

Late Diagnosis of Kawasaki Disease and its Complications. Case Report

Diagnóstico Tardio da Doença de Kawasaki e suas Complicações. Relato de Caso

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Male patient, 5 years old, healthy, is taken to a primary healthcare unit with cough and fever for 2 days, irritability and decreased appetite. Seven days after the onset of amoxicillin, he maintained fever and developed bilateral non-exudative conjunctival hyperemia. Admitted to the hospital of his city, he received intravenous antibiotic therapy for 9 days but maintained fever associated with hand and foot edema, rash, abdominal pain, labial and hand peeling, palpable lymph nodes in the bilateral cervical region. After 18 days, he was transferred to Hospital Martagão Gesteira in Salvador, BA.

On admission, he was in good general condition, hypoactive, eupneic, tachycardiac, hypochromic mucosa +2/+4, dehydrated 2+/4+, anicteric, acyanotic and with fever (39.0 °C).

Due to long-lasting fever and clinical signs, he was diagnosed with KD and immunoglobulin (IG) was initiated (2 g/kg/dose) on the first day of hospitalization.

Laboratory tests revealed hemoglobin 8.0 g/dL, platelets 575,000/mL, white blood cells 13.2/mL (67% neutrophils and 15% lymphocytes), C-reactive protein 80.78 mg/l. Negative cytomegalovirus and Epstein-Barr serology, normal chest X-ray and urine summary, negative urine culture and blood culture. On the third day of hospitalization, 100 mg/kg/day of acetyl salicylic acid (ASA) was introduced, and an echocardiogram showed diffuse coronary disorder with anterior descending (DA) aneurysm (Z score + 8.43) and circumflex artery (CX) aneurysms (Z score + 4.27) (Table 1).

On the seventh day, daily fever persisted, with hepatomegaly and peeling in the feet. One dose of GI was repeated and ASA was maintained. After 24 hours, he remained feverless for five days and ASA was reduced to 5 mg/kg/day. Another echocardiogram showed maintenance of diffuse coronary

Table 1 - Echocardiogram results.

	10/10/2017	13/10/2017	28/11/2017	11/04/2018
Proximal third, mm	4.6	5.6	2.8	3.8
Z score	+ 6.52	+9.00	+1.61	+3.2
Median portion, mm	5.8	4.9	-	-
Z score	+10.19	+7.96	-	-
Left main coronary artery, mm	3.5	4.0	2.8	4.0
Z score	+3.21	+4.49	+3.74	+3.87
Proximal/middle anterior descending artery, mm	3.2/4.6	3.1/4.9	1.8/ 4.0	2.9
Z score	+4.06 / +7.94	+3.78/+8.77	-0.44/+5.75	+2.73
Proximal / middle circumflex branch, mm	5.1/6.6	1.6/7.2	3.5/6.5	3.55/4.0
Z score	+10.19/+12.36	-0.19/+13.8	4.08/+11.28	4.0/+5.19

Keywords

Aneurysm; Conjunctivitis; Exanthema; Mucocutaneous Lymph Node Syndrome.

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disorder with moderate to severe dilation of right coronary artery (RCA), mild dilation of left coronary trunk (LCT), aneurysmal dilation of CX with saccular and DA aneurysm, mild mitral regurgitation and mild left ventricular (LV) dilation. It was chosen to introduce clexane at a dose of 2 mg/kg/day and warfarin at a dose of 2.5 mg/day.

On the thirteenth day, he returned with fever and prostration. The patient underwent pulse therapy with methylprednisolone for 3 days, with improvement. Prednisolone was maintained for 15 days.

Post-pulse therapy echocardiography (Figure 1) revealed suspected CX thrombus. Chest CT angiography (CT angiography) confirmed the findings of Kawasaki arteritis and ruled out coronary thrombus.

After the 24th day of hospitalization, the patient was discharged asymptomatic, using warfarin and ASA, for outpatient follow-up. Subsequent echocardiograms showed no regression of the aneurysms. CT angiography after 6 months showed complete regression of CX and RCA aneurysm and improvement of LMCA. However, she maintained an aneurysm with Z score > +10 in the ADA, with suspected obstruction (Figure 2 and Table 2).

