

Silent Kawasaki Disease Affecting Multiple Coronary Arteries in a 39-Year-Old Egyptian Woman

Hamdy Singab, MD, PhD¹; Gamal Sami, MD, PhD¹; Mahmoud Tag El Sabah, MD, PhD²

¹Department of Cardiac Surgery, Faculty of Medicine, Ain Shams University, Cairo, Egypt

²Department of Pathology, Misr University for Science and Technology, 6th of October City, Giza, Egypt

Kawasaki disease, an acute febrile illness, can cause vasculitis in the coronary arteries. It is the chief acquired cause of myocardial infarction and sudden cardiac death in infants, children, and young adults in developed countries. We report a case of chronic, silent Kawasaki disease complicated by multivessel thrombosis in a 39-year-old Egyptian woman. The patient presented with progressive, unstable angina but was otherwise asymptomatic and at negligible risk of ischemic heart disease. Coronary angiograms showed critical arterial stenosis with multiple aneurysms. During revascularization surgery, the patient's harvested left internal mammary artery was found to have occlusive lesions and aneurysmal areas that made it unfit for bypass grafting, and subsequent histopathologic examination revealed features characteristic of chronic Kawasaki disease-associated systemic vasculitis.

We think that this is only the second report of Kawasaki disease in the Arabian Mediterranean region. In addition to the patient's case, we discuss the epidemiology and management of Kawasaki disease, in hopes of increasing clinicians' awareness. (Tex Heart Inst J 2022;49(2):e207261)

Citation:

Singab H, Sami G, El Sabah MT. Silent Kawasaki disease affecting multiple coronary arteries in a 39-year-old Egyptian woman. *Tex Heart Inst J* 2022;49(2):e207261. doi: [10.14503/THIJ-20-7261](https://doi.org/10.14503/THIJ-20-7261)

Key words:

Adult; age factors; coronary artery disease/epidemiology/etiology; dilatation, pathologic; disease progression; mucocutaneous lymph node syndrome/complications/diagnosis/etiology/ethnology/surgery; treatment outcome; vasculitis

Corresponding author:

Hamdy Singab, MD, PhD, Department of Cardiac Surgery, Faculty of Medicine, Ain Shams University, 94 El Sheik Mohamed Gorab, Qubry El Quba, Cairo 11517, Egypt

E-mail:

drhamdy-ahmed@med.asu.edu.eg

© 2022 by the Texas Heart[®] Institute, Houston

Kawasaki disease (KD), an acute febrile illness with systemic vasculitis (SV), shares clinical features with several other medical conditions, so diagnosis is difficult.¹ It is rare in people older than 5 years of age and is most prevalent in Japan.² Coronary artery involvement is the most serious complication of KD. In developed countries, clinically silent KD is the chief acquired cause of myocardial infarction (MI) and sudden cardiac death in young adults.¹ The SV in KD is self-limiting, of unknown cause, and more prevalent in males.

We describe the case of a 39-year-old Egyptian woman with no cardiac risk factors whose symptoms of acute ischemic heart disease were caused by chronic KD-associated SV. In addition, we discuss the epidemiology and management of KD. We hope that our findings will help to increase physicians' awareness of the differential diagnosis in similar cases.

Case Report

A 39-year-old woman presented at our emergency department with chest discomfort, dyspnea, fatigue, and dizziness. On admission, she was afebrile and alert, with unstable vital signs (blood pressure, 90/60 mmHg; heart rate, 120 beats/min; and respiratory rate, 29 breaths/min) and no rash or conjunctivitis. She reported ischemic chest pain that radiated to her left shoulder at rest (Canadian Cardiovascular Society grade IV angina). The pain was not relieved with medication and was unrelated to emotional stress or physical exertion lasting longer than 30 minutes. She had no relevant medical or travel history, had received all childhood vaccinations, and was not taking medications. Her family medical history included diabetes, hypertension, and hyperlipidemia, but she had no personal history of these or of obesity or smoking. Chest radiographs and results of respiratory and abdominal examination revealed nothing notable. An electrocardiogram (ECG) showed ST-segment elevation in leads I, aVL, and V₃ through V₆.

