# CARDIAC SARCOIDOSIS-MRI FINDINGS IN 4 CASES

**M. Puvaneswary MB,BS; F.R.C.R,** [1] **D.C Sutherland MB,BS; F.R.A.C.P,** [2]

**R. A. Hackworthy MB,BS; F.R.A.C.P** [3]

## SUMMARY

Sarcoidosis is a multisystem granulomatous disease and symptomatic cardiac involvement is found in less than 5%. The diagnosis of cardiac sarcoidosis can be missed on endomyocardial biopsy because of the patchy distribution of lesions. We report 4 cases diagnosed using MRI.

**Key words:** magnetic resonance imaging(MRI); cardiac sarcoidosis

## CASE REPORTS

### CASE 1

A 69-year-old woman was admitted November 1997 for secondary AV Block.

A chest radiograph demonstrated hilar lymphadenopathy and a diagnosis of sarcoidosis was made on histology.

She was referred for an MRI of the heart to determine if there was any evidence of myocardial sarcoidosis.

MRI images demonstrated nodular lesions in the anterior and mid interventricular septum and anterolateral left ventricle at the level of the mitral valve.

Nodular lesions were hypointense to the myocardium on T1-weighted, proton density and T2-weighted sequences with a peripheral high signal intensity (Fig 1a).

The subcarinal and hilar lymph nodes were enlarged. The myocardial findings were interpreted as being consistent with either myocardial sarcoidosis or secondary deposits. In the clinical setting it was decided sarcoidosis to be the most likely cause and patient was treated with oral corticosteroids.

A follow-up MRI in August 1998 was performed with limited sequences and orientation. There was focal nodular thickening of the anterior and mid interventricular septum and anterior left ventricle and STIR sequences demonstrated increase signal intensity (Fig1b). The subcarinal and hilar lymph nodes were enlarged.

A second follow-up MRI in January 1999 was performed .There was reduction in the septal

[1] Department of Medical Imaging
[2] Medicine
[3] Cardiovascular Medicine, John Hunter Hospital, N.S.W AUSTRALIA

**Correspondence :** M.Puvaneswary John Hunter Hospital Locked Bag No1 Hunter Mail Centre NSW 2310 Phone: 49213383 Fax : 49213949

and anterior left ventricular wall thickening and fewer nodular lesions in the mid septum and anterior left ventricle were present.( Fig1c). The subcarinal and hilar lymph nodes were enlarged. An endomyocardial biopsy was not performed.

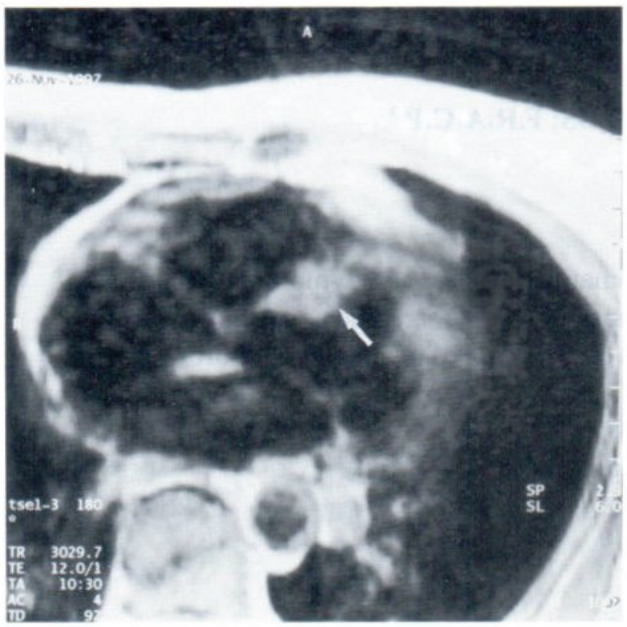


**Fig 1a** Axial proton density fast spin-echo image demonstrate hypointense nodular lesion in the mid interventricular septum with a periph eral high signal intensity.(arrow)

