Right Ventricular Involvement in Hypertrophic Cardiomyopathy: A Case Report and Literature Review

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Summary: Although hypertrophic cardiomyopathy (HCM) is classically considered a disease of the left ventricle, right ventricular (RV) abnormalities have also been reported. However, involvement of the right ventricle in HCM has not been extensively characterized. The literature regarding prevalence, genetics, patterns of involvement, histologic findings, symptoms, diagnosis, and treatment of RV abnormalities in HCM is reviewed. To highlight the salient points, a case is presented of apical HCM with significant RV involvement, with an RV outflow tract gradient and near obliteration of the RV cavity, in the absence of a left intraventricular gradient. Right ventricular involvement in HCM appears to be as heterogeneous as that of the left ventricle. The spectrum extends from mild concentric hypertrophy to more unusual severe, obstructive disease. While in some cases the extent of RV involvement correlates with left ventricular (LV) involvement, predominant RV disease can be seen as well. While the genetics of RV involvement have not been well characterized, histologic findings appear to be similar to those in the left ventricle, suggesting similar pathogenesis. Significant RV involvement may result in RV outflow obstruction and/or reduced RV diastolic filling, with potentially increased incidence of severe dyspnea, supraventricular arrhythmias, and pulmonary thromboembolism. The optimal treatment for patients with significant RV disease is unknown. Medical and surgical therapies have been attempted with variable success; experience with newer techniques such as percutaneous catheter ablation has not been reported. Further characterization of RV involvement in HCM is necessary to elucidate more clearly the clinical features and optimal treatments of this manifestation of HCM.

Key words: hypertrophic cardiomyopathy, right ventricle, review

Introduction

Hypertrophic cardiomyopathy (HCM) is typically characterized as hypertrophy of a nondilated left ventricle in the absence of a secondary cause, such as aortic stenosis or systemic hypertension.1–5 However, while HCM is classically considered a disease of the left ventricle, cases of right ventricular (RV) involvement in HCM have also been reported.6–19 While the clinical, anatomic, and genetic heterogeneity of left ventricular (LV) abnormalities in HCM have been well described, the extent and significance of RV abnormalities in HCM have not been reviewed. We present such a review, with a representative case to highlight the salient points, to increase recognition of the sometimes biventricular, and rarely predominantly right ventricular, manifestations of hypertrophic cardiomyopathy.

Case Presentation

A 39-year-old man with a cardiac murmur since young adulthood presented with shortness of breath and fatigue. He had been active and asymptomatic until 4 years previously, when he began noting dyspnea during vigorous exercise. Over 2 years his symptoms gradually worsened to New York Heart Association (NYHA) class 3; at that time he was diagnosed with “cardiomyopathy” by echocardiography and started on verapamil 240 mg daily. While his symptoms improved somewhat with verapamil, bouts of exertional dyspnea and fatigue continued, with symptoms varying unpredictably between NYHA class 2 and 3. He denied chest pain, palpitations, light-headedness, orthopnea, pedal edema, a history of hypertension, or a family history of cardiac disease or sudden death.

Physical examination revealed a healthy-appearing, comfortable man with pulse 76 beats/min and blood pressure 100/70 mmHg. The cardiac apical impulse and first and second heart sounds were normal. A grade 3/6 harsh mid-sys-
tolic murmur could be heard at the left upper sternal border, with radiation to the apex but not to the carotid arteries. The intensity of the murmur diminished to grade 1/6 with inspiration, suggestive of a right-sided obstructive murmur. The remainder of the physical examination, including jugular venous pressure and carotid upstroke, was unremarkable.