The patient's cardiac enzyme levels (creatinine kinase-MB fraction, 35 IU/L; and cardiac troponin I, 0.8 ng/mL) indicated acute coronary syndrome. Her inflammatory marker levels were normal (total leukocytes, $10 \times 10^9/L$; neutrophils, $6.5 \times 10^9/L$; lymphocytes, $2.5 \times 10^9/L$; and C-reactive protein, 4 mg/L), as were her hepatic function test results (alanine aminotransferase, 25 U/L; aspartate aminotransferase, 35 U/L; alkaline phosphatase, 32 U/L; total bilirubin, 0.1 mg/dL; direct bilirubin, 0.2 mg/dL; and albumin, 4 g/L).

The patient was admitted to our cardiac service. An echocardiogram showed global hypokinesia of both ventricles, segmental wall-motion abnormalities, and impaired left ventricular function (ejection fraction, 45%). Coronary angiograms revealed multivessel isch-

emic heart disease and critical calcific stenosis of the coronary arteries that was not amenable to percutaneous coronary intervention (Fig. 1). The diagnosis was unstable angina and acute coronary syndrome necessitating emergency coronary artery bypass grafting.

Before starting cardiopulmonary bypass, we discovered that the left internal mammary artery (LIMA) was adhering tightly to the chest wall and was not patent. The harvested vessel was occluded, had several levels of obstruction and aneurysmal dilations between lesions, and was unfit for use in bypass grafting. The use of another arterial conduit was ruled out, and revascularization was achieved by using 3 saphenous vein grafts. No intraoperative or postoperative surgical complications occurred, and antiplatelet and anticoagulant therapy

