Sudden Death and Isolated Right Ventricular Noncompaction Cardiomyopathy

Report of 2 Autopsied Adult Cases

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Abstract: A predominantly right ventricular variant of isolated noncompaction cardiomyopathy is a potentially lethal disease entity, which only recently has become recognized in the clinical and cardiac imaging literature. There are currently few established morphologic criteria for the diagnosis other than right ventricular dilation and presence of excessive regional trabeculation. To date, there have been no autopsy reports of cases following either clinical diagnosis or sudden death. We report 2 adult cases of sudden unexpected death in which unexplained right ventricular dilation and prominent apical hypertrabeculation were the principal findings. The gross and microscopic results suggest pathological similarities between, or coexistence of, right ventricular noncompaction and arrhythmogenic right ventricular cardiomyopathies.

Key Words: right ventricular noncompaction, cardiomyopathy, sudden death, forensic autopsy

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During the fifth to eighth week of fetal life, the intertrabecular spaces of the developing heart are obliterated, and the ventricular myocardium undergoes compaction from apex to base.[1] Isolated myocardial noncompaction cardiomyopathy (NCCM) is defined by arrest of the process of compaction of the spongiotic trabecular muscle layer with resulting hypertrabeculation and failure to obliterate intertrabecular recesses.[1] Although the left ventricle is the usual site of involvement, biventricular involvement is also common.[2–6] In children, NCCM is the third most common cardiomyopathy after dilated and hypertrophic forms.[7] Left ventricular NCCM (LV-NCCM) has an incidence of between 0.01% and 0.25% in adults.[8] The clinical manifestations range from asymptomatic to progressive congestive heart failure, arrhythmias, thromboembolic events, and sudden cardiac death.[1,9,10] Although LV-NCCM is well known, there are relatively few clinical reports of isolated or predominant right ventricular noncompaction (RV-NCCM) and, to our knowledge, no autopsy reports following sudden unexpected death.

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MATERIALS AND METHODS

In each case, a complete autopsy was performed, including toxicological examination. The hearts were examined after en bloc fixation in formalin. If the coronary arteries were calcified, they were dissected and decalcified before sectioning.

CASE REPORTS

Case 1

A 46-year-old white woman was found unresponsive while incarcerated. Examination revealed absence of a pulse, and immediate resuscitation was begun. Emergency medical service arrived 15 minutes later and transported the patient to the nearest hospital, where she was pronounced dead upon arrival. Two days prior, multiple bruises were noticed on her right deltoid area that she attributed to a fall secondary to being on crutches following a tibial fracture a month ago. The events that led to her unconsciousness were unwitnessed. The case was reported to the county medical examiner, who ordered an autopsy. Medical history included tobacco use, chronic obstructive pulmonary disease, pulmonary hypertension, nonspecific elevations of troponin, anemia, pneumonia, tachycardia, and remote resection of an esophageal adenocarcinoma. An echocardiography study performed 2 months before death reported a dilated, hypokinetic right ventricle with normally contracting apex and a normal-size but D-shaped left ventricle. Toxicological analysis performed on postmortem femoral blood, urine, and gastric contents was negative for alcohol and drugs. Autopsy examination revealed mild chronic respiratory bronchiolitis, normal coronary arteries, and unremarkable brain examination. The heart weighed 280 g. The 10-mm-thick left ventricle, left atrium, and mitral valve were all normal (Fig. 1A). The right atrium was dilated with mildly hypertrophic pectinate muscles. The tricuspid valve was normal, but the right ventricle anterior papillary muscle and an enlarged posterior papillary muscle were attached to a mass of trabecular muscle that filled the apex (Fig. 1B). The proximal right ventricular cavity and the infundibulum were dilated and externally demarcated from the apical region by a narrow band-like indentation running diagonally across the anterior wall. The 3- to 4-mm-thick anterior and posterior walls abruptly thinned at the apex and were focally inverted at the attachments to trabeculi, allowing cavitary protrusions between the trabecular attachment sites (Fig. 1C). The infundibulum had prominent trabecular musculature. Microscopic sections from the left ventricular apex also contained deep intertrabecular recesses. Sections of the right ventricle had extensive subendocardial hyperacute contraction band necrosis. Several trabecular muscles had centrally located microfoci of healing necrosis. The apical compact muscle wall was thin and largely replaced by fat, a histology closely resembling that of the fatty infiltrative form of arrhythmogenic right ventricular cardiomyopathy (ARVC). The presence of deep intertrabecular recesses at the left ventricle apex