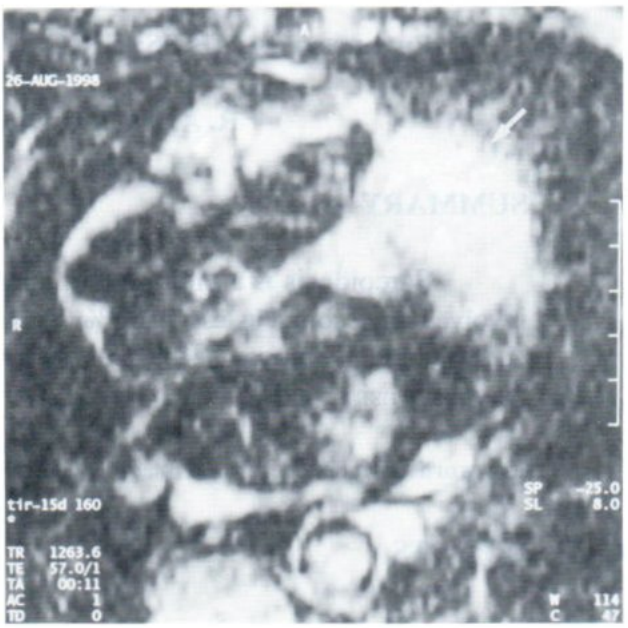


**Fig 1b** Follow-up axial STIR image demonstrate increase signal intensity and focal thickening at the anterior and mid interventricular sep tum and anterior left ventricle (arrow).

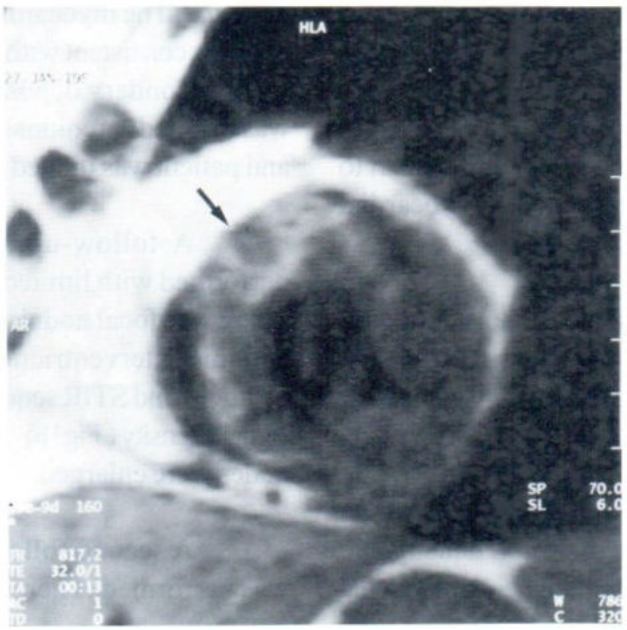


**Fig 1c** Follow-up short-axis T1- weighted fast spin-echo image reveal several hypointense nodular lesions with peripheral increase signal intensity in the interventricular septum (arrow)

## CASE 2

A 59-year-old male with known history of pulmonary sarcoidosis and echocardiographic findings of left ventricular diastolic dysfunction was referred for a cardiac MRI in June 2002.An ECG-gated MRI was performed to rule out the presence of cardiac sarcoidosis. Gadolinium-enhanced images in the axial and short-axis orientation were obtained.

Cine sequences demonstrated a focal thinning of the anterior wall of the left ventricle at the apex of the heart. (Fig2a) The rest of the left ventricular wall demonstrated hypertrophy and normal contractility. There were a few focal areas of hypointense nodule in the anterior wall of the right ventricle, anterior and lateral wall of the right ventricular out-flow tract , anterior and mid inter-ventricular septum and anterolateral wall of the left ventricle and anterior papillary muscle. There was patchy enhancement of the anterior wall of the right ventricle and interventricular septum and peripheral enhancement of the nodule in the anterior papillary muscle.(Fig2b)

Multiple enlarged paratracheal, aorto-pulmonary window ,subcarinal and hilar lymph nodes were present. An endomyocardial biopsy was not performed.