Diagnostic Evaluation

Complete blood count and renal, electrolyte, hepatic, and thyroid panels were within normal limits. An electrocardiogram was notable for markedly increased QRS voltage in the precordial leads, with ST depressions and giant inverted T waves, suggestive of the apical variant of HCM. Transthoracic two-dimensional (2-D) echocardiography showed massive thickening of the interventricular septum and hypertrophy of the RV free wall and LV apex, with relative sparing of the basal septum and LV free walls (Fig. 1). At end-diastole the mid-septum measured 29 mm, the RV free wall > 20 mm, the basal septum 10 mm, and the basal posterior wall 10 mm. During diastole most of the mass of the hypertrophied septum appeared to impinge on the RV cavity, and during systole there was near obliteration of the RV cavity, with sparing of the LV outflow tract and absence of systolic anterior motion of the mitral valve. Color-wave Doppler showed turbulent flow in the RV outflow tract; continuous wave Doppler demonstrated peak RV outflow velocity of 2.2 m/s, corresponding to a peak systolic gradient of 20 mmHg (Fig. 2). No turbulence or gradi-

![Fig. 1](image1.png)

![Fig. 2](image2.png)
ent was present in the LV outflow tract (peak velocity 0.9 m/s). With a Valsalva maneuver, LV outflow velocities remained normal; RV outflow velocities could not be assessed due to loss of Doppler windows. Overall LV systolic function and valvular structure and function were within normal limits.

Right and left heart catheterizations were performed. At rest, right atrial pressure was 3 mmHg, RV pressure was 47/12 mmHg, and a maximal systolic gradient of 12 mmHg was noted in the RV outflow tract; provocative measures were not performed. There was no gradient in the LV outflow tract. Mean pulmonary capillary wedge pressure was 17 mmHg, and aortic pressure, pulmonary and systemic vascular resistance, and cardiac index (2.8 l/min/m²) were normal. Coronary arteriography showed normal epicardial coronary vessels. During arteriography of the right coronary artery, a large pulmonary conus vessel was noted to produce a large, late “tumor” blush of significantly increased capillary flow in the interventricular septum.

Left ventriculography showed mild inward displacement at the inferior apex with otherwise normal LV dimensions and systolic function (Fig. 3). Right ventriculography showed massive inward bulging of the septum and RV apex, with severe reduction in RV diastolic filling and near obliteration of the RV cavity during systole (Fig. 4).

Because an RV tumor was considered a possibility, cardiac magnetic resonance imaging (MRI) was performed, which confirmed biventricular apical hypertrophy with disproportionate involvement of the right ventricle and near obliteration of the RV cavity (Fig. 5). Myocardial contrast enhancement was homogeneous, without evidence of tumor. The LV free wall and basal septum demonstrated normal wall thicknesses (11 and 9 mm, respectively), and the LV apex was significantly thickened (22 mm). Due to massive hypertrophy of the mid to apical RV, the septum could not be distinguished from the RV free wall, with maximal myocardial thickness to 46 mm. Right atrial enlargement was also present.

The final diagnosis was biventricular apical HCM, with significant involvement of the right ventricle. The RV involvement was notable in two respects. First, the bulk of the hypertrophied myocardium appeared to be supplied by the right coronary circulation via the pulmonary conus branch. Second, both reduced RV diastolic filling and an RV outflow systolic gradient were present, in the absence of an LV outflow gradient. While reduced LV compliance was apparent, these RV ab-

![Fig. 3](image3.png) Ventriculography of the left ventricle (LV) at end-diastole (A) and end-systole (B). Mild inward displacement of the inferior apex is seen, especially during systole, without other significant abnormalities.

![Fig. 4](image4.png) Ventriculography of the right ventricle (RV) at end-diastole (A) and end-systole (B). Note “mass-like” obliteration of the RV apex, with severe reduction in diastolic filling, and near obliteration of the RV cavity during systole. RA = right atrium, PA = main pulmonary artery.
normalities—especially the reduction in RV stroke volume—were also thought to contribute to the patient’s exertional symptoms, which were more severe than the mild symptoms typically seen with apical hypertrophic cardiomyopathy.1, 6 Metoprolol 25 mg twice daily was added to the patient’s regimen, but was not tolerated as it caused general fatigue. Verapamil was increased to 360 mg daily, with decreased dyspnea and improved subjective exercise tolerance; repeat echocardiography showed a reduction in the peak RV outflow systolic gradient to 10 mmHg.

