International Journal of Research in Medical Sciences
Sharma AK et al. Int J Res Med Sci. 2020 Jan;8(1):221-225
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20195911

Original Research Article

Cardiac magnetic resonance in tropical endomyocardial fibrosis

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Received: 01 November 2019
Revised: 18 November 2019
Accepted: 28 November 2019

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ABSTRACT

Background: Endomyocardial fibrosis has varied presentatation and difficult to diagnose. Aim to elucidate the role of Cardiac Magnetic Resonance (CMR) imaging in the evaluation of Endomyocardial Fibrosis (EMF) and to devise diagnostic criteria for the disease.
Methods: Retrospective analysis of cases of restrictive cardiomyopathy referred for Magnetic resonance imaging over a period of 5 years. All patients underwent 1.5 T CMR imaging (Magnetom Avanto, Siemens, Germany) with standard cardiomyopathy protocol. Criteria for diagnosis of RCM included normal sized ventricles, normal/reduced systolic function, uni-/bi-atrial enlargement, normal pericardium and absent septal bounce. Cases diagnosed as EMF on CMR were included in this study. Statistical analysis performed using SPSS software.
Results: EMF was diagnosed in 20 patients (31%) [12 males; age 39±18 years]. Ten patients had Right Centricular (RV) EMF, 3 had Left Ventricular (LV) EMF, while 7 had bi-ventricular EMF. Oedema indicating ongoing inflammation was seen in 4 (20%) cases. Apical thrombus was seen in 8(40%) cases and was present in 35% cases of RV and 20% cases of LV involvement. Subendocardial delayed enhancement was always present in the involved ventricle. The RV apex was obliterated in 100% of patients with RV EMF, while LV apex was similarly obliterated in 66% cases with LV disease. Mild-moderate pericardial effusion was observed in 8 patients. On the basis of CMR findings, the disease was classified as early necrotic phase in 1, thrombotic necrotic in 4 and late fibrotic phase in 13 and of different stages in ventricles in 2 cases.
Conclusions: EMF was the commonest cause of RCM in this series. Major diagnostic criteria of EMF on CMR include subendocardial delayed enhancement and apical obliteration. Oedema and thrombus are variable findings, depending on disease severity.

Keywords: Apical obliteration, Cardiac magnetic resonance, Endomyocardial fibrosis, Restrictive cardiomyopathy

INTRODUCTION

Restrictive Cardiomyopathy (RCM) is characterized by restrictive filling and reduced diastolic volume of either or both ventricles, with normal or near-normal systolic function and wall thickness.[1] It can be a part of systemic involvement (like sarcoidosis) or isolated to heart (like Endomyocardial Fibrosis [EMF]). The standard of care for all RCMs is medical therapy, although surgical treatment can be offered for diseases like EMF. If the etiology of RCM is known, it can alter the form of medical therapy. Besides, a close clinical differential diagnosis is chronic constrictive pericarditis, which is primarily treated with surgery. Therefore, diagnosis of RCM and its differentiation from chronic constrictive pericarditis is crucial for planning management. EMF is one of the forms of RCM observed especially in the tropical and subtropical regions.[2] EMF is an obliterative cardiomyopathy characterized by fibrotic thickening and obliteration of right (RV-EMF), left (LV-EMF) or Both Ventricles (BV-EMF) with a predilection to selectively

involve ventricular apices and inflow regions and sparing the outflow regions.

Although, morphological and functional evaluation of EMF can satisfactorily be done with echocardiography, and angiography is the gold standard for hemodynamic evaluation, all conventional modalities have low contrast resolution and therefore perform poorly in tissue characterization to confirm the diagnosis of EMF and its differentiation from chronic constrictive pericarditis.

Cardiac Magnetic Resonance (CMR), by virtue of its high contrast resolution and ability to assess morphology and function accurately, can serve as a virtual "one stop shop" for the assessment of RCMs including EMF. Available studies on the role of CMR in diagnostic evaluation of EMF are confined to case reports.[2-5] We describe the spectrum of CMR features in a group of patients with this disease and try and propose diagnostic criteria for the disease.

