

Case Report

Kawasaki's Disease in Remission With Cardiac Involvement: Intracardiac Thrombus in a Giant Aneurism of Both Coronary Arteries. Case Report[☆]

Karla Mendiola Ramírez^{a,*}, Jorge Omar Osorio Díaz^b, María del Rocío Maldonado Velázquez^c, Enrique Faugier Fuentes^d

^a Second Year Pediatrics Resident, Hospital Infantil de México, Mexico City, Mexico

^b Second Year Pediatric Cardiology Resident, Hospital Infantil de México, Mexico City, Mexico

^c Chief of Servicio de Reumatología Pediátrica, Hospital Infantil de México, Mexico City, Mexico

^d Attending Physician Reumatología Pediátrica, Hospital Infantil de México, Mexico City, Mexico

ARTICLE INFO

Article history:

Received 17 June 2010

Accepted 12 November 2010

Available online 9 September 2011

Keywords:

Kawasaki disease

Coronary artery aneurisms

Myocardial infarction

Palabras clave:

Enfermedad de Kawasaki

Aneurisma de arterias coronarias

Infarto de miocardio

ABSTRACT

Kawasaki disease is of relevance in pediatric practice because it is a systemic vasculitis of unknown origin and the most common cause of acquired heart disease in young patients. Its main complication is the formation of a coronary aneurism in 25% of the patients, unless they receive timely medical treatment.

We report the case of a 4-month-old male child with Kawasaki's disease, who received treatment with gammaglobulin and acetyl-salicylic acid, in which the initial echocardiogram showed aneurisms. Admitted to our hospital with cardiogenic shock, we documented, by echocardiography, the presence of coronary aneurisms with intracardiac thrombus and acute myocardial infarction. He received fibrinolytic therapy, with an adequate response: the size of aneurisms decreased, as did the intracardiac thrombus. Currently the patient is asymptomatic and receiving treatment with warfarin and acetylsalicylic acid.

The diagnosis and treatment, as well as identification of risk factors can prevent fatal complications at the cardiovascular level. The treatment in the first 10 days of illness with gammaglobulin and acetylsalicylic acid reduced cardiac complications from 4.7% to 25%.

© 2010 Elsevier España, S.L. All rights reserved.

Enfermedad de Kawasaki en fase de convalecencia con afección cardíaca: trombo intra-sacular en aneurisma gigante de ambas coronarias. Reporte de un caso

RESUMEN

La enfermedad de Kawasaki es de relevancia en la práctica pediátrica debido a que es la vasculitis sistémica de origen desconocido más común y la primera causa de cardiopatía adquirida en pacientes jóvenes. Su complicación principal es cardíaca, ya que el 25% de los pacientes sufre la formación de aneurismas coronarios si no reciben de manera oportuna tratamiento médico.

Reportamos el caso de un niño de 4 meses de edad, con enfermedad de Kawasaki, que recibe tratamiento con gammaglobulina y ácido acetilsalicílico. El ecocardiograma inicial no presenta ectasias o aneurismas. Ingresa en nuestro hospital con datos de choque cardiogénico, se documenta por ecocardiografía aneurismas coronarios, con trombo intra-sacular e infarto agudo al miocardio. Recibe terapia fibrinolítica, con respuesta adecuada: disminución del tamaño de los aneurismas y del trombo intra-sacular. Actualmente el paciente se encuentra asintomático y en vigilancia en la consulta externa, recibe tratamiento con warfarina y ácido acetilsalicílico.

El diagnóstico y el tratamiento oportuno, así como la identificación de factores de riesgo, pueden evitar complicaciones fatales a nivel cardiovascular. El tratamiento en los primeros 10 días de la enfermedad con gammaglobulina y ácido acetilsalicílico reduce del 4.7% al 25% de las complicaciones cardíacas.

© 2010 Elsevier España, S.L. Todos los derechos reservados.

[☆] Please cite this article as: Mendiola Ramírez K, et al. Enfermedad de Kawasaki en fase de convalecencia con afección cardíaca: trombo intra-sacular en aneurisma gigante de ambas coronarias. Reporte de un caso. Reumatol Clin. 2011. doi:10.1016/j.reuma.2010.11.003.

* Corresponding author.

E-mail address: karlamendiola@hotmail.com (K. Mendiola Ramírez).

