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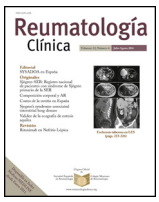

Original Article

Has Articular Involment Lessened in Kawasaki Disease?☆

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ABSTRACT

Objective: Kawasaki disease (KD) is an acute systemic vasculitis affecting medium-sized arteries, particularly the coronary arteries. Classic diagnosis is based in prolonged fever and different clinical features, including acute arthritis. Our objective is to determine the prevalence of arthritis at the moment of the diagnosis, the response to intravenous immunoglobulin infusion and the relation with cardiac findings.
Material and methods: Retrospective study through review of medical records of 42 patients with KD from 1988 to 2013. Demographic, clinical, laboratory variables and treatment were reviewed.
Results: Male sex was predominant (57%). Fever (100%), exanthema (92.9%), conjunctivitis (78.6%), oropharingeal changes (76.2%), cervical lymphadenopathy (71.4%), edema (52.4%) and peripheral desquamation (46.3%) were reported. Eight patients presented ecocardiography alterations (ectasia and aneurism). Acute articular involvement was reported in 7 (16%) patients, including oligoarticular (57%), monoarticular (29%) and polyarticular (14%) patterns. All patients had elevation of acute phase reactants with neutrophilia (57%) and hypoalbuminemia (71.5%), but showed a good therapeutic response to intravenous immunoglobulin, without sequelaes. Sixteen patients had incomplete KD nine males, with 100% of fever exanthema (75%), conjunctivitis (56%) and 50% of cervical lymphadenopathy. Whereas oropharingeal changes and edemas was described in 44% and 25% of them. Four patients with incomplete KD had coronary artery abnormalities.
Conclusions: Acute arthritis was an uncommon finding (16%) and resulted in no sequelae. Maybe the treatment with intravenous immunoglobulin and aspirin prevents the development of articular abnormalities and then leading to a decrease in its follow-up requirement by reumathologist. The cardiovascular sequelae, mainly incomplete KD, remains determining its prognosis. The presence of articular involvement seems not to have influence over cardiac involvement.

¿La enfermedad de Kawasaki ha perdido su afectación articular?

Palabras clave:
Enfermedad de Kawasaki
Afectación articular
Aneurismas
Inmunoglobulinas

RESUMEN

Objetivo: La enfermedad de Kawasaki (EK) es una vasculitis sistémica aguda de arterias de tamaño medio, especialmente las coronarias. Su diagnóstico clásico se basa en la presencia de fiebre prolongada y diversas manifestaciones clínicas. En la era preinmunoglobulinas, la artritis aguda constituía un hallazgo común. Nuestro objetivo es definir la prevalencia de la artritis al diagnóstico, su respuesta a inmunoglobulinas intravenosas y su relación con eventos cardiacos.
Material y métodos: Estudio retrospectivo de 42 pacientes con EK desde enero de 1988 a noviembre de 2013. Las variables demográficas, clínicas, laboratorio y tratamiento fueron revisadas.
Resultados: Se encontró predominio de varones (57,1%), fiebre (100%), exantema (92,9%), conjuntivitis (78,6%), afectación oral (76,2%), adenopatía cervical (71,4%), edema (52,4%) y descamación (46,3%). Ocho pacientes presentaron clínica cardiológica y ecocardiograma con alteraciones coronarias. Siete pacientes (16%) presentaron afectación articular aguda. El 57% fue oligoarticular con predominio de tobillos, 29% monoarticular de cadera y 14% poliarticular. El 100% aumentó los reactantes de fase aguda, con neutrofilia

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(57%) e hipoalbuminemia (71,5%). Todos respondieron a inmunoglobulinas intravenosas, sin afectación cardiaca ni secuelas posteriores. Hubo dieciséis EK incompletos: nueve varones, con fiebre (100%), exantema (75%), conjuntivitis (56%), adenopatía cervical (50%), alteración de mucosa oral (44%) y edemas (25%). Cuatro tuvieron afectación cardiaca (un aneurisma; tres ectasias).
Conclusiones: La artritis aguda fue poco frecuente (16%) y sin secuelas posteriores. El tratamiento con inmunoglobulinas intravenosas y ácido acetilsalicílico posiblemente previene su desarrollo, disminuyendo el seguimiento por Reumatología. La afectación cardiaca, principalmente en EK incompleta, sigue marcando su pronóstico, sin hallar empeoramiento cardíaco en pacientes con artritis.