Right Ventricular Involvement In Hypertrophic Cardiomyopathy

Several excellent reviews of LV abnormalities in HCM have been published;1–5 this discussion will focus on involvement of the right ventricle in HCM.

Prevalence: Population prevalence of HCM is estimated at between 0.02 and 0.2%.1 Although the prevalence of RV involvement in HCM is unknown, mild concentric RV hypertrophy may be common. In one series of 24 patients with HCM evaluated by 2-D echocardiography, 67% demonstrated maximum RV wall thickness ≥5 mm.7 Similarly, in another series of 37 patients with HCM evaluated with MRI, 70% demonstrated mild RV hypertrophy (right anterior wall thickness > 5 mm).8 In a third series of 73 patients with LV HCM evaluated by 2-D echocardiography, 33% demonstrated mild (<8 mm) concentric RV hypertrophy, and an additional 10% showed moderate (9–12 mm) concentric RV hypertrophy.9 Only one patient (1.4%) in this series demonstrated severe (>12 mm) RV hypertrophy. Thus, while mild concentric RV disease may be common in HCM, severe involvement of the right ventricle appears to be unusual. The incidence of hemodynamically significant RV involvement is unknown, as published reports are limited to single cases or small series of patients.6, 10–19 All age groups—from infants to the elderly—have been represented in these reports.

Genetics: Among all patients with HCM, a family history is present in approximately 50%, with autosomal dominant transmission and variable penetrance; in the remaining 50%, HCM appears to arise spontaneously.1, 2, 4 Some patients with RV involvement also have a positive family history of HCM,10, 11 and in four infants presenting with severe RV HCM in the first year of life there appeared to be autosomal recessive inheritance.10 In general, however, it is not known whether RV involvement is associated with specific genetic abnormalities or transmission patterns, as the genetic attributes of RV HCM have not been well characterized.

Patterns of involvement: Involvement of the left ventricle in HCM is typically heterogeneous: while the interventricular septum is most often involved, there may also be hypertrophy of the anterior, lateral, inferior, or posterior walls.1, 2, 4, 5 Other variations include concentric LV hypertrophy and predominant apical hypertrophy; the latter, present in our patient, is most commonly reported from Japan and Brazil.1, 2, 13

Involvement of the right ventricle appears to be similarly variable, with reported patterns including concentric RV hypertrophy and heterogeneous hypertrophy of the RV apex, mid septum, basal septum, and/or free wall.9–14 The crista terminalis and moderator band may also be involved.11 Of note, RV outflow obstruction has not been reported with concentric RV hypertrophy, but only in cases of heterogeneous RV disease.

While the majority of patients with RV HCM have significant LV involvement,11, 13–16, 18 it is unclear how LV involvement might predict RV disease. In one series of patients, there was a correlation between maximal left and right ventricular wall thickness (r = 0.643).9 In another series, RV involvement was associated with more severe hypertrophy of the LV posterior wall.8 Severe RV involvement without obstructive LV disease, as in our patient, may also be seen, although published reports are limited to isolated cases.10–13, 17

Histologic findings: In patients with LV HCM, three major histologic abnormalities have been described: (1) cellular disorganization at both the intercellular (myocyte) and intracellular (myofibrillar) levels, involving from <5% to >50% of the LV myocardium; (2) myocardial fibrosis, also either focal or extensive; and (3) intramural coronary artery wall thickening with reduction in lumen diameter.1, 2, 4 Histologic examinations of hypertrophied RV myocardium following surgical resection, at autopsy, and following endomyocardial biopsy have shown similar findings.12, 14, 15, 16 Consistent with the supposition that hypertrophy in the right and left ventricles is a manifestation of the same disease. However, as these histologic findings are neither unique to HCM nor found in all patients, the diagnosis cannot be absolutely established by their presence or excluded by their absence.1, 2

