

# KAWASAKI DISEASE UNDIAGNOSED IN CHILDHOOD, MYOCARDIAL INFARCTION IN ADULTHOOD - CASE REPORT

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**Keywords:** Kawasaki disease, acute coronary syndrome, angio-coronarography;

**Abstract:** Kawasaki disease is a vasculitis, usually diagnosed in childhood, for which reason treatment should be started as early as possible, to avoid complications. We present the case of a 37-year-old man with anterior chest pain, with coronary character, without known cardiovascular risk factors, and who, following investigations, is directed to emergency angio-coronarography due to acute coronary syndrome. Here, we highlight the characteristic coronary dilations for Kawasaki disease. It is released in very good general condition, with proper treatment.

## INTRODUCTION

Kawasaki disease is the second most common cause of vasculitis after Schoenlein Henoch in childhood and the first cause of cardiovascular disease in children due to coronary complications.

Once the disease has been diagnosed, the patient should be evaluated constantly by a cardiologist, in order to diagnose coronary aneurysms diagnosis, for optimal treatment, in order to avoid cardiovascular complications.

## CASE REPORT

We present the case of a patient, aged 37, from the rural area, admitted to the Sibiu Emergency County Clinical Hospital, who presents for constrictive anterior chest pain, of high intensity, started 24 hours prior admission.

From personal pathological records we note that during childhood he presented with febrile episodes, associated with conjunctival hyperemia, rashes, which he associated with childhood diseases. He denies any drugs consumption.

The initial clinical examination revealed: general influenced state, normal weight with body mass index (BMI) 22kg/m<sup>2</sup>, normal bilateral blood pressure (BP) 120/80mmHg, pulse 90/min, rhythmic cardiac noises, without cardiac or vascular murmurs, peripheral pulses present bilaterally, normal breath sounds present bilaterally, without signs of pulmonary congestion, spontaneous and painless abdominal pain, Temporo-Spatial Orientation.

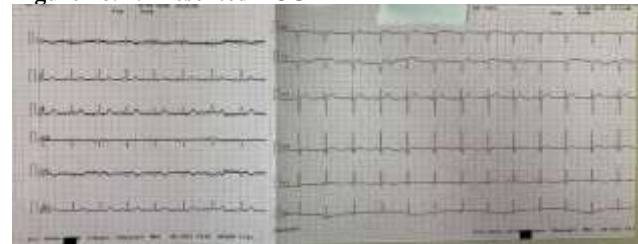
The electrocardiogram (ECG) at presentation showed sinus rhythm, with a pulse of 80 beats per minute, QRS axis + 90 °, 0.5 mm ST segment elevation and T negative in DI, aVL, V1-V2 derivations (figure no. 1).

**Biological samples** were in normal ranges, except for aspartate amino-transferase which showed high values, 148 U/L (3 times above normal value). Myocardial cytolysis markers were also elevated: high sensitivity - cTnI 16869 ng/L, TNI 17.6 ng/mL, CK-MB 71.5ng/L, BNP 136 ng/ml.

In context of patient symptomatology, of EKG changes concordant with left ventricle (LV) apex and anterior

wall hypo-kinesia, elevated myocardial cytolysis enzymes, the patient was referred for angio-coronarography.

**Figure no. 1. Presented ECG**



Angiogram revealed a right dominant coronary system, left main and circumflex coronary artery with no significant lesions, 90 % stenosis in Anterior Descending Artery (ADA) proximal segment, followed by a significant dilation, in the mid-focal stenosis of 70-80%, distally without significant angiographic lesions. Significant dilation was also found in the vertical segment of right coronary artery (typical aspect of Kawasaki disease) (figures no. 2,3) Coronary revascularization by percutaneous implantation of two drug eluting stents was performed on the Anterior Descending Artery, with TIMI III distal flow and without any periprocedural complications.

**Figure no. 2. Right coronary artery**



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## CLINICAL ASPECTS

Figure no. 3. Left coronary artery



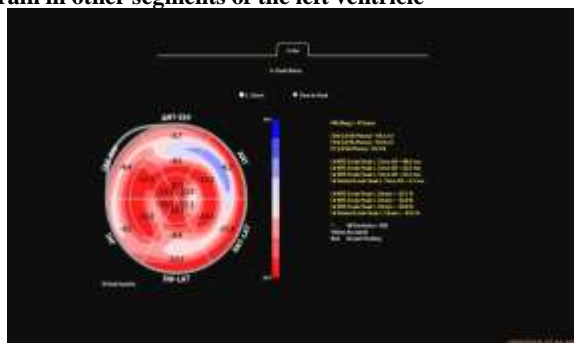
Emergency **transthoracic echocardiography** revealed a normal sized left ventricle (LV), with regional wall motion (left ventricle apex and anterior wall hypokinesia), and moderately reduced LV ejection fraction (40%). Mild mitral regurgitation was associated and no pericardial fluid was found. A more detailed transthoracic echocardiography was performed post-coronary revascularization in order to evaluate LV function, kinetics and typical changes of Kawasaki disease (figures no .4,5).

