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CME ARTICLE

Clinics in diagnostic imaging (189)

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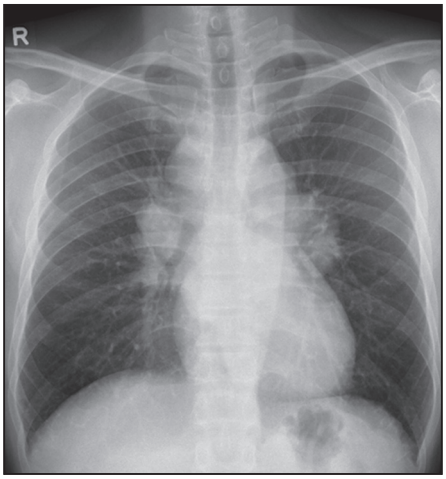

Fig. 1 Frontal chest radiograph of the patient taken at the time of presentation.

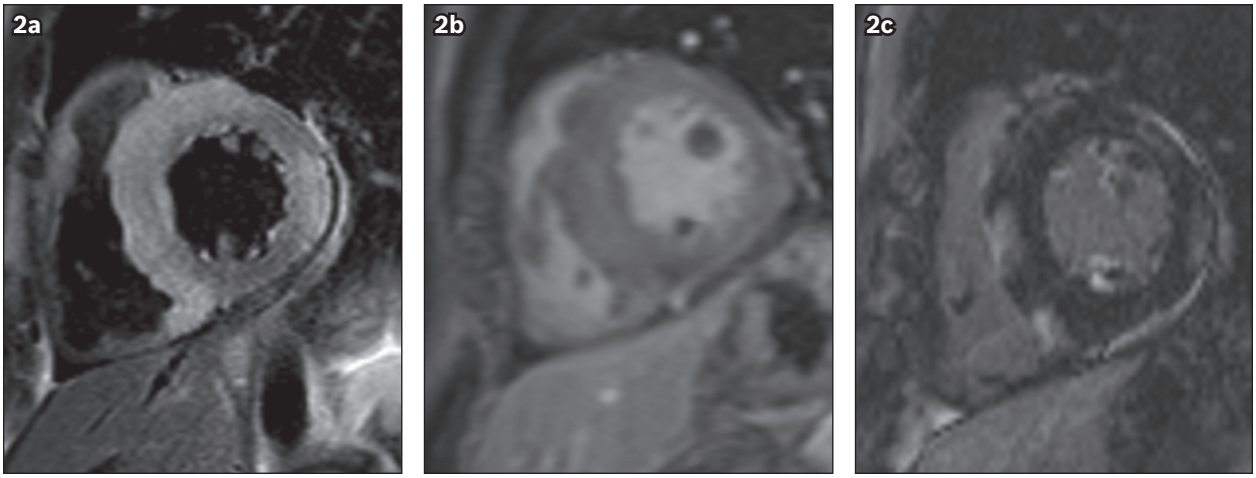

Fig. 2 Short-axis (a) T2-W, (b) early contrast-enhanced and (c) late gadolinium enhancement (LGE) MR images.

CASE PRESENTATION

A 44-year-old man presented to the emergency department with breathlessness and a history of intermittent episodes of palpitation for the past one year, which had increased in frequency to almost every day (2–3 times per day) over the last two weeks. Each episode lasted for about 10–15 minutes. The first electrocardiogram (ECG) showed features of right bundle branch block, followed by subsequent ventricular tachycardia. The patient was started on verapamil and amiodarone, and was given 150 joules of electrical cardioversion. His troponin T and creatine kinase levels were high at 175.4 (0–14.0) pg/mL and 666 (24–200) U/L, respectively. Echocardiogram showed concentric left ventricular (LV) hypertrophy with hypokinetic wall motion and LV systolic dysfunction. What do the chest radiograph (Fig. 1) and cardiac magnetic resonance (CMR) images (Fig. 2) show? What is the diagnosis?

