

# Typical and Atypical Manifestations of Intrathoracic Sarcoidosis

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Sarcoidosis is a systemic disorder of unknown cause that is characterized by the presence of noncaseating granulomas. The radiological findings associated with sarcoidosis have been well described. The findings include symmetric, bilateral hilar and paratracheal lymphadenopathy, with or without concomitant parenchymal abnormalities (multiple small nodules in a peribronchovascular distribution along with irregular thickening of the interstitium). However, in 25% to 30% of cases, the radiological findings are atypical and unfamiliar to most radiologists, which cause difficulty for making a correct diagnosis. Many atypical forms of intrathoracic sarcoidosis have been described sporadically. We have collected cases with unusual radiological findings associated with pulmonary sarcoidosis (unilateral or asymmetric lymphadenopathy, necrosis or cavitation, large opacity, ground glass opacity, an airway abnormality and pleural involvement) and describe the typical forms of the disorder as well. The understanding of a wide range of the radiological manifestations of sarcoidosis will be very helpful for making a proper diagnosis.

**S**arcoidosis is a multisystem disorder of unknown cause that is characterized by the presence of noncaseating granulomas and the proliferation of epithelioid cells (1). The diagnosis of sarcoidosis is commonly established based on clinical and radiological findings that are supported by histological findings. The clinical signs and symptoms are nonspecific and include fatigue, general malaise, weight loss, and less commonly, fever. The characteristic radiological findings associated with sarcoidosis have been well described and the findings include bilateral hilar lymphadenopathy and parenchymal abnormalities (2). As sarcoid granulomas in the lung are typically distributed along the lymphatic vessels, multiple small nodules in a peribronchovascular distribution along with irregular thickening of the interstitium are typical CT findings of sarcoidosis. However, 25% to 30% of cases show differences as compared to the aforementioned typical findings, which can make a correct diagnosis difficult (3-5).

This review is divided into two parts for typical and atypical forms of sarcoidosis. The first part of this review provides a general overview of typical sarcoidosis with bilateral hilar lymphadenopathy, small nodules with perilymphatic distribution and interstitial thickening. Other cases with atypical findings are described in the second part of this review.

## Typical Sarcoidosis

Sarcoidosis usually presents with asymptomatic lymphadenopathy with or without

pulmonary infiltrations. Bilateral hilar lymphadenopathy is the most common radiological finding. Mediastinal lymphadenopathy can also be seen and is often associated with the presence of pulmonary infiltrates (2-4). The presence of pulmonary infiltrations have been reported in approximately 60% of patients (6).

**Lymphadenopathy**

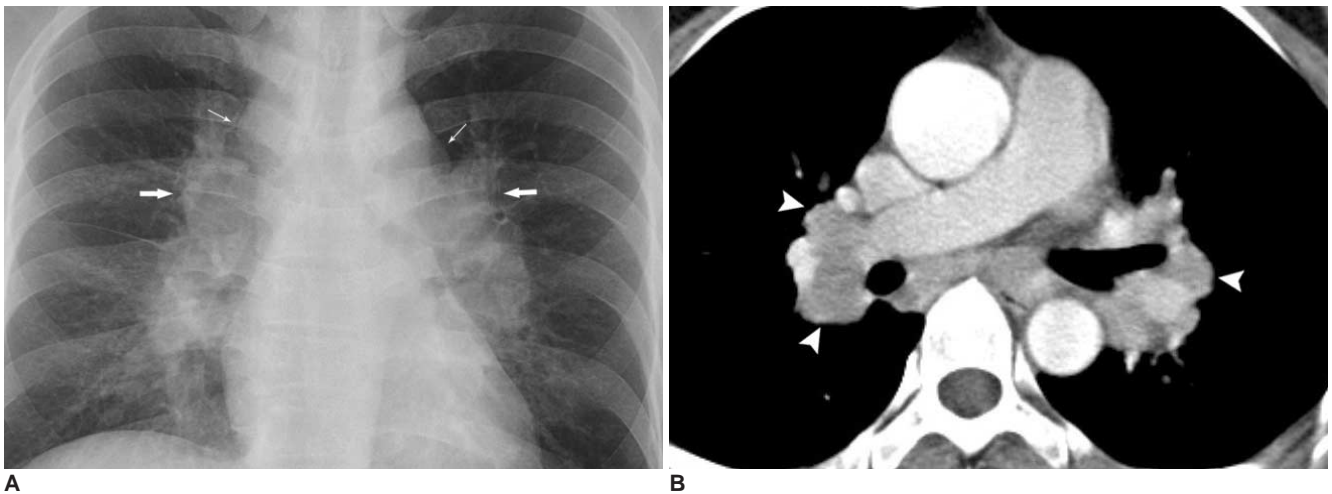
Lymphadenopathy is the most common finding in sarcoidosis and typically presents as bilateral hilar lymphadenopathy. In contrast to other causes of hilar lymphadenopathy, hilar lymphadenopathy in sarcoidosis is typically bilateral and symmetric. In addition, hilar lymphadenopathy is frequently associated with mediastinal lymph node enlargement as depicted on CT scans, especially including the right paratracheal and subaortic nodes. However, mediastinal lymphadenopathy without hilar involvement is rare (4, 5). Because of this characteristic distribution, intrathoracic lymphadenopathy typically

