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Seminars in
ROENTGENOLOGY

Thoracic Sarcoidosis: Imaging Patterns

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Introduction

Sarcoidosis is a systemic idiopathic condition characterized by caseating granulomas that can involve almost any organ. Sarcoidosis is most commonly affects adults under the age of 40, and it has a slight predominance among females.[1] In most patients, the predominant and most severe manifestations occur in the thorax, primarily in the lungs, lymph nodes, airways, and heart. Approximately 25% of patients have respiratory symptoms at the time of diagnosis, including cough and dyspnea. Other common symptoms include fatigue, weight loss, erythema nodosum, and sometimes fever. Approximately 50% of patients are asymptomatic.[2,3] Although most patients remain stable or undergo remission, up to 20% develop pulmonary fibrosis.[4] Imaging can be used to help establish the diagnosis, delineate the extent of disease, assess the course of the disease, and to identify the irreversible changes of fibrosis.

Imaging

The lungs and thoracic lymph nodes are involved in more than 90% of patients with sarcoidosis.[2] Pulmonary nodules and hilar and mediastinal lymphadenopathy are common findings on chest radiography and high-resolution computed tomography (HRCT), and fibrosis is less frequently encountered.

A radiographic staging system has been described[5,6]:

Stage 0, normal (approximately 5%-10% of patients).

Stage 1, lymphadenopathy without parenchymal findings (approximately 50%).

Stage 2, lymphadenopathy and lung disease (approximately 25%-30%).

Stage 3, parenchymal disease without visible lymphadenopathy (approximately 15%).

Stage 4, pulmonary fibrosis.

The staging system is interesting from a historical standpoint, and the severity of symptoms may be correlated to the radiographic stage.[5] However, the usefulness of the staging system may be limited because patients do not necessarily progress from stage to stage, and especially because CT is a more useful and robust modality for the diagnosis and follow-up of sarcoidosis. HRCT can be especially useful to identify areas of active inflammation, as manifested by small and large nodules and ground-glass opacities, which can be reversed with treatment.[7,8] In contrast, HRCT findings of fibrosis and honeycombing are irreversible.

Lymphadenopathy

Mediastinal and hilar lymphadenopathy is frequently seen in sarcoidosis, and more than 85% of patients have lymph node enlargement at some point.[5] Although radiographs can demonstrate both lung and lymph node abnormalities in patients with suspected or known sarcoidosis, CT scan is a more sensitive way to identify lung disease in patients with enlarged lymph nodes and suspected sarcoidosis (Fig. 1). Approximately 80% of patients with lymphadenopathy have parenchymal disease,[5,9] and conversely, more than 80% of patients with lung abnormalities have lymph node enlargement.[10]

Lymphadenopathy is often bilateral and symmetrical, and bilateral hilar involvement is the most characteristic pattern of lymph node enlargement on chest radiographs, occurring in 95% of patients with lymph node involvement (see Fig. 1a). A typical 1-2-3 distribution of lymphadenopathy on chest radiographs involves the right paratracheal and bilateral hilar lymph nodes.[6] Sarcoidosis can lead to enlargement of aorticopulmonary window, subcarinal, and prevascular lymph nodes; less commonly, internal mammary and retrocrural lymph nodes are involved.

On CT, 75%-95% of patients with sarcoidosis have mediastinal and hilar lymphadenopathy.[9,11] Approximately 67%-75%