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IMAGE INTERPRETATION

The frontal chest radiograph (Fig. 1) shows lobulated soft tissue masses in the right paratracheal and bilateral hilar regions, in keeping with enlarged lymph nodes. Both lungs are otherwise unremarkable. In view of mediastinal and symmetrical hilar lymphadenopathy, the radiographic differentials were sarcoidosis, lymphoma and metastatic lymphadenopathy. However, based on the patient's clinical presentation and radiographic and echocardiographic findings, a suspicion of sarcoidosis was raised and CMR imaging was advised.

CMR imaging confirmed mediastinal and bilateral hilar lymphadenopathy. In addition, it shows extensive confluent areas of increased T2 signal intensity (corresponding to oedema) in the septum, anterior septal segment and inferior septal segment that extended into the adjoining right ventricle wall and in the lateral wall of the LV (Fig. 2a). Scattered nodular areas of increased T2 signal intensity with focal wall thickening involving the anterior and diaphragmatic wall of the right ventricle were also noted. Correspondingly, these areas of increased T2 signal show early enhancement (Fig. 2b). Asymmetrical wall thickening that is worse in the septal region is seen in the LV. The maximum end-diastole thickness of the interventricular septum in the mid-cavity region was 2.3 cm. Late gadolinium enhancement (LGE) images show multiple discrete and confluent hyperintense foci (nodules) in the septal wall, inferior septal wall, lateral wall of the LV and anterior and diaphragmatic wall of the right ventricle (Fig. 2c). These foci are located in the mid myocardium and epicardium, sparing the subendocardial region. Scattered areas of increased T2 signal intensity in the biventricular myocardial wall correspondingly show restricted diffusion on diffusion-weighted images (Fig. 3). Cine MR images show hypokinesis involving multiple segments that is most severe in the basal septal wall.

Contrast-enhanced computed tomography of the thorax was performed, which also shows bilateral symmetrical hilar lymphadenopathy with extensive bilateral paratracheal, aortopulmonary window and left para-aortic lymphadenopathy (Fig. 4). No definite parenchymal changes in the lungs were seen.

DIAGNOSIS

Acute phase cardiac sarcoidosis (CS).

CLINICAL COURSE

The patient was referred to the rheumatology department and started on intravenous hydrocortisone for five days and

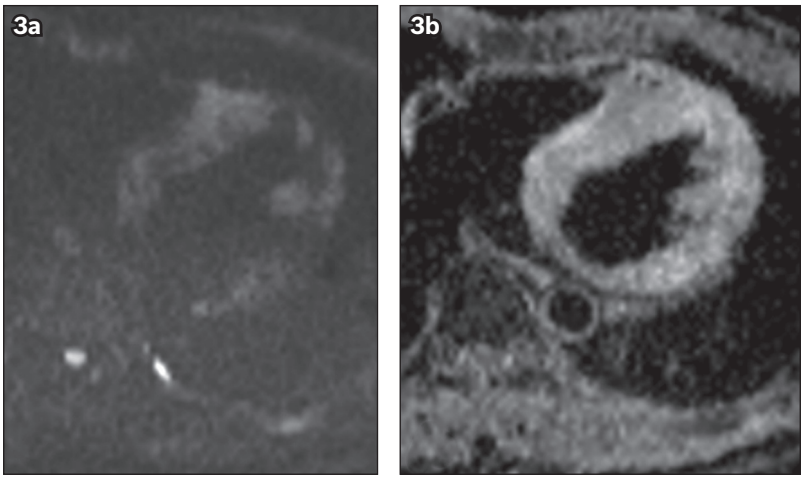

Fig. 3 (a) Axial diffusion weighted (b-1000) and (b) apparent diffusion coefficient map MR images show patchy areas of restricted diffusion in the septum and the left ventricular wall.