resembles the shape of the Greek letter ‘lambda (lambda sign)’ as seen on gallium scans (7) (Fig. 1).

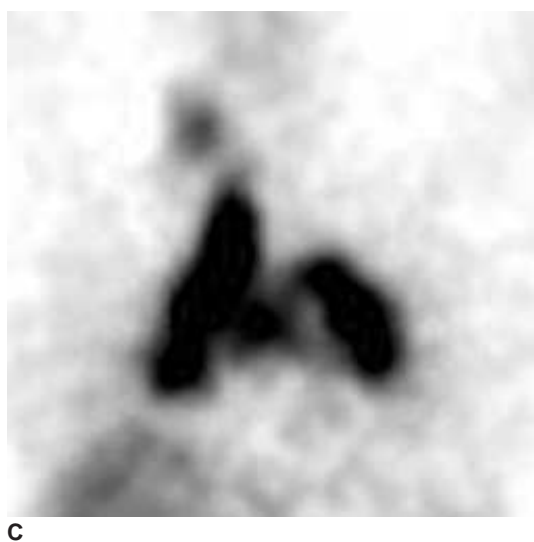
Lymph node calcification is visible in 25% to 50% of cases and may have an amorphous, stippled or eggshell appearance. Node calcification is closely related to the duration of the disease and suggests a chronic condition, a finding similar to other chronic granulomatous diseases (3, 5) (Fig. 2).

**Pulmonary Infiltrates (Nodules, Interstitial Thickening and Fibrosis)**

Characteristic CT findings of sarcoidosis include the presence of small nodules that mostly measure less than 3 mm in diameter and nodular thickening along the lymphatics in the bronchovascular sheath and, to a lesser extent, in the interlobular septa and subpleural lung regions. This distribution is referred to as perilymphatic. In addition, upper lobe predominance is common, but this finding can vary. Most sarcoid granulomas can resolve spontaneously;



**Fig. 1.** Imaging findings for bilateral, symmetrical hilar lymphadenopathy in 35-year-old man with sarcoidosis are shown.  
**A.** Chest PA shows bilateral symmetric hilar enlargement (arrows) and right lower paratracheal and subaortic lymphadenopathy (thin arrows).  
**B.** Axial CT scan shows bilateral hilar and subcarinal lymphadenopathy (arrowheads).  
**C.** Gallium scan reveals ‘lambda sign’ with bilateral hilar and mediastinal lymphadenopathy.



C

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however, sarcoid granulomas can also progress to fibrosis (2-4).

### Nodules

Although sarcoid granulomas are microscopic in size, the lesions often coalesce to form macroscopic nodules. As seen on high-resolution CT (HRCT) images, the nodules appear as small as a few millimeters in diameter and tend to be sharply defined despite a small size. Due to the perilymphatic distribution of sarcoid granulomas, HRCT images typically demonstrate the presence of multiple

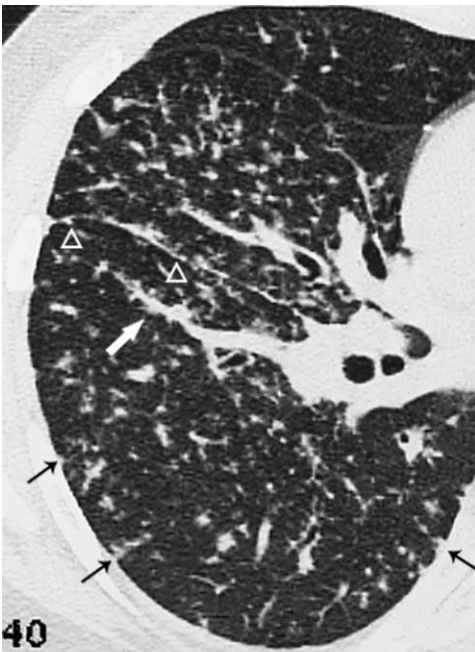
small nodules predominately in the peribronchovascular interstitium, interlobar fissures and interlobular septae (Fig. 3). The nodules may be distributed throughout both lungs with upper lobe predominance and often are distributed as foci (2-4).



