

The objective is to review a series of clinical cases highlighting that several initial manifestations can accompany an incomplete or atypical KD. Therefore, the diagnosis and therapeutic decisions are difficult for pediatricians. Various clinical-analytical characteristics were identified to determine the initial images of patients with insufficient or atypical KD.

Population and Methods

This was a retrospective case series study with incomplete or atypical KD treated at Dr. Roberto Gilbert Children's Hospital between January 2017 and April 2019. The diagnostic criteria of the American Cardiology Association were used to define KD in its incomplete or atypical form. A descriptive analysis was carried out, which is intended to calculate the frequencies and percentages for the qualitative variables and the maximum and minimum values for the quantitative measurements.

Ethical aspects

Authorization was requested from the Ethics and Teaching Committee of Dr. Roberto Gilbert Elizalde Children's Hospital, which endorsed the review of the files. The total confidentiality of the data was ensured; no names or identification numbers of the patients were noted in the information collection forms.

Results

There were 6 cases, of which 83.4% were men, while 16.6% were women. The age ranged from 4 months (minimum value) to 7 years (maximum value). There was only one patient aged two years (16.6%) and one older than five years (16.6%). This implies that 66.8% of the patients were under one year of age.

The reason for consultation was fever in 100% of cases, followed by irritability and vomiting, both present in 50% of cases.

Fever greater than five days was present in 100% of the study patients; within the current clinical criteria were rash with 66.6%, followed by conjunctival injection and changes in the extremities, both present in 50% of the cases. No case was reported that presented adenopathies. On admission, 50% of the patients only met 1 of the five criteria, 33.4% met 3, and the remaining 16.6% met 2.

Leukocytes greater than 16,000/µl were elevated in 100% of the patients, with values recorded between 16,980 (minimum value) and 28,970 (maximum value). The mean total leukocyte count was 21,720. Neutrophils greater than 60% were present in 100%; the average was 71%. Hemoglobin values were less than 10 gr/dl in 100% of the

cases, with a minimum value of 8.3 and a maximum of 10. The platelet values considered normal were found in the range of 150,000-450,000, so considering these values, limits were 66.6% of the cases, while thrombocytosis was found in 33.4% of the patients in the case series. C-reactive protein (CRP) >15 mg/l was elevated in 66.6% of the patients, while the remaining 33.4% were negative, considering average values to be less than three mg/l. General examination of pathological urine in 33% of patients. The patients' admission tests did not request the erythrocyte sedimentation rate (ESR).

One hundred percent of the cases received antibiotics from their admission. The associated manifestations were aseptic meningitis (33.4%), vesicular hydrops (16.6%), acute abdomen (16.6%), pneumonia (16.6%), and hip synovitis (16.6%). The days of hospitalization until diagnosis was an average of 3 days. The days of fever until diagnosis was an average of 9 days. Likewise, the maximum value of days of rage until treatment was ten days (66.6%), and the minimum was seven days (33.4% of cases).

Discussion

KD has been reported in more than sixty countries, and approximately twelve thousand articles have been published [10]. It is the leading cause of acquired heart disease in children, so it is essential to know the classic clinical criteria and unusual manifestations to make an early diagnosis [11].

Blatt et al. conducted a study with 37 patients with incomplete KD; of these, 45%, as they did not meet all the criteria, had a delay in diagnosis and, therefore, in treatment; cardiovascular complications developed in 24% of them [12].

Central nervous system involvement with aseptic meningitis occurs in 25% of patients, whereas anterior uveitis occurs in 80% of cases [13].

In the literature, some reviews show how KD in 15% of patients has pulmonary radiographic abnormalities, mainly in interstitial pneumonitis [14].

The gastrointestinal presentation occurs before the other significant manifestations of KD and often diverts our attention to diagnoses involving vomiting, acute diarrheal illness, abdominal pain, acute abdomen, and hepatomegaly at 40 [16]. Gallbladder hydrops or distention of the gallbladder identified by abdominal ultrasound is uncommon at 15% [15]. Sterile pyuria is the product of urethritis due to the same disease; it is frequent, reaching 30-60% in some reports [15]. Joint involvement, such as arthritis and arthralgia, affects 10-30% of cases. Other findings include erythema and induration at the BCG site, perineal rash, testicular inflammation, and macrophage activation syndrome [16]. Systemic inflammatory response syndrome (SIRS) is observed in 50-60% of cases if we analyze the presence of simultaneous infections; in the literature, many works have indicated various viruses as triggers of EK. Some studies describe that up to half of KD cases have one or more positive respiratory viruses detected by PCR, although its pathogenic role is unclear [16]. Several studies support that patients with incomplete or atypical KD require more days of evolution to reach their diagnosis [16].

These cases represent a critical situation in pediatrics in the context of a child with a prolonged fever who does not respond to conventional treatments and in whom other pathologies have been ruled out. Most of these patients are admitted with clinical data suggestive of viral and bacterial infections that may mask this disease, so it is necessary to rely on analytical and echocardiographic findings.

Taking into account the coinciding infection with which the patients were admitted, if we are dealing with a minor infant with an unexplained fever of more than seven days despite previous treatment, even if there are no clinical manifestations or nonspecific symptoms, echocardiography should be performed to rule out KD.

Early diagnosis of cases with incomplete or atypical KD should be pursued to start treatment during the inflammatory phase of the disease and limit the occurrence of coronary aneurysms or improve the prognosis of those already formed.

Quality prospective studies are needed to help establish the role of infections in KD.

Conclusions

EK can involve numerous aspects; the cases described exemplify the variety of the incomplete or atypical EK presentation form since the similarity with other infectious processes due to the initial symptoms delayed diagnosis and specific therapy. As in other works, it has been found that diagnosis continues to be a challenge and that they present a greater risk of developing coronary aneurysms. This study shows that having an associated infection in incomplete or atypical KD is frequent, so knowing the nonspecific clinical manifestations and unusual laboratory findings is essential since treatment should always be started when KD is suspected.

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Statements

Ethics committee approval and consent to participate

Not required for clinical cases.

Publication Consent

Written permission was obtained from the patient to publish the images.

Conflicts of interest

The authors declare they have no conflicts of interest.

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Editor's Note

The Revista Actas Médicas (Ecuador) remains neutral regarding jurisdictional claims on published maps and institutional affiliations.

Received: April 24, 2023.
Accepted: May 28, 2023.
Published: June 12, 2023.
Publisher: Dra. Mayra Ordóñez Martinez.

Cite::
Chavesta S, Ordóñez E, Chang J. Initial manifestations of incomplete or atypical Kawasaki disease: Case series report. Actas Médicas (Ecuador) 2023;33(1):61-65.

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