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[JACC Case Rep.](#) 2021 Nov 3; 3(15): 1674–1676.

PMCID: PMC8571792

Published online 2021 Nov 3. doi: [10.1016/j.jaccas.2021.09.002](https://doi.org/10.1016/j.jaccas.2021.09.002)

PMID: [34766016](https://pubmed.ncbi.nlm.nih.gov/34766016/)

Intraventricular Septation in the Context of Dilated Cardiomyopathy Associated With *TTN* Mutation

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Received 2021 Jun 1; Revised 2021 Aug 17; Accepted 2021 Sep 2.

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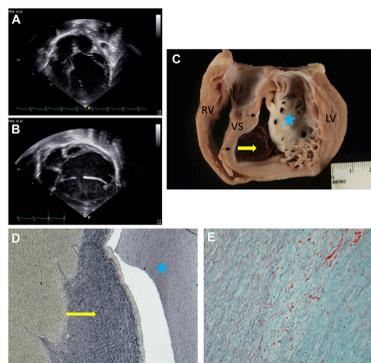
Abstract

A 6-month-old infant boy presented with symptomatic heart failure. Dilated cardiomyopathy was found in association with a mutation in *TTN*. Structural heart disease included novel septation of the left ventricle with a fenestrated membrane resulting from aberrant congenital mitral valve apparatus formation. (**Level of Difficulty: Advanced.**)

Key Words: congenital heart disease, dilated cardiomyopathy, endocardial fibroelastosis, intraventricular septation, titin gene

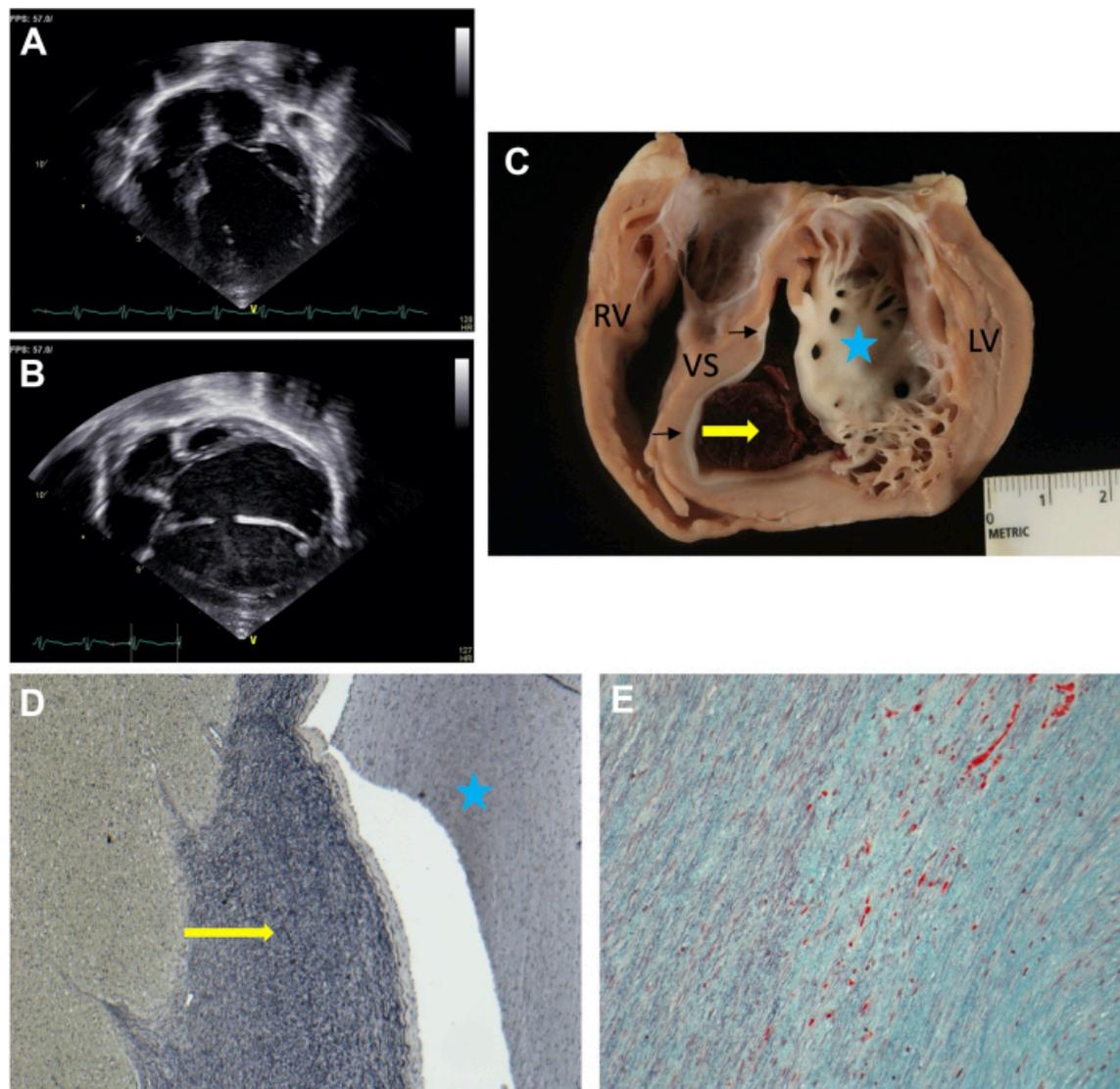
Abbreviations and Acronyms: BP, blood pressure; EFE, endocardial fibroelastosis; LV, left ventricle; *TTN*, titin gene