Symptoms: The spectrum of clinical disease with LV involvement is broad.1–5 While symptoms are generally related
to the sites and severity of LV hypertrophy, this correlation is not strict, and significant heterogeneity exists. Some patients may be asymptomatic, while others may suffer significant morbidity including dyspnea on exertion, palpitations, chest pain, lightheadedness, and syncope. These sequelae are multifactorial, thought to result from dynamic subaortic outflow obstruction due to systolic anterior motion of the mitral valve, decreased LV compliance with diastolic dysfunction or overt congestive heart failure, and atrial or ventricular tachy- and bradyarrhythmias. Myocardial ischemia may also occur, which in the absence of extramural coronary abnormalities is thought to be due to decreased myocardial blood flow from intramural coronary artery wall thickening combined with increased myocardial oxygen demand from hypertrophy and elevated filling pressures. All patients with HCM, even those without symptoms, appear to be at risk for sudden cardiac death.

Patients with HCM involving the right ventricle may similarly present with dyspnea on exertion, palpitations, lightheadedness, and syncope. Since many patients have significant LV involvement as well, it is not surprising that these symptoms mirror those described for LV HCM. It is interesting, however, that patients with RV disease and no significant LV involvement also have similar complaints, suggesting that RV hemodynamic abnormalities may, in some cases, be as symptomatically limiting as those in the left ventricle. However, because RV involvement in HCM has never been extensively characterized, it is unclear to what extent RV disease might contribute to the type or severity of symptoms. In one series, RV involvement was associated with increased incidence of ventricular tachycardia and supraventricular arrhythmias; the association with supraventricular arrhythmias persisted following stepwise logistic regression analysis. This series also showed a significant association between RV involvement and severity of dyspnea, with more patients with biventricular involvement in NYHA class 3 or 4 than those with LV involvement alone (25 vs. 7%, respectively). The contribution of RV involvement to symptoms may also be exemplified by our patient who, as noted above, exhibited more pronounced dyspnea and fatigue than typically seen with apical HCM. The pathophysiology underlying such symptoms is unclear; dynamic RV outflow obstruction and reduced cardiac output due to limited RV diastolic filling (“inflow” obstruction) may both be contributing.

Right ventricular outflow gradients, for example, have been demonstrated in patients with HCM by both echocardiogram and cardiac catheterization, with peak gradients up to 118 mmHg. These RV outflow gradients usually, but not always, are associated with LV outflow gradients. The cause of the RV gradient is controversial. In some cases, gradients have responded to beta blockade, suggesting dynamic or functional obstruction. In other cases, however, hemodynamic and pathological analyses have suggested fixed obstruction due to hypertrophied RV muscle, especially the crista supraventricularis, and resection of the involved RV tissue has resulted in reduced gradients and improved symptoms.

Moreover, while mild degrees of RV diastolic dysfunction may be common to all patients with HCM, marked RV hypertrophy can be associated with more significant diastolic abnormalities. In our patient, for example, asymmetric RV involvement appeared to limit RV diastolic volume significantly. This limitation may be particularly important during exercise, when reduction in RV stroke volume and subsequent limitation in cardiac output might result in dyspnea and fatigue. Reduced RV compliance from RV HCM has also been associated with severe right atrial enlargement and atrial fibrillation, which in one series was associated with increased risk of pulmonary thromboembolism and a poorer prognosis. Pulmonary thromboembolism may also be of concern in the absence of atrial fibrillation: one patient with biventricular HCM in normal sinus rhythm presented with RV mural thrombus associated with an RV aneurysm. Aneurysm formation in this patient was thought to be due to histologically demonstrated RV arteriolar thickening with resulting ischemia and replacement fibrosis.

**Diagnosis:** When RV involvement is suspected in the appropriate clinical setting, both echocardiography and cardiac catheterization are useful to delineate hypertrophy and systolic function, evaluate diastolic pressures, and measure outflow gradients. Cardiac MRI may be of particular utility in these patients, providing unparalleled imaging of the RV myocardium. Cardiac MRI has also been shown to demonstrate close agreement with echocardiography in assessment of the left ventricle. In our patient, cardiac MRI both clearly demonstrated the biventricular distribution of the cardiac hypertrophy and also helped exclude tumor as the cause of the ventricular abnormality.