Introduction

Kawasaki's disease (KD) is of relevance in the pediatric practice because it is the most common systemic vasculitis of unknown origin and the first cause of acquired cardiac disease in young patients.¹

The inflammatory process has a predilection for coronary arteries, leading to the formation of aneurisms, thrombus and stenosis. Aneurisms and coronary ectasia are detected in 15%–25% of patients with KD who do not receive treatment and are the main cause of myocardial infarction, ischemia and sudden death.²

The peak of mortality in KD occurs between days 15 and 45, after the resolution of fever; during this time there is vasculitis in the coronary arteries, platelet elevation and a state of hypercoagulability.²

The American Heart Association (AHA) has published guidelines for the stratification of coronary risk; it divides the disease in 5 groups according to the size of the aneurisms.³

Risk factors associated to the formation of coronary aneurisms (CA) are: age under 1 year or over 5, delay in the diagnosis and treatment of disease, an increase of inflammatory markers (ESR, CrP, procalcitonin) after the administration of gammaglobulin, leukocytosis over $30 \times 10^9/l$, thrombocytopenia, an increase in liver enzymes and low albumin levels.⁴

Treatment with gammaglobulin before day 10 of disease and aspirin reduces the risk of cardiac complications from 4.7% to 25%. Its objective is to inhibit the production of pro-inflammatory cytokines, metalloproteinases, TNF- α and platelet aggregation, reduction in the formation of CA and early identification of vaso-occlusive cardiovascular risk factors may help reduce severe cardiac disease.⁴

Timely diagnosis and treatment, identification of risk factors and close follow-up of patients may help prevent fatal cardiovascular complications.

Clinical Presentation

The patient is a 4-year-old male who was previously healthy. One month prior to his hospitalization he presented upper respiratory tract infection and difficult to treat fever, managed with antipyretics and antibiotics, without a good response.

KD diagnosis was established in a private hospital based on: (1) difficult to control fever lasting more than 5 days; (2) non-suppurative bilateral conjunctivitis; (3) changes in oral mucosa (raspberry tongue); (4) erythema polymorphus and (5) cervical

lymphadenopathy. He presented desquamation of the site of BCG vaccine application. On day 8, an echocardiogram was performed showing a healthy heart, the right coronary measuring 1.8 mm and the left one measuring 2.6 mm; there were no aneurisms. Laboratory tests showed: Hb 9.3 g/dl (NR 12–15.5 g/dl), Hto 28% (NR 36%–47%), platelets 197,000 (NR 150 000–450 000), leukocytes 14 300 (NR 6000–10 000). Harada Score: points. On day 8, the patient was treated with intravenous gammaglobulin at a dose of 2 g/kg/dose and aspirin 100 mg/kg/day for days. He was discharged without any further treatment due to improvement.

From day 12 to day 35 of the disease he presented no fever nor received medical treatment or attention.

He came to our hospital on day 36 of the disease with a 9-h episode of vomiting, abdominal pain, cyanosis, somnolence and shallow respirations. He presented cardiac arrest, metabolic acidosis and shock; after resuscitation for 5 min he achieved sinus rhythm.

He was hospitalized. An electrocardiogram showed sinus rhythm, heart rate (HR) of 136; P axis +45°; QRS axis +80°; PR: 0.11; cQt: 0.36; ST depression on V6; Q wave on DI, DII, aVL and aVR; and left ventricle hypertrophy (Fig. 1a). A chest X-ray showed *Situs solitus*; levocardia; ICT 0.62; normal pulmonary flow. The echocardiogram showed a mild pericardial effusion on the free wall of the left ventricle, subendocardial ischemia, dyskinesia of the lateral wall of the left ventricle, and paradoxical septal movement. The left coronary measured 2.8 mm; circumflex 2.3 mm, with a fusiform aneurism of 5.8 mm; anterior descending 1.7 mm with fusiform aneurisms measuring 7.5, 8.1, and 11 mm. The right coronary artery measured 2.4 mm, with a saccular aneurism measuring 7.5 mm and an intrasaccular thrombus 0.5 cm². Systolic function showed an ejection fraction of 55%, FA 27%, normal mitral EA and a Tie index of 0.26 (Fig. 1b).