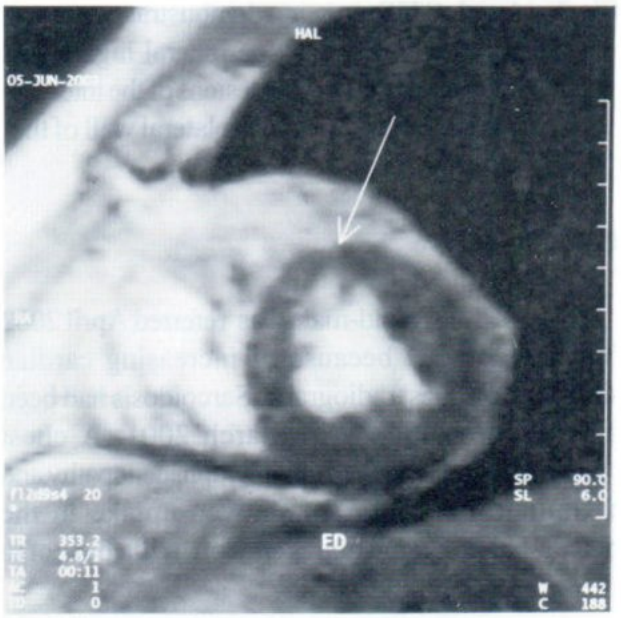


**Fig2a** Short - axis cine sequence at the apex of the heart end-diastolic (ED) image demonstrate focal thinning of the anterior wall of the left ventricle(arrow)

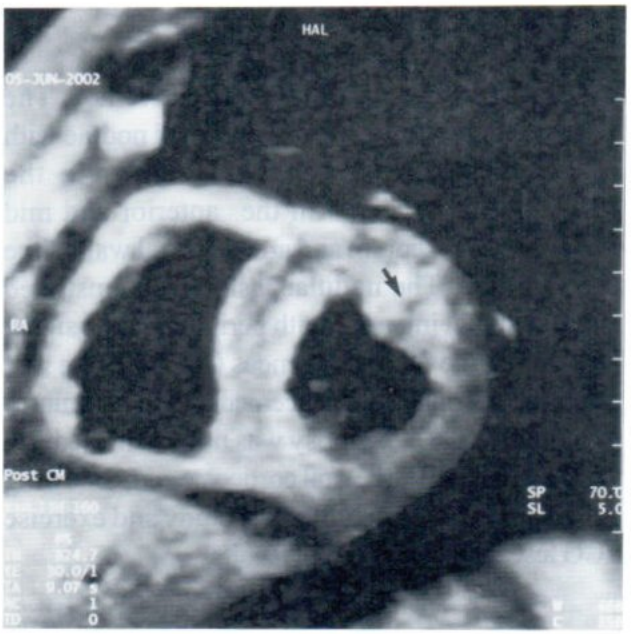


**Fig2b** Gadolininum-enhanced image in the short-axis orientation demonstrate peripheral enhance ment of the nodular lesion in the anterior papillary muscle.(arrow)

## CASE 3

A 44-year- old male was referred in August 2000 for cardiac MRI on the basis of an echocardiographic findings raising the possibility of cardiac sarcoidosis. He was on high dose steroid treatment. He had presented in March of that year with malaise, fatigue and a persistent cough. He was shown on computed tomography (CT) scanning to have multiple pulmonary nodules, and at least two low attenuation lesions in his liver. A gallium scan was normal. An ECG showed a sinus tachycardia, and transthoracic echocardiography identified mild concentric hypertrophy and hyperkinetic function of the left ventricle and mild left ventricular diastolic dysfunction, mild left and right atrial enlargement, mild tricuspid regurgitation and mild pulmonary hypertension.