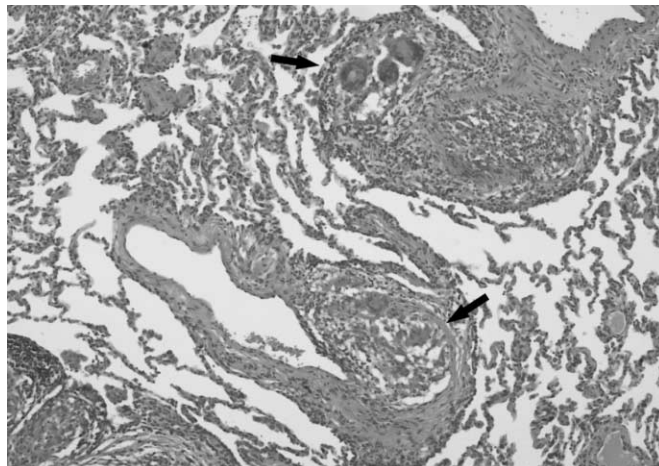
**Fig. 2.** Node calcification in sarcoidosis is shown. Axial CT scan shows typical eggshell calcification in both hilar and peribronchovascular nodes (arrows). Presence of node calcification suggests chronic condition.



**Fig. 4.** Imaging findings for interstitial thickening in sarcoidosis are presented. High-resolution CT image shows nodular thickening of interlobular septae, peribronchovascular interstitium and interlobar fissure (arrows).



**A**



**B**

**Fig. 3.** Imaging findings for sarcoid granulomas with perilymphatic distribution are shown.

**A.** High-resolution CT scan shows multiple small nodules in peribronchovascular interstitium (arrow), interlobar fissure (arrowheads) and subpleural region (thin arrows).  
**B.** Microscopic image (Hematoxylin & Eosin staining,  $\times 40$ ) reveals non-caseating granulomas with giant cells and proliferating epithelioid cells in bronchovascular interstitium (arrows).

### Interstitial Thickening

Sarcoid granulomas frequently cause nodular or irregular thickening of the peribronchovascular interstitium. As seen on HRCT images, extensive peribronchovascular nodularity is strongly suggestive of sarcoidosis (Fig. 4). However, in most patients, interstitial thickening is not extensive. In some patients, interlobular septal thickening may be a predominant feature of the disease (2-4).

### Fibrosis

Most sarcoid granulomas resolve with time. In 15% of cases, fibrosis becomes more prominent over time. As fibrosis develops, irregular reticular opacities including intralobular lines and irregular septal thickening become a prominent feature. Progressive fibrosis leads to masses of peribronchovascular fibrous tissue with conglomeration of parahilar bronchi and vessels that is typically most marked in the upper lobes (Fig. 5). Honeycombing may be seen in patients with sarcoidosis, but is uncommon. Honeycombing usually involves the middle and upper lung zones with relative sparing of the lung bases. Rarely, honeycombing may involve mainly the lower-lung zone and may mimic an appearance of idiopathic pulmonary fibrosis (2-5) (Fig. 6).

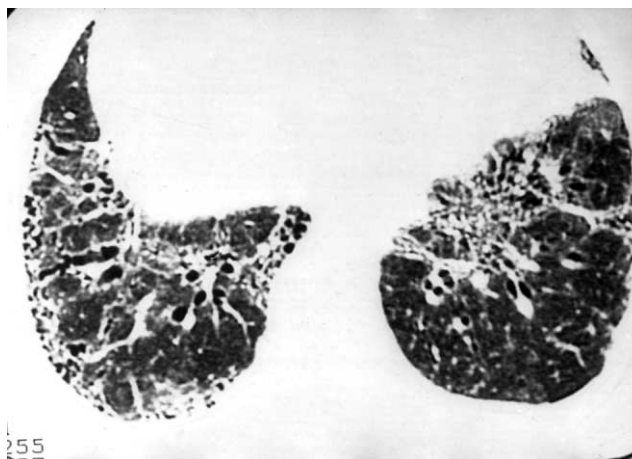
### Atypical Sarcoidosis

In addition to the typical radiological patterns of sarcoidosis as described above, less frequent and unusual manifestations may be observed in 25% to 30% of cases.

