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KAWASAKI DISEASE, A CLINICAL CHALLENGE: LITERATURE REVIEW

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Abstract: INTRODUCTION: Kawasaki disease is a rare vasculitis that predominantly affects medium-sized vessels, it is difficult to diagnose, as there is no pathognomonic finding. OBJECTIVE: To elucidate the symptoms, diagnostic criteria and treatment of patients and how this influences the closure of the case. METHODOLOGY: Data were retrieved from PubMed, Scielo and UpToDate sources for the construction of this article, using "Kawasaki Disease", "Diagnosis", "Treatment", "Signs and Symptoms" and "Complications" and their respective forms in English.RESULTS: Case reports were found in which a late diagnosis of KD is performed, leading children to multiple health services, and possibly presenting complications resulting from Kawasaki Disease.CONCLUSION: Kawasaki disease is a disease with nonspecific manifestations and a challenging diagnosis, but there is a need for early treatment in order to reduce serious and often fatal complications.
Keywords: Kawasaki disease. Signs and symptoms. Diagnosis. Treatment.

INTRODUCTION

Kawasaki Disease (KD) is a rare and systemic febrile vasculitis of unknown etiology and one of the main causes of heart disease acquired in childhood1, especially in the first year of life. The annual incidence of cases is 3/100,000 in children in South America and Japan, the country with the highest number of cases and where it was first described by Tomisaku Kawasaki, with an annual incidence between 110-150 cases per 100,000 children under five[2,3]. Occurs more often in boys, mostly in the age group 6 months to 2 years old[4].

KD has as main clinical manifestations: erythema and/or edema of hands and/or feet; persistent fever; swelling, erythema, and fissures on the lips and tongue in raspberry[5].

Diagnostic criteria are: fever for more than five days (main criterion), conjunctival hyperemia, changes in the oropharynx, polymorphic rash, changes in peripheral extremities, and cervical lymphadenopathy[6]. If not treated, up to 25% of patients may have the most serious complication of the disease, which consists of the formation of coronary aneurysms[5,7].

The treatment is eminently clinical and instituted early; surgery is reserved for specific cases[8,9].

JUSTIFICATION

KD is an important cause of cardiovascular morbidity in childhood. Therefore, this work has the importance of listing the main evolutionary, diagnostic and therapeutic aspects of the disease, in order to encourage discussion in the scientific community on the subject.

OBJECTIVES

GENERAL

Elucidate the symptoms, diagnostic criteria and treatment of patients and how this influences the closure of the case.

SPECIFICS

- Seek the difficulties of early diagnosis.
- Understand the treatment and its effectiveness.
- Assess the possible complications of the disease.

METHODOLOGY

The present work was done through a literature review on the subject "Kawasaki Disease". The databases used were "Google Scholar", "SciELO", "UpToDate" and "PubMed". For the search for articles that were used as reference, the words "Kawasaki disease", "Diagnosis", "Treatment", "Signs and

symptoms" and "Complications" and their respective forms in English were excluded, those that escaped of the central theme addressed. The inclusion criteria used for this review were: Case reports, cohort studies describing patients with KD and literature reviews describing the disease. Studies performed on animals, computational models, were excluded. Works in which there was no certainty of the diagnosis of the pathology in question were also not included.

Bibliographical references of the included articles were also searched. A first evaluation was carried out, based on the titles and abstracts of the articles, and those that did not meet the inclusion criteria or presented any of the exclusion criteria were rejected. When a study could not be included or rejected with certainty, the full text underwent secondary analysis.

After searching these databases, the titles and abstracts were read, removing those that did not meet the inclusion criteria. Then, the articles found were read, summarizing the etiological, epidemiological and clinical aspects of KD in this work.