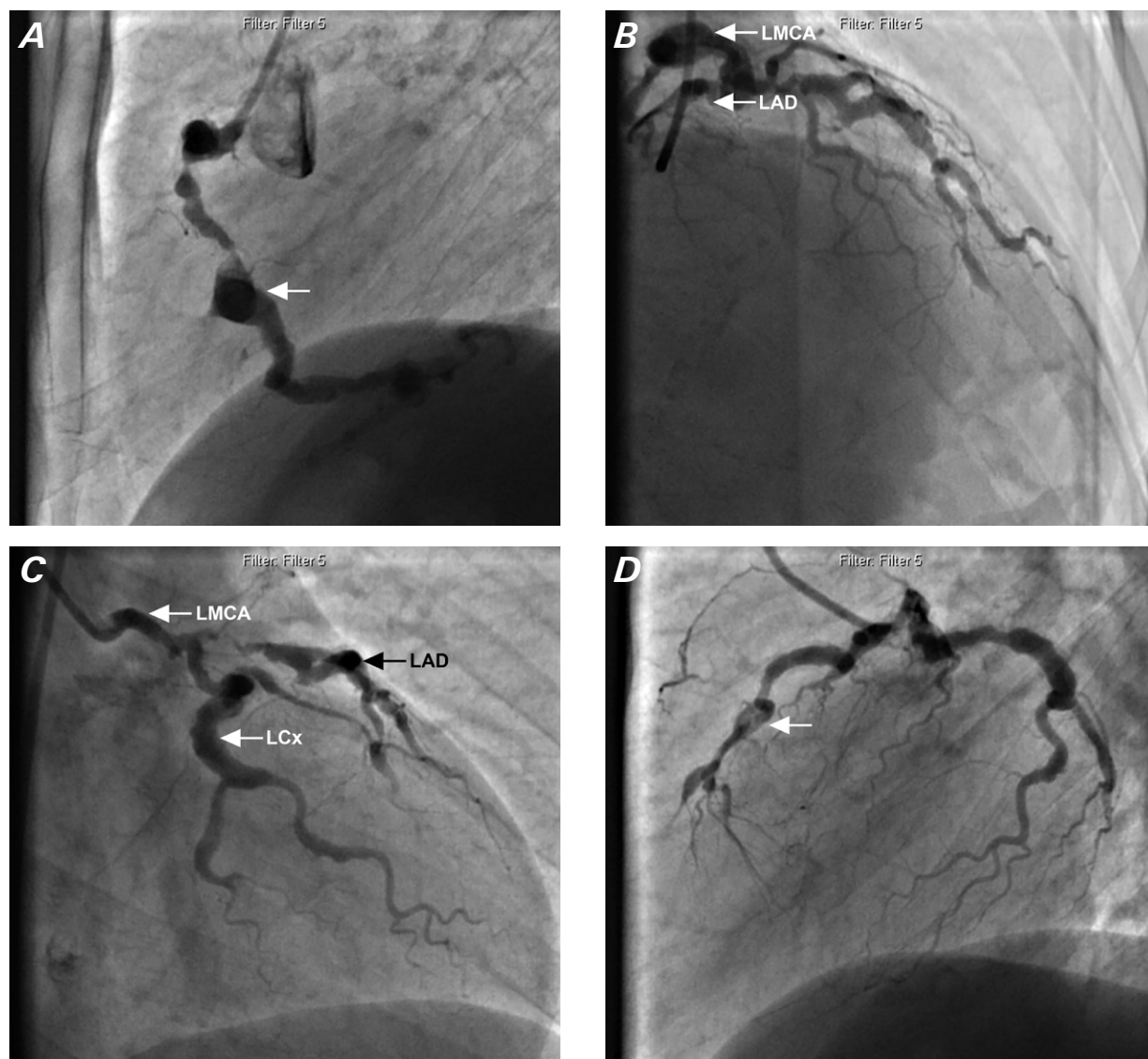


Fig. 1 Coronary angiograms. **A)** Right anterior oblique view shows critical proximal stenosis and aneurysms in the right coronary artery (arrow). Left anterior oblique caudal views show **B)** a dilated left main coronary artery (LMCA), critical stenosis of the proximal left anterior descending coronary artery (LAD) with aneurysms, and **C)** aneurysms with stenosis affecting the LMCA, proximal LAD, and proximal left circumflex coronary artery. **D)** Left anterior oblique view shows critical proximal stenosis of the LAD (arrow).

was started. She recovered uneventfully, was discharged from the hospital, and had normal follow-up echocardiographic results.

Our suspicion of KD-associated SV prompted histopathologic examination of the LIMA (Fig. 2). Disruption of the internal elastic lamina, lymphocyte infiltration of the intima, multiple recanalized luminal channels after occlusion, and remarkable arterial intimal proliferation strongly indicated the effects of KD throughout the LIMA. These findings in the presence of coronary aneurysms were all consistent with KD,¹ and our diag-

nosis was KD-associated SV with coronary artery involvement. The possibility was raised that the patient had unrecognized KD in childhood.

Discussion

Kawasaki disease is far more prevalent in children of Japanese and other Asian ancestries than in other children²; by illustration, an epidemiologic model forecasts a KD population of greater than 35,000 in Taiwan by the year 2030.³ Comparatively few cases of KD in adults