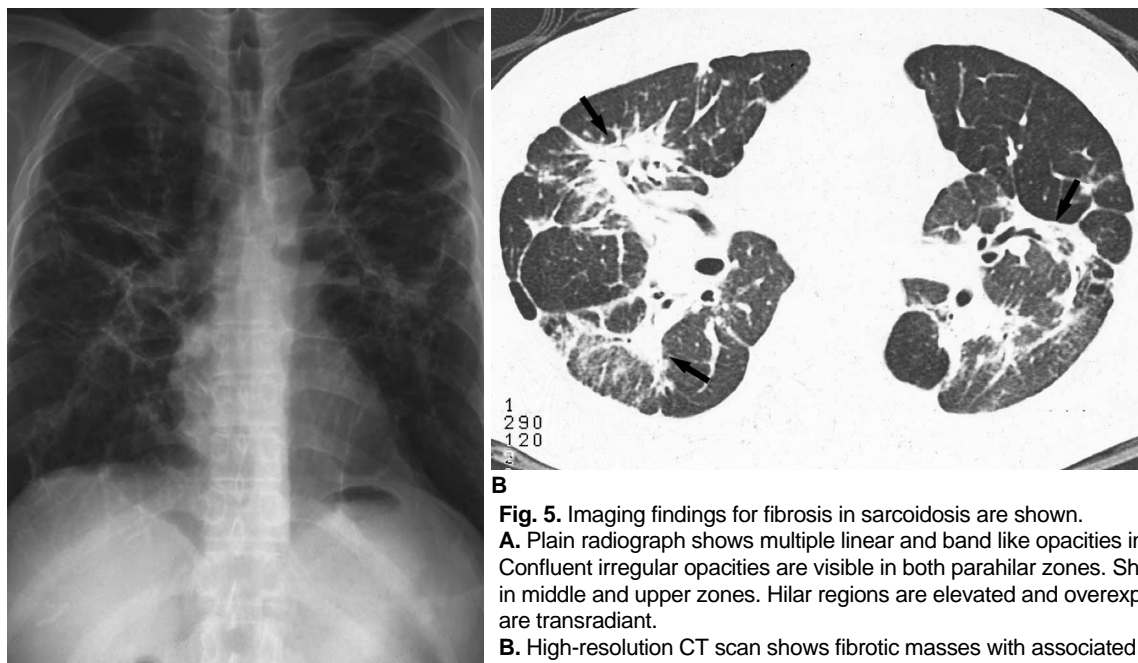
These atypical radiological patterns of sarcoidosis can make the disorder difficult to differentiate from other diseases (4, 5). In patients older than 50 years, atypical radiological patterns are relatively common (8).

### Unilateral or Asymmetric Lymphadenopathy

Hilar lymphadenopathy associated with sarcoidosis is typically bilateral and symmetric in distribution. This distribution pattern is an important diagnostic feature of sarcoidosis; a symmetric pattern is unusual for the other major diagnostic alternatives such as lymphoma, tuberculo-



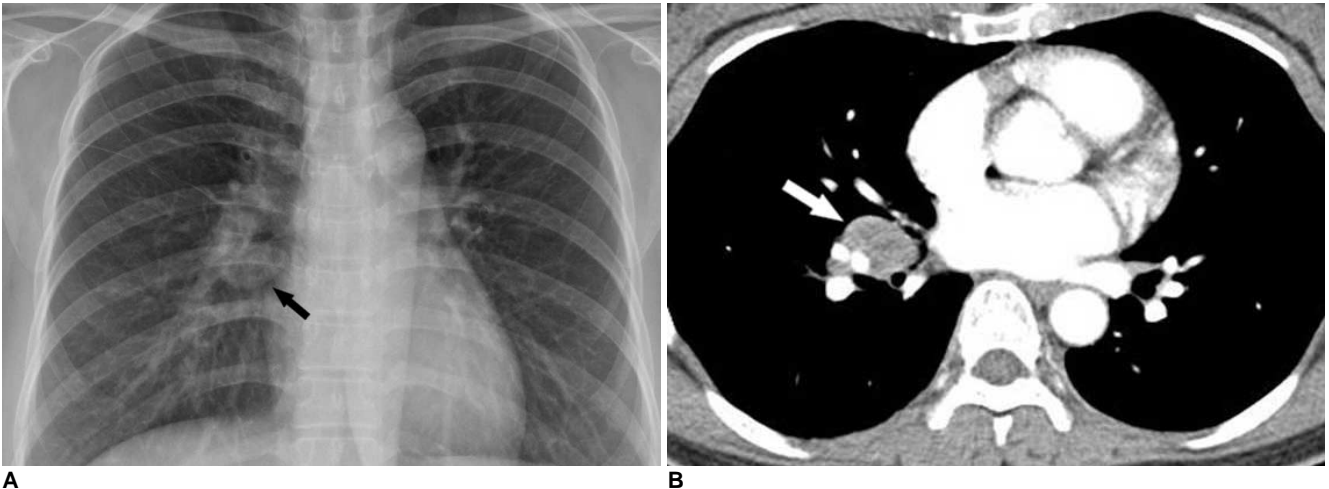
**Fig. 6.** Imaging findings for fibrosis with honeycombing in sarcoidosis are shown. High-resolution CT image shows interlobular septal thickening, reticular opacities and traction bronchiectasis. Associated subpleural honeycombing is also seen.