Laboratory results showed: Hb 7.6 g/dl (NR 12–15.5 g/dl), Hto 23% (NR 36%–47%), platelets 379 000/mm³ (NR 150 000–450 000/mm³), leukocytes 7900/mm³ (NR 6000–10 000/mm³), albumin 3.1 g/dl (NR 3.5–5 g/dl), TGO 367 UI/l (NR 15–50 UI/l), TGP 107 UI/l (NR 10–40 UI/l), DHL 321 UI/l (NR 110–295 UI/l), procalcitonin 2.44 ng/dl (NR 2.0 ng/dl), ESR 40 mm/h (NR 0–10 mm/h), CRP 5.5 mg/l (VR 0–0.300 mg/l). Urinalysis presented albuminuria, hemoglobinuria, erythrocyturia 10–12/field, abundant leukocytes, granular casts 0–2/field, epithelial cells 2–3/field. Cardiac enzymes, 12 h after admission: AP 195 UI/l (NR 150–420 UI/l), DHL 1190 UI/l (NR 110–295 UI/l), CPK Mb 5.173 UI/l (NR 0–25 UI/l), TGP 352 UI/l (NR 10–40 UI/l), TGO 269 UI/l (NR 15–50 UI/l). Lipid profile:

Day 36

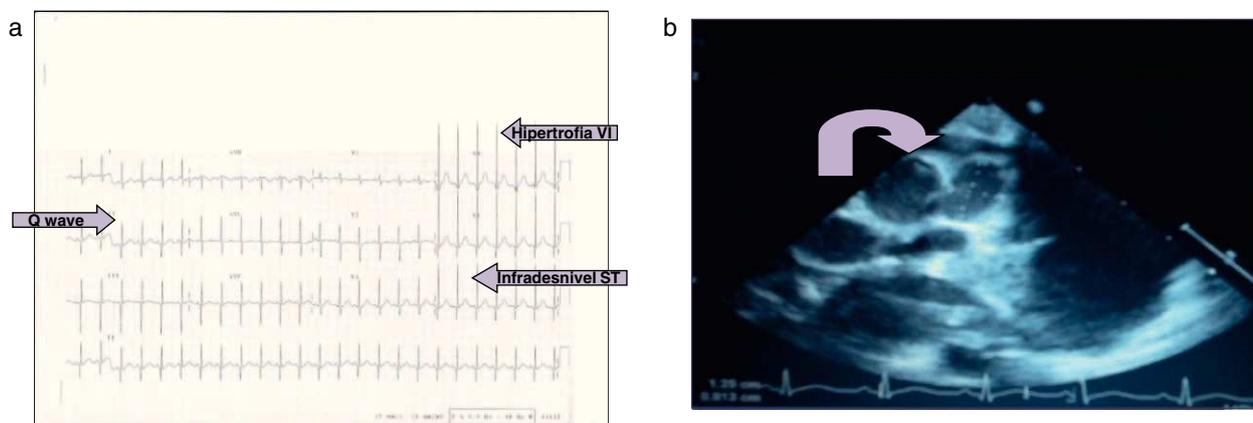


Fig. 1. (a) Electrocardiogram showing sinus rhythm, HR 136, P axis +45°, QRS axis +80°, PR 0.11, cQt 0.36, ST depression in V6, Q wave on DI, DII, aVL, and aVR, left ventricular hypertrophy. (b) Echocardiogram reflecting right coronary of 2.4 mm, with a saccular aneurism of 7.5 mm with intrasaccular thrombus of 0.5 cm².