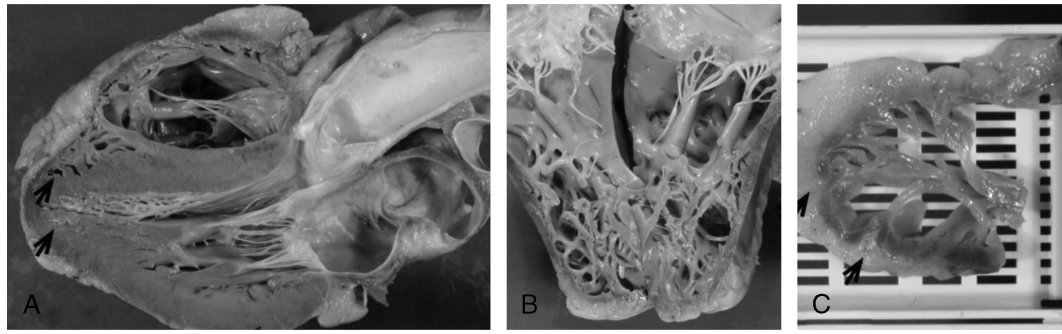

FIGURE 1. A, Long-axis section: there is an indentation of the anterior right ventricle wall at the moderator band and prominent hypertrabeculation of the right ventricle apex (upper arrow). The base of the posterior papillary muscle of the left ventricle extends to the left ventricle apex (lower arrow). B, The right ventricle posterior wall is opened to expose the tricuspid valve and the highly trabeculated apical segment. C, A long-axis section of the right ventricle apex has attenuation of the compact wall and in-foldings of the trabecular muscle layer (arrows).

implied a minor degree of biventricular involvement. Although in the present case pulmonary hypertension could not be excluded, the major cardiac pathology was predominant RV-NCCM with apical compact wall thinning and replacement by fat. The latter histology overlaps that of or is similar to ARVC. The cause of death was ventricular noncompaction of the heart.

Case 2

A 52-year-old white woman with medical history of hypertension and cerebrovascular disease was discovered lying unresponsive at home. Resuscitation efforts were unsuccessful. Postmortem toxicological examination of blood did not detect ethanol or drugs. The relevant autopsy findings were limited to the heart. The heart weighed 410 g. The epicardium had fat covering the entire right ventricular anterior surface but little of posterior surface. The right atrium and right ventricle were enlarged (Fig. 2A). The coronary artery distribution was weakly right dominant, and there was minimal atherosclerotic stenosis. The right atrium was enlarged by pectinate muscle hypertrophy. There was a shallow, leftward-bulging, 20-mm-diameter aneurysm of the fossa ovalis, without endocardial thrombosis. The tricuspid valve was diffusely opaque and mildly thickened and had minimally hooded leaflets. The nondilated left atrium measured 4.0 × 4.5 cm. The mitral valve posterior leaflet measured a normal 10 mm in breadth, but had mild hooding. The left ventricle midcavity diameter was 35 mm with a circumferential wall thicknesses of 12 to 13 mm. Short-axis sections of the right ventricle contained dense, spongy, lattice-like trabecular muscle filling the lower middle and apical segments (Fig. 2B). The right ventricular wall thickness averaged 2 mm, but the myocardium was obscured by fatty infiltration in regions of the posterior and anterior walls. Microscopic sections of the left ventricle had only a single small focus of remote scarring near the posterior left ventricle papillary muscle base. The right ventricle sections had diffusely distributed patchy, fatty infiltration with sparing of the trabecular muscles. The lateral wall of the right ventricle had near total replacement of compact myocardium by adipose tissue. The histology was consistent with fatty infiltrative ARVC (Fig. 2C). The prominent right ventricular hypertrabeculation/noncompaction associated with extensive fatty infiltrative replacement of the attenuated compact myocardium was diagnosed as isolated right ventricular cardiomyopathy with features of arrhythmogenic and noncompaction cardiomyopathies.

DISCUSSION

It is difficult to attribute sudden unexpected cardiac death to a genetic cardiomyopathy when the genotypic and phenotypic variations of the cardiomyopathy are poorly defined. Right ventricular involvement commonly occurs in cases of LV-NCCM, but the initial diagnosis is made using criteria developed on the basis of left ventricular involvement.[11] Isolated

FIGURE 2. A, Posterior view of the heart: the right atrium and ventricle are enlarged. B, A short-axis section taken apical to the papillary muscle bases has a complex spongy meshwork of trabeculi filling the dilated right ventricle cavity. There is extensive focally severe fatty infiltration with replacement of the attenuated compact wall. C, Hematoxylin-eosin–stained section of the right ventricle apex: a thick fat pad overlies the extensive fatty replacement of the compact wall, but the trabecular muscle layer is preserved.