RESRESULTS AND DISCUSSIONS

KD, also known as mucocutaneous lymph node syndrome, is a primary, rare, febrile systemic vasculitis of unknown etiology but mediated by Immunoglobulin A (IgA)[1,10]. The annual incidence of cases is 3/100000 in children in South America, 8.1/100000 in the United Kingdom, 17.1/100000 in the USA and 110-150/100000 children under five years of age in Japan, a country that leads in the number of cases and where it was first described by Tomisaku Kawasaki[2,3]. It occurs more frequently in boys, mainly in the age group of 6 months to 2 years old, and may also affect older children. About 80% of patients are younger than 4 years old and it is even rarer for the disease to appear after 11 years of age [4].

Mucocutaneous lymph node syndrome can lead to fibrinoid necrosis of the vessel wall. Compromising them from the intima layer to the perivascular region with formation of aneurysms in various stages of appearance. It is a systemic vasculitis, but with a predilection for the coronary arteries[10].

This vasculitis is one of the main causes of heart disease acquired in childhood, especially in the first year of life[7].

There are 4 most accepted theories about what would trigger KD:

1. Infectious Theory for NL-63 coronavirus;
2. Theory of Bacterial Superantigens, such as staphylococcal and streptococcal toxins;
3. Immune Theory by IgA oligoclonal response, indicating antigen-driven immune response;
4. Theory of Genetic Polymorphism, due to the increased incidence in relatives and a study that revealed 67 genes associated with KD and involved in endothelial function, lipid metabolism, platelet adhesion and immune activation[2].

KD has as main clinical manifestations: alterations in the extremities, such as erythema and/or edema of the hands and/or feet during the acute phase, alterations in the lips and oral cavity, such as edema, erythema and fissures in the lips and raspberry tongue (Figure 1), which result from damage to small and medium-sized blood vessels5. In addition, patients may present with less specific symptoms, such as arthralgia, diarrhea, vomiting, abdominal pain, irritability and fatigue[11]. The lack of correct treatment can cause 25% of patients affected by KD to have the most serious complication that is found in the formation of coronary aneurysms (Figure 2)[5,7].

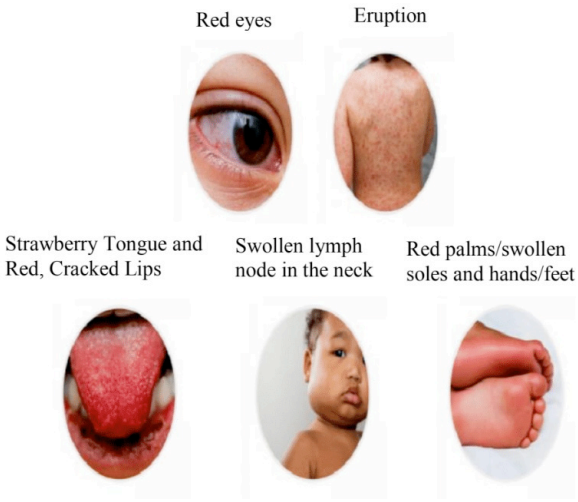

Figure 1- Changes in mucous membranes and extremities

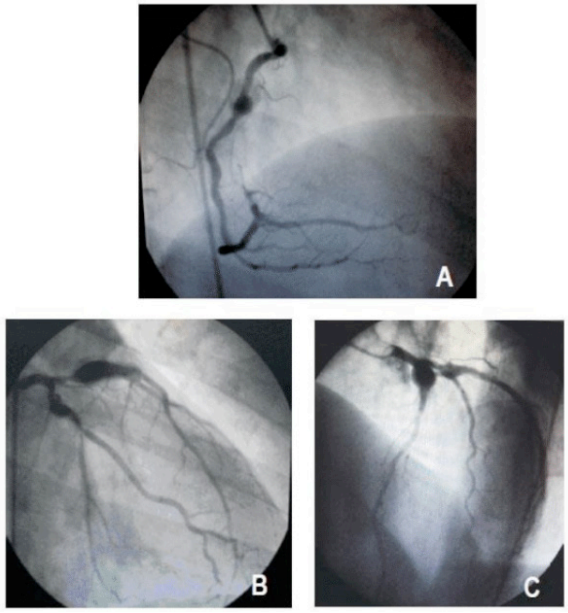

Figure 2 – Coronary Artery Aneurysm

Image taken from :https://kdfoundation.org/pt/kd-symptoms/ Image taken from:https://www.scielo.br/j/abc/a/MpjpPH6z9wPCYQ38M4w49Ch/?lang=pt#