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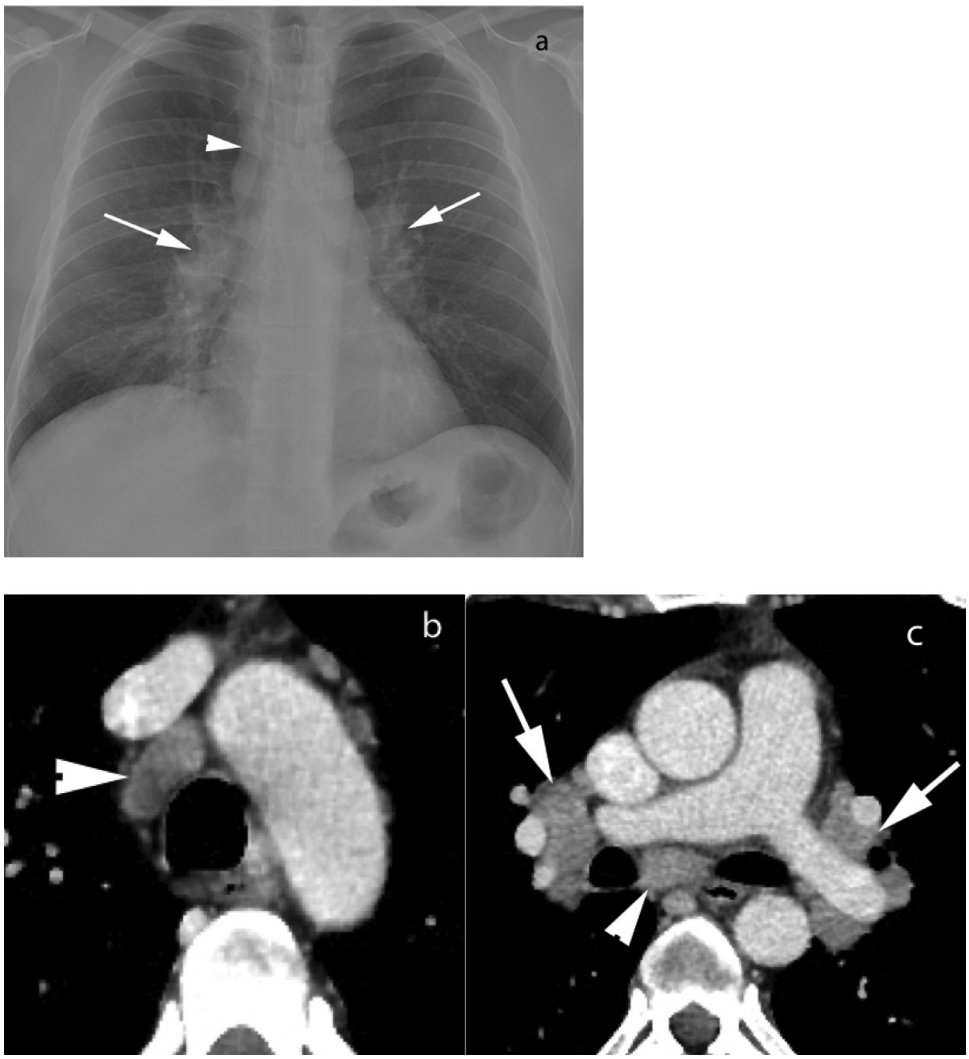

Figure 1 (a-c) Frontal chest radiograph (a) and CT showing mediastinal (arrowheads) and bilateral hilar (arrows) lymphadenopathy. CT, computed tomography.

of patients have hilar lymphadenopathy, often bilateral[9,11] (Figs. 1 and 2). Common locations of enlarged mediastinal lymph nodes include the right paratracheal and right peribronchial (at least 55%-70% of patients), left paratracheal, aorticopulmonary window, subcarinal, and paraesophageal (each approximately 50% of patients).[9] CT can demonstrate mediastinal lymphadenopathy in the absence of enlarged hilar lymph nodes in approximately 15% of patients, although this is uncommonly manifested on chest radiography.[9]

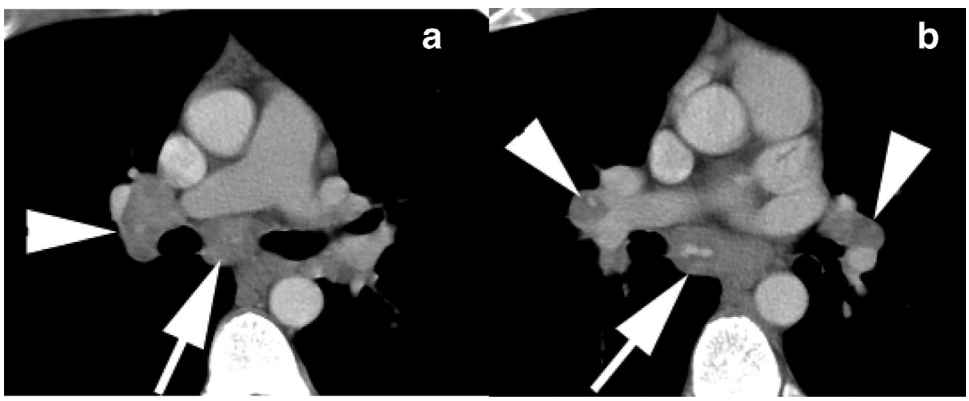

Figure 2 (a, b) CT showing symmetrical bilateral hilar (arrowheads) and mediastinal (arrows) lymphadenopathy with faint, amorphous calcifications. CT, computed tomography.