**Fig. 5.** Imaging findings for fibrosis in sarcoidosis are shown. **A.** Plain radiograph shows multiple linear and band like opacities in both lungs. Confluent irregular opacities are visible in both parahilar zones. Shadowing is maximal in middle and upper zones. Hilar regions are elevated and overexpanded lower zones are transradiant. **B.** High-resolution CT scan shows fibrotic masses with associated traction bronchiectasis at central lung region (arrows).

A

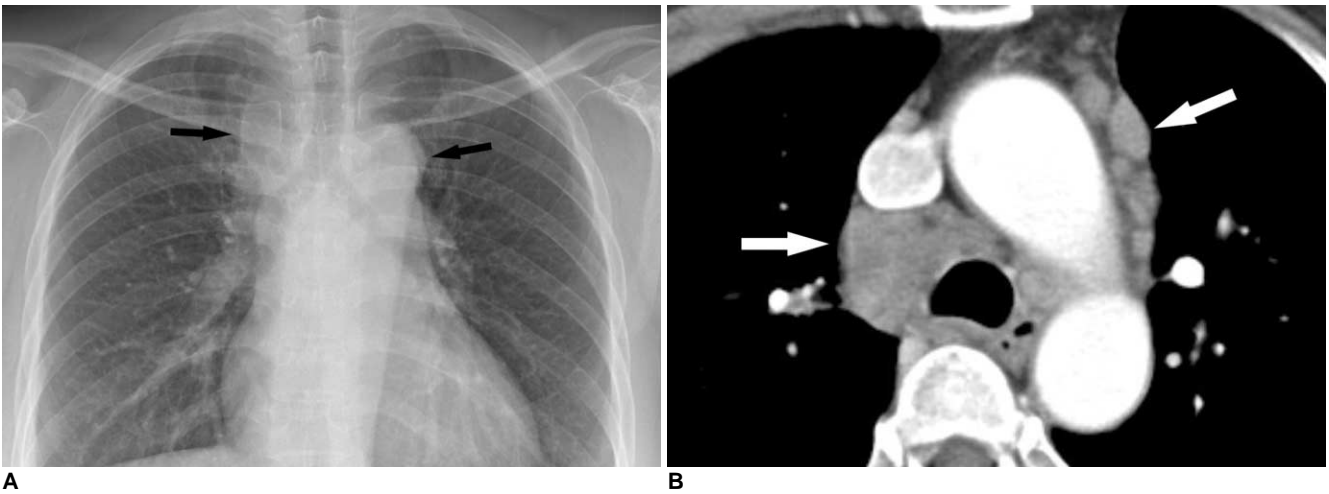
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**Fig. 7.** Imaging findings for unilateral hilar lymphadenopathy in sarcoidosis are presented.

**A.** Plain radiograph shows well-circumscribed oval mass in right infrahilar area (arrow).

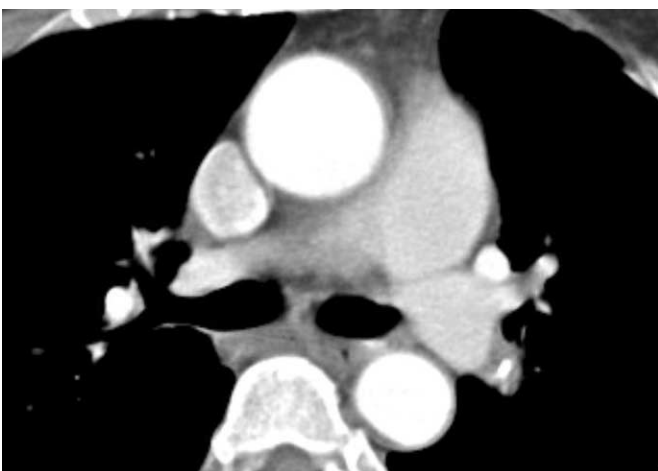
**B.** Contrast enhanced CT scan reveals presence of enlarged node (arrow) in right interlobar nodal station. Excision biopsy demonstrated presence of sarcoidosis.



**Fig. 8.** Imaging findings for mediastinal lymphadenopathy without hilar nodes are presented.

**A.** Plain radiograph shows lymphadenopathy in right paratracheal region and para-aortic area (arrows). Both hilar shadows appear to be normal.

**B, C.** Contrast enhanced CT scans show multiple enlarged nodes with homogeneous attenuation in mediastinum (arrows). However, both hilar zones are preserved.



