Typical and atypical radiologic manifestations of pulmonary sarcoidosis: Apictorial review

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Sarcoidosis is a multisystemic disorder of unknown cause that is characterized by the presence of noncaseous epithelioid cell granulomas, which may affect almost any organ. Thoracic involvement is common, being seen in approximately 90% of patients [2] and accounts for most of the morbidity and mortality associated with the condition. Although chest radiography is often the first diagnostic imaging study in patients with pulmonary involvement, high resolution computed tomography (HRCT) is more sensitive for the detection of adenopathy and subtle parenchymal disease. The characteristic radiological findings associated with sarcoidosis have been well described and 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 [1]. The understanding of a wide range of the radiological manifestations of sarcoidosis will be very helpful for making a proper diagnosis.

We propose to attend these objectives:

- Discuss the role of chest radiography and HRCT in the diagnosis and management of pulmonary sarcoidosis.

- Recognize the HRCT findings of both typical and atypical features of pulmonary sarcoidosis.
Background

Sarcoidosis is a systemic disorder of unknown cause that is characterized by noncaseating granulomas with proliferation of epithelioid cells. This disease commonly affects young and middle-aged patients, with a slightly higher prevalence in women [4]. It primarily affects the lungs and the lymphatic system in more than 90% of patients but virtually no organ is immune from the disease [6].

The clinical features at presentation are nonspecific; the most common are respiratory symptoms (cough, dyspnea, bronchial hyperreactivity..), weakness, night sweats, weight loss, and erythema nodosum [1,2]. However, about one-half of patients remain asymptomatic, with abnormalities detected incidentally at chest radiography [4]. The clinical expression, natural history, and prognosis of sarcoidosis are highly variable. Although spontaneous recovery occurs in nearly two thirds of cases, therapy is necessary in one third of cases, and some patients experience a prolonged and severe course [6]. Death from sarcoidosis is usually the result of extensive and irreversible lung fibrosis with respiratory failure or cardiac or neurologic involvement. Less than 5% of patients die of sarcoidosis [2].

The diagnosis of sarcoidosis is commonly established on the basis of clinical and radiological findings that are supported by histological findings, and especially imaging plays an important role in the diagnosis and staging of this condition.

1- Chest radiographs:

Despite the progress in new imaging technologies, conventional chest radiograph continues to have a crucial role for the diagnosis, prognosis, and follow-up of sarcoidosis. The chest radiograph is abnormal at some point in more than 90% of patients and is often the first investigation to suggest the diagnosis [6].

a- Radiographic Staging:

The Siltzbach classification system defines the following five stages of sarcoidosis : stage 0, with a normal appearance at chest radiography; stage I, with lymphadenopathy only; stage II, with lymphadenopathy and parenchymal lung disease; stage III, with parenchymal lung disease only; and stage IV, with pulmonary fibrosis [2,6].

b- Radiographic Features :

- Typical features :
- **Sarcoid lymphadenopathy**: is typically bilateral, symmetrical, and non compressive. The most characteristic feature is bilateral hilar lymphadenopathy, noted in 50 to 80% [6] (Fig.1). Bilateral hilar adenopathy, alone or in combination with mediastinal lymphadenopathy, occurs in 95% of patients with lymph node involvement [5]. These lymph nodes are classically located in both hilar, in the pre- and right paratracheal mediastinum, in the aortopulmonary window, in the subcarinal area, those latter two are less easily identified on chest radiographs. Lymph node size tends to be largest at presentation. Calcification of affected lymph nodes is related to duration of disease, occurring in 3% of cases after 5 years and in 20% after 10 years [5].

- **Parenchymal infiltration**: is noted in 25 to 50% of patients with sarcoidosis and results from interstitial involvement by the granulomatous process. It is usually bilateral and symmetrical with a patent predominance for central regions and upper lobes. The pattern of infiltration is typically micronodular or reticulomicronodular. Other well-recognized radiographic features, including focal alveolar opacities and ground-glass opacities, are less frequent [6]. Pulmonary fibrosis can also be seen (Fig.2).

**Atypical features**:

- **Sarcoid lymphadenopathy**: Unusual patterns of lymph node enlargement occasionally occur. Rarely, the middle mediastinal nodes (paratracheal, subcarinal, aortopulmonary window, retroaortic) are involved in the absence of hilar adenopathy. The posterior mediastinum is least commonly involved. Isolated unilateral hilar adenopathy is an unusual manifestation of sarcoidosis, occurring only in 1-3% of patients. In fact, enlarged mediastinal lymph nodes without hilar adenopathy or unilateral hilar adenopathy occurs more frequently in older age patients [5].