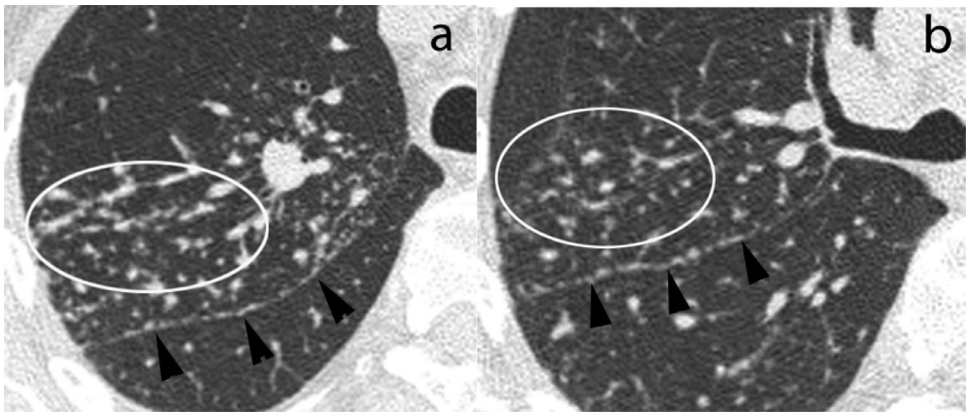

Figure 3 (a, b) CT showing nodules in the perilymphatic distribution along the bronchovascular bundles (ovals) and fissural pleura (arrowheads). CT, computed tomography.

Lymph node calcification frequently occurs in sarcoidosis[12] (Fig. 2). Focal calcification has been reported to be more common than complete calcification,[13] and calcification patterns include dense, amorphous or hazy, stippled, and eggshell. On magnetic resonance imaging (MRI), a dark lymph node sign has been described in approximately 50% of patients with sarcoidosis.[12]

Nodules

In sarcoidosis, radiographs show lung disease in at least 40% of patients (stage 1 or stage 2), and most of these patients have lymphadenopathy. Nodules are seen in radiographs in approximately half of patients with parenchymal disease, although radiographs have limited sensitivity. The nodules are typically predominant in the upper lobes, but in some patients the disease is more diffuse. Lower lobe predominance is rare.

HRCT often demonstrates small nodules (less than 1 cm in diameter), sometimes called micronodules, in patients with sarcoidosis. HRCT can depict nodules as small as 1-2 mm in diameter, and small nodules in sarcoidosis are usually sharply defined, but they can be ill-defined. Occasionally, the nodules may be calcified.

Small nodules in sarcoidosis are most typically distributed in a perilymphatic pattern (Fig. 3). The distribution along the lymphatic system corresponds to nodules identified in the peribronchovascular interstitium, the interlobular septa, and the subpleural area. These nodules tend to predominate in the upper lobes, and a patchy distribution is common, with areas of disease interspersed with normal lung.

The differential diagnosis of perilymphatic distribution of nodules includes silicosis, coal worker's pneumoconiosis, and lymphangitic spread of tumor. In sarcoidosis, small nodules are characteristically present in the peribronchovascular interstitium and in the subpleural areas along the fissures. In contrast, nodules in silicosis and coal workers are often associated with areas of fibrosis, and peribronchovascular and septal nodules are less common and less conspicuous than in sarcoidosis.[14] In lymphangitic spread of carcinoma, the nodules tend to be sparser and are frequently associated with thickened interlobular septa, yielding a beaded appearance.