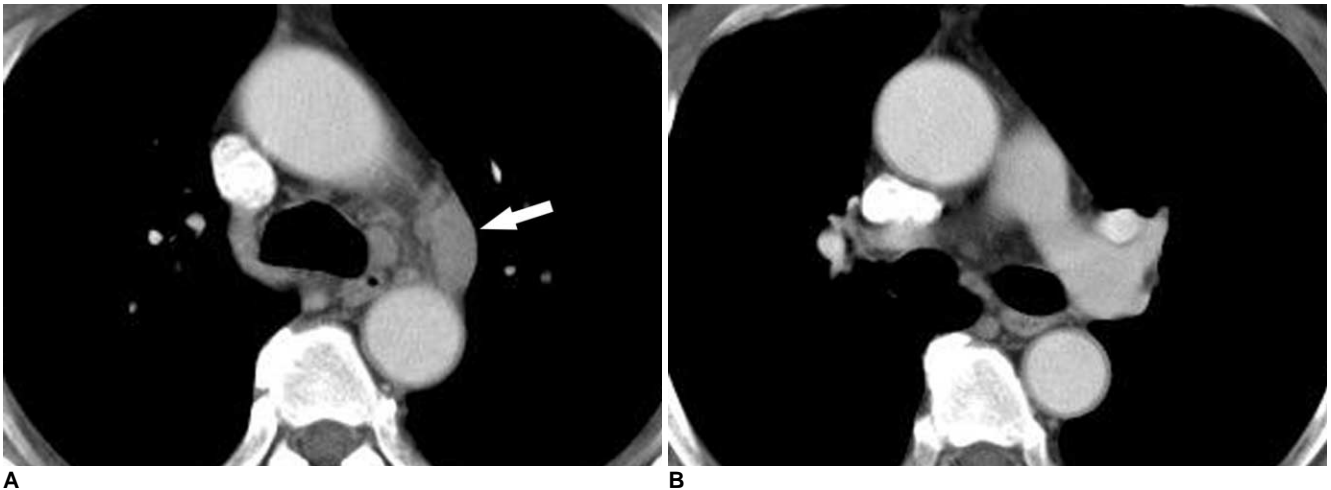
**C**

sis and metastatic disease (2-5). However, unilateral hilar lymphadenopathy is seen in less than 5% of cases, and is especially seen in patients older than 50 years of age. Unilateral hilar lymphadenopathy is approximately twice as common on the right side as compared to the left side and can occur either alone or with right paratracheal lymphadenopathy (Fig. 7). Mediastinal lymphadenopathy without hilar lymphadenopathy is even less common (Fig. 8). Moreover, isolated paratracheal or isolated subaortic

lymphadenopathy has been rarely reported in sarcoidosis (4, 5, 8, 9) (Fig. 9).

**Necrosis or Cavitation in Sarcoidosis**

Although non-necrotizing granulomas are characteristic of sarcoidosis, necrosis or cavitation occurs in less than 1% of patients; necrosis is thought to be due to either ischemic necrosis within conglomerated areas of sarcoid granulomas or extrusion of ischemic hyaline fibrous tissue (Fig. 10). To



**Fig. 9.** Imaging findings for isolated subaortic lymphadenopathy in sarcoidosis are shown. **A, B.** Contrast enhanced CT scans show presence of enlarged subaortic node (arrow) without hilar and paratracheal lymphadenopathy.



**Fig. 10.** Imaging findings for necrosis in sarcoidosis are shown. Axial CT scan with lung window setting shows ill-defined irregular consolidation with two small cavities at subpleural region of right middle lobe.



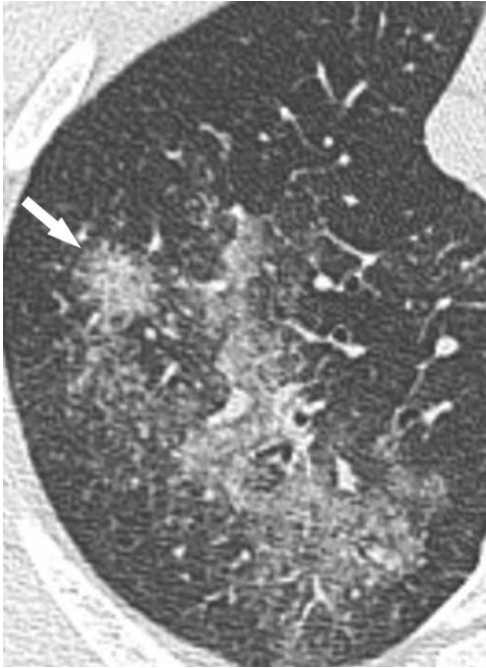
**Fig. 11.** Imaging findings for alveolar sarcoidosis are shown. Axial CT scan with lung window setting shows ill-defined round consolidation with air bronchogram in right upper lobe.

