

Atrioventricular Block Pathology in Cardiomyopathy by Desmin Deposition

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Generally, restrictive cardiomyopathy due to desmin deposition is characterized by restriction to ventricular diastolic filling and different degrees of atrioventricular block (AVB). In this report, we describe the pathological changes of the cardiac conduction system related to AVB. The sinus node, the compact node, and the penetrating bundle (bundle of His) had no abnormalities, however, there was extensive fibrosis of the terminal portions of the branching bundle and the beginning of the left and right bundles at the top of the ventricular septum. The pathogenesis of this fibrous replacement is probably the same that leads to extensive fibrosis of the working ventricular myocardium, and remains to be elucidated.

Introduction

Restrictive cardiomyopathy by deposition of desmin is a rare genetic disease characterized by deposition of electron-dense granulo-filamentous material immunoreactive for desmin in the cytoplasm of cardiomyocytes. Besides the restriction to diastolic ventricular filling, patients usually present clinical or subclinical skeletal myopathy and varying degrees of atrioventricular block (AVB)¹⁻³. Although several cases of the disease have been previously reported, the morphological basis for the development of AVB has not been studied.

In our study, we describe the pathological findings of the cardiac conduction system in a patient who died due to restrictive cardiomyopathy due to deposition of desmin with AVB.

Case report

After recurrent episodes of syncope, a 13-year-old boy was diagnosed with complete AVB (Figure 1A) and treated with implantation of a two-chamber pacemaker. There was no family history of cardiomyopathy or skeletal muscle

Keywords

Atrioventricular block/pathology, restrictive cardiomyopathy, desmin, heart conduction system.

disorders. The patient remained asymptomatic for 7 years, after which he developed symptoms and signs of progressive heart failure. At that time, the electrocardiogram showed atrial flutter and normal activity of the pacemaker (Figure 1B). The patient was treated with medication for heart failure and showed clinical improvement.

At 25 years of age, the patient presented decompensated heart failure and was admitted into the hospital for investigation and treatment. On that occasion, transthoracic echocardiography showed enlarged atria, especially the right atrium, and tricuspid valve insufficiency. The left ventricle had normal volume, moderated hypertrophy, preserved systolic function and restrictive diastolic dysfunction. The right ventricle presented dilation, hypertrophy and moderate hypokinesia. Pulmonary artery systolic pressure was estimated at 46 mmHg. Pulmonary angiography was negative for pulmonary embolism. The clinical diagnosis was restrictive cardiomyopathy with atrioventricular block, probably secondary to infiltrative myocardial disease. There was an attempt to perform right ventricular endomyocardial biopsy, but it was not possible to remove enough fragments for analysis. Despite the drug therapy for heart failure, the patient died due to cardiogenic shock, and an autopsy was asked to clarify the etiology of the heart disease.

The heart weighed 392 g. There was a moderate atrial increase, especially the right atrium. The ventricles had a normal volume and the myocardium was firm. Left and right ventricular thickness was 11 and 4 mm, respectively. The pacemaker wires were correctly impacted; one on the right atrial wall and the other in the right ventricular apex. Histological examination revealed diffuse hypertrophy of the cardiomyocytes, which showed foci of cytoplasmic vacuolar degeneration and disarray. There was extensive fibrosis of the myocardium, with bundles of collagen fibers surrounding groups of cardiomyocytes, especially in the middle-wall of the left ventricle. Ultrastructural examination (transmission electron microscopy) revealed extensive depositions of electron-dense granulo-filamentous material in the cytoplasm of the cardiomyocytes (Figure 2A). Immunohistochemical test for desmin revealed irregular granular positivity in the cytoplasm of cardiomyocytes consistently with the depositions observed by electron microscopy (Figure 2B). The pathological diagnosis was restrictive cardiomyopathy due to desmin deposition.

The junction of the superior vena cava and the right atrium in the topography of the sinus node and the atrioventricular junctional area were removed en bloc, sectioned serially and processed for routine histological inclusion in paraffin. Serial sections at 4 μ m of thickness of each paraffin block

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Figure 1 - Electrocardiograms: AVB at age 13 (A) and atrial flutter and normal activity of the pacemaker at age 20 (B).

were stained with hematoxylin-eosin or Masson's trichrome. The sinus node showed normal histological appearance with prominent fibrous matrix and areas of fat infiltration (Figure 2C). The compact atrioventricular node and the penetrating bundle (bundle of His) had no abnormalities (Figure 2D). There was extensive fibrosis in the terminal portion of the branching bundle (Figure 2E) and the top of the ventricular septum, in the projection of initial segments of the left and right bundles (Figure 2F), with interruption of the continuity of the axis of atrioventricular conduction. There was no calcification of cardiac structures related to the area of the atrioventricular junction or obstructive coronary disease.

