Myocardial siderosis due to hemochromatosis in an individual with hypertrophic cardiomyopathy

Ainslie M Hildebrand MD¹, Kapil M Bhagirath MD², Vignendra Ariyaratnam MD², Jonathan R Walker BSc³,
Donald S Houston MD PhD FRCPC⁴, Shelley Zieroth MD FRCPC², James W Tam MD FRCPC²,
Iain DC Kirkpatrick MD FRCPC⁵, Davinder S Jassal MD FACC FRCPC^{2,3,5}

AM Hildebrand, KM Bhagirath, V Ariyaratnam, et al. Myocardial siderosis due to hemochromatosis in an individual with hypertrophic cardiomyopathy. *Can J Cardiol* 2009;25(12):e424-e425.

A patient with hypertrophic cardiomyopathy (HCM) and transfusion-dependent sideroblastic anemia, who presented with decompensated heart failure, is described. The present case demonstrates the usefulness of cardiac magnetic resonance imaging as a noninvasive imaging modality to assess the etiology of new systolic dysfunction in the setting of HCM. Cardiac magnetic resonance imaging is able to differentiate between the dilated 'burned-out' phase of HCM and a concomitant dilated cardiomyopathy secondary to myocarditis or hemosiderosis.

Key Words: Cardiac MRI; Hemochromatosis; Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is the most common genetic cardiovascular disease, occurring in 0.2% of the population (1). A small proportion of HCM cases (5% to 10%) evolve into a stage resembling the morphological and functional features of dilated cardiomyopathy (DCM) with systolic dysfunction, left ventricular dilation and wall thinning (1). This end stage (or 'burned-out' phase) results in progressive and irreversible heart failure (1).

Previous reports have described the usefulness of cardiac magnetic resonance (CMR) imaging in identifying myocarditis as a cause of clinical deterioration during the progression of HCM (2). However, to our knowledge, myocardial siderosis has never been reported as such. We report a case of a patient with HCM and transfusion-dependent sideroblastic anemia who presented with decompensated heart failure and new systolic dysfunction. CMR imaging confirmed the presence of myocardial iron overload as the etiology for this DCM. This finding was confirmed by the improvement of cardiac function that occurred with intensive iron chelation.

CASE PRESENTATION

A 23-year-old man with a longstanding history of HCM presented with acute onset of fatigue, orthopnea, paroxysmal nocturnal dyspnea and peripheral edema. His medical history was significant for transfusion-dependent sideroblastic anemia poorly responsive to pyridoxine therapy, for which he had been receiving monthly transfusions and iron chelation therapy since the age of four years. Due to poor compliance, he was switched to oral chelation therapy with deferasirox four months before his current presentation.

The diagnosis of HCM had been prompted by a dynamic grade 3/6 systolic murmur that increased with the Valsalva manoeuvre, first noted at 15 years of age. Transthoracic echocardiography (TTE)

Sidérose myocardique due à une hémochromatose chez un patient atteint de cardiomyopathie hypertrophique

On décrit ici le cas d'un patient souffrant de cardiomyopathie hypertrophique (CMH) et d'anémie sidérolastique dépendante des transfusions qui s'est présenté en insuffisance cardiaque décompensée. Ce cas montre l'utilité de l'imagerie par résonance magnétique cardiaque comme modalité diagnostique non effractive pour découvrir l'étiologie d'une nouvelle dysfonction systolique dans le contexte de la CMH. L'imagerie par résonance magnétique cardiaque permet de distinguer la phase dilatée hypokinétique de la CMH de la myocardiopathie dilatée concomitante secondaire à une myocardite ou à une hémosidérose.

revealed hyperdynamic systolic function with a left ventricular ejection fraction of 70% to 80%, asymmetric left ventricular hypertrophy and a peak left ventricular outflow tract gradient of 56 mmHg at rest.

On initial physical examination, the patient was hypotensive and appeared ill. The cardiorespiratory examination was remarkable for an elevated jugular venous pressure at the angle of the jaw, a third heart sound and bibasilar crackles in both lung fields with decreased air entry to the right lung base. The abdominal examination revealed hepatosplenomegaly. In addition, he had significant bilateral peripheral edema to the knees.

A twelve-lead electrocardiogram revealed sinus tachycardia with Q waves in leads V₅ and V₆, and T wave inversions in leads V₁ to V₆. Serum ferritin was 2990 µg/L and transferrin saturation was 82%. TTE revealed severe asymmetric septal hypertrophy with a septal thickness of 2.0 cm to 2.5 cm (Figure 1). There was mild systolic anterior motion of the leaflet tips, but no significant left ventricular outflow tract obstruction at rest. The overall left ventricular systolic function was moderately impaired with an ejection fraction of 30% to 35%. The right ventricular systolic function was severely impaired with a right ventricular systolic pressure of 42 mmHg. These findings were significant for new DCM, compared with the echocardiogram three years previously.