Large nodules and masses, typically 1-4 cm in diameter or later, are often ill-defined and can contain air bronchograms and resemble consolidation (Figs. 4-6). Sometimes these nodular opacities have been termed “alveolar sarcoid,” though they arise from the conglomeration of smaller interstitial granulomas. Large nodules can be identified on radiographs, and they are found in CT in 15%-25% of patients.[6] Small nodules may surround the larger nodular opacities, a pattern that has been called the “galaxy sign” (Figs. 5 and 6). The differential diagnosis for the galaxy sign includes other granulomatous diseases and lung cancer.[6]

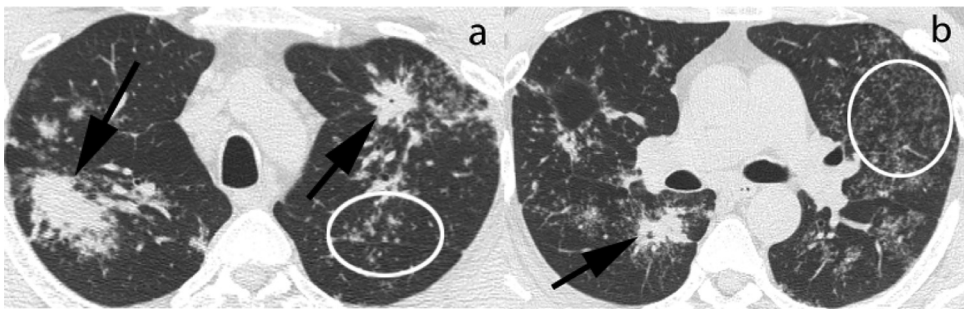

Figure 4 (a, b) CT showing nodular consolidation (arrows) and small nodules (ovals) in the perilymphatic distribution. CT, computed tomography.

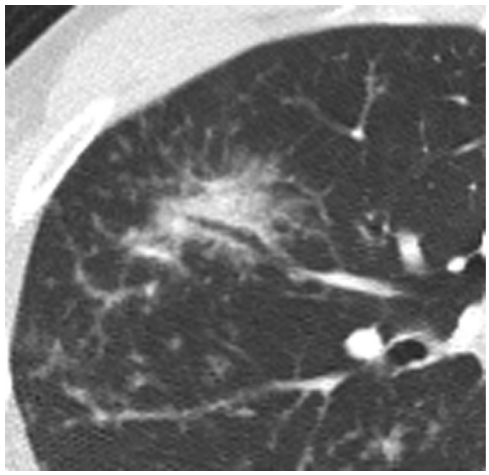

Figure 5 CT showing nodular consolidation with surrounding small nodules ("galaxy sign"). CT, computed tomography.

Ground-Glass Opacity

On HRCT, approximately 40% of patients with parenchymal sarcoidosis manifest patchy ground-glass opacities, which occur as a consequence of the confluence of small nodules and interstitial fibrosis.[7] The appearance results from a conglomeration of granulomas, as occurs in alveolar sarcoidosis.[6] Patchy ground-glass opacities typically occur only when other radiological findings, such as small nodules, are present (Fig. 6). Diffuse ground-glass opacities are unusual in sarcoidosis.

Fibrosis

Although parenchymal findings usually resolve, approximately 15%-20% of patients with thoracic sarcoidosis develop fibrosis.[4,6] On chest radiographs, the fibrosis can manifest as reticular opacities with an upper lobe predominance, along with upper lobe volume loss and upward hilar retraction (Fig. 7). Fibrosis tends to progress, and perihilar mass-like opacities can result from peribronchial fibrosis.

On HRCT, findings of fibrosis include reticulation, architectural distortion, traction bronchiectasis, and volume loss (Figs. 7 and 8). The distribution is typically patchy with upper lobe or central lung predominance. With progression of fibrosis, mass-like consolidation can develop in the perihilar regions (Fig. 8). The differential diagnosis for this appearance includes silicosis and talcosis.[6] Honeycombing and lung cysts can occur, but they are primarily located in the upper or mid lungs, as opposed to the basilar-predominant fibrosis and honeycombing that occurs in usual interstitial pneumonia and idiopathic pulmonary fibrosis.

Airways

Sarcoidosis can involve small airways and large airways. Granulomas or fibrosis in the small airways can result in mosaic attenuation and, on expiratory CT, air trapping[15,16] (Fig. 9). Air trapping is common and can occur in up to 95% of patients.[7,16] In the large airways, HRCT can demonstrate small granulomas in the tracheal or bronchial walls, wall thickening or irregularity, or focal bronchiectasis. Tracheobronchial stenosis is relatively common,[6] but symptomatic stenosis is rare.[7] Stenosis of the large airways can result in atelectasis, especially in the right middle lobe.

Pleura

Pleural disease is a rare manifestation of sarcoidosis.[6] Patients can develop plaque-like abnormalities in the lung periphery caused by subpleural aggregations of small parenchymal nodules,[7] sometimes termed "pseudoplaques" (see Fig. 6).