Referred for better coronary evaluation in cardiac catheterization, where ADA showed saccular aneurysmal dilation in the proximal portion of the vessel, with the presence of subocclusion in its mid-distal section. Also, CX with ectasia in the middle section and RCA with ectasia in the proximal section.

Expectant management was adopted, as there were no signs of myocardial ischemia or cardiac dysfunction on echocardiogram. Patient remains anticoagulated, in outpatient follow-up.

Discussion

the patient was diagnosed late, partly due to the late onset or perception of symptoms and late transfer to the tertiary center, presenting severe cardiac involvement and immunoglobulin resistance. Fever only reappeared after pulse therapy.

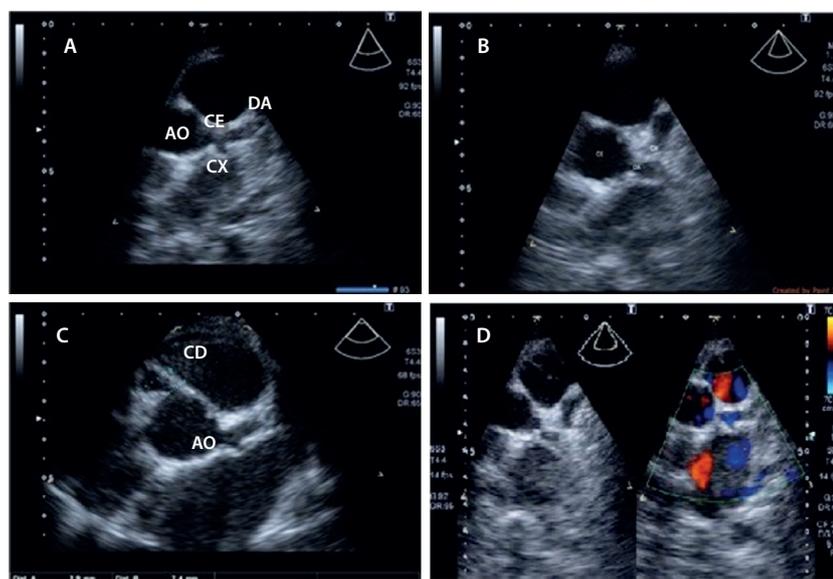
Coronary artery involvement is observed in about 25% of untreated patients before 10 days of fever. It is observed that the diagnostic criteria for KD have good specificity with low sensitivity, making early diagnosis difficult in some patients.¹⁻³

In all suspected or confirmed cases echocardiogram is mandatory. Coronary evaluation on echocardiogram is important not only in suspected cases of KD, but also in routine tests. Coronary artery dilation is usually not detected by echocardiography in the first week of the disease. It should then be repeated after 7 days in incomplete cases and 10 to 15 days in complete cases, with weekly follow-up in case of abnormalities.^{1,4,5}

Diseases such as measles, scarlet fever, toxic shock syndrome, staphylococcal scalded skin syndrome, erythema multiforme, Stevens-Johnson syndrome, mononucleosis and allergic drug reactions are differential diagnoses. Clinical history and laboratory data help rule out these diseases.^{1,2,6}

Ten to 20% of KD patients develop persistent fever at least 36 hours after GI infusion and are termed resistant GI, in which case additional therapies are recommended.^{1,3}

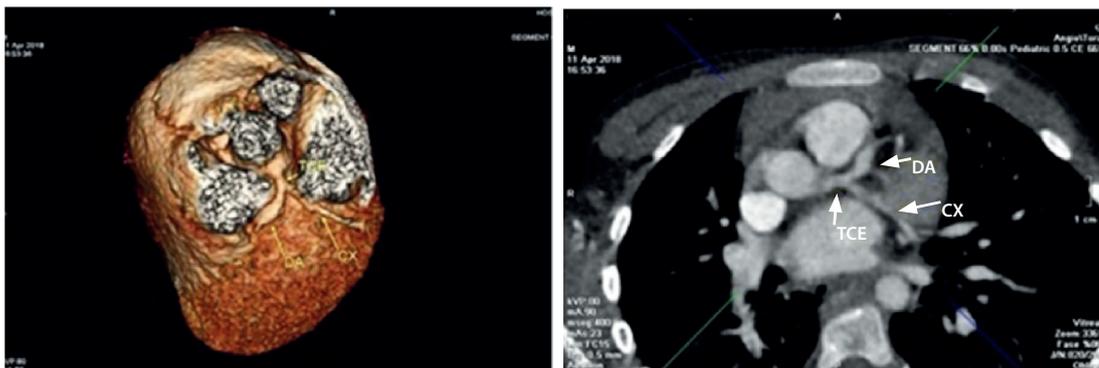
Immunoglobulin has an effect on reducing the occurrence of coronary artery disease. Even when properly treated, 20% of children develop transient coronary dilation in proximal ADA or proximal right coronary artery by the Z-score criterion, 5%



