G27 Fatal Kawasaki Disease Associated With Cardiac Rhabdomyomas in an Infant

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The purpose of this report is three-fold: to present a hitherto undescribed association (Kawasaki disease and cardiac rhabdomyoma); to illustrate an extremely rare cause of sudden death in infants (cardiac tamponade due to a ruptured Kawasaki aneurysm); and to demonstrate the co-existence of two coronary complications of Kawasaki disease: proximal coronary aneurysm (common) and nonaneurysmal stenosis (rare).

This presentation will impact the forensic community and/or humanity by presenting a hitherto undescribed association in a rare cause of death (cardiac rhabdomyomas in fatal case of Kawasaki disease due to rupture of a coronary aneurysm in an infant).

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Introduction: Kawasaki disease (KD), or mucocutaneous lymph node syndrome, is an inflammatory disease of infants and children that is often associated with a systemic vasculitis preferentially involving the coronary arteries. Although the acute illness usually resolves spontaneously, 15-30% of untreated children develop cardiovascular complications, including proximal coronary artery aneurysms and rarely coronary stenosis without aneurysm formation. Fatal complications are uncommon, occurring in an estimated 0.5% of cases. Sudden deaths are usually related to myocardial ischemia secondary to thrombosis of coronary aneurysms or coronary scarring. Among fatal cases of KD, coronary artery rupture has been reported in approximately 5% of those autopsied.

KD usually afflicts children under five years of age, and the diagnosis is based on a constellation of clinical features. The signs include fever unresponsive to antibiotics, cervical lymphadenopathy, bilateral conjunctival injection, labial and oropharyngeal mucosal erythema and fissuring, and cutaneous erythema and exanthema that often involves the palms and soles. Infants under six months of age can present with aggressive coronary vasculitis with aneurysms in the absence of the typical clinical signs.

The etiology of KD is unknown. Although a number of toxins and infectious agents have been implicated, acting as direct pathogens or via superantigen mediated autoimmunity, no constant associations have been identified. Moreover, case reports have described rare cases of KD occurring in association with other medical conditions, including congenital anomalies of the coronary arteries, Beckwith-Weidemann syndrome, and cystic fibrosis. To our knowledge, KD has not been previously reported in association with cardiac rhabdomyomas.

Cardiac rhabdomyomas are rare congenital hamartomatous tumors usually discovered in infants and children. Most are multiple, occurring anywhere in the myocardium. Rhabdomyomas of the heart are strongly associated with tuberous sclerosis. The clinical presentation and prognosis depend on the size and location of the tumors.

Clinical History: The decedent was a four-month-old white male infant who was the product of a 38 week gestation, delivered via cesarean section for maternal pre-ecclampsia. The early neonatal period was marked only by transient hyperbilirubinemia, which resolved spontaneously. The infant was healthy until approximately three months of age, when he developed a cough and intermittent fevers that reportedly responded to treatment with acetaminophen. He was seen by his primary pediatrician several times during the ensuing 2-3 weeks and diagnosed with otitis media. Despite treatment with antibiotics, fevers and cough persisted, prompting an emergency department visit. At the time, his temperature was recorded at 102.1. He had no lymphadenopathy, rash, or oral mucosal abnormalities, although redness of the eyes was noted. He was discharged home with continued antibiotics and symptomatic treatment. Ten days after being examined in the emergency department, the infant became suddenly unresponsive while being dressed by his mother. Resuscitative efforts were unsuccessful.

Autopsy Findings: The body was that of a well-developed, wellnourished white male infant who was large for the age of four months. The skin was pale and free of exanthema. The oral mucosa was free of lesions, and the conjunctivae were clear. There was no lymphadenopathy. The brain was free of tubers, and the kidneys had no masses. The pericardial sac was distended with 400 cubic centimeters of partially clotted, bright red blood. The heart was normally formed. The epicardial coronary arteries were markedly thickened and firm, most with a cord-like appearance. Focally (predominantly in the distal left obtuse marginal branches), the arteries had a beaded appearance, with areas of thickening alternating with thin, grossly normal-appearing segments. The proximal right coronary artery had a 0.8 x 0.8 x 0.7 centimeter thin

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walled aneurysm with a 0.1-0.2 centimeter rupture in the epicardial surface. Transverse sections of the thickened arterial segments demonstrated firm, yellow-white, circumferentially thickened arterial walls surrounding narrow, focally pinpoint residual lumina. The cardiac valves and chamber dimensions were normal. The myocardium was firm, red-brown, and free of gross abnormalities. A 0.2 x 0.2 x 0.2 centimeter smooth excrescent nodule was on the right ventricular aspect of the septum, just below the right ventricular outflow tract. The endocardial surfaces were otherwise unremarkable. The pulmonary artery, the aorta, and the major systemic arterial branches were free of thickening or other gross abnormalities.

Microscopic examination: Histologic sections of the coronary arteries demonstrated diffuse chronic and mixed inflammatory infiltrates involving the intima, media, and adventitia. Focally, the inflammation was accompanied by intimal hyperplasia and non-occlusive adherent luminal surface thrombi. The media was focally disrupted and obliterated. Both the media and the adventitia had large areas of sclerosis and neovascularization resembling granulation tissue. Sections of the right coronary aneurysm demonstrated attenuation of the arterial wall with destruction of the media and transmural mixed inflammation with eosinophils. The thin wall was focally disrupted, with transmural fibrin deposition at the rupture site. Myocardial histologic sections revealed multiple small subendocardial and intramural rhabdomyomas in the left and right ventricles, characterized by well demarcated foci of large, clear cells, some with spider cell morphology.

Discussion: Coronary artery aneurysm rupture due to KD and cardiac rhabdomyomas are both independently rare. To our knowledge, they have not been previously reported together. In addition, the coexistence of proximal aneurysm with diffuse non-aneurysmal stenosis in the acute phase of KD is described. The relationship, if any, between the these entities is not clear, and the rhabdomyomas may represent an incidental finding in this case of fatal KD.

Kawasaki Disease, Rhabdomyoma, Coronary Aneurysm

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