Despite slight improvement of LV ejection fraction after stent implantation (48%), LV myocardial deformation abnormality was noted on speckle tracking imaging (figures no.4,5). LV Global Longitudinal Strain was reduced (-14%), the most significant decrease being highlighted in the LV anterior wall.

Figure no. 4. Transthoracic echocardiography two-chamber apical view: 2D speckle tracking shows a moderate reduction of the anterior wall longitudinal strain, with a slight reduction of the ejection fraction (48%)



Figure no. 5. “Bull’s Eye” type imaging that shows a low global longitudinal strain (-14%), with infarction in the anterior territory, as well as a reduction of the longitudinal strain in other segments of the left ventricle



During the hospitalization, after coronary revascularization, the patient evaluation was favourable, with chest pain remission, ECG normalization and LV ejection fraction improvement. After three days of hospitalization the patient is discharged on request, with the following treatment recommendations: ACETYLSALICYLIC ACID 75mg 0-1-0, TICAGRELOR 90mg 1-0-1, RAMIPRIL 2.5 mg 0-0-1, ATORVASTATIN 80mg 0-0-1, BISOPROLOL 2.5 mg 1-0-0.

## DISCUSSIONS

Kawasaki disease is an acute vasculitis of unknown etiology, which predominantly affects children younger than 5 years. Initially, when the first cases of Kawasaki disease was described, coronary heart disease was not a problem, but today is the most common cause of acquired heart disease in children from developed countries. Data from the literature describe a 25% incidence in coronary aneurysms, in patients not receiving treatment during the acute period, the incidence being reduced to 4%, in patients who received early immunoglobulin treatment.(1)

### Pathogenesis

In the acute, febrile phase, there is a systemic inflammation in the medium - sized arteries, with important coronary artery disease, with extension in different tissues and organs, so the clinical presentation may include associated clinical manifestations: hepatitis, interstitial pneumonia, abdominal pain, vomiting, diarrhea stools, vesicular hydrops, aseptic meningitis, myocarditis, pericarditis, valvulopathy, pyuria, pancreatitis, adenopathy. Three pathological processes have been described in the arterial changes. The first one is the necrotizing arteritis produced by infiltration of arterial wall with neutrophils, which occurs two weeks after the onset of fever, a process that causes the progressive destruction of the adventitia, with the formation of aneurysm. The second process is subacute/chronic vasculitis, formed by asynchronous infiltration of lymphocytes, plasma cells and eosinophils, a process that begins two weeks after the onset of febrile syndrome, which may continue for months or even years, in a small number of patients. The third process describes a myofibroblast proliferation, which starts also in the first two weeks, and lasts for years, with the potential to cause progressive arterial stenosis.(2,3)

Coronary artery disease depends on the severity of the lesions. The arteries with slight dilatations can regain their original shape. Large-scale saccular aneurysms, in which the intima and media have been affected, can no longer undergo regeneration processes. Fusiform aneurysms, in which the middle layer has not been affected, may have partial thrombosis, or even progressive stenosis through myofibroblast proliferation. Large aneurysms develop successive layers of thrombi, with subsequent calcification. Myocardial infarction may occur through the process of acute thrombosis, or by the formation of progressive arterial stenosis.

In the present case, the presence of fever, conjunctivitis and rash were affirmative, according to the anamnesis, without clear clinical evidence, but the suggestive changes of Kawasaki disease were described in patients' coronary angiography.

The condition should be suspected when a marked ectasia or aneurysm is detected in the proximal coronary arteries (especially ADA and RCA) in a young patient who does not present risk factors for atherosclerotic coronary artery disease. Characteristics of coronary arteries, which should support Kawasaki disease, include marked proximal ectasia with or without calcification, followed by a sudden passage to a normal distal angiographic segment.

**Cardiovascular impairment assessment**

The “gold standard” for evaluating coronary complications, especially in the adult patient, is angiography, which provides a detailed picture of the vascular lumen, assessing the degree of stenosis. Coronary flow reserve, measured during angiography, is a common method, useful in determining ischemic potential in atherosclerotic stenosis. In patients with Kawasaki disease, with coronary artery disease, the discrete coronary artery stenosis can also be evaluated using the same method. An additional perspective regarding the coronary flow reserve in Kawasaki disease concerns the impact of coronary aneurysms on blood pressure. Loss of pressure related to blood turbulence in the dilated segments may cause pressure drop along the artery, but the flow reserve evaluated at several microenvironments associated with Kawasaki disease has documented pressure drops, but without physio pathological significance.(1,4)

