Case in Point

Adult Kawasaki Disease

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Adult cases—such as that which occurred in this young, healthy military recruit—are rare. If left untreated, however, this disease can cause serious cardiovascular complications in patients of any age.

Kawasaki disease, also called mucocutaneous lymph node syndrome, is an acute febrile illness first reported in 1967 by Tomisaku Kawasaki.[1] Considered one of the most common vasculitides affecting children, the cardinal manifestations include fever, cervical lymphadenopathy, rash, mucositis, conjunctivitis, and extremity changes. Other less common symptoms include headache, arthralgia, diarrhea, and abdominal pain. The incidence of Kawasaki disease peaks between the ages of six months and two years, with the majority presenting at less than four years old.[1] Adult presentations of the disease are extremely rare.[2]

The disease is typically self-limiting, though complications—such as coronary artery aneurysm, myocarditis, heart failure, and arrhythmias—may develop if not treated promptly. Proper diagnosis and treatment can prevent the catastrophic complications of coronary aneurysms and sudden cardiac death.

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We present a case of Kawasaki disease in a young, healthy military recruit, as well as the novel diagnostic use of computed tomographic (CT) angiography. Additionally, we review the overall clinical presentation, treatment, and prognosis of Kawasaki disease.

INITIAL EXAM

A 20-year-old, previously healthy man presented to the emergency department at the Naval Medical Center, San Diego, CA with a two-day history of malaise, sore throat, dry lips, rash, and subjective fevers. The patient reported experiencing general myalgias and arthralgias. His vital signs showed a temperature of 102.9°F, heart rate of 107 beats per minute, blood pressure of 120/70 mm Hg, and a respiratory rate of 15 breaths per minute. Physical examination was notable for bilateral conjunctival injection; a beefy, red tongue; and an erythematous posterior oropharynx. The patient also had enlarged, tender, anterior, unilateral cervical lymphadenopathy. Inspection of his skin revealed a morbilliform rash covering his abdomen and upper and lower extremities, along with bilateral palmar erythema. Cardiac, lung, and abdominal exams, along with a baseline electrocardiogram and chest radiograph, were all normal.

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On admission, a complete blood count revealed a white blood cell (WBC) count of 14 x 10^3/μL (normal, 4 to 11 x 10^3/μL), with 93% neutrophils (normal, 37% to 80%), 2% lymphocytes (normal, 20% to 45%), and 5% monocytes (normal 0.5% to 10%). The patient's hemoglobin level of 12.4 g/dL and hematocrit of 35.7% were slightly below normal (13 to 18 g/dL and 38% to 54%, repectively). His platelet level of 2.47 x 10^3/μL was within the normal range.

Urinalysis showed positive leukocyte esterase with 15 to 20 WBCs

per high power field on microscopy. Erythrocyte sedimentation rate was 50 mm/hr with a C-reactive protein level of 14 mg/dL. Blood cultures and throat cultures were negative for abnormalities. HIV, rapid plasma reagin, cytomegalovirus immunoglobulin M, Epstein-Barr immunoglobulin M, hepatitis panel, rheumatoid factor, and antinuclear antibody tests also were negative. Transthoracic echocardiogram showed normal left ventricular function without any structural abnormalities.

The patient remained febrile over his first 24 hours of hospitalization. Due to the absence of an apparent infectious etiology, he was diagnosed with Kawasaki disease.

TREATMENT COURSE

Prompt treatment with immune globulin IV (IVIG) 130 g was initiated over eight hours, in addition to aspirin PO 1,300 mg every six hours. After the second day of hospitalization, the patient's fever curve diminished, with complete resolution of his presenting symptoms. Skin desquamation was noted on his upper and lower extremities. He was discharged after five days with a prescribed regimen of aspirin 325 mg daily.

The patient underwent routine outpatient follow-up and surveillance for the development of coronary aneurysms. Repeat echocardiography showed normal left ventricular systolic function and no evidence of coronary aneurysms (Figure 1). Using the Aquilion 16 (Toshiba America, Inc., New York, NY), serial multislice CT angiography with intravenous iodinated contrast also was performed as an adjunctive, noninvasive study of his coronary vasculature (Figure 2). After six months, the patient underwent exercise stress testing and was able to complete stage 5 of the standard Bruce protocol without experiencing chest pain and with no electrocardiographic changes. He was permitted to return to his military unit at full duty status.

