

Late diagnosis of Kawasaki disease with major cardiovascular complications: a case report

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Background

Kawasaki disease (KD) is an acute systemic vasculitis syndrome, mostly targeting children under 5 years old. If untreated, coronary artery abnormalities develop to approximately one out of four patients who suffered from KD. As KD might be easily missed in childhood, managing cardiovascular complications might become a real challenge at an advanced age.

Case summary

A 25-year-old woman was presented to a skiing resort hospital with discomfort in chest, shortness of breath, cold sweat, and dizziness after skiing. Based on increased troponin level and ECG findings, the specialists diagnosed myocarditis and initiated treatment with non-steroidal anti-inflammatory drugs. After the symptoms recurred in half a year, there was a need for further clarification of the diagnosis of myocarditis. The patient received a comprehensive cardiac imaging evaluation at Vilnius University Santaros Clinic to differentiate the cause of the recurrent chest pains. Coronary artery computed tomography revealed presence of aneurysm with wall calcification in left anterior descending artery S6—10 mm in diameter and aneurysm of circumflex artery S11—7 mm in diameter as well as occlusion of calcified right coronary artery. After taking a detailed medical history, a presumption about a former case of KD has been made.

Discussion

Coronary artery aneurysm is a cardiovascular sequelae of KD if it is left untreated. Due to atypical presentation, it might be overlooked, while the key of successful KD management is an early diagnosis and therapy.

Keywords

Case report • Kawasaki disease • Vasculitis • Coronary arteries • Complication • Aneurysm

ESC curriculum

2.3 Cardiac magnetic resonance • 2.4 Cardiac computed tomography • 3.4 Coronary angiography • 7.5 Cardiac surgery

Learning points

- Kawasaki disease (KD) is diagnosed for a patient having fever for ≥ 5 days with at least four out of five following clinical features: mouth mucosal changes, conjunctivitis, polymorphous rash, oedema, and erythema of the extremities, cervical lymphadenopathy > 1.5 cm. Not all five major criteria of KD are necessarily present. A clinician must have a suspicion in any child (especially ≤ 5 years old) with persistent unexplained fever accompanied by any other major clinical feature.
- When a young person presents with clinical symptoms and findings suggesting myocardial ischaemia, the coronarography or coronary computed tomography angiography (CCTA) should be performed. Coronary artery aneurysm in young adults should raise suspicion of KD in the past.