Echocardiography has a fast, noninvasive, diagnostic role. During the first week of illness the echocardiogram may be in normal relations, but when the suspicion is increased, treatment should not be postponed. Once the condition is diagnosed, especially during childhood, the patients should be evaluated by echocardiography, in order to diagnose coronary aneurysms, which most commonly occur two weeks after the febrile syndrome, and once diagnosed, they must be evaluated for the following interventions. The echocardiographic evaluation should include measuring the diameters of the vessels using the Z-score, highlighting the associated structural anomalies, possible valvulopathies, the presence of the pericardial fluid.(1)

**Treatment**

Thromboembolic prophylaxis plays an important role, especially in patients who have been diagnosed in childhood with Kawasaki disease and coronary heart disease, in order to prevent thrombosis. In patients with large aneurysms, in addition to antiaggregant treatment, an anticoagulant may be used, when the thrombotic risk exceeds the hemorrhagic risk. In patients who cannot receive anticoagulant therapy, dual antiplatelet therapy may remain an option. As regards anti-aggregation treatment, Aspirin in doses of 80-100 mg remains the main component. If the patient does not tolerate Aspirin, or has contraindication, another class of platelet anti-aggregates may be chosen.

Regarding anticoagulant treatment, Warfarin was the drug of choice and studied in patients with Kawasaki disease and coronary artery disease, with the INR being maintained at 2-2.5. Low molecular weight heparins may be an alternative to patients who are not compliant with warfarin treatment. LMWH has similar thromboembolic effects and bleeding risk lower than warfarin. (5)

Statins represent the key in primary and secondary prevention of atherosclerotic cardiovascular events in adults.(5) In addition to lowering cholesterol levels, statins have beneficial effects on inflammation, oxidative stress, coagulation and fibrinolysis.

In Kawasaki disease the pathogenic process does not include atheroma plaque formation and the use of statins is controversial. Patients with Kawasaki disease have been shown to have chronic inflammation and low levels of HDL cholesterol, endothelial dysfunction, increased vascular rigidity with thickening of the intima and media, both at the coronary and systemic arteries. Small, short-term studies have shown improvement in endothelial dysfunction in patients with coronary aneurysms and Kawasaki disease, thus empirical treatment with statins may be considered in patients with aneurysms, regardless of age or sex. In this case, the patient

received high-dose statin treatment, as indicated in the adult acute coronary syndrome guidelines.(5)

Angiotensin converting enzyme inhibitors (ACEI), in patients with atherosclerotic diseases, have a prophylactic role in decreasing the debut of acute coronary events and decreasing cardiovascular mortality, an effect not shown in patients with coronary artery disease in Kawasaki disease. In our patient ACEI administration is supported by the presence of left ventricular dysfunction after acute myocardial infarction, influencing the process of left ventricular remodeling. If ACEI are not tolerated, or have contraindications, treatment with angiotensin receptor blockers (ARBs) can be followed, presenting similar effects.

Beta blockers reduce acute cardiovascular events as well as cardiac mortality by decreasing myocardial oxygen consumption. The use of beta-blockers in patients who have already suffered an acute coronary event, or in patients with a left ventricular ejection fraction  $\leq 40\%$  is a class IA indication in European Society of Cardiology (ESC) guidelines. Beta blockers can be used at any age, regardless of sex, prophylactically, especially in patients with Kawasaki disease and large coronary aneurysms and increased thromboembolic risk. The dose of beta blocker used in our patient represented the lowest starting dose, in order to not influence blood pressure or ventricular allure, which were within normal limits.(5)

As for patients with ST elevation myocardial infarction (STEMI) and Kawasaki disease, they must undergo emergency angiography, with the restoration of coronary flow in the involved artery. (Class I. Record level C). Percutaneous coronary implantation (PCI) is preferred at the expense of aorto-coronary bypass (CABG), in patients with univascular, or focal multivascular (Class I, level C). The use of drug eluting stents (DES) is indicated in patients who do not receive long-term anticoagulant treatment. CABG is preferred in place of PCI in patients with left main disease, multivascular coronary artery disease, with reduced left ventricular function, or triconary diabetic patients (Class I, record level B).(5)

In this case, the patient presented with the diagnosis of acute coronary syndrome STEMI, with onset at 24 hours, with indication of emergency angiography, for coronary reperfusion. Patient age, male gender, typical angiographic changes, as well as lack of cardiovascular risk factors, sustained the diagnosis of Kawasaki disease.

**CONCLUSIONS**

Imaging evaluation of patients diagnosed with Kawasaki disease in childhood, plays an important role, especially since in some cases the aneurysms formation occurs time away from the acute episode. In young patients, most commonly males, with no cardiovascular risk factors, and who present with stable angina, or even acute coronary syndrome, elective or emergency angio-coronarography should be performed in order to diagnose coronary sequelae in Kawasaki disease, as well for reperfusion therapy.

Coronary angiography is the gold standard for both diagnosis and treatment of coronary aneurysms. Antithrombotic prophylaxis in patients with coronary aneurysms is important, and anticoagulation should be considered when the thrombotic risk exceeds the hemorrhagic risk.

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