Hamartomas of mature cardiac myocytes

Shaji C. Menon¹*, Dylan V. Miller², Allison K. Cabalka¹, and Donald J. Hagler¹

¹Pediatric Cardiology, Mayo Clinic, 200 First Street SW, Gonda 6, Rochester, MN 55905, USA; and ²Division of Anatomic Pathology, Mayo Clinic, Rochester, MN, USA

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We present two paediatric cases of a very rare, pathologically benign, and primary cardiac tumour composed of mature cardiac myocytes with disorganized cytoarchitecture called hamartoma of mature cardiac myocyte. The patients are usually asymptomatic, may have non-specific electrocardiogram findings, and rarely have associated sudden death. The clinical presentation and pathological and imaging findings of this rare tumour are discussed. Cardiac magnetic resonance imaging may help differentiate this tumour from other common differential diagnosis like cardiac fibroma and hypertrophic cardiomyopathy.

KEYWORDS
Cardiac hamartoma; Paediatric; Imaging

Introduction

Paediatric primary cardiac tumours are rare and are usually considered benign, although they may locally infiltrate the myocardium.¹ Hamartomas of mature cardiac myocyte are extremely rare; only a handful of such tumours have been reported in the literature.¹⁻⁷ Differentiating this rare tumour from other tumours, such as fibroma, rhabdomyoma, and angiosarcoma, or rarely from hypertrophic cardiomyopathy may pose considerable difficulty.⁴,⁵ We describe the clinical presentation, diagnostic dilemmas, and imaging findings in two paediatric patients with this rare tumour.

Case 1

A 16-year-old-female lost 25 pounds over 6 months. During evaluation for possible associated eating disorder, she underwent a routine electrocardiogram. The electrocardiogram revealed right axis deviation, right ventricular hypertrophy, and inverted T waves in II, III, AVF, and chest leads (Figure 1A). She had no history of cardiac symptoms, including chest pain, palpitation, breathlessness on exertion, presyncope, or syncope. An echocardiogram was performed at an outside institution and revealed a large (8 x 7 x 3 cm) homogenous mass. She was referred to our institution for further evaluation. Her echocardiogram revealed the mass, extending along the posteroinferior free wall of the right ventricle from right atrioventricular groove to the right ventricular apex (Figure 2) (see Supplementary data online, Videos 1⁻3). Medially, the mass also involved the lower aspect of interventricular septum. The echodensity of the mass was similar to the remainder of the myocardium; there was no clear line of demarcation between the mass and rest of the myocardium. A small pericardial effusion was also noted. Overall systolic function was normal, and there was no notable valvular pathology. However, the tumour itself was non-contractile with severely reduced tissue Doppler velocities. A 24 h Holter study did not reveal any significant ectopy or arrhythmia. To further delineate the mass, a cardiac magnetic resonance imaging (CMR) scan was performed. Cardiac magnetic resonance imaging clearly delineated the size and extent of tumour (Figure 3) (see Supplementary data online, Videos 4 and 5). There was markedly increased T2 signal intensity (Figure 4), rapid intense enhancement (first pass) after gadolinium contrast (see Supplementary data online, Video 6), and persistent delayed enhancement (Figure 5). All these features suggested increased vascularity of the tumour.

In view of the extensive cardiac involvement, with history of weight loss, suggested high vascularity of the tumour, and the associated small pericardial effusion, the possibility of a malignant tumour, such as angiosarcoma, was considered. The patient underwent a right ventricular endomyocardial biopsy. Histopathological examination revealed areas of hypertrophied, disorganized, mature myocytes, variably interspersed among fibroblasts and collagen (Figure 6). In addition, there was myocyte vacuolization, dilated venules, and thick-walled arteries. All these findings confirmed the histological diagnosis of a hamartoma of mature cardiac myocytes. On 4 month follow-up, she continues to remain asymptomatic without change in echocardiographic appearance or the occurrence of arrhythmias. Behavioural
therapy and counselling for her eating disorder has resulted in weight gain.

Case 2

A 10-year-old Italian male was referred to our institution for resection of a possible left ventricular fibroma. This tumour was diagnosed on screening echocardiography following a routine pre-sports electrocardiogram that showed left axis deviation and widespread ST-T wave changes in limb and lateral chest leads (Figure 1B). He had no history of cardiovascular complaints, including palpitations, arrhythmias, chest pain, presyncope, or syncope. He was an avid soccer player, in excellent physical condition. It was recommended that he undergo surgical resection of the tumour in order to continue to participate in competitive soccer, as the initial diagnosis was presumed fibroma, which may be associated with ventricular arrhythmias and risk for sudden death. An echocardiogram at our institution revealed a mass along the anterosuperior aspect of the left ventricular free wall, measuring $3 \times 2$ mm (Figure 7) (see Supplementary data online, Videos 7 and 8). Similar to the previous case, the tumour appeared isointense with no clear line of demarcation between the tumour and rest of the myocardium. The echocardiographic features were consistent with a left ventricular free wall fibroma. A 24 h Holter study did not show any significant arrhythmia or ectopy. Cardiac magnetic resonance imaging showed an elliptical tumour, along the anterosuperior, free wall of the left ventricle (Figure 8) (see Supplementary data online, Videos 9 and 10). On gadolinium contrast, imaging the tumour did not show any significant early enhancement. The tumour was mildly hyperintense on T2-weighted image (Figure 9). However, there was diffuse delayed enhancement.