METHODS

This retrospective study included 100 patients presenting to facility from January 2005 onwards till October 2009 with suspicion of RCM in which cardiac MRI had been performed as part of diagnostic work up. The clinical characteristics, lab data, echocardiography findings, cardiac catheterization and endomyocardial biopsy findings (if performed) were recorded. CMR with gadolinium enhancement was performed with 1.5 T MRI (Magnetom Avanto, Siemens, Germany) after obtaining written informed consent from the patients.

Inclusion criteria

- Diagnosis of RCM on CMR included normal sized ventricles, normal/reduced systolic function, uni-/bi-atrial enlargement, normal pericardium and absent septal bounce.

Exclusion criteria

- Patients with metallic implants, Pacemakers, End stage renal disease and allergy to gadolininium were excuded.

Of the 100 patients, 64 patients were found to have RCM based upon a combination of clinical, ECG and imaging findings. Cases diagnosed as EMF had their CMR features analyzed in detail and formed the cohort group for this study. Statistical analysis performed using SPSS software.

Cardiac MR protocol

Following scout images in axial, sagittal and coronal planes, axial set of Steady State Free Precession (SSFP) were obtained. Then cine SSFP images were obtained along the short axis, vertical long axis and 4-chamber planes. Similarly, turbo spin echo T1 and T2 weighted images were obtained along the same planes as above. Afterwards, 0.05-0.1 mmol/kg IV bolus of gadolinium contrast, followed by 30ml saline flush at 3-7 ml/sec was given and delayed enhanced images were acquired, 10 min after contrast injection. The inversion time was set to null normal LV myocardium. Two dimensional (2D) segmented inversion recovery gradient recalled echo imaging was done during diastole in same view as for cine-imaging (short-axis and long-axis views) with in-plane resolution 1.4-1.8 mm. Following features on CMR were analyzed: (1) Sidedness of involvement (RV, LV or both) (2) Presence of myocardial oedema (3) Presence of apical thrombus (4) Pattern and site of subendocardial enhancement (5) Presence of pericardial effusion.

The frequency of each of the different findings was recorded as a percentage. Then an attempt to classify the disease stage was made according to pathological pattern6 as follows: (A) Necrotic with endocardial micro abscesses (corresponds to presence of myocardial edema and delayed enhancement on CMR) (B) Thrombotic-necrotic: thrombus forming on the surfaces of denuded myocardium (corresponds to presence of myocardial edema, delayed enhancement and apical thrombus on CMR) (C) Fibrotic: fibrosis, scarring of chordae tendinea (corresponds to presence of myocardial delayed enhancement without edema or apical thrombus). Due to the characteristic features of EMF on CMR, etiological confirmation beyond CMR was not considered necessary for establishing the diagnosis.

RESULTS

Of the total patients that underwent CMR, EMF was diagnosed in 20 patients (31%) [12 males; age 39±18 years]. This was the most common cause of RCM in this series (Figure 1).

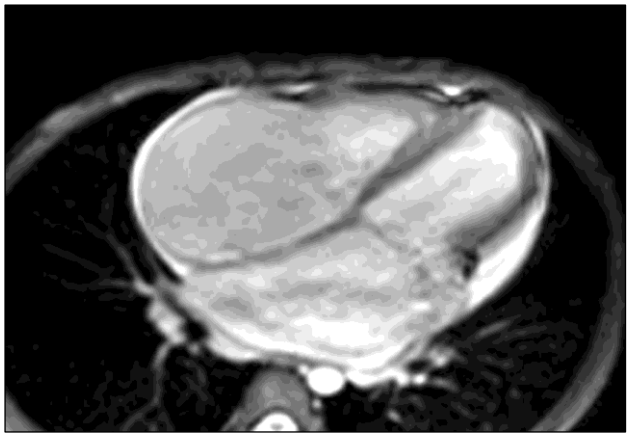

Figure1: Restrictive cardiomyopathy. Steady State Free Precession (SSFP) image in 4-chamber view shows typical imaging features: normal sized ventricles with smooth outline, dilatation of both atria and normal thickness of pericardium. Small pericardial effusion is also present.

