VIA MEDICA
CASE REPORT
2012, Vol. 19, No. 6, pp. 646–649
10.5603/CJ.2012.0120

ISSN 1897–5593

Progressive breathlessness in an Afro Caribbean hypertensive subject

Girish Dwivedi[1], Robert J. MacFadyen[2], Chetan Varma[2], Vishal Sharma[1], Desley Neil[1], Richard P. Steeds[1]

[1]University Hospital Birmingham NHS Foundation Trust and University of Birmingham, Birmingham, United Kingdom
[2]Sandwell and West Birmingham NHS Trust, City Hospital, Dudley Road, Birmingham, United Kingdom

Abstract

The sensitivity and specificity of structural assessment of the heart by echocardiography in black hypertensive patients presenting with symptoms of heart failure is often incomplete. Cardiovascular magnetic resonance, mainly by virtue of its ability to characterize myocardial tissue composition, may be of value in differentiating some of the common pathologies noninvasively. We present an illustrative case of hypertrophic cardiomyopathy in a British Afro Caribbean hypertensive patient where at least some features of familial amyloidosis were present on screening echocardiography. Cardiovascular magnetic resonance examination of this case established not only the usefulness of this technique, but also highlighted the importance of recognizing the variations and departure from the usual which one associates with hypertrophic cardiomyopathy, so as to arrive at the final diagnosis. (Cardiol J 2012; 19, 6: 646–649)

Key words: breathlessness, Afro Caribbean, hypertrophic cardiomyopathy, amyloidosis, left ventricular hypertrophy, cardiac magnetic resonance

Introduction

The sensitivity and specificity of structural assessment of the heart by echocardiography in black patients with hypertension is poor [1]. In such subjects, there is a need to differentiate a range of structural changes that manifest as increased wall thickness: hypertensive heart disease; hypertrophic disease (inherited cardiomyopathies) as well as infiltrative heart disease such as familial transthyretin-related (TTR) amyloidosis and Anderson Fabry disease [2–4]. This can be challenging using echocardiography alone, as the sensitivity and specificity of changes are generally inadequate for any purpose other than as a screening tool.

Cardiovascular magnetic resonance (CMR), by virtue of its ability to assess structure and function, define valvular and/or pericardial changes, and give information on myocardial tissue characterization, has the potential to differentiate such pathology in these subjects [5–7]. Differing hyperenhancement patterns are observed in a variety of non-ischemic cardiomyopathies on delayed inversion recovery sequences following gadolinium injection [5–7].

We illustrate the potential of CMR techniques in Afro Caribbean subjects using an indicative case where hyper-enhancement patterns on CMR proved valuable in differentiating hypertrophic cardiomyopathy (HCM).

Address for correspondence: Dr. Girish Dwivedi, MD, DM, MRCP (UK), PhD, Clinical Lecturer in Cardiology, Department of Cardiovascular Medicine, The Medical School, University of Birmingham, Edgbaston, Birmingham B15 2TT, United Kingdom, tel: +44 121 5075080, e-mail: g.dwivedi@bham.ac.uk

Received: 16.11.2011 Accepted: 19.11.2011

Case report

A 57 year-old Afro Caribbean, hypertensive male was referred from his family doctor with undiagnosed progressive breathlessness on exertion over six months. He had a history of arterial hypertension for 18 years (secondary causes excluded) and had undergone partial left (18 months prior) and right (12 months prior) nephrectomy for bilateral renal cell carcinoma. There was no personal or family history of any form of heart disease or sudden cardiac death. He was not affected by orthopnea or paroxysmal nocturnal dyspnea, and complained only of non-specific exercise limitation. There were no relevant respiratory symptoms, occupational history or exposures.

General physical examination revealed a heavily built man with a pulse rate of 80 bpm and treated (candesartan, doxazozin, minoxidil and metalozone) clinic blood pressure of ~134/68 mm Hg on repeated readings in the left arm. Jugular venous pressure was normal with no pedal edema. Chest and cardiovascular system were otherwise unremarkable.

A 12-lead electrocardiogram demonstrated voltage left ventricular (LV) hypertrophy with a typical lateral strain pattern. Echocardiography confirmed severe concentric LV hypertrophy (max LV wall thickness: 2 cm) with mild biatrial dilatation and a global pericardial effusion (maximum depth: 1.4 cm). The LV ejection fraction was normal. The LV and right ventricular (RV) long axis functions (mitral and tricuspid annular excursions) were clearly preserved. The ratio of early mitral inflow velocity (E) to lateral mitral annulus early velocity (e') indicated elevated LV end-diastolic pressure (E/e' = 18). Notably, the echocardiography showed thickening of the RV (free wall: 1 cm), atrial septum, and valvular structures along with the non-specific granular pattern of myocardial reflectivity characterized as septal 'speckling' of myocardial texture (Fig. 1). No systolic anterior motion of the mitral valve or LV outflow tract gradient suggestive of obstructive cardiomyopathy was observed at rest.