Day 52

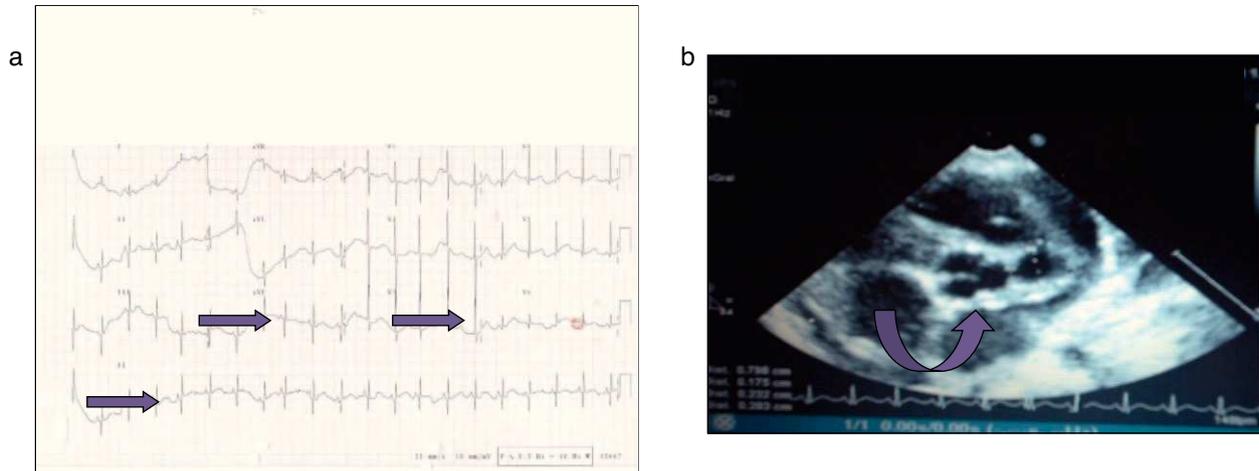


Fig. 2. (a) Electrocardiogram showing sinus rhythm, HR 125, a P +30°, QRS axis +60°, PR 0.12, cQt 0.40, Q waves on DII, aVF, and V6. (b) Echocardiogram showing aneurism of the right coronary of 0.1 cm²; left anterior descending coronary of 6.8 mm; origin of both coronaries of 3 mm; EF 61%.

cholesterol 159 mg/dl (NR 150–200 mg/dl) and triglycerides 233 mg/dl (NR 30–86 mg/dl).

Treatment with dobutamine and levosimendan was started, as well as assisted mechanical ventilation. The patient underwent a transfusion once and thrombolysis was carried out with recombinant plasminogen activator and heparin, suspended after bleeding through the ventilation type, and low molecular weight heparin (enoxaparin) was prescribed as well as antiplatelet therapy (aspirin). He was managed in the ICU for 10 days, vasoactive drugs for 4 days and mechanical ventilation for 6 days.

On day 50 of hospitalization he underwent a myocardial thallium-201 perfusion SPECT; there was no evidence of necrosis. No stress test with dipyridamole was found due to the age of the patient. He was stratified as AHA V due to the obstruction of the coronary artery, treated with low molecular weight heparin and later received warfarin and aspirin.

On day 55 an electrocardiogram showed sinus rhythm, HR 125, aP +30°, QRS axis +60°, PR 0.12, cQt 0.40, Q waves on DII, aVF and V6 (Fig. 2a). The echocardiogram showed minimal pericardial effusion, no paradoxical movement or dyskinesia; there is a reduction in the size of the intrasaccular thrombus in the right coronary aneurism of 0.1 cm², fusiform aneurism of the left descending anterior coronary of 6.8 mm, origin of both coronaries of 3 mm; EF 61% (Fig. 2b). Laboratory data showed Hb 11.2 g/dl (NR 12–15.5 g/dl), Hto 33.8% (NR 36%–47%), platelets 461 000/mm³ (NR 150 000–450 000/mm³), leukocytes 8100/mm³ (NR 6000–10 000/mm³). BUN 8 mg/dl (NR 5.0–18 mg/dl), uric acid 2.9 mg/dl (NR 2.4–6.4 mg/dl), creatinine 0.2 mg/dl (NR 0.2–0.4 mg/dl), DB 0.08 mg/dl (NR 0.2 mg/dl), IB 0.28 mg/dl (NR 0.2 mg/dl), TB 0.36 mg/dl (NR 0.2–1.0 mg/dl), proteins 7.2 g/dl (NR 4.2–7.4 g/dl), albumin 3.8 g/dl (NR 3.5–5.0 g/dl), TGO 38 UI/l (NR 15–50 UI/l), TGP 62 UI/l (NR 10–40 UI/l), LDH 321 UI/l (NR 110–295 UI/l), urinalysis: granular casts 0–1/field, erythrocyturia 7–9/field, leukocytes 3–5/field, bacteria++, epithelial cells 2–4/field, negative nitrites. Urine culture was negative.

The patient is currently asymptomatic and under surveillance by Rheumatology and Cardiology. The echocardiogram after 4 months of the onset of KD showed: right coronary of 3.6 mm, with an intrasaccular thrombus of 0.1 cm², left coronary of 2.5 mm, anterior descending of 5.37 mm, ectasia of the long circumflex of 2.5 mm, treatment with warfarin 0.1 mg/kg/day and aspirin 3 mg/kg/day.

Discussion

We have presented the case of a patient with KD who had CA and intrasaccular thrombus, surviving a myocardial infarction and showing a progressive reduction of the CA and thrombus. No adequate follow-up was carried out and was initially discharged, mainly because of lack of knowledge regarding the disease.