The demographic profile and baseline characteristics of these patients are provided in Table 1. Ten patients had Right Ventricular (RV) EMF (Figure 2), 3 had Left Ventricular (LV) EMF, while 7 had bi-ventricular EMF. Oedema indicating ongoing inflammation was seen in 4(20%) cases. Apical thrombus was seen in 8(40%) cases and was present in 35% cases of RV and 20% cases of LV involvement. Subendocardial DE was always present in the involved ventricle.

The RV apex was obliterated in 100% of patients with RV involvement, while LV apex was similarly obliterated in 66 % cases with LV disease. Mild-moderate pericardial effusion was observed in 8 patients. These features are summarized in Table 2.

It was possible to differentiate the different stages (in increasing order of severity and chronicity) on the basis of CMR findings. The disease was classified as stage A in 1, stage B in 4 (Figure 3) and stage C (Figure 4) in 13 cases. It was of different stages between ventricles in 2 cases, with LV being predominantly involved.

Table 1: Baseline characteristics of study patients.

Characteristics	Number of patients (n=20)
Age, mean±SD (years)	39±18
Male, n (%)	12 (60%)
Duration of illness, mean±sd (months)	19.3±0.35
NYHA Class I, n (%)	2 (10%)
NYHA Class II, n (%)	10 (50%)
NYHA Class III, n (%)	8 (40%)
Congestive heart failure, n (%)	15 (75%)
Syncope, n (%)	4 (20%)
Pre-syncope, n (%)	1 (5%)
Palpitation, n (%)	4 (20%)
History of documented VT, n (%)	2 (10%)
History of neck pulsations, n (%)	1 (5%)
Fatigue, n (%)	10 (50%)
Angina on exertion, n (%)	0 (0%)
Atypical chest pain, n (%)	1 (5%)

Table 2: MRI findings in EMF (n=20).

MRI findings	No. of patients (n=20)
Right ventricular endomyocardial fibrosis, n (%)	10(50%)
Left ventricular endomyocardial fibrosis, n (%)	3(15%)
Bi-ventricular endomyocardial fibrosis, n (%)	7(35%)
Myocardial edema, n (%)	4(20%)
Obliteration of ventricular apex, n (%)	11(55%)
Apical thrombus, n (%)	8(40%)
Pericardial effusion, n (%)	8(40%)
Subendocardial delayed enhancement, n (%)	20(100%)

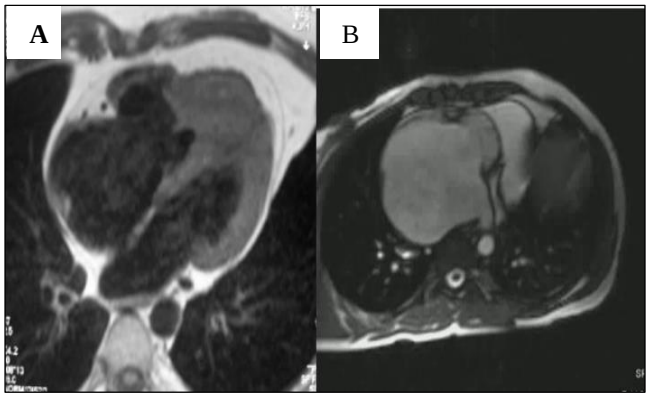

Figure 2: Isolated Right ventricular EMF. Turbo spin echo T1 weighted (A) and SSFP (B) images to show the thickening and obliteration at the RV apex with enlarged right atrium.

