CASE REPORT

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Sudden Death in an Adolescent Four Years after Recovery from Mucocutaneous Lymph Node Syndrome (Kawasaki Disease)

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ABSTRACT: A case is presented of sudden death during physical activity in a 15-year-old boy with clinically inactive mucocutaneous lymph node syndrome (Kawasaki disease). At autopsy, the coronary arteries were involved by multiple aneurysms and obstructive thrombi, and the left ventricular myocardium was extensively scarred. Although Kawasaki disease most commonly occurs in infants and young children, it may be a cause of sudden death in adolescents.

KEYWORDS: pathology and biology, death, Kawasaki disease, coronary arteritis, mucocutaneous lymph node syndrome, nonatherosclerotic ischemic heart disease, sudden death

Sudden death among adolescents most commonly is due to accidents, homicide, suicide, or drug overdose [*1*]. Less commonly observed are cases caused by cardiovascular disorders such as myocarditis, hypertrophic cardiomyopathy, or congenital malformations. Herein is reported an example of sudden coronary death in a 15-year-old boy with clinically inactive mucocutaneous lymph node syndrome (Kawasaki disease).

Case Report

Clinical History

A 15-year-old boy had been admitted to a hospital 4 years previously, at age 11 years, with a 3-day history of fever and cervical lymphadenopathy. In spite of treatment with oral erythromycin and intravenous Cleocin®, the fever continued (twice daily spikes to 40.5°C), the

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adenopathy progressed to involve both axillas, a blanching maculopapular erythematous rash appeared over the trunk and extremities, and iridocyclitis developed. Tissue from a cervical lymph node biopsy showed reactive hyperplasia and negative cultures for bacteria and fungi. The patient then developed hallucinations, increasing weakness and loss of reflexes in the lower extremities, bilateral facial nerve palsies, hypocomplementemia, elevated erythrocyte sedimentation rate, and abnormal liver and renal function studies. A skin biopsy revealed perivascular leukocytic infiltrates. The diagnosis of mucocutaneous lymph node syndrome was made, and the patient was treated with prednisone. His condition improved, and he was dismissed on the 22nd hospital day. At that time, an electrocardiogram and serum creatine phosphokinase levels were normal.

The patient had slow but continued improvement of symptoms. However, nine months later, he again developed cervical adenopathy. This responded to treatment with prednisone and erythromycin, and within five months, the symptoms had abated and laboratory tests had returned to normal.

Two years after the initial illness, the boy was involved in strenuous athletic competition and lettered in football, basketball, and track. His only symptoms were recurrent urticaria and intermittent light-headedness and vertigo. He continued to have enlarged and palpable cervical lymph nodes.

Four years after the initial illness, during evaluation for urticuria, the patient described two recent episodes of severe exertional chest pain that were relieved by rest. At that time, a chest roentgenogram and electrocardiogram were normal, and the chest pain was considered to be noncardiac in origin. However, three months later, while participating in gym class, the boy experienced the sudden onset of chest pain and then collapsed. Cardiopulmonary resuscitation was begun immediately but was unsuccessful.

Autopsy Findings

The pertinent findings were limited to the heart. All of the major epicardial coronary arteries were involved by aneurysms (Fig. 1). The largest aneurysm measured 1.6 cm in diameter and involved the left main coronary artery and the proximal 2 cm of the left anterior descending and circumflex branches (Fig. 2); it was occluded by thrombus. Multiple aneurysms involved the dominant right coronary artery, and some were partially obstructed by old thrombi.

Microscopically, the structural abnormalities in the coronary aneurysms were considered to be the result of healed arteritis (Fig. 3). These changes included medial thinning or fibrotic disruption, intimal fibrosis and cellular proliferation, luminal obstruction by necrotic and partially organized thrombi, adventitial lymphoplasmacytic infiltrates, and adventitial proliferation and dilatation of vasa vasorum with extension through the media and intima and anastomoses with vascular channels in the luminal thrombi. There was no evidence of *acute* coronary arteritis or thrombosis and no evidence of active or healed arteritis in other organs.

The left ventricle was mildly dilated and hypertrophied (435-g heart) and was the site of a healed transmural inferobasal infarction with subendocardial inferolateral extension (Fig. 2). Moreover, microscopically, all regions of the left ventricle were involved by patchy interstitial fibrosis that was considered indicative of chronic myocardial ischemia. In the inferobasal subendocardium was an area of acute myocardial ischemia less than 12 h old (Fig. 4), and from this site may have originated a fatal arrhythmia.