The probable diagnosis of HCM or hypertensive heart disease was considered. However, given the Afro Caribbean phenotype, CMR was organized to exclude TTR amyloidosis. This has been described in the African American population, and was a possibility due to the unexpected findings of a pericardial effusion, atrial septal, RV and valvular thickening along with the granular speckling pattern of myocardium seen on the echocardiogram [3, 4]. In addition, a ventricular biopsy from the right internal jugular vein under lidocaine local anesthetic was completed to provide three samples of septal myocardium for histological analysis.

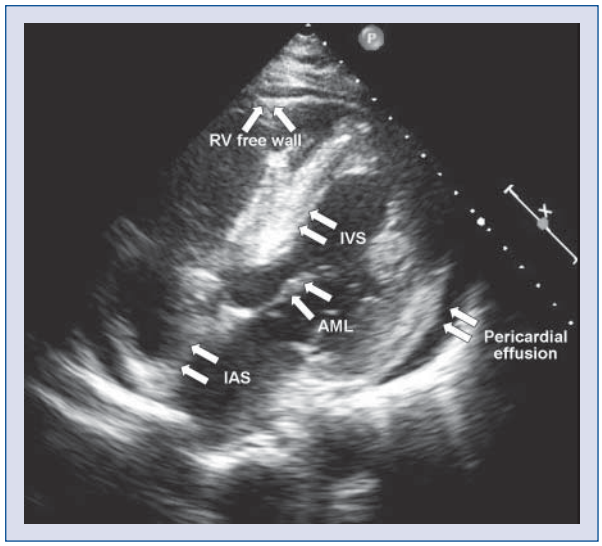

Figure 1. Modified apical five-chamber view demonstrating significant pericardial effusion, thickened cardiac structures (IAS — inter atrial septum; IVS — inter ventricular septum; AML — anterior mitral leaflet; right ventricle [RV] free wall) and characteristic granular speckling myocardial architecture.

The CMR examination revealed a global pericardial effusion [maximum depth 1 cm adjacent to the anterolateral wall], concentric severe LV hypertrophy [maximum dimension of 2.3 cm; LV mass of 364 gm absolute] (Fig. 2A) with a small LV end systolic cavity and flow acceleration within the LV cavity (Fig. 2B). The RV wall thickness was increased (0.7 cm) with normal systolic function. On longitudinal relaxation time (T1) mapping there was a strong suspicion of early subendocardial passage through the null point. The late gadolinium enhancement images showed generally poor nulling with diffuse linear mid-myocardial wall hyper-enhancement that was most apparent in the mid and basal inferolateral and anterolateral LV segments (Fig. 3). In addition, the basal insertion points of the RV into the septum also demonstrated mid myocardial wall hyper-enhancement. These appearances were compatible with either HCM or Anderson Fabry disease. However, primary cardiac amyloidosis could not be excluded on the basis of the T1 mapping findings. Anderson Fabry disease was excluded by demonstrating normal level of alpha-galactosidase activity. Cardiac amyloidosis was excluded by the cardiac biopsy which was consistent with a tissue diagnosis of HCM.

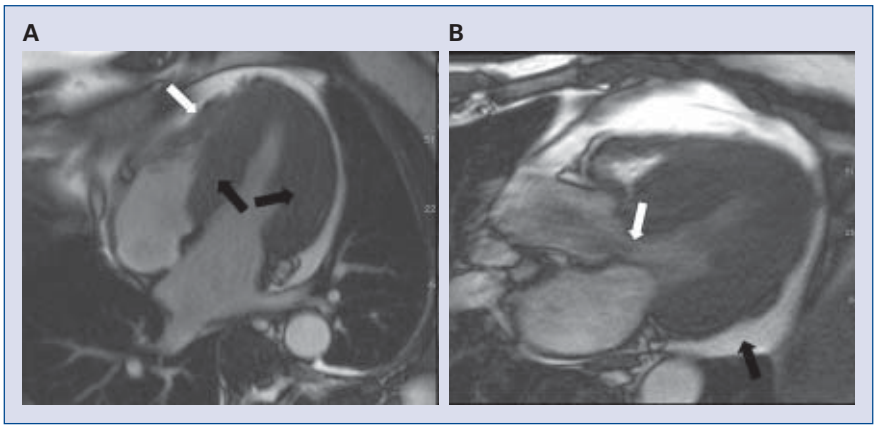

Figure 2. A. Apical four-chamber view on cardiovascular magnetic resonance (CMR) showing thickened septal and lateral walls (black arrows) and thickened right ventricle free wall (white arrow); **B.** Flow acceleration seen within the left ventricle (white arrow) and pericardial effusion (black arrow) on CMR. Note small end systolic cavity size.

