

# Kawasaki Disease: Heart Disease During Childhood

Ana M. Schroh, Pablo Domínguez, Lidia B. Laghezza, Pablo A. Melonari, Marisa Olguin, and Roberto Miatello

Servicio de Cardiología Infantil, Hospital Pediátrico Dr. Humberto J. Notti, Mendoza, Argentina.

The aim of this study was to determine risk factors for coronary lesions, the type of heart lesion present, and long-term outcome in Kawasaki disease. We studied 150 children, aged 3 months to 9.5 years, who met the criteria for a diagnosis of Kawasaki disease. Of the 18% who were diagnosed with heart disease, 100% had coronary artery abnormalities, 11.1% had pancarditis, and 3.7%, mitral insufficiency. The coronary abnormalities were classified according severity as follows: diffuse ectasia in 40.7%; a small-to-medium-sized solitary coronary artery aneurysm in 33.3%; numerous small-to-medium-sized aneurysms in 11.1%; giant aneurysms in 11.1%; and coronary artery stenosis in 3.7%. The presence of pancarditis was a predictor of a giant coronary artery aneurysm. Mortality was 3.7%. Coronary aneurysm was the predominant heart lesion. The risk factors for coronary aneurysm in Kawasaki disease included age less than 27 months, fever lasting more than 8 days, erythrocyte sedimentation greater than 70 mm, and pancarditis.

**Key words:** *Kawasaki disease. Coronary aneurysm.*

## Enfermedad de Kawasaki: afección cardíaca durante la infancia

Con objeto de determinar los factores de riesgo para la coronariopatía, el tipo de lesión cardíaca y la evolución a largo plazo en la enfermedad de Kawasaki, evaluamos a 150 niños con criterios de la enfermedad, de 3 meses a 9,5 años de edad. El 18% desarrolló cardiopatía, en todos los casos lesiones coronarias; el 11,1%, pancarditis y el 3,7%, insuficiencia mitral. Las lesiones coronarias fueron clasificadas en: ectasia difusa en el 40,7%, aneurisma solitario en el 33,3%, aneurismas múltiples en el 11,1%, aneurismas gigantes en el 11,1% y estenosis coronaria en el 3,7%. La pancarditis fue predictora de aneurismas gigantes. La mortalidad fue del 3,7%. Los aneurismas coronarios fueron las lesiones cardíacas predominantes. La edad menor de 27 meses, la fiebre durante más de 8 días, la velocidad de sedimentación globular > 70 mm y la pancarditis fueron factores de riesgo para aneurismas coronarios.

**Palabras clave:** *Enfermedad de Kawasaki. Aneurismas coronarios.*

## INTRODUCTION

Kawasaki Disease (KD) is an acute febrile childhood disease<sup>1</sup> capable of damaging the coronary arteries and causing aneurysms, which can then become complicated with thrombosis or coronary obstruction, leading to myocardial ischemia.<sup>2</sup>

## METHODS

Between October 1988 and April 2004, we assessed 150 children with KD. The mean age was 44.8 months

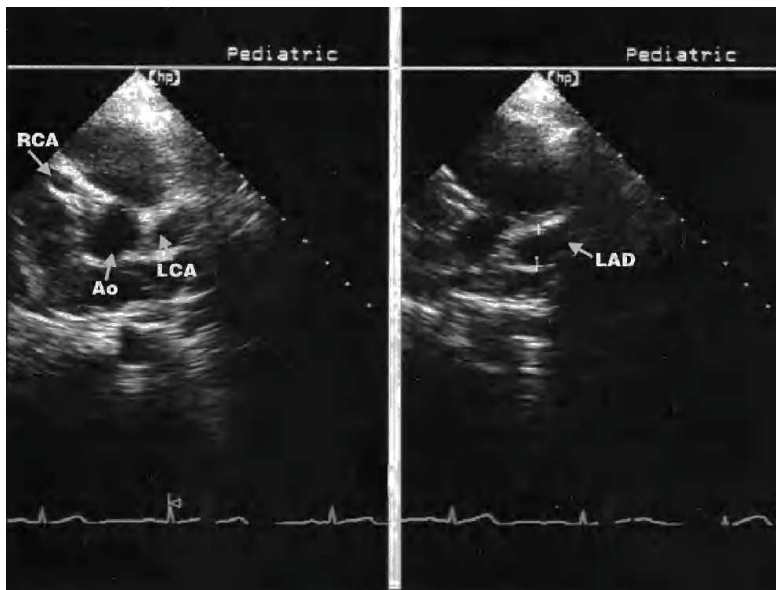
(range, 3-114); 56 were girls and 94 were boys. Patients with "typical" American Heart Association (AHA)<sup>3</sup> criteria were included: prolonged fever ( $\geq 5$  days) plus 4 of the following criteria: *a)* changes in extremities, *b)* polymorphic exanthem, *c)* bilateral conjunctivitis without exudate, *d)* changes in oral cavity, and *e)* cervical lymphadenopathy. "Atypical or incomplete" cases with fever  $\geq 5$  days and fewer than 4 criteria, but with coronary artery complications on echocardiography, were also included.<sup>4</sup>

