



G56 Sudden Death in Duchenne Muscular Dystrophy With Noncompaction of the Ventricular Myocardium: A New Cardiomyopathy or a Compensatory Regression to Fetal Myocardiogenesis?

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The goal of this presentation is to evaluate morphologic changes in the myocardium critically in order to gain insight into their role in the pathogenesis of apparent cardiomyopathies. What may appear initially to be a primary derangement in cardiac muscle (the definition of cardiomyopathy) may in fact be a secondary response to another primary insult.

This presentation will impact the forensic community and/or humanity by creating an awareness of an abnormal morphologic pattern within the myocardium and the spectrum of its association with disease states, particularly the muscular dystrophies.

Noncompaction of the ventricular myocardium (NVM) is a condition describing a rare type of cardiomyopathy believed to be due to an interruption in cardiac development. It refers specifically to persistence of the trabecular network of sponge like cardiac muscle that accompanies mid- to late embryonic development, during which time the myocardial blood supply is provided by direct diffusion from the intertrabecular spaces that communicate directly with the cardiac chambers. NVM may occur either as an isolated condition, in association with other structural heart derangements, or as part of a syndrome of anomalies. NVM has been described as a component of several muscular disorders and mitochondriopathies, including Barth syndrome, Becker muscular dystrophy, Emery-Dreifuss muscular dystrophy, myoadenylate deaminase deficiency, myotubular and metabolic myopathies, and with mutations in the G4.5 and α -dystrobrevin genes (Xq28 chromosome region), with possible X-linked inheritance. However, until quite recently, an association between NVM and Duchenne muscular dystrophy (DMD) had not been realized. This presentation describes a case of sudden death in the setting of DMD complicated by dilated cardiomyopathy (DCM) in which autopsy revealed a prominent finding of NVM; in doing so, this study attempts to explore a potential causal relationship between the DCM and NVM.

The deceased was a 21-year-old African-American man with DMD (wheelchair-bound) and DCM; a recent echocardiogram documented global hypokinesis with a left ventricular ejection fraction ranging from 20-30%. Five days before his death, he presented with an acute exacerbation of congestive heart failure and tricuspid regurgitation. On the day of his death, his caregiver called 911 for complaints of profound weakness; paramedics recorded a mean blood pressure of 65 mm Hg. He was transported to the Emergency Department and was administered crystalloid intravenous fluids, which restored his blood pressure to 91/51. However, despite being stable for the next few hours, he experienced a witnessed seizure that was followed by a thready carotid pulse, and shortly after, by pulseless electrical activity (PEA). Resuscitative efforts were initiated and were carried out for approximately 10-15 minutes but were unsuccessful and he was pronounced dead.

At autopsy, the deceased exhibited marked flexion contractures of the hips and knees and there was extensive fatty replacement of the calf and psoas muscles. There were unequivocal features of DCM, including a 550-g heart (expected for body weight: 223 g), moderate to marked left ventricular dilatation and patchy but focally confluent areas of dense white fibrosis, individually up to 0.6 cm, involving the posterior and lateral left ventricular walls. In addition, there was marked exaggeration of the trabeculae carneae within the left ventricular chamber, with numerous anastomosing trabeculae that imparted a distinctly "spongy" appearance, particularly at the left ventricular apex. Microscopic cardiac examination revealed confluent replacement fibrosis and fatty ingrowth within the compact outer myocardial half, while the inner half consisted of an anastomosing network of trabeculae forming irregular "staghorn"-like spaces. The cause of death was certified as complications of DCM (associated with NVM) due to DMD.

In late 2005, NVM was described for the first time in a patient with DMD by a group of investigators in Vienna, Austria. They proposed that in the setting of DMD, replacement fibrosis of the compact myocardium following myocyte loss is the principal pathologic finding and accounts for the clinical spectrum of ventricular dysfunction in these patients, while NVM represents a compensatory response generated by a failing heart to regenerate its nonfunctional myocardium. The case presented represents the second reported association between NVM and DMD. This study proposes that the precise molecular signals governing the events in embryonic myocardiogenesis may be recapitulated in certain clinical settings, such as this one; identification and isolation of such signals would corroborate this hypothesis and enhance the understanding of such events.

Noncompaction of the Ventricular Myocardium, Dilated Cardiomyopathy, Duchenne Muscular Dystrophy