CMR imaging confirmed severe global left ventricular systolic dysfunction with regional variation and an ejection fraction of 26%. Various iron-sensitive protocols were performed, which revealed a lower signal than expected on all sequences within the left ventricular myocardium (Figure 2). T2-star (T2*) mapping was performed with a multiecho gradient-echo sequence (time to repetition 200 ms; times to echo 4.8 ms, 7 ms, 9.3 ms, 11.5 ms, 13.7 ms, 16 ms and 18.2 ms) on a Siemens Avanto 1.5 T magnet (Siemens AG, Germany). The T2*

¹Department of Internal Medicine; ²Section of Cardiology, Department of Cardiac Sciences; ³Institute of Cardiovascular Sciences; ⁴Section of Hematology, Department of Internal Medicine; ⁵Department of Radiology, University of Manitoba, Winnipeg, Manitoba

Correspondence: Dr Davinder S Jassal, Department of Cardiology, Radiology and Physiology, Bergen Cardiac Care Centre, Cardiology Division, Room Y3010, Department of Cardiac Sciences, St Boniface General Hospital, 409 Tache Avenue, Winnipeg, Manitoba R2H 2A6.

Telephone 204-237-2023, fax 204-233-2157, e-mail djassal@sbgh.mb.ca

Received for publication March 5, 2009. Accepted May 17, 2009

Figure 1) Parasternal long-axis view of transthoracic echocardiography demonstrating asymmetric septal hypertrophy consistent with hypertrophic cardiomyopathy. LA Left atrium; LV Left ventricle; RV Right ventricle

value was 16 ms (normal greater than 20 ms). These findings were consistent with myocardial iron overload.

The patient received appropriate oral chelation therapy with deferasirox for 10 months. Follow-up echocardiography and CMR imaging at 10 months revealed a significant improvement in left ventricular ejection fraction from 30% to 35%, to greater than 60%.

DISCUSSION

While TTE remains the most common noninvasive diagnostic test for HCM, CMR is superior in identifying atypical patterns of hypertrophy. CMR provides high-resolution images with uniform contrast at the endocardial borders, encompassing all regions of the left ventricle, resulting in virtually complete reconstruction of the chamber (3). Furthermore, with late gadolinium enhancement imaging, CMR has the capability of identifying myocardial fibrosis, a potentially arrhythmogenic substrate for ventricular tachyarrhythmias (4).

It is well known that HCM may transition to a dilated phase characterized by systolic dysfunction and left ventricular dilation, resembling DCM (1). One potential cause of DCM, which may be implicated in a potentially destabilizing role in HCM patients, is iron overload. Heart failure due to iron overload is a leading cause of death in patients with thalassemia and is a recognized complication of other transfusion-dependent anemias and hereditary hemochromatosis (5). Because intensive chelation therapy may attenuate or reverse ventricular dysfunction in these patients, the ability to identify and monitor myocardial iron overload is of clinical interest (5).

CMR permits the simultaneous assessment of both myocardial iron loading and cardiac function, making it well suited for the assessment of iron overload cardiomyopathy. CMR incorporates a measurement of myocardial T2*, a magnetic relaxation property that is highly reproducible for detecting early tissue iron overload (5). For this reason, it is also a useful parameter for longitudinal tracking of myocardial iron deposition. As iron accumulates in the heart, the T2* begins to fall. At the point at which iron storage reserve is exhausted, cardiac function

Figure 2) Short-axis gradient echocardiography image of the heart without inversion preparation (time to repetition 200 ms; time to echo 7 ms; slice thickness 10 mm) shows marked hypointensity of the left ventricular myocardium. The large arrow points to the hypertrophied septum, which measured up to 2.5 cm in diastole

deteriorates rapidly. Identification of left ventricular systolic dysfunction is, therefore, a late sign of iron overload.

CONCLUSION

Myocardial siderosis due to transfusional iron overload is an uncommon cause of functional deterioration in HCM. CMR is a useful modality to determine the etiology of DCM resulting in abrupt clinical decompensation in the setting of HCM.

REFERENCES

1. Maron BJ. Hypertrophic cardiomyopathy: A systematic review. *JAMA* 2002;287:1308.
2. Frustaci A, Verardo R, Caldarulo M, Acconcia MC, Russo MA, Chimenti C. Myocarditis in hypertrophic cardiomyopathy patients presenting acute clinical deterioration. *Eur Heart J* 2007;28:733-40.
3. Friedrich MG, Sechtem U, Schulz-Menger J, et al. International Consensus Group on Cardiovascular Magnetic Resonance in Myocarditis. Cardiovascular magnetic resonance in myocarditis: A JACC White Paper. *J Am Coll Cardiol* 2009;53:1475-87.
4. Adabag AS, Maron BJ, Appelbaum E, et al. Occurrence and frequency of arrhythmias in hypertrophic cardiomyopathy in relation to delayed enhancement on cardiovascular magnetic resonance. *J Am Coll Cardiol* 2008;51:1375-6.
5. Westwood M, Anderson LJ, Firmin DN, et al. A single breath-hold multiecho T2* cardiovascular magnetic resonance technique for diagnosis of myocardial iron overload. *J Magn Reson Imaging* 2003;18:33-9.