At surgery, the mass appeared indistinguishable from rest of the normal ventricular myocardium. Externally, the left ventricle free wall mass appeared tumour-like. A fresh frozen section performed during surgery revealed the diagnosis of a hamartoma of mature cardiac myocytes with histological findings identical to the case 1. Resection was abandoned at this stage. The patient continues to be asymptomatic at 5 month follow-up.

Discussion

Hamartoma of mature cardiac myocytes was first described in 1988; since then very few cases have been described. Hamartomas are defined as tumours consisting of disorganized collections of tissue components native to the organ in which they occur.  Although hamartomas of mature cardiac myocytes lack primitive or aberrant cellular elements, their tissue architecture is distinctly abnormal, and markedly enlarge myocyte forms can be seen. Still, hamartomas are benign and slow growing tumours that usually do not involve surrounding structures. Their origin

Figure 1 (A) Resting electrocardiogram of case 1 showing right axis deviation, right ventricular hypertrophy, and inverted T waves in II, III, AVF, and chest leads. (B) Resting electrocardiogram of case 2 showing left axis deviation and widespread ST-T wave changes in limb and lateral chest leads.

Figure 2 (A) Apical-long-axis view, angled posteriorly showing the extent of tumour. (B) Subcostal coronal view showing the tumour and small pericardial effusion. (C) Parasternal short axis view showing the septal involvement and lack of line of demarcation between normal myocardium and tumour. LA, left atrium; LV, left ventricle; RV, right ventricle.
is unknown, but congenital anomalous development of embryonic cells seems most likely.

Hamartoma of mature cardiac myocyte should be distinguished from the more common rhabdomyoma and histiocytoid (oncocytic) cardiomyopathy, both of which have also been referred to as ‘cardiac hamartoma’. Rhabdomyomas, often seen in the setting of tuberous sclerosis, may be multiple and can often be detected during foetal or neonatal echocardiographic examination and generally regress over time. Rhabdomyomas are composed of mature cardiac tissue, but show massive vacuolation of the myocytes, giving the appearance of ‘spider cells’ on histology. Histiocytoid (oncocytic) cardiomyopathy is characterized by well-defined collections of myocytes showing pale granular material filling the sarcoplasm, presents in similar age group with presenting symptoms including tachyarrhythmia or sudden death, and tends to regress over time.

Hypertrophic cardiomyopathy may share some histological findings with a hamartoma of mature cardiac muscle. However, these two disorders can be distinguished by lack of increased vascularity, more diffuse myocardial involvement, and characteristic septal localization of hypertrophic cardiomyopathy.

Finally, a hamartoma of mature cardiac myocyte may be confused with cardiac fibroma, as described in our second case. Cardiac magnetic resonance imaging may provide valuable clues to help differentiate these entities.
Figure 6  Histopathology from case 1 (A) and case 2 (B) showing hypertrophied, disorganized, mature myocytes, variably interspersed among fibroblasts and collagen. A also shows dilated venules and thick-walled arteries.

Figure 7 (A) Parasternal-short-axis showing the isointense mass with no demarcating area on left ventricular left free wall. (B) Apical-four-chamber view showing the mass. RA, right atrium.

Figure 8  (A & B) Steady-state free precision cardiac magnetic resonance imaging, axial (A) and sagittal (B) view, showing the extent of tumour (arrow). (C) Short axis view showing the tumour.
Hamartomas of mature cardiac muscle appears to be a vascular tumour with rapid early and persistent delayed enhancement following gadolinium contrast CMR. In the presence of increased vascularity, a hamartoma appears hyperintense on T2-weighted image and first-pass perfusion scan. In contrast, fibromas appear hypointense on first-pass perfusion image due to low tumour vascularity. On delayed myocardial enhancement images, fibromas demonstrate high signal intensity of the mass compared with the nulled normal myocardium. On cardiac computed tomogram, large fibromas may also contain areas of calcification.

The clinical presentations in hamartoma of mature cardiac myocytes range from asymptomatic cases brought to attention secondary to non-specific electrocardiogram changes (as with our 2 cases), to presentation with ventricular and supraventricular tachycardia, and sudden death. Although, the tumour may be large and alters the ventricular shape, resection of the mass is difficult due to the lack of clear demarcation from the normal myocardium.

These two cases highlight the asymptomatic clinical presentation and imaging findings associated with an extremely rare, pathologically benign, and primary cardiac tumour ‘hamartomas of mature cardiac muscle’ presenting in paediatric age group. Wider clinical recognition of this rare entity may help to further differentiate this tumour from other relatively common causes of cardiac masses by non-invasive means.

Supplementary data

Supplementary data are available at European Journal of Echocardiography online.

References


Figure 9 (A) T1-weighted cardiac magnetic resonance image showing and isointense mass. (B) T2-weighted image showing a mildly hyperintense mass.