Introduction

Kawasaki disease (KD) is a systemic vasculitis affecting medium-sized arteries, mainly in boys under the age of 5 years.[1] It is most prevalent in Japan and Korea, especially during the winter and autumn months. It shows a predilection for the coronary arteries, a feature that originates its major complication, as it is accountable for the associated mortality and a more extensive and accelerated atherosclerosis in these children.[2] At the present time, it is the main cause of acquired heart disease in pediatric patients in developed countries. Its etiology remains to be determined. An inappropriate immune response to external or infectious agents (staphylococcal and streptococcal toxins) that would act like triggering superantigens in genetically susceptible individuals and in which IgA plasma cells would play an important role.[3–5] The diagnosis of KD is mainly based on certain clinical criteria, in which fever is a key, in addition to 4 of the following characteristics: (1) changes in extremities (erythema and edema in palms and soles, desquamation of the fingers and toes); (2) polymorphous exanthema; (3) bilateral nonexudative bulbar conjunctival injection; (4) changes in lips and oral cavity (erythema of the lips or mucosa, cracked lips, strawberry tongue); (5) unilateral cervical lymphadenopathy greater than 1.5 cm in diameter.[3] However, for the early diagnosis and treatment of KD, incomplete KD is defined as those cases in which less than 4 criteria are met, but the typical changes in the coronary arteries are identified (measured by echocardiogram or arteriography).[6]

Although cardiac involvement is the most important prognostic factor, arthritis has been considered a common manifestation of KD, having been reported in up to 31% of the patients in different publications from the preimmunoglobulin era.[7] Moreover, a close relationship between early acute arthritis and a poorer cardiac outcome has been demonstrated in the literature, including the development of coronary aneurysms in 39% of the patients with arthritis,[6] versus an overall average of 19%. The introduction of intravenous immunoglobulins (IVIG) meant an advance in the control of the disease, reducing the fever and systemic inflammatory processes, as well as the incidence of coronary artery involvement. The prognosis marked by the clinical signs of cardiac disease has led to the publication[7] of a number of studies focusing on the outcome of this manifestation, and there are few articles devoted to joint involvement. The objective of this report was to define the prevalence of arthritis in KD at the time of diagnosis, its response to IVIG and its relationship to cardiac events.

Material and Methods

This retrospective descriptive study deals with children with KD admitted to Hospital Universitario Severo Ochoa in Madrid, Spain, between January 1988 and November 2013. This report was approved by the hospital ethics committee.

We reviewed the clinical histories of all the pediatric patients who had been classified under the diagnostic code for "Kawasaki disease" or "mucocutaneous lymph node syndrome" provided by the information system of our records department. In our hospital, those children in whom KD is suspected are assessed and admitted by the pediatric department. They begin to receive rheumatology care during admission, following a request on the part of the pediatricians. The children included in this study were diagnosed with KD in accordance with the criteria proposed by the American Academy Of Pediatrics/American Heart Association.[3]

The clinical signs were recorded, particularly those concerning the criteria of the diagnostic classification, as were the demographic variables (age, sex, race), the season of the year in which the disease presented, history of infections and the analytical variables at diagnosis (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], biochemical data, albumin, hemoglobin, platelets, leukocytes and urinalysis results). In the analytical variables collected, any value that was outside the normal range established by the central laboratory services of our center was defined as anomalous. For acute-phase reactants, we considered CRP > 10 mg/L and ESR > 20 mm/h.

Cardiac involvement was based on the presence of abnormal findings in the electrocardiogram and/or echocardiogram. Coronary aneurysm was defined as a maximum diameter of the coronary artery greater than 3 mm in patients under 5 years of age, and greater than 4 mm in those aged 5 years or older.[8] Moreover, they were classified by size as small (less than 5 mm), medium (5–8 mm) or giant (greater than 8 mm). In the absence of aneurysms, coronary ectasia or dilatation was considered to be the presence of a coronary artery with a diameter greater than normal.

Joint involvement was based mainly on clinical signs, and on the findings derived from the musculoskeletal ultrasound study (since 2004). It was classified as oligoarticular if the number of affected joints was ≤4 and polyarticular with ≥5 affected joints. In addition, we included in the study the presence of any chronic clinical manifestation (sequelae) of cardiac or articular nature.

The existence of a protocol-guided therapeutic management of KD, adopted in the pediatric department of our hospital, meant that all the children received the same treatment during the first 7–10 days after diagnosis. During the acute phase, according to the protocol, patients should rest, and acetylsalicylic acid (ASA) together with IVIG are prescribed at admission. Initially the ASA dose is anti-inflammatory (80–100 mg/kg body weight [bw]/day), up to 48 h after the fever and clinical signs have disappeared. At that time, the amount is reduced to the levels of antiplatelet therapy, with a single dose of 3–5 mg/kg bw/day.[9] Intravenous immunoglobulins are given once, in a single dose of 2 g/kg bw, administered slowly (duration of the injection 10 h), and the fever usually disappears by the time the administration has finished. If this treatment is followed within 36 h by clinical and analytical improvement, but the fever returns, a second dose of IVIG should be administered.

Perhaps ≥10% of cases of KD are resistant to IVIG, and are defined by persistence of fever and acute-phase reactants and/or clinical signs ≥36 h after IVIG administration. An increase in the risk of coronary artery aneurysms has also been reported in these patients.[10]