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diagnose the presence of cavities associated with sarcoidosis, cultures for acid-fast bacilli and fungi should be negative and radiologically similar lesions, such as bullae and bronchiectasis, should be ruled out (5, 9, 10).

### Large Opacities

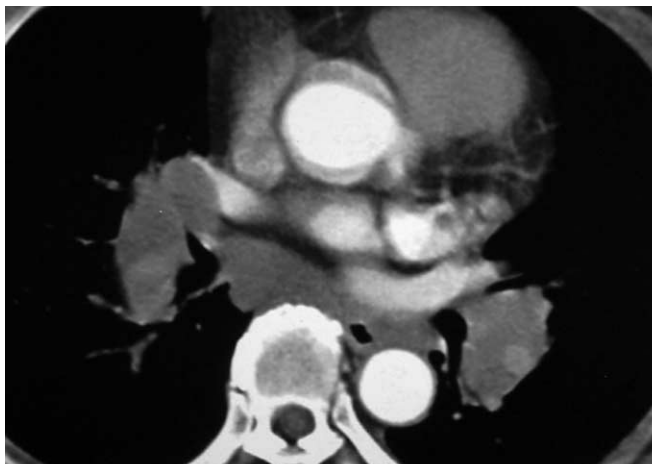
Large opacities refer to the presence of high attenuation areas, ranging in diameter from 1 cm to 4 cm. Large opacities can be seen on chest radiographs and CT scans in



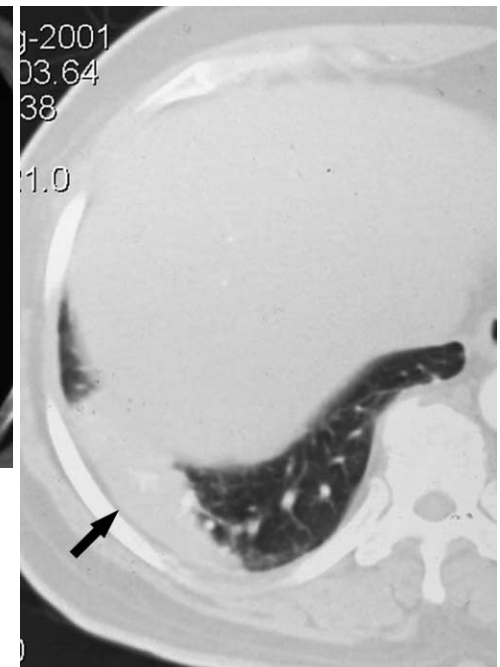
**Fig. 12.** Galaxy sign in alveolar sarcoidosis is demonstrated. High-resolution CT scan shows ill-defined nodular opacity resulting from confluence of interstitial granulomas (arrow). Another ill-defined large area with ground glass attenuation is seen with similar appearance as nodular lesion, also suggestive of alveolar sarcoidosis.



**Fig. 14.** Ground glass opacity in sarcoidosis is demonstrated. Axial CT scan with lung window setting shows localized area of ground glass opacity at posterior segment of right upper lobe. Note nodular thickening of peribronchial interstitium (arrow).



A



B

**Fig. 13.** Imaging findings for subpleural consolidation in sarcoidosis are presented. **A.** Axial CT scan shows bilateral symmetric hilar lymphadenopathy. **B.** Axial CT scan with lung window setting shows well-defined, elongated consolidation adjacent to pleura (arrow). Percutaneous CT guided biopsy revealed presence of sarcoidosis.



**Fig. 15.** Imaging findings for bronchial narrowing in sarcoidosis are presented. Axial CT scan with lung window setting shows focal narrowing of lateral segmental bronchus of right middle lobe, caused by enlarged peribronchovascular nodes (arrow). Associated ground glass opacity in right upper lobe is seen.

15% of patients with sarcoidosis. These opacities have a rounded or elongated shape, irregular edges and blurred margins with or without air bronchograms, and are located in the parahilar or peripheral region of the lungs (3) (Fig. 11).

These opacities have been referred to as alveolar sarcoid opacities, even though the opacities result from the confluence of a large number of interstitial granulomas. Therefore, on CT scans, small nodules are often visible at the periphery of these large opacities. This appearance has been referred to as the 'galaxy sign' (11) (Fig. 12). When the large opacities are located in the subpleural region, they occasionally manifest as elongated opacities adjacent to the pleura with a well-defined margin and regular edges (Fig. 13).

#### **Ground Glass Opacities**

Patients with sarcoidosis often show patchy areas of ground glass opacities (GGO) on HRCT images that are superimposed on a background of interstitial nodules or fibrosis (Fig. 14). The areas of GGO are usually due to the presence of extensive interstitial sarcoid granulomas or fibrosis rather than alveolitis (12).