An ECG-gated MRI was performed. The MRI study demonstrated several small nodule with surrounding increase signal intensity in the T1-weighted spin-echo in the anterior and mid interventrcular septum and anterolateral wall of the left ventricle. The nodular lesions demonstrated increase signal intensity with peripheral high signal intensity in the STIR sequences (Fig3). There was patchy and peripheral enhancement with gadolinium. An endomyocardial biopsy was not performed. He improved on high dose oral corticosteroid, following which an ECG , Holter monitor study and exercise ECG test all yielded normal results.

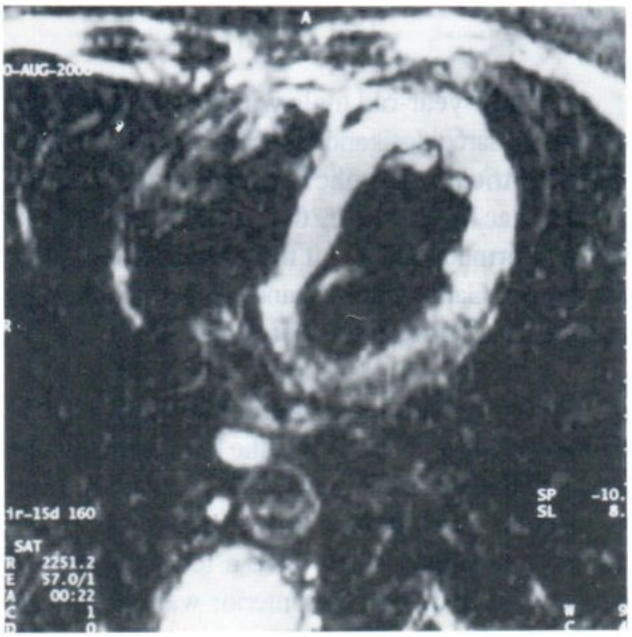


**Fig 3** Axial STIR image demonstrate increase signal intensity with peripheral high signal intensity of the nodular lesions of the interventricular septum and anterolateral wall of the left ventricle.

## CASE 4

A 75-year-old-male was referred April 2002 for cardiac MRI because of increasing cardiac silhouette on chest radiograph. Sarcoidosis had been diagnosed on biopsy in March 2001. A chest radiograph demonstrated hilar lymphadenopathy and a Gallium-67scintigram showed uptake in the bilateral hilar lymph nodes and left axilla but not in

the heart. A HRCT performed in April 2001 confirmed enlarged hilar lymph nodes but there was no evidence of interstitial lung disease. He was started on high oral corticosteroids.

A repeat HRCT in March 2002 demonstrated persistent enlargement of the hilar lymph nodes and increasing size of the heart. A transthoracic echocardiography demonstrated moderate left ventricular diastolic dysfunction, and right and left atrial enlargement .There was moderate pulmonary hypertension but no evidence of cardiac sarcoidosis. A MRI scan was suggested for evaluation of cardiac sarcoidosis. MRI demonstrated moderate right and left atrial enlargement and pulmonary hypertension. There was concentric hypertrophy of the left ventricular myocardium. The interventricular septum was thickened and demonstrated mild diffuse increase signal intensity in T1-weighted sequences which was more prominent in the T2-weighted images. There was patchy enhancement of the interventricular septum and peripheral enhancement of a nodule in the anterior interventricular septum at the level of the mitral valve (Fig4). The hilar lymph nodes were enlarged. The patient underwent an endomyocardial biopsy which did not reveal sarcoid granuloma, giant cells, inflammation or fibrosis.