Laboratory tests, including complete blood counts, erythrocyte sedimentation rate (ESR), and platelet count, were performed. The cardiac complications of KD were assessed by color Doppler echocardiography from the fifth day, except in three patients due to a late echocardiographic finding, a retrospective diagnosis of KD in one child with angina, and a postmortem diagnosis in 1 infant with prolonged fever. The presence

Correspondence: Dra. A. M. Schroh.  
Paso de los Andes, 812. Mendoza (5500). Argentina.  
E-mail: schroh\_md@hotmail.com

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**Figure.** Echocardiographic image (short axis of large vessels) showing coronary aneurysms. Ao indicates aorta; LAD, left anterior descending artery; LCA, left coronary artery; RCA, right coronary artery.

**TABLE 1. Classification of Patients With Coronary Aneurysms According to Severity and Risk**

Risk Group	Patients, n	Percentage
1	11	40.7
2a	9	33.3
2b	3	11.1
3	3	11.1
4	1	3.7

and degree of valvular, myocardial, and pericardial compromise were determined, as well as the presence and type of coronary lesions, which were classified as follows:

1. Diffuse ectasia or dilation (diameter greater than that expected for the body surface area).<sup>5</sup>
2. Coronary aneurysm (segmental dilation >1.5 times the adjacent segment)<sup>6</sup>; it was also indicated whether the aneurysm was single or multiple, small and/or medium-sized (up to 8 mm) or giant (over 8 mm).<sup>7</sup>
3. Coronary stenosis.

Echocardiography was repeated in 4-6 weeks and at 1 year from the onset of symptoms in patients with no heart disease, every 6 months in those who had small to moderately sized aneurysms, and every 1-3 months in children with giant aneurysms. From 5 years of age, the patients were evaluated by a yearly stress test. Patients with residual moderate or giant coronary aneurysms also underwent perfusion myocardial testing (single photon emission computed tomography [SPECT]) at rest and

with pharmacologic challenge every two years after 10 years of age.<sup>8</sup> Coronary angiography was indicated in a child who consulted for angina and experienced an acute myocardial infarction (AMI).

The comparison of quantitative variables between patients who developed an aneurysm and those who did not was done by one-way analysis of variance in the case of parametric distributions and the Mann-Whitney/Wilcoxon test for 2 samples in the case of nonparametric distributions. The association between the qualitative characteristics and the development of aneurysms was assessed by a  $\chi^2$  test using the Yates correction or by Fisher's exact test.

## RESULTS

A total of 27 patients (18%) experienced cardiac complications.

Mitral regurgitation was mild, transient, and uncommon (3.7%). Three male patients who developed giant coronary aneurysms presented pancarditis (Figure). There were no cases of aortic valvulitis.

All had coronary lesions, which were classified as follows:

- Group 1: transient dilation (ectasia) in 11 patients.
- Group 2: single aneurysm of small or moderate size in 9 patients (group 2a) and multiple aneurysms of small or moderate size in 3 patients (group 2b).
- Group 3: giant coronary aneurysms in 3 patients.
- Group 4: coronary stenosis in 1 patient (Table 1).