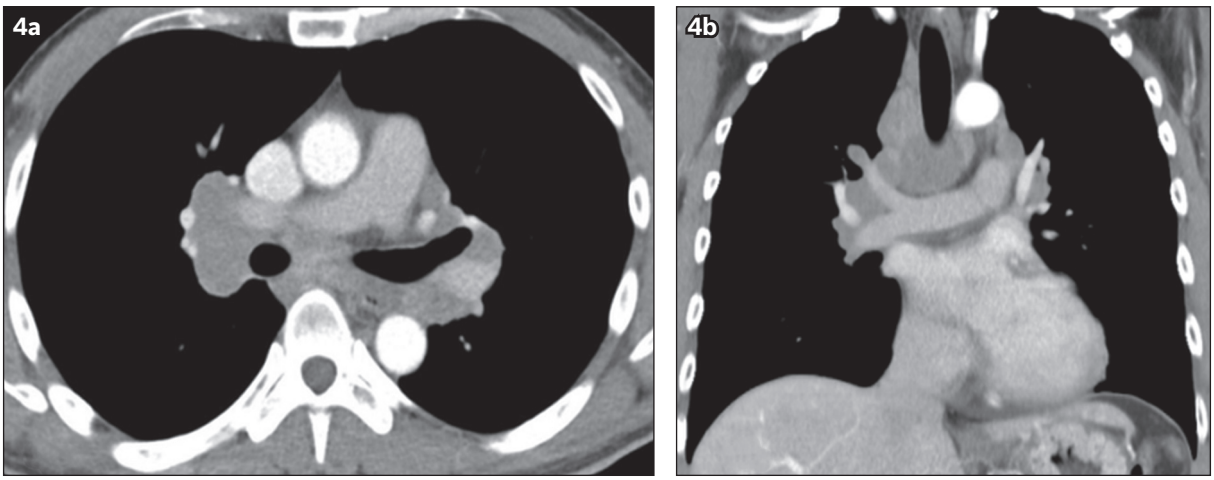

Fig. 4 (a) Axial and (b) coronal reformatted contrast-enhanced CT images of the thorax show bilateral symmetrical hilar and mediastinal lymphadenopathy.

intravenous methylprednisolone for three days. Following video mediastinoscopy and mediastinal lymph node biopsy, histopathology confirmed the diagnosis of sarcoidosis. An automated implantable cardioverter-defibrillator was inserted a few days later, and the patient was discharged and started on oral amiodarone 200 mg, bisoprolol 2.5 mg and prednisolone 60 mg. A month later, the patient presented with acute renal failure due to nephritis and blurring of vision due to posterior uveitis, both secondary to sarcoidosis. No further imaging was performed in the last three months (from the time of first presentation).

DISCUSSION

Sarcoidosis is characterised by the formation of non-caseating granulomas affecting multiple organs.[1] Sarcoidosis typically manifests as bilateral hilar lymphadenopathy and pulmonary nodules. Other organs commonly involved include the skin, eye and central nervous system.[2] Cardiac involvement, characterised by infiltrative cardiomyopathy, is clinically rare and diagnosed in only 5% of patients, even though around 20%–50% patients may show non-caseating granulomas within the myocardium on autopsy.[2,3] Patients with CS may be completely asymptomatic or may present with non-specific symptoms such as chest pain, palpitations, dyspnoea and syncope.[2] It can be life-threatening, causing fatal ventricular or supraventricular tachyarrhythmia, LV dysfunction, conduction disturbances and sudden death.[1] Approximately 12%–65% patients with CS can succumb to sudden death from dysrhythmias.[2]

CS histologically progresses through three stages: oedema, granulomatous inflammation and fibrosis leading to scarring.[3] Myocardial biopsy is highly specific and the gold standard method for diagnosing cardiac sarcoidosis. However, it is invasive and may have a false-negative result due to the patchy pattern of the disease.[1,4]