Discussion

The mucocutaneous lymph node syndrome (Kawasaki disease) most commonly affects infants and children [*2-5*]. Melish [*5*] has reported that 50% of the cases are less than two

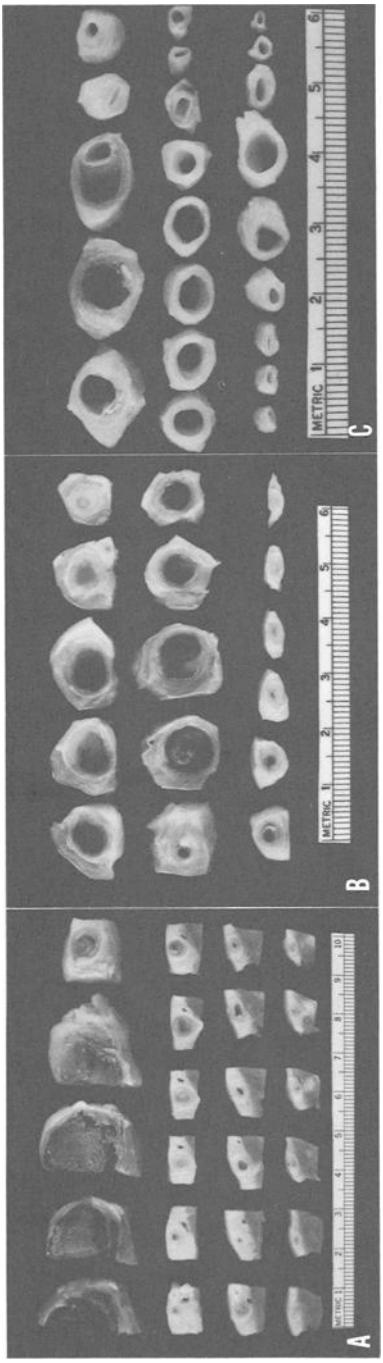

FIG. 1—*Coronary artery aneurysms with thrombotic obstruction. Gross serial sections of left anterior descending* (a), *left circumflex* (b), *and right* (c), *coronary arteries.*

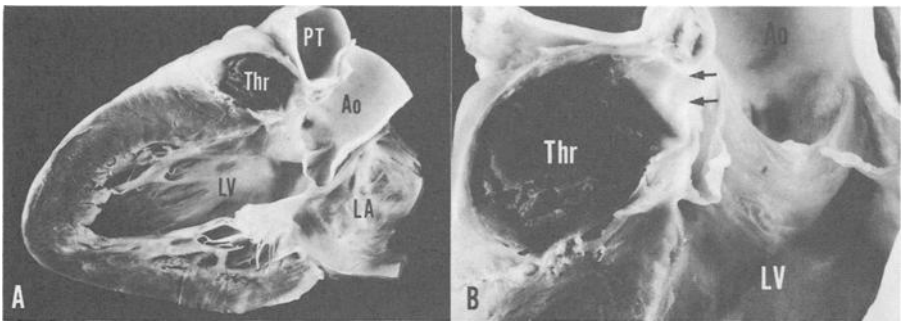

FIG. 2—*Thrombosed* (Thr) *aneurysm of left main coronary artery, with dilated left coronary ostium* (arrows); b *is close-up of* a. *Pale mottling of inferior left ventricular wall represents ischemic fibrosis.* Ao = *aorta,* LA = *left atrium,* LV = *left ventricle, and* PT = *pulmonary trunk.*

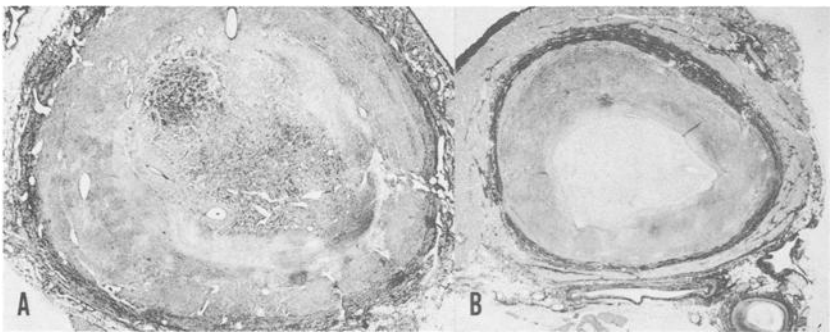

FIG. 3—*Coronary obstruction. Medial destruction, intimal fibrosis, organized luminal thrombus, and ingrowth of vasa vasorum, in left anterior descending* (a) *and circumflex* (b) *branches.* (a,b, *elastic-van Gieson.* ×*18 and 9, respectively).

years old, and 80% are less than four years old. Only rarely has the disease been reported in persons older than ten years [*5–7*]. Although the syndrome occurs predominantly in Japan [*2,3*], it is not rare in the United States [*4,5*].