**Treatment:** The most appropriate therapy for patients with HCM and significant RV involvement is unknown. Symptomatic patients with RV disease have been treated with beta blockers and calcium-channel blockers; while in some patients these medications have diminished symptoms and reduced right (and left) intraventricular gradients, not all patients have responded. The effects of these medications on the risk of sudden death are unknown.

In patients with HCM and atrial fibrillation, anticoagulation with warfarin is recommended to decrease risk of systemic thromboembolism. When significant RV diastolic dysfunction and right atrial enlargement are present, there may also be increased risk of pulmonary thromboembolism, although experience is limited to case reports and treatment recommendations cannot be made based on such limited data. The utility of treatment with aspirin is unknown.

Surgical intervention has been reported. In 1993, Maron et al. described a series of five patients with HCM and RV involvement, ages 18–55. All had resting RV outflow gradients > 50 mmHg, with NYHA class 3 or 4 symptoms. Four of five patients also had significant LV outflow gradients (12–110 mmHg at rest). In four patients, right ventriculotomy was performed, with substantial resection of hypertrophied RV tissue (2.2–22.0 g). Three of these patients also received a septal myotomy-myectomy (Morrow procedure) or septal myotomy alone. The fifth patient received septal myotomy-myectomy alone, without right ventriculotomy. Two patients died perioperatively. In the survivors, resting RV gradients were reduced...
from 60 to 0, 60 to 11, and 118 to 0 mmHg, respectively. Symptoms were also reduced, from NYHA class 3 to 2 in two patients, and class 3 to 1 in the third.

The potential for nonsurgical interventional treatment of RV HCM is unclear. Recently, a series of 91 patients with HCM and significant LV outflow tract gradients treated with percutaneous transluminal septal myocardial ablation was reported. This intervention significantly reduced mean LV outflow gradients (from 73.8 to 16.6 mmHg) and patient symptoms (from mean NYHA class 2.8 to 1.1). There were two periprocedure deaths. To our knowledge, there are no reports of this technique having been utilized in patients with RV gradients. Given the echocardiographic reductions in septal thickness which have been observed, this technique may be promising for reducing the hemodynamic abnormalities of obstructive RV disease in patients in whom an appropriate coronary vessel is available for ethanol injection. If our patient were more severely symptomatic, for example, the conus branch of the right coronary artery might be considered for this therapeutic approach.

Conclusions

Mild, concentric RV hypertrophy appears to be relatively common in HCM. Significant, heterogeneous RV involvement is unusual; when present it is often, but not always, associated with severe LV hypertrophy. Significant RV disease may result in RV outflow obstruction, reduced RV compliance, and reduced RV diastolic filling. While severe RV disease is usually associated with obstructive LV disease, it can be seen in isolation as well. It is unclear to what extent RV hypertrophy may contribute to symptoms; significant RV involvement has been associated in some cases with increased prevalence of severe dyspnea and increased incidence of supraventricular arrhythmias. When atrial fibrillation and severe RV diastolic dysfunction are present, increased risk of pulmonary thromboembolism has been reported, although data are limited. Surgical intervention in patients with high resting RV gradients appears to have potential for substantial reduction in both intraventricular gradients and symptoms, but the associated operative mortality may be high. Percutaneous catheter ablation techniques show preliminary success in treatment of hemodynamic abnormalities and symptoms due to LV gradients and may therefore hold promise for the treatment of selected patients with RV disease as well.

Many unanswered questions remain. The true incidence of significant RV involvement in HCM as well as the relation of such disease to type and severity of symptoms requires definition. Given the varied and significant symptoms potentially associated with RV involvement, it is interesting to speculate whether unrecognized RV disease might in some cases explain the variable correlation between the extent of LV hypertrophy and symptoms in patients with HCM. In addition, if clinical course is affected by significant RV involvement, as suggested by reported experience to date, the resulting consequences for optimal therapy and long-term prognosis are unknown.

Increased awareness of the potential for RV involvement in HCM is necessary to characterize further this manifestation of HCM and to elucidate these important issues.

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