#### **Airway Abnormalities**

Airway involvement is common in sarcoidosis. Bronchial abnormalities primarily consist of nodular bronchial wall thickening or small endobronchial lesions. Obstruction of lobular or segmental bronchi resulting in collapse may occur because of the presence of endobronchial granulomas or enlarged peribronchovascular lymph nodes (Fig. 15). Bronchiolar involvement due to granulomas or fibrosis



**Fig. 16.** Pleural involvement in sarcoidosis is demonstrated. Axial CT scan shows bilateral hilar and subcarinal lymphadenopathy, indicating sarcoidosis. Right pleural effusion is present. Note pleural thickening (arrow). Pleural biopsy revealed presence of sarcoidosis.

may result in air trapping as depicted on HRCT images (5).

#### **Pleural Involvement**

Approximately 1% of patients with sarcoidosis develop pleural abnormalities associated with sarcoidosis (5). Effusions are generally observed in cases with extensive pulmonary or systemic involvement. Lymphocytic, often bloodstained pleural aspirates are characteristic of involvement. A diagnosis can be made when pleural biopsies demonstrate the presence of noncaseating granulomas with no acid-fast bacilli by staining or under culture conditions (13) (Fig. 16).

#### **CONCLUSION**

Sarcoidosis is a relatively common disease with characteristic imaging findings (5). However, a diagnosis might be difficult for several reasons. These reasons include nonspecific clinical features and difficulty in the histopathological differentiation from granulomatous infections such as tuberculosis. In addition, atypical manifestations on radiological images can make diagnosis difficult. However, most cases of atypical sarcoidosis also show some typical radiological findings such as areas of typical sarcoid granulomas seen as nodules with a perilymphatic distribution or bilateral hilar lymphadenopathy. Therefore, it is important to consider both the typical and atypical radiological findings associated with sarcoidosis for a correct diagnosis.

#### **References**

1. Colby TV, Carrington CB. *Infiltrative lung disease*. In:



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- Thurlbeck WM, ed. *Pathology of the lung*. Stuttgart: Thieme Medical, 1988:425-517
- Müller NL, Kullnig P, Miller RR. The CT findings of pulmonary sarcoidosis: analysis of 25 patients. *AJR Am J Roentgenol* 1989;152:1179-1182
  - Koyama T, Ueda H, Togashi K, Umeoka S, Kataoka M, Nagai S. Radiologic manifestations of sarcoidosis in various organs. *Radiographics* 2004;24:87-104
  - Hamper UM, Fishman EK, Khouri NF, Johns CJ, Wang KP, Siegelman SS. Typical and atypical CT manifestations of pulmonary sarcoidosis. *J Comput Assist Tomogr* 1986;10:928-936
  - Rockoff SD, Rohatgi PK. Unusual manifestations of thoracic sarcoidosis. *AJR Am J Roentgenol* 1985;144:513-528
  - Baughman RP, Teirstein AS, Judson MA, Rossman MD, Yeager H Jr, Bresnitz EA, et al. Clinical characteristics of patients in a case control study of sarcoidosis. *Am J Respir Crit Care Med* 2001;164:1885-1889
  - Sulavik SB, Spencer RP, Weed DA, Shapiro HR, Shiue ST, Castriotta RJ. Recognition of distinctive patterns of gallium-67 distribution in sarcoidosis. *J Nucl Med* 1990;31:1909-1914
  - Conant EF, Glickstein MF, Mahar P, Miller WT. Pulmonary sarcoidosis in the older patient: conventional radiographic features. *Radiology* 1988;169:315-319
  - Miller BH, Rosado-de-Christenson ML, McAdams HP, Fishback NF. Thoracic sarcoidosis: radiologic-pathologic correlation. *Radiographics* 1995;15:421-437
  - Nakatsu M, Hatabu H, Morikawa K, Uematsu H, Ohno Y, Nishimura K, et al. Large coalescent parenchymal nodules in pulmonary sarcoidosis: "sarcoid galaxy" sign. *AJR Am J Roentgenol* 2002;178:1389-1393
  - Rohatgi PK, Schwab LE. Primary acute pulmonary cavitation in sarcoidosis. *AJR Am J Roentgenol* 1980;134:1199-1203
  - Nishimura K, Itoh H, Kitaichi M, Nagai S, Izumi T. Pulmonary sarcoidosis: correlation of CT and histopathologic findings. *Radiology* 1993;189:105-109
  - Huggins JT, Doelken P, Sahn SA, King L, Judson MA. Pleural effusions in a series of 181 outpatients with sarcoidosis. *Chest* 2006;129:1599-1604