Imaging diagnosis of CS is challenging and requires good clinical, radiological and pathological collaboration. CMR imaging, with its high spatial and soft tissue contrast, has the capability to detect the acute inflammatory phase of the disease and the chronic phase, which includes fibrosis and scarring.[5] In the acute inflammatory phase, CMR imaging shows focal wall thickening and regional wall motion abnormalities, while the granulomas demonstrate patchy nodular areas of increased T2 signal intensity within the myocardium, with early enhancement and LGE due to oedema associated with inflammation.[5,6] CS commonly involves the septum, particularly the basal septum and LV free wall, whereas right ventricular involvement is quite rare.[6,7] With septal involvement, contiguous involvement of the right ventricular insertion point is often seen, as in our case.[3] CS may affect any portion of the myocardium, the commonest being transmural involvement. Focal non-transmural lesions commonly affect the subepicardial or mid-myocardial portion and less commonly, the subendocardial portion.[2,8] In severe cases, CMR imaging may show diffuse myocardial thickening secondary to massive granulomatous infiltration, resulting in significant contraction abnormalities and cardiac failure.[6] The myocardial thickening and LGE usually resolve after steroid treatment, while increased T2 signal within the myocardium may persist.[9]

In the chronic phase, CMR imaging usually shows focal or diffuse thinning of the myocardial wall with LGE, without high T2 signal or early gadolinium enhancement, indicative of myocardial damage, fibrosis and scarring.[5,10] The LGE occurs due to increased volume of contrast material in the extracellular space secondary to underlying myocardial fibrosis.[2] LGE is considered to be the strongest hallmark of CS and a marker of adverse events such as ventricular arrhythmias and sudden death.[2,5] Cine CMR images are useful in demonstrating regional wall motion and contraction abnormalities associated with advanced disease.[2] CMR imaging was shown to have a sensitivity and specificity of 100% and 78%, respectively, for diagnosing sarcoidosis.[1,11] LGE sequence is a very important CMR imaging protocol for identifying both active and chronic phases of CS, and plays a key role in both diagnostic and prognostic assessments and in evaluating response to steroid treatment.[1,2] Patel et al showed that the rates of adverse events and cardiac death were nine and 11.5 times higher, respectively, in patients with LGE on CMR imaging in CS than in patients who did not exhibit LGE.[12] After the initiation of treatment, patients with lower LGE show good response compared to those with severe LGE who either show no response or have worse outcomes.[9] Associated findings that may be identified on CMR imaging, such as right ventricular hypertrophy and dilatation, are probably due to pulmonary hypertension secondary to underlying lung disease.[6]

Other noninvasive imaging modalities, such as echocardiography and nuclear scintigraphy (thallium-201 and gallium-67), may be used to diagnose CS but have limited success. Fluorine-18 fluorodeoxyglucose positron emission tomography (i.e. 18F-FDG PET) may be useful for diagnosing CS, but is limited by cost and availability.[1]

Other cardiomyopathies that may demonstrate overlapping imaging features with CS include myocarditis, hypertrophic cardiomyopathy, ischaemic cardiomyopathy and amyloidosis.[2] These conditions, however, show different patterns of myocardial involvement. Myocarditis shows increased T2 signal in the myocardium with early enhancement and LGE, particularly in the epicardial distribution. Unlike CS, myocarditis frequently involves the lateral free wall of the LV rather than the interventricular septum (Fig. 5).[2,13]

In CS, diffuse granulomatous infiltration may result in extensive myocardial thickening, as in our case, and this can morphologically mimic hypertrophic cardiomyopathy. The diagnostic criterion for hypertrophic cardiomyopathy on CMR imaging is LV wall thickness ≥ 15 mm at end-diastole and characteristically involves the interventricular septum, most obviously in the anteroseptal myocardium.[2,14] In hypertrophic cardiomyopathy, LGE commonly involves the septum (particularly the basal portion) and the junction between the right ventricular free wall and interventricular septum, and is more likely to be mid-myocardial.[2] In contrast to CS, hypertrophic cardiomyopathy does not commonly show myocardial oedema, which is seen as increased T2 signal (Fig. 6).[2] Unlike CS, CMR imaging in