- **Parenchymal infiltration**: may be unusual. Opacities may be basal or confined to part or all of one lung. Among a multiplicity of atypical patterns, the most frequent are multiple large, round nodules and alveolar consolidations, named "nodular" or "alveolar sarcoidosis", diffuse ground-glass opacities, tumorlike opacities, cavitation, pleural involvement, including effusion, pleural thickening or calcification, and pneumothorax; and atelectases. These features may occur in isolation but are often admixed with more typical abnormalities [6].

**c- Diagnostic role of chest radiography**:

In the absence of histological confirmation, clinical and/or radiological features may be diagnostic in stage I (reliability of 98%) or stage II (89%), but are less accurate for patients with stage III (52%) or stage 0 (23%) disease [6].

**d- Prognostic role of chest radiography**:
The purely descriptive nature of chest radiographic staging should be stressed. In individual cases, findings do not reliably discriminate between active inflammation and fibrosis, but they do identify major prognostic differences. Spontaneous resolution occurs in 55 to 90% of patients with stage I, 40 to 70% with stage II, 10 to 20% with stage III, and does not occur with stage IV disease [6].

2- High resolution computed tomography (HRCT):

Although probably not necessary in every patient, HRCT can play an important role in the diagnosis and staging of thoracic sarcoidosis. CT cannot only demonstrate subtle mediastinal adenopathy, which may be hardly visible on a chest radiograph, but can also better show lung parenchymal involvement [3]. The thin-section collimation and high-spatial-frequency reconstruction algorithms that are used to generate HRCT images allow improved detection of intrathoracic lesions observed in sarcoidosis.

The spectrum of disease on HRCT is extraordinarily variable. Several characteristic HRCT profiles have now been identified, but in many cases appearances are atypical.

a- Typical HRCT features:

• **Thoracic lymphadenopathy:**

CT is more sensitive in detecting enlarged lymph nodes than a chest radiograph. In sarcoidosis, lymph nodes typically present as bilateral and symmetric hilar lymphadenopathy associated with mediastinal lymph node enlargement, especially including the right paratracheal and subaortic nodes. Hilar and/or mediastinal lymphadenopathy is present on CT in 47 to 94% of patients with sarcoidosis, irrespective of radiographic staging [1,2,6]. Middle mediastinal nodes (at the left paratracheal level, subcarinal level, and level of the aortopulmonary window), prevascular nodes, or both are involved in approximately 50% of patients [2].

• **Parenchymal lesions and patterns:**

• **Micronodules with a perilymphatic distribution:**

A perilymphatic distribution of micronodular lesions is the most common parenchymal disease pattern seen in patients with pulmonary sarcoidosis (75%-90% of cases). HRCT shows sharply defined, small (2-4 mm in diameter), rounded nodules, usually with a bilateral and symmetric distribution, predominantly but not invariably in the upper and middle zones. The nodules are found most often in the subpleural peribronchovascular interstitial and less often in the interlobular septa. Although sarcoid granulomas arise as micronodular lesions, they may coalesce over time, forming larger lesions *(Fig. 3)* [2].
• **Interstitial thickening:**

Sarcoid granulomas frequently cause nodular or irregular thickening of the peribronchovascular interstitium (*Fig.4*). Extensive peribronchovascular nodularity on HRCT images is strongly suggestive of sarcoidosis. However, in most patients, interstitial thickening is not extensive [1,2].

• **Fibrosis:**

In most patients, sarcoid granulomas resolve with time. However, in an estimated 20% of patients, fibrosis becomes more prominent over time, producing HRCT findings of linear opacities, traction bronchiectasis, and architectural distortion (displacement of fissures and bronchovascular bundles) (*Fig.5*). Fibrosis is seen predominantly in the upper and middle zones, in a patchy distribution. Honeycombing may be seen in patients with sarcoidosis, but is uncommon. Extensive interstitial fibrosis can cause pulmonary arterial hypertension and resultant right heart failure [1,2].

• **Bilateral perihilar opacities:**

Confluent nodular opacities that appear on HRCT images as bilateral areas of lung consolidation with irregular edges and blurred margins, radiating from the hilum toward the periphery, are often seen with or without air bronchograms. These areas of consolidation are usually accompanied by micronodules [2].

b- **Atypical HRCT features:**

• **Thoracic lymphadenopathy:**

Occasionally, radiologic findings of lymph node enlargement may be asymmetric or seen in unusual locations (internal mammary, paravertebral, and retrocrural regions). Isolated unilateral hilar lymph node enlargement (usually on the right side) is seen in less than 5% of cases (*fig.6*). Enlargement of mediastinal lymph nodes without hilar lymph node enlargement is even less common [2]. Moreover, isolated paratracheal or isolated subaortic lymphadenopathy has been rarely reported in sarcoidosis [1].