Source: Hospital Martagão Gesteira.

RCA: right coronary artery; LCA: left coronary artery; CX: circumflex artery and ADA: anterior descending artery.

Figure 1 – Echocardiograms (10/10/2017 and 13/10/2017) show diffuse coronary impairment with aneurysm.



Source: Hospital Martagão Gesteira.

Figure 2 – Computed tomography angiography (11/04/2018)

Table 2 – Comparative table with computed tomography angiography findings.

	18/10/2017	11/04/2018
Left main coronary artery	4.2 × 5.8 mm	3.7 × 4.0 mm
	Z score: +8.78	Z score: +4.18
Right coronary artery	5.4 × 5.1 mm	1.9 × 1.4 mm
	Z score: +8.19	Z score: -0.40
Anterior descending artery	7.5 × 5.3 mm	6.0 × 5.2 mm
	Z score: +15.56	Z score: +11.4
Circumflex artery	6.1 × 5.3 mm	2.2 × 2.3 mm
	Z score: +10.73	Z score: +1.35

Source: Hospital Martagão Gesteira.

will develop coronary artery aneurysms ($Z > +2.5$) and 1% will develop giant aneurysms.⁷

In the coronary arteries, inflammatory disorders are observed in the middle layer that surrounds the entire vessel. With the loss of structural integrity of this vessel, there is aneurysm formation and fibroblast proliferation. This remodeling contributes to the formation of thrombi, as well as stenoses and calcifications, as shown in this case.^{4,5,8}

The Z-score-based scheme was recommended in 2017 by the American Heart Association, allowing a better assessment of the severity of coronary dilation.^{1,7,8} No involvement: $< +2$; Dilatation only: $+2$ to < 2.5 ; or if initially $< +2$, Z score decreases during follow-up ≥ 1 ; Small aneurysm: $\geq +2.5$ to $< +5$; Median aneurysm: $\geq +5$ to $< +10$ and absolute dimension < 8 mm; Large or giant aneurysm: $\geq +10$ or absolute dimension ≥ 8 mm.¹

Severe but partially preserved aneurysms may decrease in lumen diameter over time as a result of thrombi and may

become stenotic. Large aneurysms do not get smaller, rarely burst and almost always contain thrombi. And anticoagulation is recommended for these patients.^{1,4,6,9}

Cardiovascular complications such as endothelial dysfunction, lipid metabolism disorders and intimal thickening of coronary artery walls appear to be directly implicated in the development of atherosclerosis, increasing the risk of acute coronary events, requiring strict control of lipid profile. These occurrences are assumed to be more frequent in patients with giant coronary artery aneurysms (> 8 mm). Mortality rate is higher in young adults with a history of KD compared to the general population.^{1,2,10}

Conclusion

Late diagnosis and introduction of appropriate therapy has led to an unfortunate outcome. A high level of suspicion in children with fever of undetermined origin is necessary for the clinical diagnosis and immediate institution of treatment, leading to less coronary complications in Kawasaki disease.

Authors' contributions

Research creation and design: Martins LSC, Alcântara NGA. Data acquisition: Martins LSC, Alves MS, Costa PCRM. Data analysis and interpretation: Martins LSC, Alves MS, Costa PCRM. Statistical analysis: Martins LSC, Alves MS, Costa PCRM. Funding: Martins LSC. Manuscript writing: Martins LSC, Alves MS, Costa PCRM. Critical revision of the manuscript for important intellectual content: Martins LSC, Alves MS, Costa PCRM.

Conflict of interest

The authors declare that there is no conflict of interest regarding this manuscript.

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