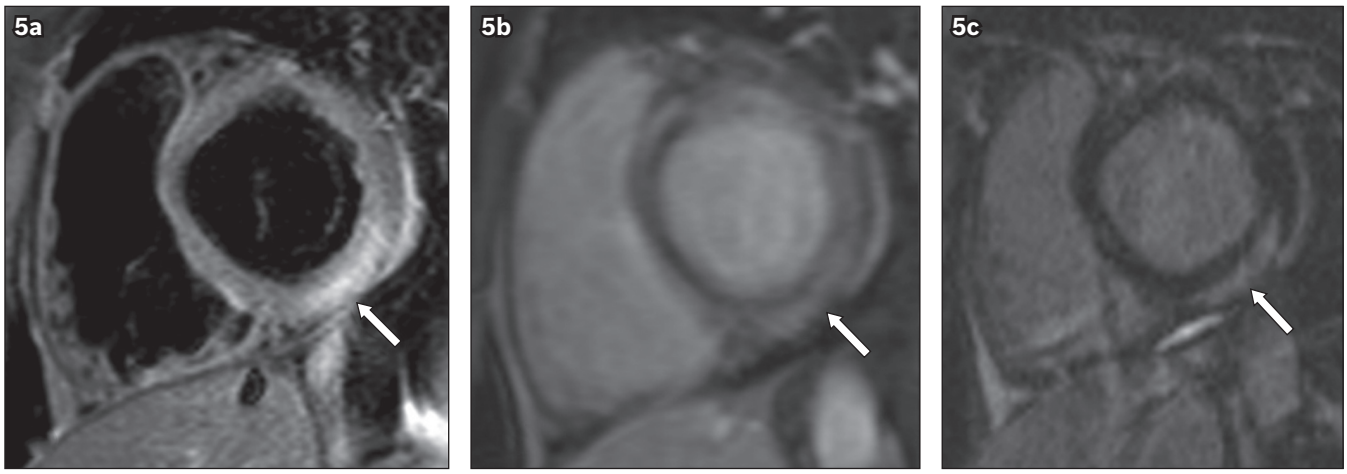

Fig. 5 A 39-year-old man with acute myocarditis. (a) Short-axis T2-W MR image shows high signal intensity in the lateral and inferior segments (arrow), indicative of oedema. (b) Short-axis early contrast-enhanced and (c) LGE MR images show subepicardial early enhancement and LGE in the inferior and inferolateral segments (arrow in b & c).

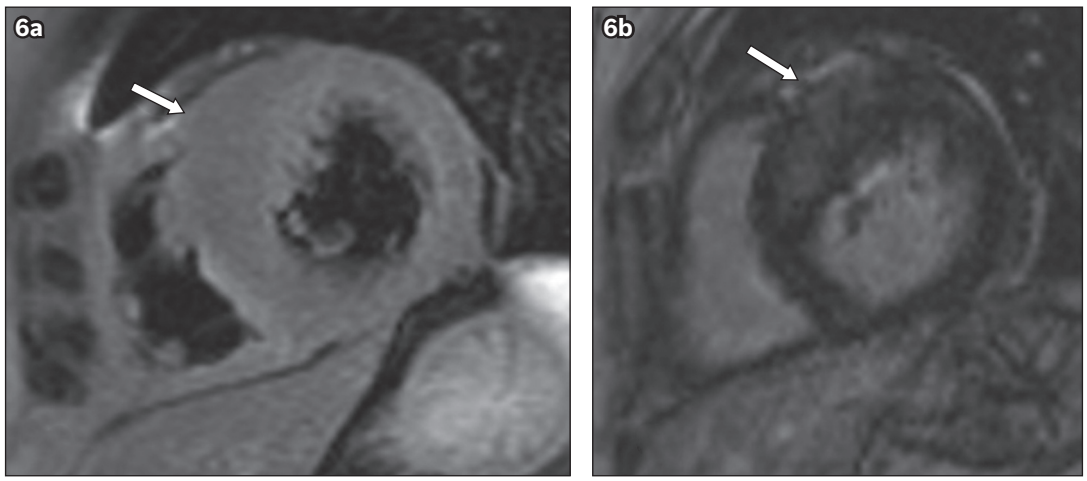

Fig. 6 A 50-year-old man with asymmetrical (septal) hypertrophic cardiomyopathy. (a) Short-axis T2-W MR image shows asymmetric septal wall hypertrophy at the anteroseptal wall, with the maximal thickness (arrow) measured as 18 mm at end-diastole. (b) Short-axis LGE MR image shows mid-myocardial LGE in the anteroseptal wall (arrow).