**HRCT** = Hilar Region CT.

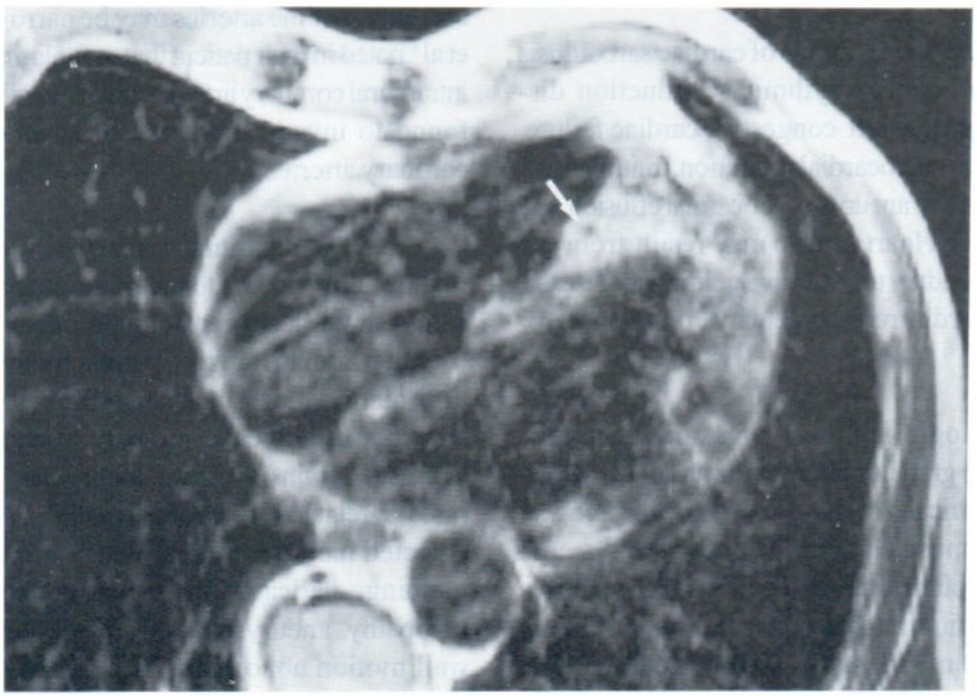

**Fig 4** Axial gadolinium-enhanced image demonstrate peripheral enhancement of the nodule in the anterior interventricular septum.(arrow)

## DISCUSSION

Sarcoidosis is a multisystem granulomatous disease .Cardiac involvement is symptomatic in less than 5% of patients,[1] but myocardial involvement in autopsy series has been identified in 20-27% of cases.[2] Sudden death due to ventricular tachyarrhythmias or conduction disturbances has been reported in 30-65% of identified cases of cardiac sarcoidosis [3,4] Most patients with cardiac sarcoidosis causing sudden death have preceding evidence of ventricular arrhythmias or evidence of high degrees of heart block.

Sudden death may be the initial manifestation of undiagnosed sarcoidosis and extensive cardiac infiltration with cardiac dysfunction are infrequently associated with dysfunction of another organ.[5]

Clinical presentations of cardiac sarcoidosis include ventricular arrhythmia, conduction disturbances , right and left congestive cardiac failure, cardiomyopathy, myocardial infarction, mitral insufficiency ,ventricular aneurysm, pericardial effusion and sudden death.[6,7] Heart failure may result from cor pulmonale secondary to extensive pulmonary disease, or from myocardial replacement by inflammation or fibrous tissue.[6]

Pathologic features of sarcoid cardiac disease include granulomatous infiltration of myocardium ( interventricular septum, left ventricular free wall and papillary muscles) and fibrous scars.[2] Sarcoid involvement is often patchy.[6] The lesions occur mainly in the myocardium and the endocardium, and rarely in the epicardium. The septum is involved in 90% of autopsy cases with cardiac sarcoidosis, and the posterior part of the septum appears to be more commonly involved.[2,7] Sarcoid infiltration initially results in a thickened myocardium principally involving the interventricular septum, resulting in some cases, in asymmetric septal hypertrophy. Later, either due to corticosteroid therapy or as a result of natural course of the disease,resolution or scar occurs.[7] Left ventricular aneurysms, and congestive cardio-myopathy may develop secondary to myocardial fibrosis and scarring in healed sarcoid granulomas.[6]

The atrioventricular node and His bundle are involved frequently and this is thought to be responsible for the cardiac arrhythmias and conduction disturbances. Extensive granulomatous involvement of the sinus node has been reported in a patient who presented with sudden death.[4] Pericardium, coronary vessels, and cardiac valves are less commonly involved.

