

FORENSIC SCIENCE NEWSLETTER
Forensic Pathology and Neuropathology

William A. Cox, M.D., FCAP

www.forensicjournals.com

March 15, 2016

FORENSIC PATHOLOGY

An Unusual Cause of Sudden Death in an Infant

In the January Issue of the Journal of Forensic Science an article was published entitled "A Case of Sudden Infant Death Due to Incomplete Kawasaki Disease." The cause of death for this infant was acute myocardial infarction due to platelet aggregated emboli, soon after discharge from the hospital, where he had been treated for fever and suppuration at the Bacille de Calmette et Guerin (BCG) vaccination site. Following a review of this article there are a number of key points which need to be understood in either Kawasaki Disease or Incomplete Kawasaki Disease.

Incomplete Kawasaki Disease (IKD) is a form of **Kawasaki Disease (KD)** in which all of the clinical diagnostic criteria for a diagnosis of Kawasaki Disease are not met. A diagnosis of Incomplete Kawasaki Disease should not be looked upon as a milder form of the disease nor regarded as a less potentially lethal form.

Although the cause of KD is not known, there are epidemiologic and clinical features which suggest an infectious origin. This infant had received BCG inoculation at 1.5 months of age, following which he developed suppuration at the injection site, as well as a fever (100.4°F/38°C) for 7 consecutive days requiring a hospital admission.

A genetic predisposition also appears to play a role in the genesis of KD, as evidence by the higher risk of KD in Asian children regardless of the country or residence. The infant was born in Japan.

An interesting side note, a KD-associated antigen has been described in cytoplasm inclusion bodies within ciliated bronchial epithelial cells from some acute fatal cases. These inclusions appear consistent with viral protein aggregates and support the hypothesis of a respiratory entrance for the unknown etiologic agent. Other collaborative supporting evidence for an exogenous agent is during the subacute phase of KD illness, levels of all immunoglobulins are elevated, indicating a substantive antibody response.

Although KD is a necrotizing arteritis, which synchronously involves large, medium and small arteries, it predominantly affects the medium sized arteries with a predilection for the coronary arteries. It can also involve cerebral arteries, causing a cerebral hypoperfusion, strokes or diffuse encephalopathy. The necrotizing arteritis leads to loss of vascular wall structural integrity, which results in dilatation or aneurysm formation. As a result, thrombi may form in the lumen of the affected vessel, which in turn can cause the formation of platelet embolic aggregates leading to obstruction of blood flow.

Ultimately, necrotizing arteritis can lead to fibrosis of the vascular wall accompanied by marked intimal proliferation causing arterial stenosis or occlusion.

Cardiac involvement is the most important manifestation of KD or IKD. Myocarditis occurs in most patients with acute KD, manifesting as tachycardia out to proportion to fever along with a decrease in left ventricular systolic function. Mitral regurgitation is present in approximately 25% of patients. Thus, it should not be surprising a so affected infant can develop an acute arrhythmia leading to sudden death.

The autopsy on this infant did not show dilatation or aneurysm of the coronary vessels but did show microscopic platelet aggregated emboli within a number of coronary arteries in the left ventricular wall and ventricular septum, which led to an acute myocardial infarction and sudden death.

The article does suggest early treatment with a high-dose intravenous immunoglobulin to prevent serious complications from KD or IKD. There is no evidence this infant ever received such treatment. The article also does not mention the role of high-dose aspirin in the treatment of KD or IKD, which also was not used in this infant.

Patients with acute KD and IKD should be treated with 2g/kg of intravenous gammaglobulin (IVIG) as well as high-dose aspirin (80-100 mg/kg/day divided q6h) as soon as possible, ideally, within 10 days of the onset of the disease. Such treatment can lead to resolution of the disease in 85-90% of patients. Although coronary disease occurs in 20-25% of those with KD who are treated with aspirin alone, it is only 2-4% in those treated with IVIG and aspirin within the first 10 days of the onset of the disease. Hence, recognition of the disease and giving the appropriate treatment is essential if these children are to survive.

NEUROPATHOLOGY

Epidural Glucocorticoid Injections

Several types of spinal injections, including epidural, root, and facet blocks, have been used for decades in the treatment of chronic pain (neuropathic pain) involving the neck and back. Injections of epidural corticosteroids or mixtures of corticosteroids and analgesics have in some cases been helpful in the relief of lumbar or thoracic nerve root pain, and occasionally in painful peripheral neuropathy. However, although used, the precise criteria for the use of this form of therapy has never been well established. Also, several studies do not show evidence of a beneficial effect from this form of therapy for back pain. There is no doubt however, a few patients do experience relief from discomfort albeit for only a few days to, in some cases, weeks. What is not understood, even though epidural glucocorticoid injections are commonly used for back pain, the FDA has never approved any injectable glucocorticoid product for epidural administration.

Over the past 20 years there have been at least 90 serious and sometimes fatal neurologic events including cases of paraplegia, quadriplegia, spinal cord infarctions, and strokes. Compounded glucocorticoids (glucocorticoids combined with another compound to increase the duration of action) have been associated with fungal meningitis.

In 2014, the FDA issued a requirement that all injectable glucocorticoid products carry a label cautioning that serious neurologic events, some resulting in death, have been reported with epidural injections of corticosteroids.