Heart

Cardiac involvement is diagnosed clinically in only 5% of patients with sarcoidosis, although it has been shown by autopsy that the heart is affected in approximately 25% of patients with sarcoidosis.[17] The frequency of involvement can be higher in some countries, including Japan. Noncaseating granulomas form in the heart, most commonly in the left ventricle, leading to edema, granulomatous inflammation, and fibrosis and scarring.[18] Clinical manifestations include arrhythmias and conduction abnormalities, congestive heart

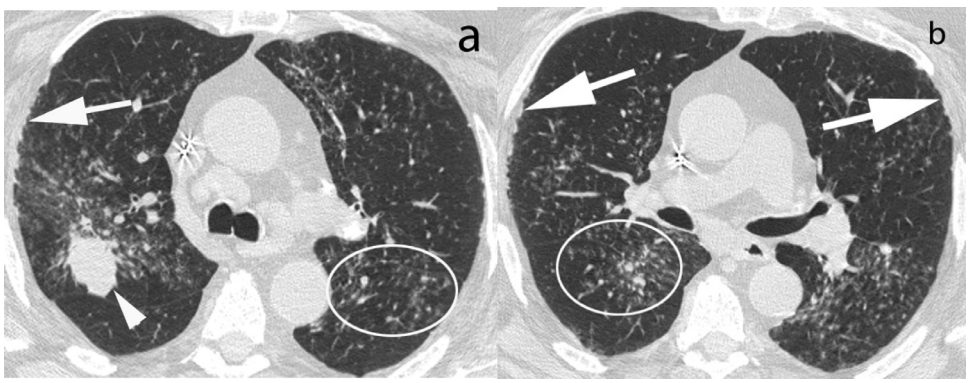

Figure 6 (a, b) CT showing small nodules in the subpleural distribution giving pseudoplaque appearance (arrows) and along the bronchovascular bundles (ovals). Nodular consolidation (arrowhead) in the right upper lobe with surrounding small nodules ("galaxy sign") and ground-glass opacity. CT, computed tomography.