James [8] reported granulomas surrounding the intramural coronary arteries of atria,ventricles or both, and lumen of the arteries may be narrowed. Virmani et al [9] noted in their patient that granulomas surrounded intramural coronary arteries, and epithelioid cells were found to invade the walls of several intramural coronary arteries.

50% of patients with systemic sarcoidosis without clinical evidence of cardiac involvement demonstrate electrocardiographic changes The most common findings are repolarisation changes, conduction disturbances, and arrhythmias. Transmural infarction occurs less commonly.[11] Echocardiography is a useful non-invasive technique for detecting sarcoid -related cardiac abnormalities. Abnormalities detected include abnormal septal thickening and thinning, pericardial effusion , congestive cardiomyopathy, aneurysm of the left ventricle , and focal wall motion abnormalities.[7,12] Focal wall motion abnormality localised to the basal portion of the ventricular septum is unusual in coronary artery disease and suggests the possibility of cardiac sarcoid even in the absence of recognised systemic disease.[1]

However, early diagnosis of cardiac infiltration is difficult.[11]

Cardiac sarcoid may occur in the absence of radiological evidence of pulmonary or systemic disease , and the diagnosis should be suggested by cardiomegaly, congestive heart failure, pericardial effusion, or left ventricular aneurysm.[6]

Radionucleotide studies may be helpful in this regard.[6]

Isotope scans can detect cardiac involvement in patients with sarcoidosis but are limited by poor spatial resolution. Extensive cardiac sarcoidosis may be diagnosed by defect on scintigraphy using Gallium-67, Thallium-201 or Technetium-99m pyrophosphate in the absence of ischaemic heart disease.[10]

Endomyocardial biopsy or open heart biopsy is essential in the definitive diagnosis of cardiac involvement. However a negative biopsy does not exclude the diagnosis as sarcoid infiltrationis often is focal or patchy. Corticosteroid therapy converts sarcoid granulomas into dense scar tissue and the granulomas may disappear entirely.[9] A non-invasive diagnostic means of identifying cardiac sarcoid is required to detect patient with high risk of life threatening cardiac arrhythmias or cardiac damage.[7] Patient with sarcoidosis could then be evaluated regularly.

In 1988 ,Riedy et al(13) first reported the MR appearance of myocardial sarcoidosis.

The MR study demonstrated multiple,discrete high signal intensity masses in the first- echo which increased in signal intensity on the second-echo image. The masses were within the anterolateral and posterior left ventricular wall and the basal portion of the septum. The basal portion of the septum was thickened. The initial endomyocardial biopsy before the MR study was non-diagnostic, but a repeat biopsy of the interventricular septum, directed by MR findings revealed typical sarcoid granuloma.

Matsuki et al [3] first reported gadolinium -enhanced MRI findings in cardiac sarcoidosis. The T1-weighted spin-echo images demonstrated nodular lesion with low signal intensity within the basal portion of the ventricular septum, with a central portion of even lower signal intensity. The T2-weighted images demonstrated peripheral areas of the nodule with high signal intensity. Gadolinium-enhanced T1-weighted images revealed peripheral enhancement. The central portion of the nodule showed low signal intensity in both the T1- and T2-weighted images.

Otake et al (14) reported nine patients with the nodular type of muscular sarcoidosis. The lesions consisted of a star-shaped area of low signal intensity in both T1-and T2 -weighted spin-echo surrounded by an area of high signal intensity Histopathology of nodular sarcoidosis involving the skeletal muscle demonstrated that low signal intensity on both T1-and T2-weighted images surrounded by an area of high signal intensity on T2-weighted images arose from central areas of hyaline fibrotic tissue and peripheral areas of active inflammatory granulomatous tissue.