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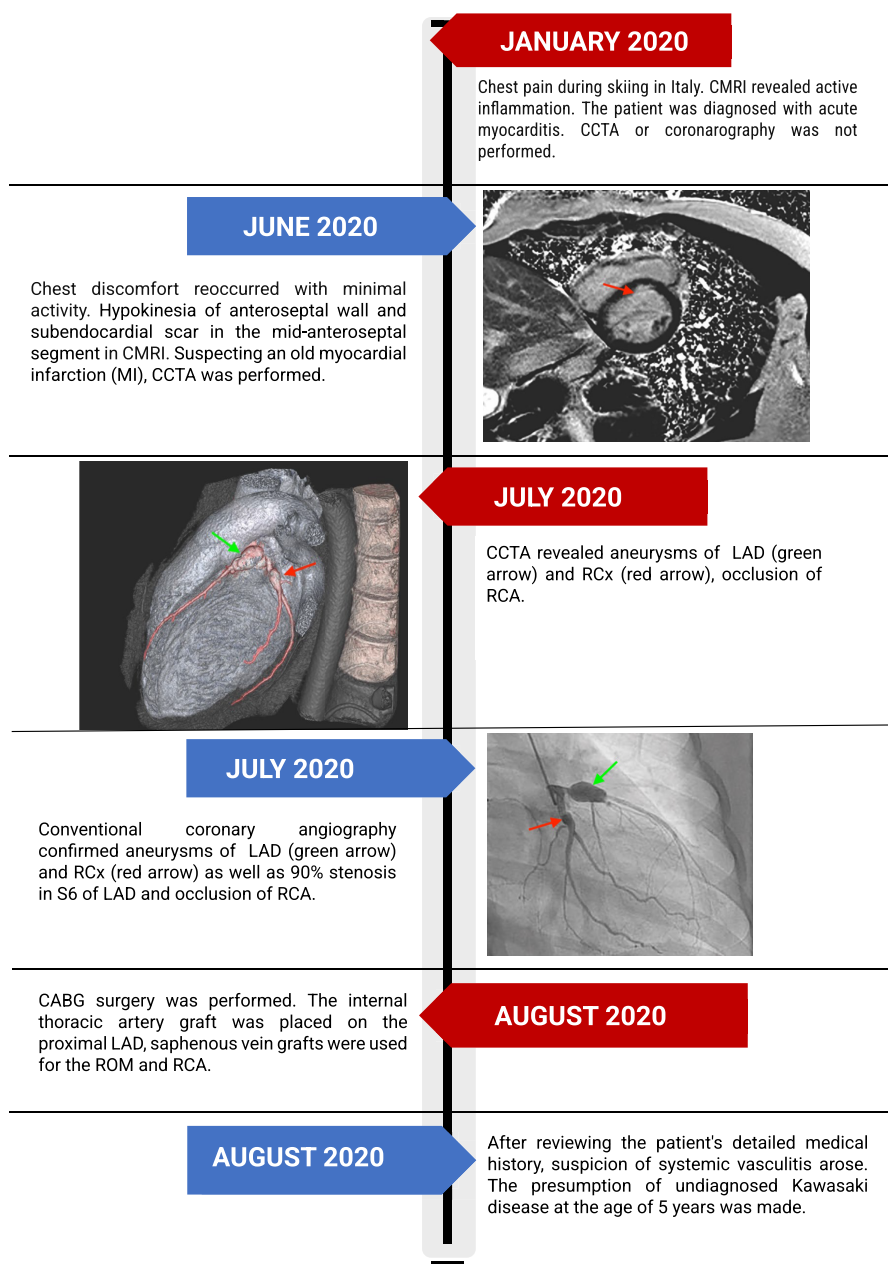
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Introduction

Kawasaki disease (KD) is an acute systemic vasculitis which predominantly affects children under 5 years old. The aetiology of KD remains unknown with immune-mediated inflammatory cascade being a leading theory.¹ According to American Heart Association criteria, KD is diagnosed for a patient having fever for ≥ 5 days with at least four out of five following clinical features: mouth mucosal changes, conjunctivitis, polymorphous rash, oedema, and erythema of the extremities, cervical lymphadenopathy > 1.5 cm.² Not all the symptoms are necessarily present, therefore, KD diagnosis might be missed in childhood and adult

patients might not have a recollection of the illness from such a young age. The most complicated manifestation of KD is coronary artery aneurysm (CAA). The overall CAA incidence rate is reduced from 25% in patients without therapy to $\sim 4\%$ by initiating the treatment with intravenous immunoglobulin within 10 days after the onset of fever.² We report a case of KD missed in childhood and presented with cardiovascular sequelae of complicated CAA and myocardial infarction (MI) in young adults.

Summary figure



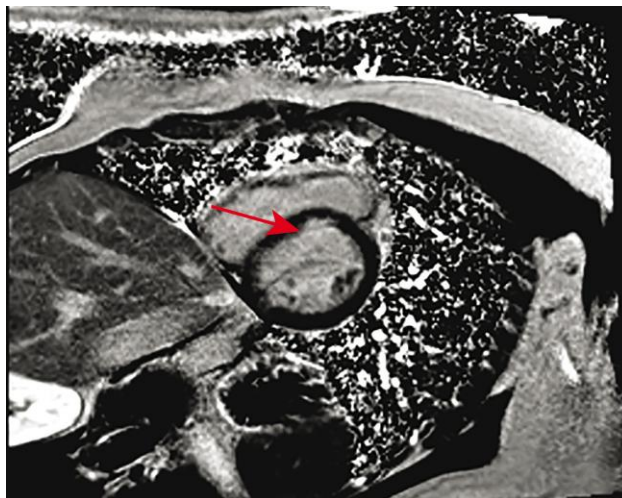


Figure 1 CMRI with subendocardial scar in mid-antero-septal segment of left ventricle on late gadolinium enhancement.