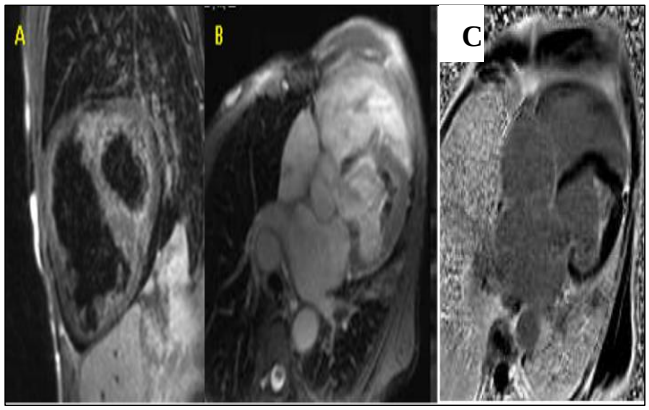

Figure 3: EMF- stage B. short axis (A) image of the TSE T2 weighted sequence demonstrates myocardial edema. (B) is an SSFP image in 4-chamber plane show the LV apical thrombus and obliteration. (C) is a delayed enhancement image in the same plane that reveals subendocardial enhancement with thrombus at the LV apex.

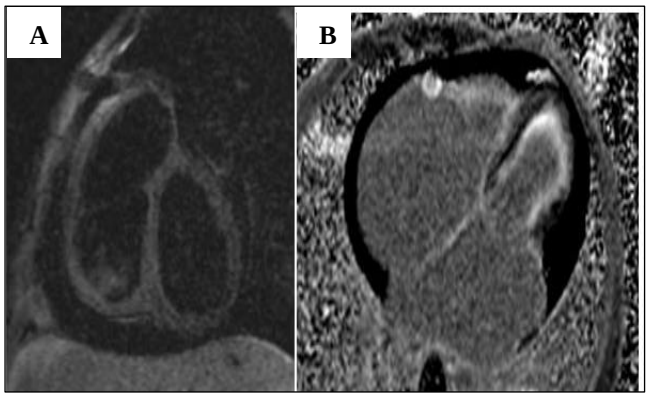

Figure 4: EMF-stage C. short axis (A) image of the TSE T2 weighted sequence shows absence of any myocardial edema. (B) is a delayed enhancement image in the 4-chamber plane that shows only subendocardial enhancement without thrombus.

DISCUSSION

There are two disease entities that have similar pathological features but have very different geographical distribution and clinical features- these include Loffler's Endocarditis (LE) and EMF. LE is seen in non-tropical countries and is associated with hyper eosinophilia that can be secondary to neoplasm, infection, allergy or idiopathic.[7] On the other hand, EMF is seen in tropical countries and is typically not associated with eosinophilia.

Oslen described three stages of EMF, namely, necrotic, thrombotic necrotic and fibrotic thrombotic.[6] Necrotic phase is characterized by eosinophilic infiltration of myocardium predominantly in the subepicardial region of the apex and inflow portion of both ventricles. Outflow tracts are usually spared. Inflammation leads to myocardial necrosis and micro-abscess formation. As disease progresses, denudation of sub endocardium leads to formation of thrombus in ventricular cavity. As disease becomes chronic, organization leads to fibrosis in subendocardial region and overlying thrombus.[8] Fibrosis leads to reduced compliance and restrictive physiology. Involvement of papillary muscles and inflow portion is common and can lead to valvular regurgitation.[9] It can involve one or both ventricles, more commonly right side. Isolated involvement of left ventricle is uncommon.[10]

Angiocardiography used to be the mainstay for making the diagnosis, the classical findings being apical obliteration, dilatation of outflow tract with atrial enlargement and tricuspid incompetence. However, these typical features are only seen late in the disease. Early EMF with changes in myocardium without alteration in lumen outline may go undetected with angiography.

Echocardiography is most often the first imaging test performed in suspected RCM including EMF due to its non-invasive nature, high temporal resolution, ability to image in any plane, portability and short procedure time. However, due to its inherent poor tissue characterization, echocardiography by itself is not capable of confirming the diagnosis of EMF in most case. Furthermore it has a limited field of view and assessment of right ventricle and ventricular apex and the pericardium is limited.