Discussion

Restrictive cardiomyopathy by deposition of desmin is usually associated with electrophysiological abnormalities of

cardiac stimulus conduction, particularly different degrees of AVB¹⁻³. Ventricular tachycardia may also occur in this disease. A case of prophylactic implantation of cardiac defibrillator has been previously reported⁴. Although ventricular arrhythmias are probably related to extensive myocardial fibrosis, the basis of AVB morphology is uncertain; it has been previously described in only one case: focal calcification of the bundle of His in a 57-year-old patient with severe skeletal myopathy and complete AVB without cardiac failure⁵.

The complete AVB is usually associated with anatomical interruption of the atrioventricular conduction system and may occur in various diseases. In a series of 200 patients who died from complete AVB and underwent autopsy, the most common site of interruption was the branching bundle or the initial segment of the left and right bundles, accounting for 66% of the cases^{6,7}. The interruption of the continuity of the axis of the ventricular conduction system with fibrous

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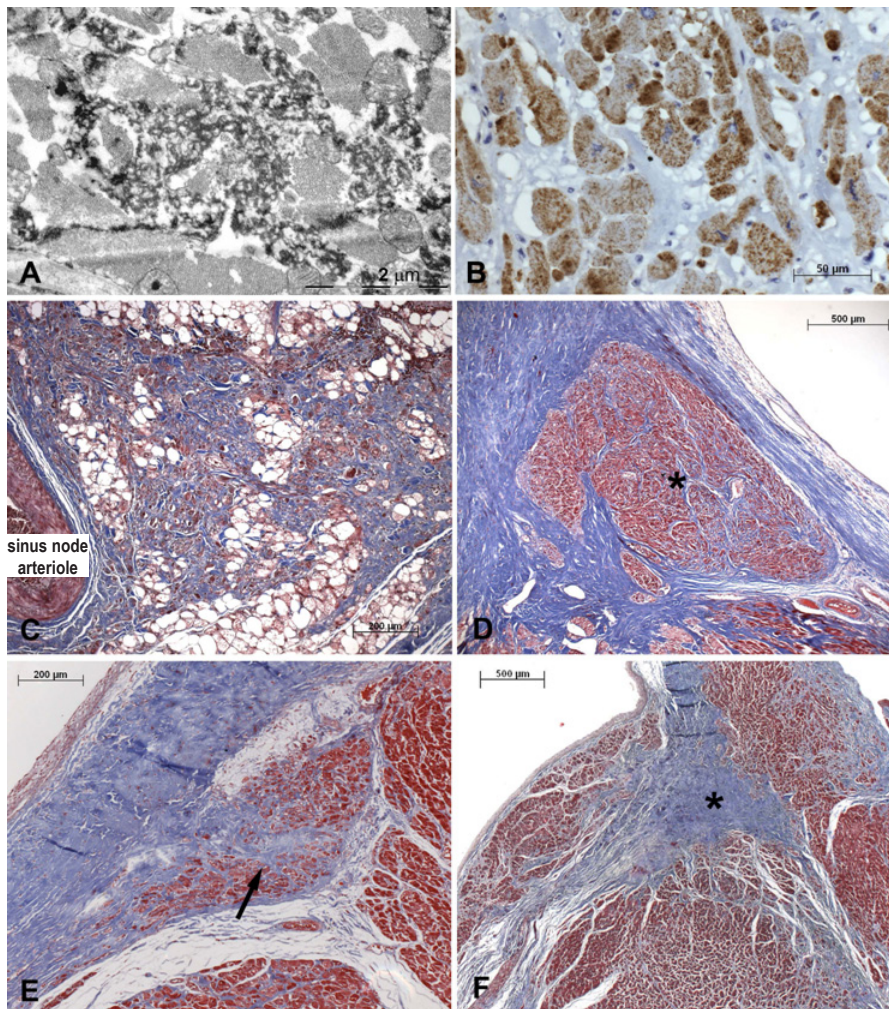


Figure 2 - Myocardial electron microscopy revealed deposition of electron-dense granulo-filamentous material among the myofibrils of cardiomyocytes (A). Immunohistochemistry for desmin showed irregular positivity in the cytoplasm of cardiomyocytes (B). Masson's trichrome staining in serial sections of the conduction system showed normal aspect of the sinus node (C) and the penetrating bundle (D, asterisk), and fibrosis of the terminal portion of the branching bundle (E, arrow) and the top of the ventricular septum in the projection of the initial segments of the left and right bundles (F, asterisk).

replacement is generally acquired and rarely congenital. When it is acquired, it may either have an ischemic origin due to obstructive coronary artery disease or be idiopathic. The latter is the most common form of complete AVB in adults^{6,7}.

In our report, we characterize the site and the morphological changes that substantiate the AVB in this case of restrictive cardiomyopathy due to desmin deposition, i.e., fibrosis of the terminal portion of the branching bundle and the initial portion of the left and right bundles at the top of the ventricular septum. The pathogenesis of this fibrous replacement is probably the same that leads to extensive fibrosis of the working ventricular myocardium, and remains to be elucidated.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any post-graduation program.

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