The acute phase is characterized by prolonged fever, sterile conjunctivitis, diffuse oropharyngeal erythema with a strawberry tongue and fissuring or crusting of the lips, induration of the hands and feet with a desquamating erythematous rash of the palms and soles, a polymorphous truncal exanthem, and nonsuppurative cervical lymphadenopathy [*2–5*]. Subacute manifestations include urethritis, arthralgia or arthritis, aseptic meningitis, diarrhea with abdominal pain, carditis, and hepatitis [*2,3,5*]. Leukocytosis, thrombocytosis, and an elevated erythrocyte sedimentation rate typically are observed, and proteinuria and pyuria may occur [*2,5*].

Arteritis is the underlying histopathologic lesion and may involve multiple organ systems [*3,5*]. In most instances, the disease remits, without sequelae, and does not recur [*3,5*]. However, the occurrence of cardiac symptoms may be associated with serious complications [*3,5*].

The cardiac manifestations of the mucocutaneous lymph node syndrome develop in at least 20% of the cases [*5*] and include myocarditis, pericarditis, endocarditis with valvulitis, conduction system lesions, and coronary arteritis [*8–16*]. The latter may result in the forma-

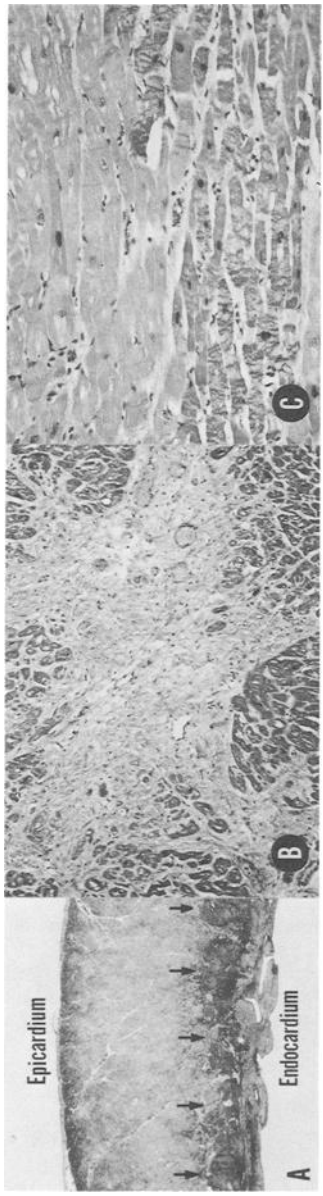

FIG. 4—*Ischemic injury of left ventricle:* (a) *old subendocardial infarction* (arrows) *of lateral wall,* (b) *microfocal patchy fibrosis of inferior wall, and* (c) *acute myocardial ischemia* (lower half) *involving inferobasal wall.* (a, *Masson trichrome,* ×*3;* b, c, *hematoxylin and eosin,* ×*90 and 180, respectively.)*

tion of coronary artery aneurysms with or without thrombotic obstruction [*3,5,8,11,12*]. Coronary aneurysms tend to develop between one and eight weeks after the onset of the acute illness [*17*] and to develop more often in infants than in older children [*13*]. Angiographically, coronary aneurysms have been demonstrated in about 20% of the cases and have been shown to regress in more than half of these [*5,8,13,14,18,19*]. Echocardiographically, regression of aneurysms has been related to their initial size; small aneurysms may disappear in several months, medium-sized aneurysms may regress in several years, and large aneurysms may persist [*17*], as in the present case. It is possible that some cases of multiple coronary artery aneurysms in adults may represent the aftermath of previous Kawasaki disease [*20*].

Thrombotic obstruction of the coronary aneurysms may produce myocardial ischemia or infarction, with resultant left ventricular wall motion abnormalities, mitral regurgitation, or sudden death [*3,5,8,11,12,21*]. Death occurs in 1 to 2% of the patients with Kawasaki disease [*4,5*] and almost invariably is associated with obstructive coronary lesions [*3,5,8, 11,12*]. Sudden death tends to occur within two months of the onset of symptoms but occasionally has been reported to occur one to eight years after diagnosis [*5,21*]. Kegel et al. [*21*] reported a case of sudden coronary death in a twelve-year-old boy who had been clinically asymptomatic for four year following the diagnosis of Kawasaki disease. Our case was similar.

The present case exemplified the usual clinical manifestations of this disease, but had two unique features. First, the patient's sudden death occurred late in the course of his illness, four years after the onset. In retrospect, his exertional chest pain probably was related to myocardial ischemia. Second, the boy was older than most patients with mucocutaneous lymph node syndrome. This case demonstrates that Kawasaki disease may be associated with unexpected sudden death several years after the acute manifestations have abated. Accordingly, the investigation of sudden death in adolescents should include a careful gross and microscopic evaluation of the coronary arteries.

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