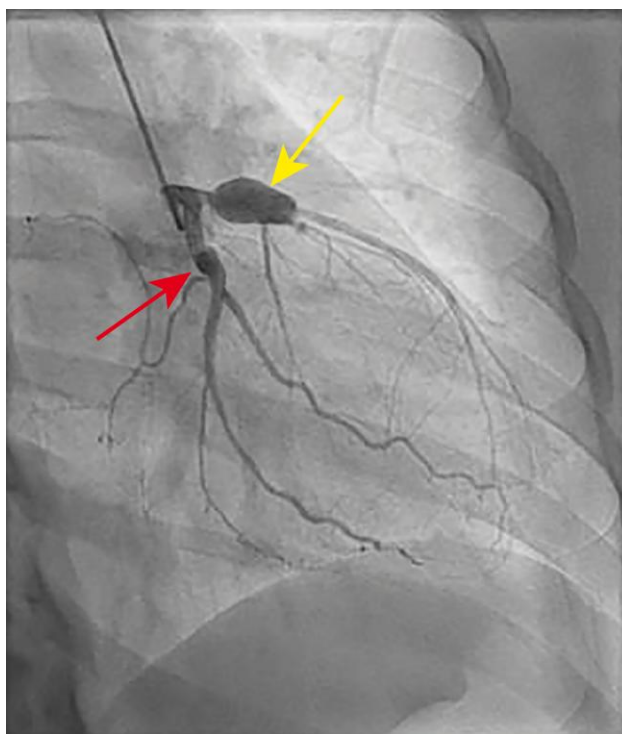


Figure 2 Conventional coronary angiography with aneurysm and 90% stenosis in S6 of left anterior descending artery (right yellow arrow) and aneurysm of RCx (left red arrow).

Case report

A 25-year-old woman presented to a ski resort hospital in January 2020 with chest pain and dyspnoea while skiing. She had no fever or flu-like symptoms. Smoking (5 cigarettes/day) was the only risk factor for coronary artery disease. Past medical history included suspicion of

myocarditis at the age of 5. Her physical exam revealed a heart rate of 86 b.p.m., blood pressure of 110/65 mmHg, and respiratory rate of 26 breaths/min. Auscultation of the chest revealed vesicular breath sounds without crackles and normal heart sounds. No peripheral oedemas present. Elevated troponin (14 809 ng/L) and creatinine phosphokinase (972 mmol/L) levels, along with negative T wave findings on the

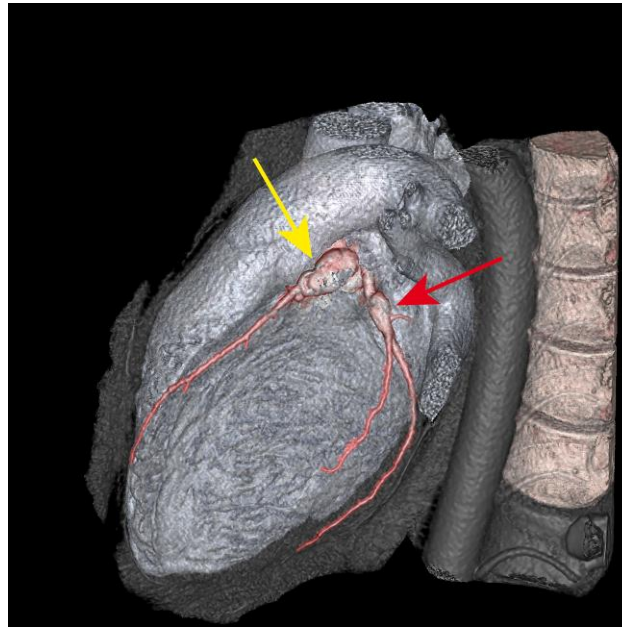


Figure 3 Coronary computed tomography three-dimensional reconstruction with aneurysm of left anterior descending artery (left yellow arrow) and RCA (right red arrow).