Central Illustration



Case Presentation

A previously healthy 6-month-old full-term infant boy was brought to an emergency department with a 2-day history of vomiting, pallor, and poor feeding. Upon transfer to a tertiary pediatric referral center, his blood pressure (BP) was 85/39 mmHg, pulse 145 beats/min, respirations 36/min, weight 6.4 kg (1st percentile), and length 69 cm (50th percentile). Significant physical examination findings included a gallop rhythm, hepatomegaly, and low-set ears with fatty and thickened helices. A chest x-ray demonstrated massive cardiomegaly with increased pulmonary vascular markings ([Supplemental Figure 1](#)). The presenting electrocardiogram demonstrated normal sinus rhythm, nonspecific interventricular block, right ventricular hypertrophy, and T-wave inversion in the inferior leads ([Supplemental Figure 2](#)). An echocardiogram demonstrated dilated cardiomyopathy with severe left ventricular dilation, systolic dysfunction ([Supplemental Tables 1 to 3](#)), and the unique finding of a septating band within the left ventricle (LV) ([Figures 1A and 1B](#)). This was further characterized as a multiply fenestrated membrane. Multiple left ventricular thrombi were noted, both within the true left ventricular cavity and within the false chamber. Genetic studies indicated a titin (*TTN*) mutation-associated dilated cardiomyopathy (1G) ([Supplemental Table 4](#)).



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Figure 1

Novel Intraventricular Septation in Multiple Imaging Modalities

(A) 2-dimensional (2D) image by transthoracic echocardiogram in the 4-chamber view, demonstrating severe dilation of the left ventricle with the mitral valve apparatus and intraventricular septation seen. (B) 2D image by transthoracic echocardiogram in the subcostal coronal view, demonstrating the fenestrated left ventricular septation within the severely dilated left ventricle. (C) Cross-section on gross examination of the explanted heart. Corresponding plane of dissection demonstrating left ventricle (LV), right ventricle (RV), and ventricular septum (VS) with endocardial fibroelastosis (EFE) (**black arrows**) and “apron” (**blue star**). Apical mural thrombus is also present (**yellow arrow**). (D) Microscopic section of the ventricular myocardium on Verhoeff-Van Gieson stain at 10× magnification, demonstrating EFE of VS highlighted as black region (**yellow arrow**). (E) Microscopic cross-section of the delaminated ventricular apron on Movat stain at 20× magnification, demonstrating thin strands of elastin (**black**) with prominent sea-green to blue myxomatous stroma.

Despite maximal pharmacologic therapy for systolic failure, left ventricular ejection fraction remained depressed, and orthotopic cardiac transplantation was performed. Gross pathologic examination of the native explanted heart revealed severe biventricular dilation and hypertrophy, as well as interstitial fibrosis with myocytolysis. Within the LV, there was endocardial fibroelastosis with a “sheetlike” partition consisting of partially fenestrated fibromyxomatous tissue that was intertwined with and extended from the chordae tendineae of the mitral valve to an area of noncompaction-like change of the left ventricular endomyocardium (Figure 1C). Histologic examination confirmed endocardial fibroelastosis (EFE) (Figures 1D and 1E). In addition, features of a dilated cardiomyopathy, including subendocardial myocytolysis, interstitial fibrosis, and T cell (CD3+) lymphocyte infiltration were observed. The septating band itself consisted of valve tissue components, including fibromyxomatous stroma and minimal collagen with decreased amounts of elastin relative to normal chordae tendineae or valve leaflets.

Discussion

Within current published reports, this case is not consistent with typical classifications of intraventricular findings such as intramyocardial delamination, congenital diverticula, congenital aneurysms, or EFE. Failure of myocardial delamination has been implicated in congenital valvular conditions such as Ebstein’s anomaly but does not result in defects containing multiple myocardial layers (1). Congenital LV diverticula and aneurysms involve dilations of the left ventricle wall that contain all three layers of the ventricular wall contracting synchronously within the heart, which was not observed in this case (2). The pathologic specimen contained features of EFE, which is generally limited to the endocardial layer but was observed here as a separate intracavity sheet or septation (3).

The case presentation, echocardiographic imaging, and gross pathologic changes fail to meet the diagnostic criteria for any known condition. The presence of EFE raises an interesting question about the functional consequences of this finding within the dilated cardiomyopathy diagnosis. Early identification of significant anatomic abnormalities, as observed in this case, may have an impact on clinical management. These patients may be at greater risk for medical treatment failure and require early cardiac transplantation.

Funding Support and Author Disclosures

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Footnotes

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors’ institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

Appendix

For supplemental figures and tables, please see the online version of this paper.

Appendix

Supplemental Figures 1 and 2 and Supplemental Tables 1–4:

[Click here to view](#). (5.4M, docx)

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