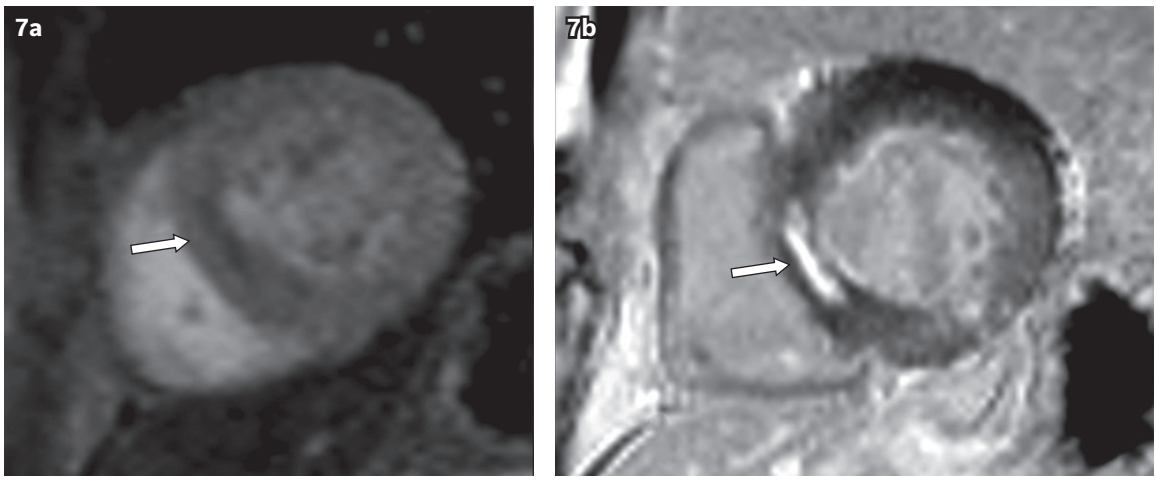

Fig. 7 A 63-year-old man with ischaemic cardiomyopathy. (a) Short-axis perfusion image shows a subendocardial perfusion defect in the interventricular septum (arrow). (b) Short-axis LGE MR image shows LGE in the corresponding subendocardial septum (arrow).

ischaemic cardiomyopathy demonstrates segmental perfusion defect in the early phase, with LGE corresponding to the distribution of coronary arteries, and is often subendocardial or transmural (Fig. 7).[6]

In cardiac amyloidosis, the amyloid protein is deposited in the myocardium and involvement of all four chambers is common, as it is a systemic process. Thus, a specific finding for cardiac amyloidosis on CMR imaging is an increase in the thickness of the

interatrial septum and right atrial free wall of more than 6 mm.[7] The most characteristic and distinct imaging pattern of cardiac amyloidosis is global LGE, which is most pronounced over the entire subendocardial circumference (Fig. 8). This is in contrast to CS, in which LGE is typically focal and subepicardial. This finding has high specificity and sensitivity for cardiac amyloidosis.[7,15] Other imaging features commonly seen in cardiac amyloidosis are atrial thickening and atrial LGE, differentiating this condition from CS.[2]

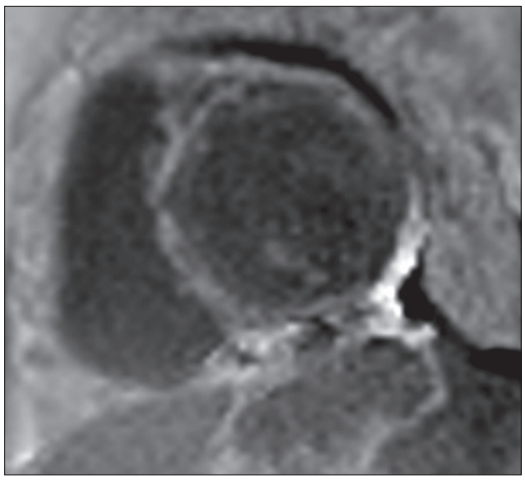

Fig. 8 A 55-year-old man with amyloidosis. Short-axis LGE MR image shows diffuse subendocardial LGE involving the left ventricle and the interventricular septum.