Shimada et al [11] in a study of histologically proven cardiac sarcoidosis in 8 patients demonstrated localised enhancement, indicating interstitial odema and inflammation.

Cardiac lesions were demonstrated as areas of high signal intensity on T1-weighted spin-echo images and they suggested these findings to represent active inflammation. Following a month of steroid therapy, the enhanced areas were markedly diminished in size and signal intensity, indicating reduce interstitial odema associated with active inflammation and the response to steroid therapy.

Vignaux et al [15] described a range of abnormalities on MRI in cardiac sarcoidosis. These included focal myocardial thickening, focal intramyocardial increased signal intensity on T2-weighted sequences, focal intramyocardial

increased signal intensity on gadolinium DTPA -enhanced T1-weighted images, or a combination of these findings. The MRI findings were grouped into three patterns: the pure nodular pattern with a peripheral increased and a central decreased intramyocardial signal intensity on both T2-weighted and gadolinium-DTPA-enhanced T1-weighted images, the inflammatory focal or patchy pattern with increased signal intensity on gadolinium-DTPA -enhanced T1-weighted images with or without myocardial thickening, and the post-inflammatory pattern with focal increased intensity on T2- weighted images (but no gadolinium enhancement) with or without myocardial thinning. The focal increased signal intensity on T2-weighted images without gadolinium enhancement occurs in scar tissue with a fibrotic component and may occur in chronic ischaemic heart disease.[15] Inoue et al [10] demonstrated enhancement of active inflammation and during the healing stage of cardiac sarcoid but not in scar tissue.

MRI is capable in demonstrating post inflammatory scarring from healed sarcoid granulomas. MRI due to its high spatial resolution , can detect scarring even limited to the subendocardium with both static and functional imaging techniques. Both regional and global ventricular function can be evaluated. Hilar and mediastinal lymphadenopathy can be imaged.[16] MRI is non-invasive and is recommended in early detection of myocardial involvement, as many as 60% of these patients sudden death may be the first manifestation of cardiac sarcoidosis.[15]

The present study demonstrated hypointense irregular nodules in T1-weighted, proton density, and T2-weighted sequences with surrounding high signal intensity. STIR sequences demonstrated increased signal intensity at the centre of the nodule and high signal intensity in the periphery in the third case and focal thickening and increase signal intensity in the first case. There was patchy enhancement and few nodules demonstrated peripheral enhancement.

In addition , in the second patient nodular lesions were demonstrated in the right ventricle. There was a focal thinning and reduced thickening during systole in the anterior wall of the left ventricle with hypertrophy of the remainder of the left ventricular myocardium, indicating focal scarring.

The first patient in our series underwent serial MRI over a period of 2 years confirming the abnormalities. Gadolinium-enhanced sequences were not obtained in the first two MRI studies. Only a few nodule demonstrated peripheral enhancement suggesting active inflammation. Lesion without enhancement are thought to be most likely to be scar tissue.[15] In patients three and four , the clinical cardiological abnormalities resolved with high dose corticosteroid therapy, and repeat MRI studies could not be justified.

Our study has limitation that endomyocardial biopsy was not performed in all the patients and ,we are unable to correlate MRI appearances with histologic findings. The patchy distribution of lesions means that the diagnostic yield from biopsy is low and significant cardiac disease may be missed . The patchy distribution and predilection for left ventricle and interventricular septum (usually the basal portion) is characteristic. Differential diagnosis of multiple myocardial lesions include other granulomatous diseases, abscesses, and metastases The diagnosis of cardiac sarcoidosis was strongly suspected in these 4 patients and other causes of cardiac disease were excluded.

## CONCLUSION

Early diagnosis of myocardial involvement is important so that steroid treatment can be initiated to prevent malignant arrhythmias and improve left ventricular function. Myocardial infiltration is patchy and focal, and sampling error may occur with endomyocardial biopsy. With relevant clinical findings, the security of a provisional diagnosis of cardiac sarcoid can be greatly increased with MRI.