ECG, slightly reduced left ventricle (LV) systolic function [LV ejection fraction (EF) –58%], and preserved right ventricle (RV) (tricuspid annular plane systolic excursion–28 cm), raised suspicion of acute myocarditis. Cardiac magnetic resonance image (CMRI) revealed active inflammation in the LV and focal inflammation on the diaphragmatic wall of the RV. Left ventricle wall abnormalities included akinesia of basal inferior wall and hypokinesia of mid-infero-lateral wall, as well as akinesia of basal and mid-anterior wall. T2-weighted images revealed oedema on the medio-basal inferior wall. Focal intra-myocardial scar on antero-septal wall and basal diaphragmatic wall on late gadolinium enhancement was present. Based on these findings and symptoms, the patient was diagnosed with acute myocarditis. After 1 week of treatment with non-steroidal anti-inflammatory drug (NSAID), patient's condition improved.

Dyspnoea and chest pain with minimal activity reoccurred after 6 months, and patient was referred to our centre. ECG and physical exercise tests showed no abnormalities, and blood tests for systemic diseases or cardiopathies were negative. CMRI indicated slightly reduced LV systolic function (LV EF-57%) with hypokinesia of antero-septal wall and subendocardial scar in the mid-antero-septal segment, occupying 25–50% of the LV wall on late gadolinium enhancement (Figure 1). Suspecting an old MI, CCTA was performed.

CCTA revealed a 10 mm in diameter aneurysm with wall calcification and proximal S6 90% stenosis in LAD (Figure 3), a 7 mm in diameter aneurysm in the S11 of RCA, as well as occlusion of the calcified RCA. Conventional coronary angiography confirmed these findings (Figures 2 and 4). Due to ongoing recurrent grade III angina, clinical symptoms and medical findings revascularization possibilities were discussed in a heart team meeting. As there are no technical possibilities of successful angioplasty percutaneous coronary intervention in case of giant CAAs, patient was referred to a cardiac surgeon. In August 2020, coronary artery bypass graft (CABG) surgery was performed (Figure 5). An internal thoracic artery graft was placed on the proximal LAD, and saphenous vein grafts were used for the Ramus obtusus

marginalis and RCA with no intraoperative or post-operative complications.

Uncharacteristic aneurysmal changes in a young patient raised suspicion of vasculitis, leading to a multidisciplinary analysis involving a cardiologist and rheumatologist. The rheumatologist conducted a comprehensive analysis for systemic diseases, but all specific enzyme tests were negative. After reviewing the patient's detailed medical history, suspicion of systemic vasculitis arose: at the age of 5, the patient experienced persistent fever episodes for over 6 months, a red 'raspberry' tongue, and enlarged lymph nodes. The suspicion of myocarditis has been made at the age of 5 without any further analysis: no cardiac MRI has been performed or cardiotropic enzymes analysed according to medical data. Treatment with oral NSAIDs was prescribed. Upon reviewing the old medical data, which fulfilled three out of five diagnostic criteria (fever, red 'raspberry' tongue, and enlarged lymph nodes), the presumption of undiagnosed KD at the age of 5 was made. There is no specific treatment for an old KD, but it would clarify the origin of coronary artery aneurysms as of being a complication of undiagnosed and untreated [with intravenous immunoglobulins (IVIG)] KD. Unfortunately, we were not aware of KD in childhood at time of CABG, so no myocardial biopsy was completed to clarify histological changes.

In December 2021, the patient was referred to a cardiologist due to persistent chest pain. Physical tolerance remained unchanged. Electrocardiogram (ECG), echocardiography, and myocardial perfusion scintigraphy showed no abnormalities. Troponin levels were within normal limits. CCTA confirmed that all three bypass grafts were patent with normal contrast flow. In the 2022 follow-up, the myocardial scintigraphy and dobutamine stress test revealed no abnormalities. Further medical follow-up includes regular examinations for recurrent ischaemia (pharmacological stress test) once a year or in case of recurrent symptoms.

Discussion

The aetiology of CAA in adults is predominantly atherosclerotic, while KD represents the second most common cause of CAA in adults.^{3,4}



Figure 4 Coronarography with occlusion of right coronary artery.