ABSTRACT A 44-year-old man presented with breathlessness and episodes of palpitations for the last one year. The imaging diagnosis of cardiac sarcoidosis was made based on chest radiography and cardiac magnetic resonance (MR) imaging findings, and was further confirmed by biopsy. Cardiac sarcoidosis is an uncommon entity, yet is potentially fatal with nonspecific clinical manifestations, including sudden cardiac death. Hence, it is important to diagnose and treat this entity at an early stage to improve morbidity and mortality. Cardiac MR imaging plays a pivotal role in facilitating diagnosis and monitoring therapeutic response. We describe the MR imaging features of cardiac sarcoidosis and discuss imaging features of other cardiomyopathies that may mimic cardiac sarcoidosis.

Keywords: cardiac magnetic resonance, cardiac sarcoidosis, cardiomyopathy, radiograph

In summary, CS is not an uncommon entity. When present, it can produce significant symptoms and even sudden cardiac death. Hence, timely diagnosis of CS is essential. However, difficulty arises due to its overlapping clinical manifestations and imaging features with those of other inflammatory and infiltrative cardiac disorders. Imaging diagnosis of CS is challenging. However, in suspected cases, after echocardiography, CMR imaging helps to further characterise the inflammatory and/or fibrotic stages of CS. CMR imaging is also useful in providing comprehensive information regarding the distribution and patterns of cardiac morphological changes and ventricular function. In addition, the LGE phase of CMR imaging is also useful in prognosis and risk stratification.

REFERENCES

1. Komada T, Suzuki K, Ishiguchi H, et al. Magnetic resonance imaging of cardiac sarcoidosis: an evaluation of the cardiac segments and layers that exhibit late gadolinium enhancement. Nagoya J Med Sci 2016; 78:437-46.
2. Jeudy J, Burke AP, White CS, Kramer GB, Frazier AA. Cardiac sarcoidosis: the challenge of radiologic-pathologic correlation: from the radiologic pathology archives. Radiographics 2015; 35:657-79.
3. Hulten E, Aslam S, Osborne M, et al. Cardiac sarcoidosis-state of the art review. Cardiovasc Diagn Ther 2016; 6:50-63.
4. Uemura A, Morimoto S, Hiramitsu S, et al. Histologic diagnostic rate of cardiac sarcoidosis: evaluation of endomyocardial biopsies. Am Heart J 1999; 138(2 Pt 1):299-302.
5. Ipek E, Demirelli S, Ermis E, Inci S. Sarcoidosis and the heart: a review of the literature. Intractable Rare Dis Res 2015; 4:170-80.
6. Vignaux O. Cardiac sarcoidosis: spectrum of MRI features. AJR Am J Roentgenol 2005; 184:249-54.
7. Chun EJ, Choi SI, Jin KN, et al. Hypertrophic cardiomyopathy: assessment with MR imaging and multidetector CT. Radiographics 2010; 30:1309-28.
8. Roberts WC, Chung MS, Ko JM, Capehart JE, Hall SA. Morphologic features of cardiac sarcoidosis in native hearts of patients having cardiac transplantation. Am J Cardiol 2014; 113:706-12.
9. Rajiah P, Raza S, Saboo SS, Ghoshhajra B, Abbara S. Update on the role of cardiac magnetic resonance in acquired nonischemic cardiomyopathies. J Thorac Imaging 2016; 31:348-66.
10. Greulich S, Deluigi CC, Gloekler S, et al. CMR imaging predicts death and other adverse events in suspected cardiac sarcoidosis. JACC Cardiovasc Imaging 2013; 6:501-11.
11. Smedema JP, Snoep G, van Kroonenburgh MP, et al. Evaluation of the accuracy of gadolinium-enhanced cardiovascular magnetic resonance in the diagnosis of cardiac sarcoidosis. J Am Coll Cardiol 2005; 45:1683-90.
12. Patel MR, Cawley PJ, Heitner JF, et al. Detection of myocardial damage in patients with sarcoidosis. Circulation 2009; 120:1969-77.
13. Yilmaz A, Ferreira V, Klingel K, et al. Role of cardiovascular magnetic resonance imaging (CMR) in the diagnosis of acute and chronic myocarditis. Heart Fail Rev 2013;18:747-60.
14. Hoey ET, Teoh JK, Das I, et al. The emerging role of cardiovascular MRI for risk stratification in hypertrophic cardiomyopathy. Clin Radiol 2014; 69:221-30.
15. Vogelsberg H, Mahrholdt H, Deluigi CC, et al. Cardiovascular magnetic resonance in clinically suspected cardiac amyloidosis: noninvasive imaging compared to endomyocardial biopsy. J Am Coll Cardiol 2008; 51:1022-30.

SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME

(Code SMJ 201808B)

	True	False
Question 1. Regarding sarcoidosis:		
(a) It is characterised by formation of non-caseating granulomas in the affected organs.	☐	☐
(b) It typically manifests as bilateral hilar lymphadenopathy.	☐	☐
(c) Cardiac involvement is common.	☐	☐
(d) Cardiac involvement is seen in around 5% of cases.	☐	☐
Question 2. Regarding the clinical presentation of cardiac sarcoidosis (CS):		
(a) Patients may be asymptomatic.	☐	☐
(b) Patients may present with chest pain and palpitations.	☐	☐
(c) Patients may succumb to sudden death from dysrhythmias.	☐	☐
(d) CS is never fatal.	☐	☐
Question 3. Regarding cardiac magnetic resonance (CMR) imaging of CS in the acute phase:		
(a) Patchy nodular areas of increased T2 signal intensity are seen within the myocardium.	☐	☐
(b) The nodular areas show early and late gadolinium enhancement (LGE).	☐	☐
(c) CS commonly involves the right ventricular wall.	☐	☐
(d) In CS, focal non-transmural lesions commonly affect the subendocardial portion.	☐	☐
Question 4. Regarding CMR imaging of CS in the chronic phase:		
(a) LGE is absent.	☐	☐
(b) LGE occurs due to increased volume of contrast material in the extracellular space secondary to underlying myocardial fibrosis.	☐	☐
(c) LGE is considered to be the strongest hallmark of CS and a marker of adverse events associated with CS.	☐	☐
(d) CMR imaging has been shown to have a specificity of 100% for diagnosing sarcoidosis.	☐	☐
Question 5. Regarding CMR imaging diagnosis and the differential diagnoses of CS:		
(a) Myocarditis frequently involves the lateral free wall of the left ventricle.	☐	☐
(b) Septal wall oedema, seen as increased T2 signal, is frequently seen in hypertrophic cardiomyopathy, differentiating it from CS.	☐	☐
(c) Ischaemic cardiomyopathy demonstrates segmental perfusion defect in the early phase with LGE, which is often subendocardial.	☐	☐
(d) Cardiac amyloidosis shows global LGE, which is most pronounced over the entire subendocardial circumference.	☐	☐

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(1) Answers will be published online in the SMJ October 2018 issue. (2) The MCR numbers of successful candidates will be posted online at the SMJ website by 12 October 2018. (3) Passing mark is 60%. No mark will be deducted for incorrect answers. (4) The SMJ editorial office will submit the list of successful candidates to the Singapore Medical Council. (5) One CME point is awarded for successful candidates. (6) SMC credits CME points according to the month of publication of the CME article (i.e. points awarded for a quiz published in the December 2017 issue will be credited for the month of December 2017, even if the deadline is in January 2018).

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