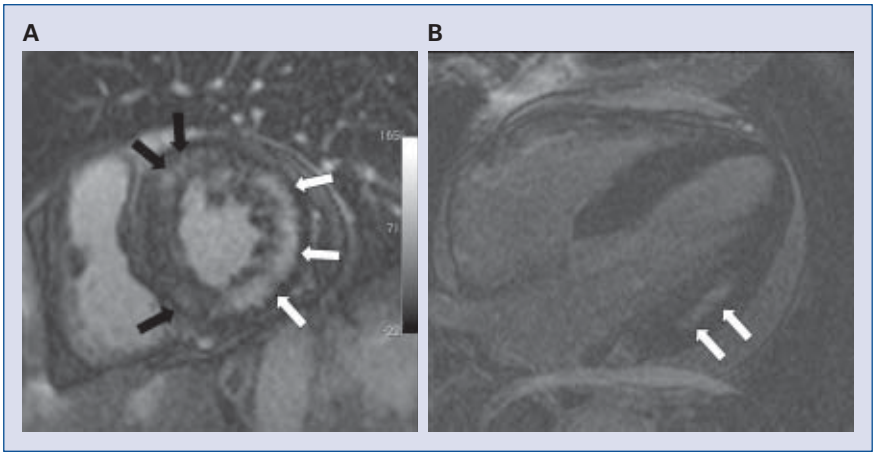

Figure 3. A. Basal short axis late gadolinium enhancement image demonstrating diffuse linear mid myocardial wall hyper-enhancement in anterolateral and inferolateral walls (white arrows). Note: Hyper-enhancement also seen at right ventricle insertion points into the septum (black arrows); **B.** Apical four-chamber view showing mid myocardial wall hyper-enhancement in the basal inferolateral left ventricle segment (white arrows).

Discussion

Hypertensive Afro Caribbean patients present specific diagnostic challenges due to their increased susceptibility to cardiac complications secondary to hypertension and their different relative responsiveness to a range of anti-hypertensive drug treatments [1]. Differentiating these subjects from more generalized forms of inherited HCM, or indeed dilated cardiomyopathy (which may simply be an end stage response to poor long term blood pressure control), is often attempted using echocardiography. This is compromised by poor image quality, the non-specific and insensitive nature of the findings and a failure to consider alternative tissue diagnoses.

HCM is a broad range of inherited primary myocardial diseases characterized by abnormal myocyte proliferation and interstitial thickening of the myocardium. CMR using late gadolinium profiling in HCM patients typically demonstrates patchy, multi focal hyper-enhancement occurring within the hypertrophied regions. The junction of the RV free wall with the interventricular septum (i.e. RV insertion points) is frequently affected [8, 9]. Recent reports suggest that the extent of delayed hyper-enhancement in HCM may have adverse prognostic implications [7–9]. It is believed that the patchy enhancement in HCM is due to the presence of abundant connective tissue within the hypertrophic myocardium, although it could also be due to necrosis caused by relative ischemia [8, 9].

Familial cardiac amyloidosis in Afro Caribbean patients, usually due to TTR valine substitution, is a complex inherited phenotype but frequently coexists with hypertension in old age in this community [3, 4]. This generally involves diffuse infiltration of myocardium and valvular tissue with fibrillar amyloid protein, typically displaying subendocardial linear global and diffuse hyper-enhancement [10, 11]. Early gadolinium kinetics may also have a role in the diagnosis of cardiac amyloidosis. The subendocardial T1 time in patients with cardiac amyloid is shorter than normal individuals and the decrease is inversely correlated with markers of cardiac amyloid load such as LV mass, wall thickness, atrial septal thickness and diastolic function [11]. The outlook for such patients is unclear in the absence of specific therapy.

Less frequently, mycocardial thickening may be due to Anderson Fabry disease with cardiac involvement, and this can mimic HCM phenotypically. However, these patients (50%) typically show basal inferolateral LV segment hyper-enhancement with sparing of the subendocardial portion [12].

This case illustrates the value of using CMR to provide a more integrated investigation in the central diagnosis and the management of cases of non-specific cardiomyopathy and apparent wall thickening and/or infiltration. It also highlights the critical importance of recognizing the variations and departure from the norm (as illustrated by the unusual pattern of T1 relaxation in this patient). It is incorrect to simply categorize such individuals as hypertensive heart disease where several different pathophysiological processes with variable outcomes and management structures exist. This differentiation may not be possible with standard screening echocardiography alone.

Conflict of interest: none declared

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