Rapid technological advances have made CMR the modality of choice for the diagnosis of EMF. Previous reports on role of CMR in EMF are restricted to case reports.[2-5,11] (Table 3). This series is the largest till date reported in the literature. Author found EMF to be the commonest cause of RCM (31%). Interestingly, while EMF is considered endemic in coastal belt of Kerala in India and its incidence in North India is said to be much less, all this patients were from the northern parts of this country. Late enhancement of ventricular apices with gadolinium along with apical obliteration and thrombus formation has been described in EMF in various case reports in literature. Similar finding were observed in this study. Of the 20 patients, 50% had RV involvement, similar to previously described in histopathological studies. All (100%) had evidence of subendocardial delayed enhancement while 40% had apical thrombus. The RV apex was obliterated in 100% of patients with RV involvement, while LV apex was similarly obliterated in 66 % cases with LV disease.

By virtue of its ability for tissue characterization, it was possible to stage the disease severity on CMR in all this cases. This information may be critical to planning appropriate therapy. Recognition of early EMF (stage A), may allow timely institution of steroids that can prevent further progression to fibrotic phase.[12] The endomyocardial infiltration was seen as high T2 signal intensity in endocardial and subendocardial portions of ventricular apices and inflow portions, indicated oedema. In the absence of thrombus, this is the earliest stage of the disease and was seen in 1 patient. As the disease progresses, a thrombus can form overlying the involved endocardium (stage B). This was appreciated in 4 patients and was seen as a hypointense band on SSFP sequences and non-enhancing hyopintensity between enhancing endocardium and bright blood pool on DEIR sequences (referred to as the "sandwich appearance").

As fibrosis develops, the apex may become obliterated and dense fibrosis develops (stage C). Majority of patients (13) were seen to be in this stage. This was manifest on CMR as an enhancing endomyocardial band without any evidence of oedema or thrombus formation. An interesting observation in this study was the differential severity of involvement of the two ventricles in 2 cases. This has not been previously described. One of these cases revealed obliteration of LV apex along with apical LV thrombus and DE with gadolinium. However, RA and RV were enlarged without any other finding. The other patient had evidence of apical RV obliteration, RVOT aneurysm and focal LV lateral wall thickening without any DE.

This study conclusively establishes that EMF can be easily diagnosed and staged accurately with contrast MRI. We propose following criteria for diagnosis of EMF by MRI:-

Unilateral/bilateral obliteration of ventricular apex with fibrous tissue

Apical thrombus

DE of ventricular apex with gadolinium indicating accumulation of fibrous Tissue.

Overall EMF carries a poor prognosis. Medical treatment is usually ineffective, though Lombardi et al, in one case have demonstrated reduction in myocardial obliteration and infiltration on serial CMR after medical therapy.[13] Some patients may benefit from surgical procedures in the form of endocardial resection and AV valve replacement. One surgical series has described 10 year survival of 68% after surgery.[9]

Table 3: Reported studies on role of cardiac magnetic resonance in endomyocardial fibrosis.

	Cury RC, 20054	Valls MF, 20072	Goo HW, 200111	Salanitri GC, 20053	Alter P, 20065	Present study
Number of patients	1	1	1	1	1	20
Apical obliteration	Present	Present	Not Present	Present	Present	11(55%)
Apical thrombus	Present	Present	Absent	Present	Present	8(40%)
Delayed enhancement	Present (apical)	Present (apical)	Present (RVOT)	Present (apical)	Present (apical)	20(100%) (various sites)
Pericardial effusion	Present	Absent	Absent	Absent	Absent	8(40%)
Comments	Normal AEC	Normal AEC	RVOT involved	Hypereosinophilia	Hypereosinophilia	No eosinophilia

CONCLUSION

CMR is an accurate technique for the demonstration of the entire spectrum of morphological and functional abnormalities in EMF. To the best of knowledge, this is the largest case series reported till date, reporting role of CMR in the evaluation of this disease. We found the major diagnostic criteria to be the presence of apical subendocardial delayed enhancement and apical obliteration. Other findings reflected disease stage. CMR findings thus help to obviate the need for biopsy and plan appropriate therapy in patients with EMF.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Sharma AK, Kumar T, Ramakrishnan S. Cardiac magnetic resonance in tropical endomyocardial fibrosis. Int J Res Med Sci 2020;8:221-5.