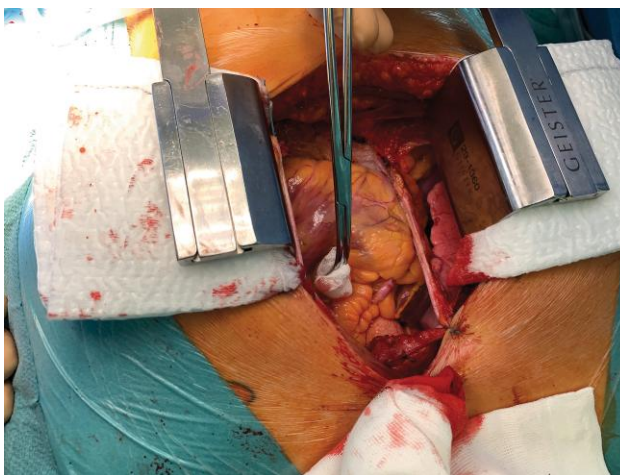


Figure 5 Aneurysm of the left anterior descending artery during coronary artery bypass graft.

Diagnosing atypical or incomplete KD, particularly when not all criteria are met, is challenging. Our patient met only three out of the five diagnostic criteria: fever, mucosal changes, and lymphadenopathy. The prolonged fever episode lasting approximately 6 months should have raised suspicion of KD in childhood.

Histologically, coronary artery arteritis typically begins within 6–8 days after KD onset. Therefore, treatment should start immediately (in 10 days) with daily administration of 30–100 mg of Aspirin and a

single infusion of IVIG at a dose of 2 g/kg.^{5,6} If untreated, coronary artery abnormalities develop in approximately one in four patients. In a clinical trial, the incidence of CAA decreased from 25% to 4% after high-dose IVIG infusions.² Early diagnosis and timely initiation of IVIG and aspirin therapy are the key to successful KD management.

Kawasaki disease patients with giant aneurysms have a higher risk of early atherosclerotic disease and MI. Meta-analysis of 30 studies has shown that cardiac complication of KD limited solely to patients with

CAAs.^{7,8} Undiagnosed KD in childhood can lead to MI in adulthood.⁹ In a retrospective study of 1073 patients with KD, followed for median of 6.7 years, 48% of patients with giant aneurysms experienced myocardial ischaemia, MI, or death.¹⁰ Another study found that approximately half of the patients with giant aneurysms required CABG within 20 years from the onset of KD.¹¹ A KD prevalence study revealed that over 5% of adults younger than 40 years undergoing coronary angiography for suspected myocardial ischaemia have CAA associated with prior KD.¹² Coronary artery aneurysm in young adults should raise suspicion of KD in the past.

Typical angina on exertion with ECG findings and elevated cardiac enzymes should raise the suspicion of coronary arteries pathology, despite young age, no family history and only one risk factor. Even with myocarditis present or suspected—as ambiguous CMRI findings can confuse the diagnosis—anatomical analysis of coronary arteries remains crucial. Despite typical symptoms and medical findings suggesting ischaemia, CCTA or coronarography was not performed, therefore, we suspect that a possible case of non-ST-elevation myocardial infarction was misdiagnosed. Due to recurrent symptoms, patient underwent analysis for myocardial ischaemia detection in our centre. As synergies together with subendocardial scar on CMRI suggested ischaemic origin. CCTA revealed giant aneurysm with critical stenosis in left anterior descending artery (LAD), aneurysm of RCx, and RCA occlusion.

Kawasaki disease is the second most common cause of coronary artery aneurysms in young adults.⁴ Deep medical history analysis could add to the differential diagnosis of unclear cases and rule out the consequences of undiagnosed disease in the past.^{9,11} Clinicians must have a suspicion of KD in any child (especially under 5 years) with persistent unexplained fever accompanied by any other major clinical features.^{2,7}

The key takeaway from this clinical case is that when a young person presents with clinical symptoms and laboratory changes suggesting myocardial ischaemia, coronarography, or CCTA should be performed to exclude potentially dangerous conditions at the earliest, even in the presence or suspicion of myocarditis, as it is the key point in differential diagnosis.¹³ CAA in young adults should raise suspicion of KD in the past.^{7,11}

Lead author biography



Egle Uzdavinyte Gateliene graduated from Vilnius University Faculty of Medicine where she also got her doctoral degree in 2014. Since 1998, she has been employed as a Cardiologist at the Center of Angiology and Cardiology, Vilnius University Hospital Santaros Clinic. Her scientific research interests include ischaemic heart disease, mitral valve pathology in coronary artery disease, and heart failure.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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