Due to the lack of a specific symptom or laboratory findings, it is difficult to establish a rapid diagnosis, in addition to the fact that the disease can be confused with other febrile childhood illnesses. KD makes the differential diagnosis with viral infectious diseases (infectious mononucleosis, measles, adenovirus, arboviruses) or bacterial (scarlet fever, bacterial cervical adenitis, retropharyngeal abscess) or non-infectious diseases (systemic juvenile idiopathic arthritis, sarcoidosis, systemic lupus erythematosus, hematological neoplasms and reactions to drugs)[12,13].

Given the need for early diagnosis, diagnostic criteria were established, four of which must be present, accompanied by fever for five days. Such criteria described in the literature are: bilateral conjunctival hyperemia, changes in the oropharynx (lip erythema, or cleft lip or erythema in the oropharynx, or raspberry tongue), polymorphic rash, changes in the peripheral extremities (edema of hands or feet, or erythema palm-plantar, or periungual desquamation) and cervical lymphadenopathy (diameter greater than 1.5 cm)[6]. The aforementioned elements are described in the table below:

Fever for 5 days (main criterion)	Changes in the peripheral extremities
bilateral conjunctival hyperemia	cervical lymphadenopathy
Changes im the oropharynx	polymorphic rash

Table 1: Diagnostic criteria for Kawasaki disease

When a case presents with fever for five days or more, associated with at least two of the criteria described above, in addition to laboratory data consistent with systemic inflammatory disease, without any other explanation for the condition, the incomplete form of KD is characterized [12].

KD treatment consists of: immunomodulation with intravenous gammaglobulin (2 g/kg) as the first line; Acetylsalicylic acid (80-100 mg/kg/day) in the febrile phase or while thrombocytosis persists, or if there are coronary aneurysms, being prescribed in the latter two cases in reduced doses (3-5 mg/kg/day). In situations

where pharmacological therapy does not show promising effects, the gammaglobulin infusion must be repeated. If fever persists, pulse therapy with methylprednisolone at a dose of 30 mg/kg/day for 3 days is started[8]. Surgical treatment can be performed at different times of the disease and in different parts of the body, such as coronary stenosis, correction of aneurysms mainly of the iliac arteries and intestinal vascular occlusions[9].

It is noted in studies that the frequency of development of coronary artery aneurysms and their mortality are drastically reduced with intravenous immunoglobulin. This therapy is effective in preventing coronary artery abnormalities, but the benefits in children who have already developed coronary artery aneurysms are uncertain. In partial presentations of the disease, treatment must be started in the same way as in complete presentations. In patients who showed resistance to immunoglobulin, glucocorticoids have been shown to decrease the rate of abnormalities in the coronary arteries, the protocol consists of administering 2 mg/kg/day of intravenous prednisolone for 5 days, then switching to the oral route, maintaining dose for 5 days, then 1 mg/kg/day for 5 days and finally 0.5 mg/kg/day for 5 days or until patient is afebrile[13].

There is a recurrence of cases in the literature in which a late diagnosis of KD is performed. According to reports by Tanaka (2003) and Lacerda (2016), children are often taken multiple times to health services, where they are not diagnosed at first. In view of the information found, possible difficulties faced for early diagnosis are suggested: the rarity of the disease, the lack of specificity of the clinical manifestations, the shortage of experienced and trained professionals to raise the clinical suspicion and obstacles inherent in the difficulties of referral and monitoring by the health system. Brazilian[14, 15]. Once treatment is postponed, the risk of complications increases. In addition, multiple visits to the emergency room are often made, increasing unnecessary expenses.

CONCLUSIONS AND PROPOSALS

KD is a disease with nonspecific manifestations and a challenging diagnosis, and it is up to the physician to be aware of its clinical manifestations for a correct early diagnosis. This way, clinical treatment reduces the risks of serious and often fatal complications.

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