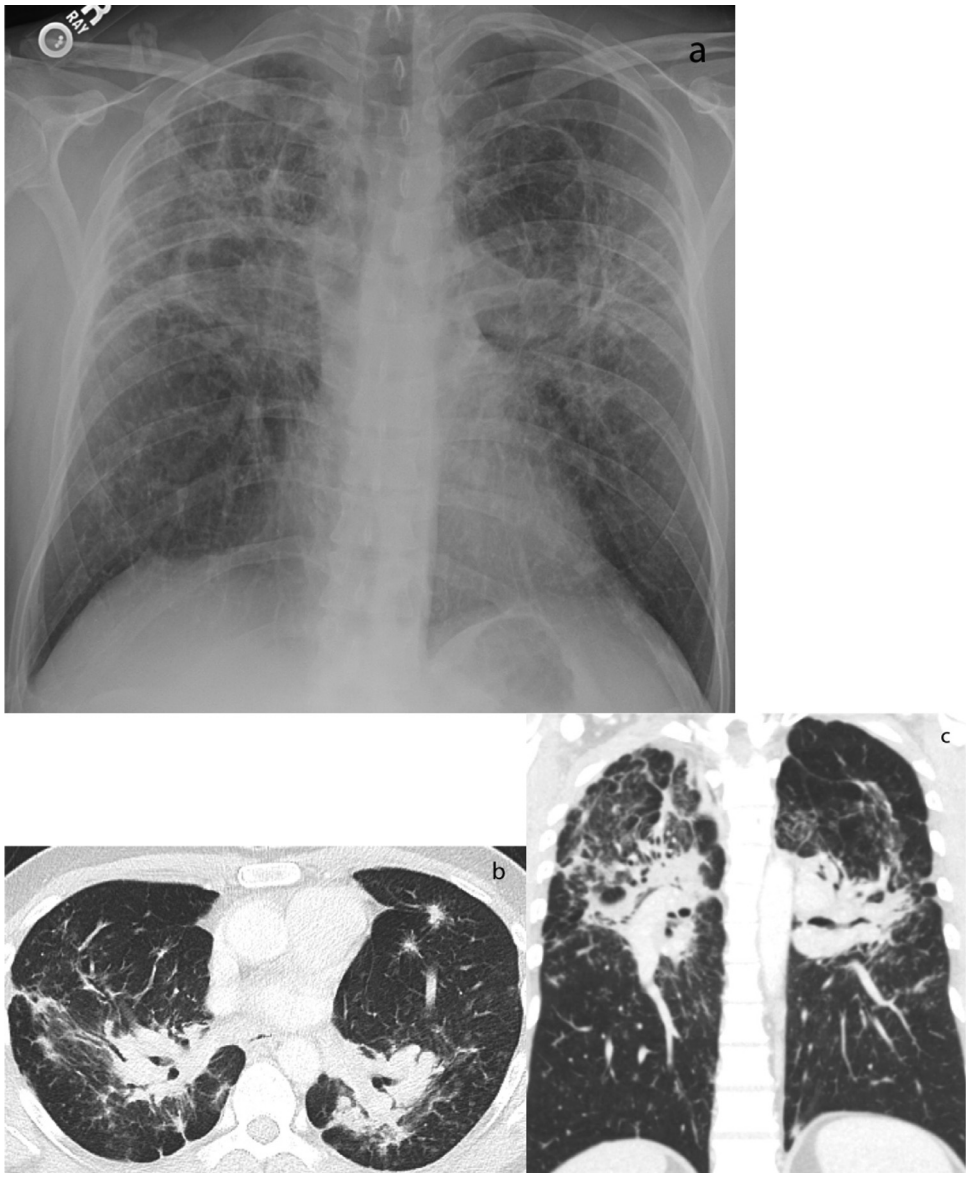

Figure 7 (a-c) Chest radiograph (a) and CT (b, c) showing upper lung predominant fibrosis and architectural distortion. CT, computed tomography.

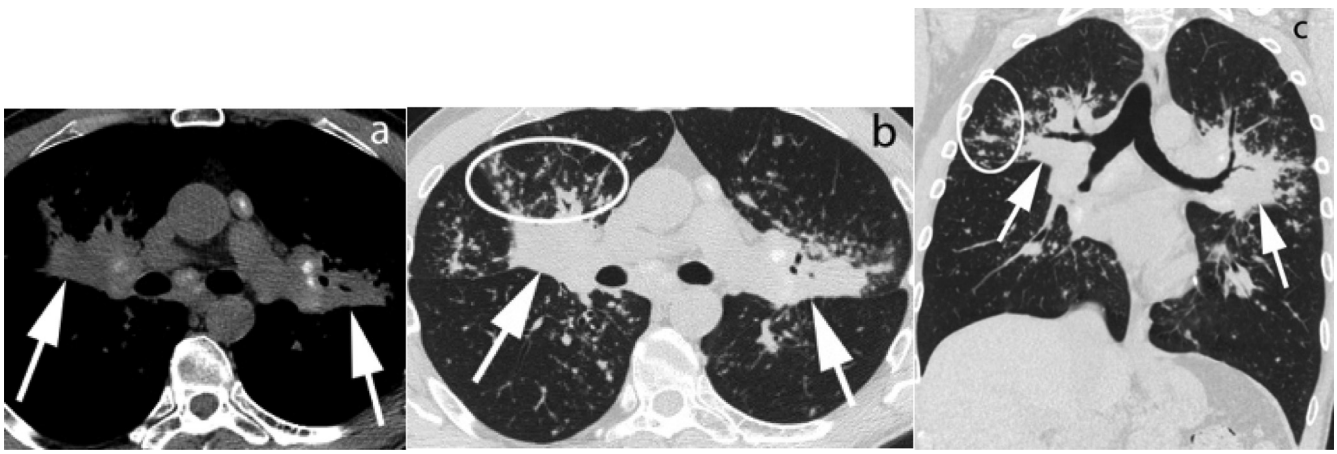

Figure 8 (a-c) CT showing bilateral perihilar mass-like fibrosis (arrows in a-c), perilymphatic nodules (ovals in b and c) and calcified mediastinal and hilar lymphadenopathy. CT, computed tomography.