Follow-up was from 1 to 16 years (mean, 8.5 years). In total, 147 children received treatment following the diagnosis: oral acetylsalicylic acid (ASA) (80 mg/kg/day) and intravenous gamma globulin (400 mg/kg for 4

**TABLE 2. Clinical Characteristics of Patients With Kawasaki Disease According to Whether or Not Coronary Aneurysms Developed\***

Patient Type	Age, Median	Sex	Days of Fever, Average ( $P<.05$ )	ESR ( $P<.05$ )	Complete Clinical Evidence
No aneurysms	43.5 months	Male, 60%	6 days	48 mm	28%
Aneurysms	27 months	Male, 66%	8 days	71 mm	44%

\*ESR indicates erythrocyte sedimentation rate.

consecutive days until 1992 and later 2 g/kg as a single dose). In 43 patients, treatment was administered after 8 or more days of fever; 13 patients already had coronary aneurysms. On the third day of apyrexia, ASA was reduced to 3-5 mg/kg/day, maintaining it until the sixth week from the onset of symptoms in patients with no aneurysms or until the aneurysms were no longer visualized on echocardiography. No new lesions occurred after the administration of gamma globulin.

We compared the clinical and laboratory data of the patients without (group A) and with (group B) coronary compromise.

In group B, coronary lesions predominated in children under 2 years and in school-aged children (5-10 years). Boys were affected more often in both groups, but only boys had serious coronary lesions. In group B, 44% presented typical KD and 56%, incomplete forms of the disease (without statistical significance).

Group B had more prolonged fever than group A (8 vs 6 days;  $P<.05$ ) and the average ESR was 70 mm in group B and 48 mm in group A ( $P<.05$ ) (Table 2).

There were no differences in the number of leukocytes or platelets.

In the patients with coronary ectasia, diameters returned to normal within the first 45 days of KD; the aneurysm regressed in 100% of group 2a patients within the first 3 years of follow-up and persisted in 66% of group 2b patients, although without complications during clinical follow-up and with stress and/or myocardial perfusion testing.

Among the 4 patients with giant aneurysms, 1 died undiagnosed; another had an AMI (which required coronary bypass surgery) and the other 2 were asymptomatic, with no ischemia detectable by noninvasive tests (3 and 15 years of follow-up).

## DISCUSSION

Kawasaki disease is an acute vasculitis of unknown origin that occurs in childhood<sup>1</sup> and is predominantly observed among boys under 5 years of age.<sup>9</sup> Our patients under 27 months, but also those of school age (5-10 years), had a higher incidence of cardiac complications.<sup>10</sup>

Kawasaki disease can affect the valvular endocardium, myocardium, and/or pericardium.<sup>7</sup> In our series, mitral valvulitis was mild and transient, although pancarditis

was always accompanied by giant aneurysms, which determined an adverse prognosis.<sup>11</sup>

Among children with coronary lesions, 56% presented an incomplete form of the disease, an incidence similar to that described in the literature.<sup>4</sup> In our population, male sex, age <27 months, prolonged fever, ESR>70 mm, and pancarditis were factors associated with coronary abnormalities.<sup>12</sup>

Generalized microvasculitis is expressed in 30%-50% of the patients as coronary ectasia. In all of these patients the condition resolved within the first 45 days of the disease. Coronary aneurysms can regress or progress. All aneurysms in group 2a involuted, compared with only 66% in group 2b. Giant aneurysms accounted for 15% of the total. These aneurysms do not involute, but can lead to obstruction.

Stress testing and myocardial perfusion (SPECT) images were used to detect myocardial ischemia.<sup>8</sup> Coronary angiography should be performed<sup>7</sup> if the patient is symptomatic or the noninvasive studies indicate myocardial ischemia, in order to assess feasibility of myocardial revascularization surgery,<sup>13</sup> as occurred in 1 patient in our series.

## CONCLUSIONS

Coronary aneurysms were the predominant cardiac lesions in our series. The risk factors for coronary aneurysms were age <27 months, prolonged fever of more than 8 days, ESR>70 mm, and pancarditis.

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