NCCM primarily involving the right ventricle is rarely reported, but this may be due to the normal variable trabeculation of the right ventricle, which has precluded the establishment of anatomic criteria for diagnosis. Despite the absence of well-defined anatomic criteria, right ventricular hypertrabeculation cardiomyopathy has become recognized as a distinct entity on the basis of clinical imaging studies. In 2008, Song[10] published the first clinical case report using echocardiography and magnetic resonance imaging to describe a syndrome of combined right ventricular hypertrabeculation/noncompaction associated with arrhythmogenic ventricular cardiomyopathy. The description was of a 2-layered myocardium with prominent apical trabeculations and deep intertrabecular recesses. In 2009, Zhang et al[9] reviewed the literature and submitted an additional case of isolated RV-NCCM in a 23-year-old woman diagnosed by cardiac magnetic resonance imaging and angiograms on the basis of a ratio of trabecular to compact myocardium of more than 3. Fazio et al[12] in 2010 reported magnetic resonance results of 2 additional cases, one of which died suddenly, and suggested that a diagnosis can be made only when the spongy-to-compact myocardial ratio is greater than 2 in association with dilatation of the right ventricle. Song[13] in 2011 reported a 69-year-old man with right ventricular dyskinesia and diagnosed the case by 3-dimensional echocardiography on the basis of right ventricle wall thickness and deep intertrabecular recesses as isolated right ventricular noncompaction. Song discussed the lack of established imaging criteria for diagnosis of right ventricular noncompaction and suggested that the identification of true trabeculi, deep intertrabecular recesses, and a thin compact layer are necessary to confirm the diagnosis. In the present report, the cardiac abnormalities encountered at autopsy closely mirror those described in these clinical reports.

Predominant right ventricular noncompaction was present in the 2 cases comprising this report, but neither can be viewed as truly "isolated" examples of RV-NCCM. The coexistence of biventricular involvement, right ventricle fatty infiltration, and attenuation of the compact wall in areas of noncompaction is a combination of anatomic features consistent with clinical reports pointing out similar features of noncompaction and arrhythmogenic cardiomyopathies. We are aware of only 1 previous report of a patient diagnosed with ARVC whose heart had a prominent constriction crossing the right ventricle anterior wall at the level of the moderator band.[14] Arrhythmogenic right ventricular cardiomyopathy has been described as 2 subtypes: the infiltrative type, seen as a lattice-like fatty infiltration with intervening normal residual cardiomyocytes, findings that were noticed in both the hearts; the other subtype is the cardiomyopathic ARVC, with massive fatty replacement of the myocardium with associated myocyte hypertrophy and myofibril loss.[15] Some clinical reports have proposed that NCCM and ARVC may coexist as a distinct clinical syndrome.[10,16,17] Although noncompaction during fetal development implies underdevelopment of the compact muscle layer of the ventricular wall, the pathophysiologic effects of hypertrabeculation on ventricular wall morphogenesis in later life are unknown. Although the genetic and pathogenetic mechanisms may differ, the common anatomic features of right ventricular dilation in the adult, attenuation of the compact myocardial wall, and the imposition of fat may preclude unequivocal distinction of noncompaction and arrhythmogenic cardiomyopathies at autopsy. Also, the presence of microinfarcts within the trabeculi, as seen in the first case, suggests impaired trabecular blood flow and ischemia, a possible mechanism of arrhythmia.

In conclusion, it is yet to be resolved as to whether isolated RV-NCCM occurs as a distinctive pathological diagnosis or only in association with ARVC or with obligatory biventricular involvement.[8] In any case, the literature suggests an association of RV-NCCM with cardiac arrhythmias and sudden death. Cases of sudden cardiac death that at autopsy have insignificant coronary disease and unexplained right ventricular dilation warrant suspicion of a cardiomyopathy. If right apical hypertrabeculation, compact wall attenuation, and/or deep intertrabecular recesses into the right side of the interventricular septum are present, the differential diagnosis would include isolated RV-NCCM, regardless of whether there are additional features of ARVC. Further investigations will be necessary to establish diagnostic criteria and determine whether isolated right ventricle hypertrabeculation per se exists as a cause of sudden unexpected death, independent of ARVC or LV-NCCM.

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