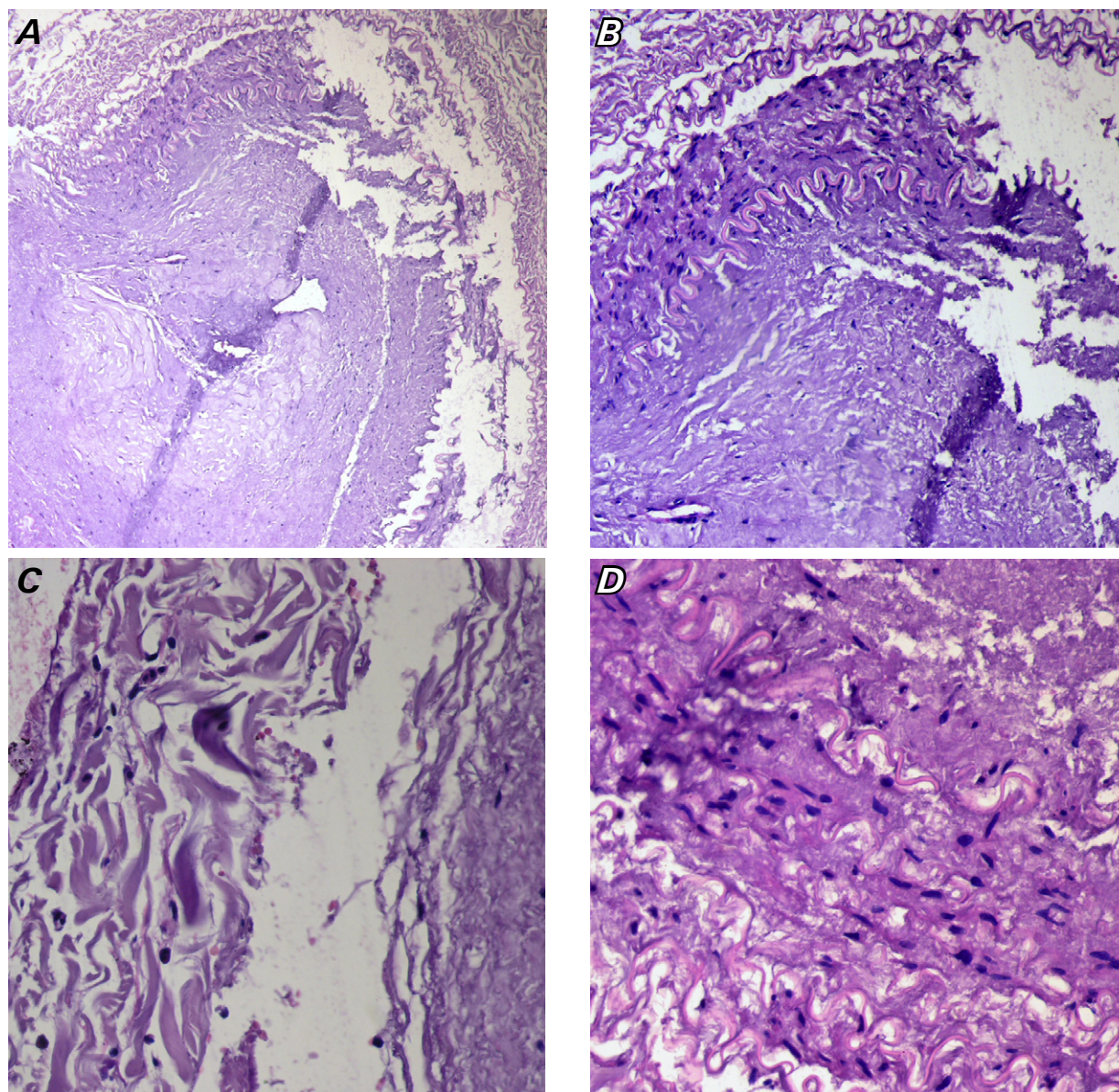


Fig. 2 Photomicrographs of the left internal mammary artery show histopathologic features suggesting Kawasaki disease systemic vasculitis. **A)** Vessel specimen shows active necrotizing polyarteritis nodosa (PAN) arteritis with residual chronic changes, a friable wall containing debris and a few neutrophils, and no inflammatory cell infiltration in the adventitia because active inflammation was in the past (H & E, orig. $\times 16$). **B)** Chronic necrotizing process in the adventitia is associated with endothelial degeneration (H & E, orig. $\times 40$). **C)** Arterial area's appearance is consistent with chronic PAN arteritis with a few inflammatory cells and no infiltration (H & E, orig. $\times 63$). **D)** The area of chronic necrotizing PAN arteritis is composed predominantly of a few neutrophils (H & E, orig. $\times 63$).