Such imaging also provide information about the extent of cardiac involvement and assist in guiding endomyocardial biopsy.

The indications for treatment in sarcoidosis are symptoms, hypercalcemia and evidence of organ damage. Thus cardiac MRI may be invaluable in guiding the initiation and duration of such therapy. This limited series suggests that MRI should be employed more frequently in the diagnosis and management of cardiac sarcoidosis.

## REFERENCES


1. Valentine H, McKenna WJ, Nihoyannopoulos P, Mitchell A, Foale RA, Davies MJ, Oakley CM. Sarcoidosis : a pattern of clinical and morphological presentation. Br Heart J 1987; 57: 256-263.
2. Silverman KJ, Hutchins GM, Bulkley BH. Cardiac sarcoid : a clinicopathologic study of 84 unselected patients with systemic sarcoidosis. Circulation 1978; 58: 1204-1211
3. Matsuki M, Matsuo M. MR findings of myocardial sarcoidosis. Clin Radiol 2000; 55:323-325
4. Abeler V. Sarcoidosis of the cardiac conducting system. Am Heart J 1979; 97:701-707
5. Roberts WC, McAllister HA Jr, Ferrans VJ : Sarcoidosis of the heart ; a clinicopathologic study of 35 necropsy patients (GroupI) and review of 78 previously described necropsy patients (GroupII). Am J Med 1977 ; 63 : 86-108
6. Chiles C, Adams G W, Ravin C E. Radiographic manifestations of cardiac sarcoid. AJR 1985; 145:711-714
7. Lewin R F, Mor R, Spitzer S , Arditti A, Hellman C, Agmon J . Echocardiographic evaluation of patients with systemic sarcoidosis. Am Heart J 1985;110: 116-122.
8. James T N.Sarcoid heart disease.Circulation 1977; 56: 320-326.
9. Virmani R, Bures J C, Roberts W C. Structure - function correlations in cardiovascular and pulmonary diseases(CPC) Chest 1980 ; 77 : 423-428.
10. Inoue SI , Shimada T, Murakami Y. Clinical significance of Gadolinium - DTPA - enhanced MRI for detection of myocardial lesions in a patient with sarcoidosis. Clinical Radiology 1999;54: 70-72.
11. Shimada T, Shimada K, Sakane T, Ochiai K, Tsukihashi H, Fukui M, Inoue S, Katoh H, Murakami Y, Ishibashi Y, Maruyama R. Diagnosis of cardiac sarcoidosis and evaluation of the effects of steroid therapy by Gadolinium - DTPA - enhanced magnetic resonance imaging. Am J Med 2001; 110 : 520-527.
12. Lull RJ, Dunn BE, Gregoratos G, Cox WA, Fisher G W : Ventricular aneurysm due to cardiac sarcoidosis with surgical cure of refractory ventricular tachycardia. Am J Cardiol 1972; 30: 282- 287
13. Riedy K, Fisher MR, Belic N , Koenigsberg DI. MR Imaging of Myocardial Sarcoido sis. AJR 1988; 151:915-916.
14. Otake S, Banno T, Ohba S , Ohba S, Noda M, Yamamoto M. Muscular sarcoidosis : findings at MR imaging .Radiology 1990;176: 145-148.
15. Vignaux O, Dhote R, Duboc D, Blanche P, Devaux J-Y, Weber S, Legmann P.Detection of myocardial involvement in patients with sarcoidosis applying T2- weighted, contrast -enhanced, and cine magnetic resonance imaging: initial results of a prospective study. J.Comput Assist Tomogr 2002;26:762-7671
16. Chandra M, Silverman M, Oshinski J, Pettigrew R. Diagnosis of Cardiac Sarcoidosis Aided by MRI. Chest 1996 ; 110 : 562-565.