ABOUT THE CONDITION

Although Kawasaki disease presented in this patient at the age of 20, it rarely occurs in adulthood. In fact, a 2003 French clinical review article refers only to 52 reported adult presentations of Kawasaki disease.[3] In children, however, it is the leading cause of acquired heart disease in North America and Japan.[4]

Kawasaki disease occurs worldwide,[4] though the incidence is greater in people of Asian descent, and the disease tends to be more prevalent in the winter and spring seasons.[1] Major epidemics have been reported to occur in both Japan and North America.[4]

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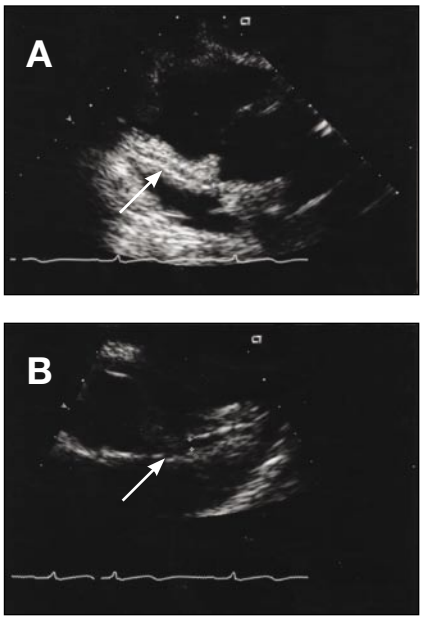

Figure 1. Echocardiograms at one-month follow-up, showing (A) a normal left anterior descending artery and (B) a normal left circumflex artery in a 20-year-old man who presented with Kawasaki disease.

Diagnosis is based on the presence of fever lasting five or more days, accompanied by four of the following five physical findings: bilateral conjunctival injection; oral mucous membrane involvement, including fissuring of the lips, injected pharynx, or "strawberry tongue"; peripheral extremity involvement, including erythema of palms or soles followed by desquamation; a truncal, polymorphous, nonvesicular, morbilliform rash; and cervical lymphadenopathy.[5]

Laboratory findings include leukocytosis with left shift, anemia, thrombocytosis, elevated erythrocyte sedimentation rate and C-reactive protein levels, and abnormal levels of serum aminotransferases.[6] Examination of the cerebrospinal fluid

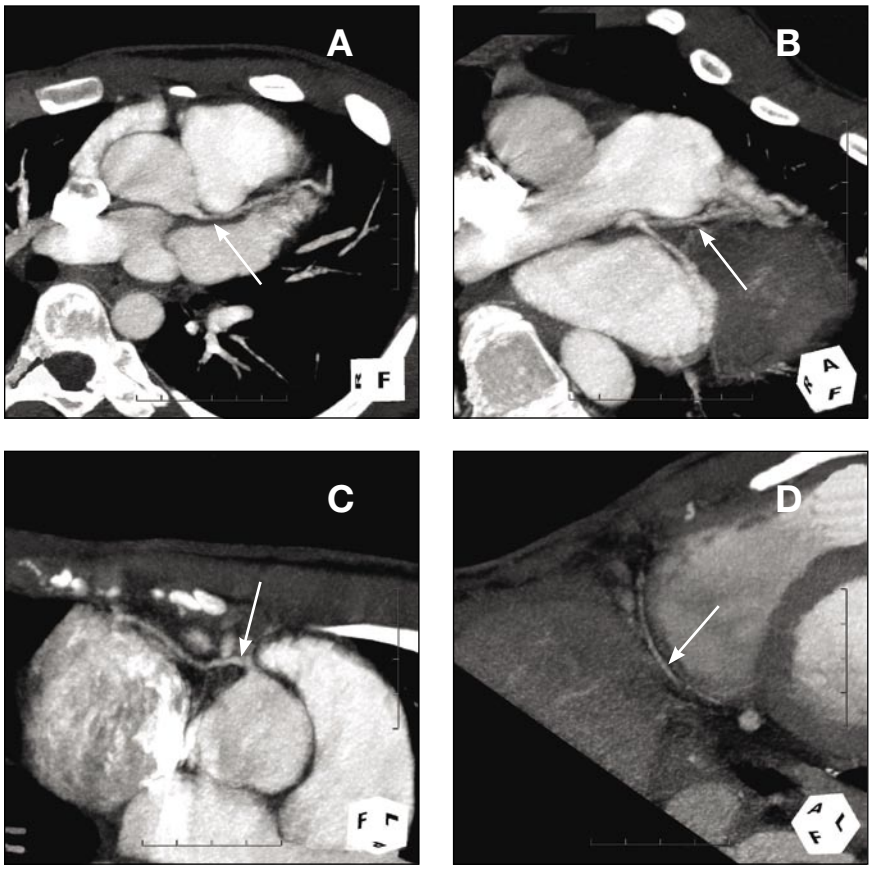

Figure 2. Computed tomographic angiogram at one-month follow-up, showing (A) a normal proximal left anterior descending artery, (B) a normal left anterior descending coronary artery, (C) a normal proximal right coronary artery, and (D) a normal right coronary artery in a 20-year-old man who presented with Kawasaki disease.

may show a pleocytosis with normal protein and glucose levels consistent with aseptic meningitis. Urine examination may yield a sterile pyuria or mild proteinuria.[2] Without treatment, the acute phase of the disease lasts an average of 12 days.

Complications of Kawasaki disease are most often cardiovascular and can range from subtle echocardiographic changes to myocarditis, coronary aneurysm formation, acute myocardial infarction, and even sudden cardiac death.[7]

Myocarditis may develop during the acute phase, depressing myocardial contractility and occasionally progressing to overt congestive heart failure.[4] On physical examination, an S_3 gallop may be auscultated. Cardiomegaly may be seen on a chest radiograph. Echocardiography may reveal a small pericardial effusion, left ventricular dilatation, or reduced left ventricular systolic function.