TABLE I. Clinical Differences in Presentations of Kawasaki Disease

Typical Presentation (usually pediatric)	Atypical Presentation (usually adult)
Fever ≥ 5 d with 5 major clinical presentations or Fever ≥ 5 d with 4 major clinical presentations and coronary artery aneurysms	Respiratory system changes Rhinorrhea Sore throat Dyspnea Nonproductive cough Acute respiratory distress
Major clinical presentations	Diffuse lymphadenopathy
Extremity changes (hands and feet)	Hepatic inflammation changes Right upper quadrant pain Jaundice Hepatomegaly Cholestatic hepatitis
Erythema of palms and soles	Renal changes Dysuria Mild renal failure
Desquamation of fingers and toes	Coronary artery involvement Myocardial infarction
Beau's lines (deep transverse grooves across the nails with peeling of surrounding skin)	Gastrointestinal changes Nausea Vomiting Stomach cramps Epigastric pain Dysphagia Abdominal pain or distention Diarrhea
Peripheral edema of fingers and toes	Musculoskeletal system changes Arthralgia Arthritis of big joints Back pain Myalgia Painful synovial thickening with or without effusion
Bilateral painless bulbar nonexudative conjunctivitis (painless red-eye syndrome)	Peripheral gangrene
Cervical lymphadenopathy ≥ 1.5 cm	Lethargy
Polymorphous rash	Irritability
Diffuse maculopapular rash over trunk and peripheral area	
Oropharyngeal changes	
Lip erythema, crusting, or fissuring	
Strawberry tongue	
Diffuse oropharyngeal mucositis	

have been reported, and coronary vasculitis rarely develops in adults who have silent KD. To our knowledge, the prevalence of KD among Mediterranean Arabs has not been determined, and we think that our report is only the second of KD from this region.⁴

The exact cause of KD is unknown, although infection or inappropriate immune responses to infection may be involved. A coronavirus may have a role in causing KD,⁵ and superantigen-mediated inflammation may underlie the associated SV. Landing and Larson⁶ defined Kawasaki coronary vasculitis as an aneurysmal malformation related to the increased collagen synthesis

and fibrosis that can develop in adults late after the onset of KD.

The higher incidence of KD among Japanese and other Asian populations suggests the influence of genetic and environmental factors.⁷ Vasculitis develops in up to 25% of patients and is characterized by endothelial proliferation, necrosis, and adhesion of CD4 and CD8 polymorphonuclear cells, with high levels of circulating cytokines, immunoglobulin (Ig) G, and IgM.¹ The vasculitis, which is associated with infantile polyarteritis nodosa, occurs predominantly in proximal arterial segments. It can involve multiple coronary vessels as well

as the renal, iliac, axillary, intercostal, and mammary arteries.¹

No definitive diagnostic test exists for KD, so diagnosis is by exclusion. Many cases are therefore missed and persist in clinical silence until adolescence or adulthood, when MI, congestive heart failure, or sudden death may occur.

Table I shows typical (pediatric) and atypical (adult) presentations of KD. At least 5 major signs or symptoms must be present for a diagnosis of typical KD, or 4 if accompanied by coronary artery aneurysms.¹ Laboratory findings include leukocytosis, thrombocytosis, and elevated erythrocyte sedimentation rates and C-reactive protein levels. Cardiac findings include S₄ gallop, non-specific ECG changes or mild pericardial effusions, impaired left ventricular systolic function on echocardiograms, and cardiomegaly on chest radiographs.¹ Of importance, cardiac catheterization poses distinct risks in pediatric patients who have systemic arterial damage from KD.⁸