Our patient presented several poor prognosis markers and high risk for the development of cardiac complications, which could have been avoided with periodic evaluation in an outpatient clinic.

Heaton et al. described the only fatal cases of KD in patients 6 months and 4 years of age; autopsy reports describe the presence of CA, as well as intrasaccular thrombi. Initial echocardiographic studies showed an absence of CA and the initial treatment was with gammaglobulin and aspirin; the development of CA was detected between days 15 and 50 of the convalescence phase.⁵

Some risk factors for the early formation of CA have been identified: age under year or over 5, delay in diagnosis and treatment of the disease, an increase in inflammatory markers (ESR, CRP and procalcitonin) after therapy with gammaglobulin, leukocytosis over $30 \times 10^9/l$, thrombocytopenia (platelets under 100 000), an increase in liver enzyme levels and low levels of albumin.⁶

Myocardial infarction in children with KD is one of the main causes of sudden death, with a mortality rate of 22%. Signs and symptoms are non-specific or present uncontrolled crying, vomiting, diarrhea, dyspnea, chest pain, abdominal pain, vascular collapse and shock. Electrocardiographically, the patients present ST segment elevation, Q waves, and T wave inversion. Echocardiographically he presents dyskinesia or hypokinesia, effusions, valvulopathy and paradoxical septal movement. Laboratory tests show an elevation of CPK, MB fraction (maximum peak in the first 24 h, normalized after 48–96 h), elevation of troponin I, elevation of muscle enzymes (aminotransferases). The start of fibrinolytic therapy during the first hours improves patient prognosis.⁷

Treatment of KD before day 10 reduces cardiac complications in 4.7% to 25%. 15% of patients will not respond to the first dose of gammaglobulin, requiring a second dose. Intravenous steroid therapy as a second line therapy in combination has shown usefulness in the reduction of coronary risk and aneurism formation.⁷

Recent studies have shown that the combination of warfarin and aspirin in patients with a high cardiovascular risk reduces the risk of myocardial infarction in 5%–33%.⁸

Diagnosis and treatment with gammaglobulin before day 10 of KD can prevent fatal cardiovascular complications.

Conflict of Interest

The authors have no conflict of interest to declare.

Acknowledgement

The authors wish to thank Dr. Abraham Galicia Reyes, cardiologist and electro physiologist, for sharing his expertise on these types of patients.

References

1. Newburger JW, Takahashi M, Gerber Mewitz MH, Tani LLY, Shulman ST, Bolge AF, et al. Diagnosis, treatment and long term management of Kawasaki disease: a statement for Health Professionals from the Comitè on Rheumatic Fever, Endocarditis and Kawasaki Disease. Council on cardiovascular disease in the young, American Heart Association. *Circulation.* 2004;110:2747–71.
2. Thèrese H, Dubos F, Hue V, Godart F, Francart C, Vicent P, et al. Increased detection rate of Kawasaki Disease using new diagnostic algorithm, including early use of echocardiography. *J Pediatr.* 2009;155:695–9.
3. Gordon JB, Kahn AM, Burns J. When children with Kawasaki Disease grow up. Myocardial and vascular complications in adulthood. *J Am Coll Cardiol.* 2009;54:1911–20.
4. Wood LE, Tulloh RMR. Kawasaki disease in children. *Heart.* 2009;95:787–92.
5. Heaton P, Wilson N. Fatal Kawasaki disease caused by early occlusive coronary artery disease. *Arch Dis Child.* 2002;87:145–6.
6. Chen YO, Yu-Fang T, Chen-Liang L, Yee-Hsuan C, Kai-Sheng H. Significant relationship between serum high sensitivity C-reactive protein, high density lipoprotein cholesterol levels and children with Kawasaki Disease and coronary artery lesion. *J Formos Med Assoc.* 2009;108:719–24.
7. Ganesh A, Seth G, Ponniah T. Corticoesteroid therapy for primary treatment of Kawasaki disease, weight of evidence: a meta-analysis and systematic review of the literature. *Cardiovasc J Afr.* 2009;20:233–6.
8. Suda K, Kudo Y, Higaki T, Nomura Y, Miura M, Matsumura M, et al. Multicenter and retrospective case study of warfarin and aspirin combination therapy in patients with giant coronary aneurysms caused by Kawasaki disease. *Circ J.* 2009;73:1319–23.