The mortality rate of Kawasaki disease is reported to be less than 2%. Death is typically the result of cardiac dysrhythmia or myocardial infarction.[6] Sudden cardiac death has been reported in older children and young adults after an untreated, presumed episode of Kawasaki disease in childhood.[7]

Treatment

Treatment with IVIG and high dose aspirin can improve the initial symptoms of the disease and, if given within the first 10 to 14 days of symptoms, can prevent complications and progression of this disease.

Aspirin was the first medication used in the treatment of the disease and is useful for both its anti-inflammatory and antiplatelet effects. Aspirin does not, however, decrease the incidence of coronary aneurysm.[2] The recommended dosage during the acute phase of the illness is 80 to 100 mg/kg per day in four divided doses. Therapy at this dosage should continue until the fever resolves, at which time the dosage can be decreased to 3 to 5 mg/kg per day. Aspirin use should be continued at this lowered dosage until the erythrocyte sedimentation rate and platelet counts normalize, at which time it may be discontinued. If coronary aneurysms are present, however, aspirin therapy should be continued until they regress.[8]

IVIG is administered as a single dose of 2 g/kg over eight to 12 hours.[9] As opposed to aspirin, IVIG therapy has been shown to decrease the incidence of coronary aneurysm by approximately 15% to 20%—to less than 5%. Approximately 10% of patients diagnosed with Kawasaki disease fail to defervesce with the initial IVIG therapy. In these patients, a second dose of IVIG is indicated if fever persists for longer than 36 hours.[10] Since IVIG is a pooled product from multiple donors, it is important to draw serology titers for other suspected organisms prior to its administration.

Although corticosteroids are the mainstay of therapy in most vasculitides, they are contraindicated in the treatment of Kawasaki disease because they have been shown to increase the risk of coronary aneurysm formation.[6]

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Who's at high risk for aneurysms?

Coronary artery involvement is a serious complication of Kawasaki disease. Aneurysms may develop in 20% to 25% of patients who go untreated or receive only aspirin,[6] and they usually occur from one to four weeks after the onset of illness. The prevalence is reduced to less than 5% in patients treated with IVIG within the first 10 days of symptom onset.

In 1998, the U.S. Multicenter Kawasaki Disease Study Group proposed a classification system for the purposes of identifying patients at high risk for aneurysmal formation. The system is based on the following factors: a patient's baseline hemoglobin and platelet values, baseline neutrophil and band counts, and body temperature on the day after receiving IVIG (Table).[11]

Prognosis is directly related to aneurysm size. Small- to medium-sized aneurysms (less than 8 mm in diameter) are associated with a very good prognosis and typically regress with IVIG and aspirin therapy.[12] Giant coronary aneurysms (greater than 8 mm in diameter) are associated with a poor prognosis—they are less likely to regress and may result in ischemic heart disease secondary to thrombosis and stenosis.[4]

Even in those patients whose aneurysms completely regress, a predisposition to accelerated atherosclerotic coronary artery disease is a concern.[13] The coronary artery damage incurred during the acute inflammatory stage of the disease may lead to endothelial dysfunction. Previous reports of patients whose aneurysms regressed had coronary arteries that demonstrated abnormalities in function and morphology.[14]

Echocardiography is recommended early in the acute phase and then again at six to eight weeks after disease onset.[2] If an aneurysm is found, coronary angiography is warranted. Surgical revascularization is recommended for patients with giant aneurysms or significant stenosis.[4]

Table. Parameters indicating high risk for developing coronary aneurysm as a complication of Kawasaki disease[11]

Parameter	High risk levels
Baseline white blood cell (WBC) count	• Neutrophil count greater than 50% of total WBCs • Band neutrophil count greater than 50% of total neutrophils OR • Neutrophil count greater than 75% of total WBCs • Band neutrophil count greater than 10% of total neutrophils
Baseline hemoglobin	Less than 10 mg/dL
Baseline platelets	Less than 350,000/μL
Temperature on day following immune globulin IV administration	Greater than or equal to 38°C

The role of CT angiography

Along with echocardiography, CT angiography is a noninvasive method of studying coronary anatomy. Studies using CT angiography to delineate obstructive coronary disease have shown high sensitivity, specificity, and diagnostic accuracy when compared to gold standard invasive angiography.[15] As far as we can determine, this is the first case reported in medical literature using CT angiography for surveillance of coronary aneurysm formation in Kawasaki disease.

Although quite rare in adults, Kawasaki disease should be considered in any patient who presents with fever and rash—especially since prompt therapy with IVIG decreases the serious complications of the disease. Additionally, follow-up should continue for six months to ensure early detection of accelerated atherosclerotic coronary artery disease. In this case, CT angiography proved to be a reliable, noninvasive imaging modality that might serve as an initial screening and surveillance imaging tool to monitor affected patients for cardiovascular complications of Kawasaki disease. ●

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