Six days after the onset of KD, acute inflammatory vasculitis involving all arterial layers begins, resulting in severe structural damage to arterial wall components. This leads to arterial dilation and aneurysm formation around the 12th day after onset. Inflammatory cell infiltration by neutrophils and macrophages continues for up to 25 days, after which these cells gradually decrease in number. Arterial remodeling and recanalization may continue for much longer, specifically after aneurysmal thrombotic occlusion.⁹

Patients with clinically silent SV generally have no symptoms until a cardiac event occurs. The most important predictor of related MI is aneurysm size. Giant coronary artery aneurysms (≥ 8 mm or a Z score ≥ 10) are found in 5% of patients. They do not regress, rarely rupture, and almost always contain potentially occlusive thrombi. The oldest thrombi may calcify.¹

When KD is diagnosed, prompt surgical or medical treatment is essential.¹⁰ Coronary revascularization with the use of venous grafts is recommended for patients with clinically silent SV who have substantial stenosis and multiple aneurysms; cases without aneurysm can be managed by infusing IgG and IgM.¹

As children who have had KD-associated coronary artery aneurysms reach adulthood, a purposeful transition of care from the pediatric cardiologist to an appropriate, knowledgeable adult cardiologist should be planned.¹¹ Children who have had aneurysm-free KD need not undergo long-term cardiology monitoring, so a transition to adult care is not necessary.¹

Conclusion

The case of our 39-year-old patient with KD-associated SV is unusual from an epidemiologic and clinical perspective. We hope that our report improves clinicians' awareness, should similar presentations be encountered.

Published: 14 April 2022

References

1. McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association [published erratum appears in *Circulation* 2019;140(5):e181-4]. *Circulation* 2017;135(17):e927-99.
2. Uehara R, Belay ED. Epidemiology of Kawasaki disease in Asia, Europe, and the United States. *J Epidemiol* 2012;22(2):79-85.
3. Huang SK, Lin MT, Chen HC, Huang SC, Wu MH. Epidemiology of Kawasaki disease: prevalence from national database and future trends projection by system dynamics modeling. *J Pediatr* 2013;163(1):126-31.e1.
4. Nugud AA, Nugud A, Wafadari D, Abuhammour W. Kawasaki shock syndrome in an Arab female: case report of a rare manifestation and review of literature. *BMC Pediatr* 2019;19(1):295.
5. Esper F, Shapiro ED, Weibel C, Ferguson D, Landry ML, Kahn JS. Association between a novel human coronavirus and Kawasaki disease. *J Infect Dis* 2005;191(4):499-502.
6. Landing BH, Larson EJ. Pathological features of Kawasaki disease (mucocutaneous lymph node syndrome). *Am J Cardiovasc Pathol* 1987;1(2):218-29.
7. Lee KY, Han JW, Lee JS. Kawasaki disease may be a hyperimmune reaction of genetically susceptible children to variants of normal environmental flora. *Med Hypotheses* 2007;69(3):642-51.
8. Gurofsky RC, Sabharwal T, Manlhiot C, Redington AN, Benson LN, Chahal N, McCrindle BW. Arterial complications associated with cardiac catheterization in pediatric patients with a previous history of Kawasaki disease. *Catheter Cardiovasc Interv* 2009;73(6):809-13.
9. Takahashi K, Oharaseki T, Yokouchi Y. Histopathological aspects of cardiovascular lesions in Kawasaki disease. *Int J Rheum Dis* 2018;21(1):31-5.
10. Burns JC, Shike H, Gordon JB, Malhotra A, Schoenwetter M, Kawasaki T. Sequelae of Kawasaki disease in adolescents and young adults. *J Am Coll Cardiol* 1996;28(1):253-7.
11. Kovacs AH, McCrindle BW. So hard to say goodbye: transition from paediatric to adult cardiology care. *Nat Rev Cardiol* 2014;11(1):51-62.