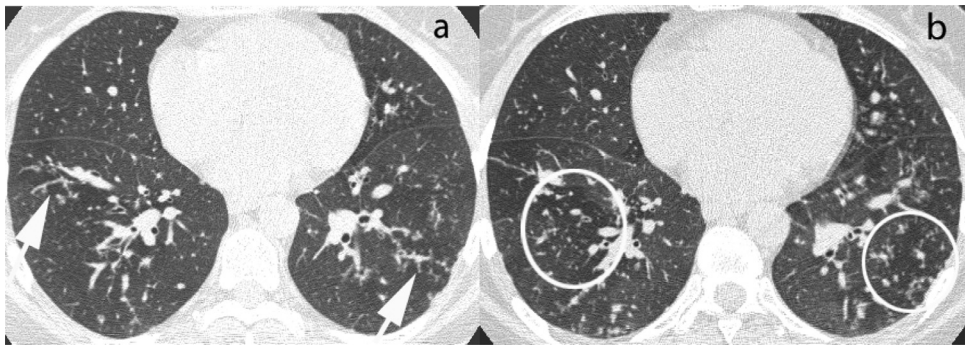

Figure 9 (a, b) CT during inspiration (a) and expiration (b) showing perilymphatic nodules (arrows) and scattered areas of air trapping (circles). CT, computed tomography.

failure, and sudden death, and left ventricular ejection fraction is an important parameter for the prediction of death in patients with cardiac involvement.[18] Restrictive physiology often occurs in the setting of cardiac sarcoidosis.

Diagnosis of cardiac sarcoidosis can be difficult, and clinical criteria are unreliable. Although endomyocardial biopsy can be considered to be a standard of reference, it has a low yield and thereby a low sensitivity. There is no definitive diagnostic examination, but both MRI and fluorine 18 fluorodeoxyglucose positron emission tomography (18F-FDG PET) can be used to identify patients with cardiac sarcoidosis. An expert consensus statement[19,20] avers that patients should undergo cardiac MRI or PET if they meet 1 or more of 3 criteria (1) diagnosis of extracardiac sarcoidosis with cardiac signs or symptoms; (2) unexplained conduction abnormalities, ventricular dysrhythmias, syncope, or nonischemic heart failure before the age of 55, even without a known diagnosis of sarcoidosis; and (3) known cardiac sarcoidosis.

In the active (edema and inflammation) and chronic (fibrosis and scarring) phases of sarcoidosis, MRI can be used to detect functional deficits. Cine steady-state free precession technique can be applied to demonstrate regional wall motion abnormalities.[20] Late gadolinium enhancement (LGE) MRI can identify abnormalities in both the active and chronic phases of cardiac sarcoidosis. The distribution of LGE is variable and can be midmyocardial, transmural, or even epicardial (Fig. 10). Although the left ventricle is most commonly involved, LGE can also be seen in the right ventricle. Ohira et al found a sensitivity of 75% and a specificity of 77% of MRI for the detection of cardiac sarcoidosis, compared to a sensitivity of 88% and a specificity of 39% of 18F-FDG PET.[21] MRI is often used as the first advanced imaging modality in cardiac sarcoidosis, and PET is an alternative or additional option.

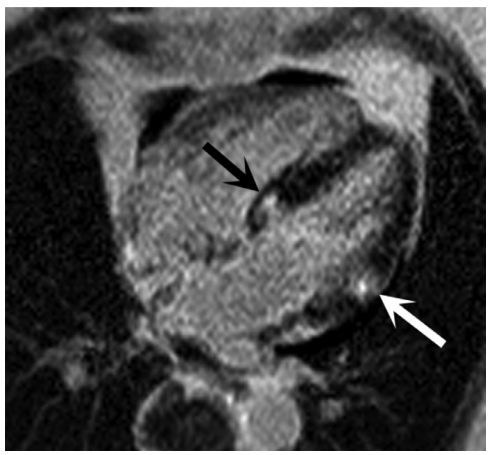

Figure 10 Four-chamber inversion recovery MRI demonstrating late gadolinium enhancement (LGE) in a patient with sarcoidosis. There is focal transmural LGE in the lateral wall of the left ventricular (white arrow) and midmyocardial LGE in the septal wall (black arrow). MRI, magnetic resonance imaging.

Conclusion

Sarcoidosis can affect almost any organ, but thoracic involvement causes the most morbidity and mortality, and up to 20% of patients develop irreversible fibrosis. HRCT is the mainstay of imaging in pulmonary sarcoidosis and can be used for diagnosis, assessment of extent and course, and identification of fibrosis. MRI and PET are important imaging tools in the assessment of cardiac sarcoidosis.

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