Calcification of enlarged lymph nodes is visible in 25% to 50% of cases and may have an amorphous, punctuate, or eggshell-like appearance. This is closely related to the duration of the disease and suggests a chronic condition [1,4].

• **Parenchymal lesions and patterns:**

• **Pulmonary Nodules and Masses:**
Pulmonary nodules and masses are seen in 15%-25% of patients with parenchymal opacities. At HRCT, they usually appear as ill-defined irregular opacities measuring 1-4 cm in diameter and represent coalescent interstitial granulomas. These lesions are typically multiple and bilateral, and they may be located in perihilar or peripheral regions, with or without air bronchograms [2]. Small satellite nodules are often visible at the periphery of these masses, producing an appearance that has been termed the "galaxy sign" [1,2].

A solitary lung mass or nodule is rarely seen in sarcoidosis; however, individual granulomas that coalesce may produce the appearance of solitary masslike opacities. Multiple well-defined rounded macronodules (nodules with diameters exceeding 5 mm) might mimic a metastatic process [2].

• **Ground Glass Opacities** :

Ground-glass opacification is defined as hazy areas of slightly increased attenuation in which vessels and bronchi remain visible [6]. Patients with sarcoidosis often show patchy areas of ground glass opacities on HRCT images that are superimposed on a background of interstitial nodules or fibrosis. The areas of ground glass opacities are usually due to the presence of extensive interstitial sarcoid granulomas or fibrosis rather than alveolitis [1].

• **Necrosis or Cavitation in Sarcoidosis** :

Although non-necrotizing granulomas are characteristic of sarcoidosis, necrosis or cavitation occurs in less than 1% of patients. To 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 (*fig.7*) [1].

• **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 peribronchial lymph nodes [1]. The most common manifestations of airway involvement at high-resolution CT in patients with sarcoidosis are a mosaic attenuation pattern, air trapping, bronchial stenosis, and atelectasis [1]. The right middle lobe bronchus is particularly vulnerable to obstruction because of its length, its relatively small caliber, the acute angle of its origin from the bronchus intermedius, and its proximity to lymph nodes that drain the right lower lobe as well as the middle and upper lobes [2] (*fig.8*).
• **Pleural Involvement:**

Approximately 1% of patients with sarcoidosis develop pleural abnormalities associated with sarcoidosis. Effusions are generally observed in cases with extensive pulmonary or systemic involvement [1]. Manifestations of pleural involvement include exudative or transudative pleural effusion, hemorrhagic or chylous pleural effusion, pneumothorax, pleural thickening, and, rarely, pleural calcification [2].

c- **Diagnostic role of HRCT:**

In the appropriate clinical context, the observation of typical HRCT features of sarcoidosis (bilateral hilar lymph node enlargement with a perilymphatic micronodular pattern) and the anatomic distribution of those abnormalities (upper lobe predominance) may point to a highly specific diagnosis. HRCT may also facilitate and orientate the diagnosis when standard diagnostic tests are negative or equivocal or when a biopsy of an extrapulmonic site is considered too risky. Moreover, the value of HRCT in the detection of complications has been clearly demonstrated [6].

d- **Prognostic role of HRCT:**

The reversibility of HRCT features has been learned in several studies. Architectural distortion, traction bronchiectasis, honeycombing, and bullae are consistently irreversible. Micronodules, nodules, peribronchovascular thickening, and consolidation are wholly or partially reversible in most cases. However, HRCT could not discriminate between active inflammation and irreversible fibrosis [6].

3- **Pathologic findings :**

The diagnosis of sarcoidosis is established most securely when clinicoradiologic findings are supported by histologic evidence of widespread noncaseating granulomas. Histologic findings in sarcoidosis consist of noncaseating granulomas with epithelioid cells and large, multinucleated giant cells [4]. These granulomas in the lung parenchyma have a characteristic distribution in relation to lymphatics in the peribronchovascular interstitial space, subpleural interstitial space, and, to a lesser extent, the interlobular septa [2].

In fact, the thickened bronchovascular bundles and small perivascular nodules seen at HRCT correspond to granulomas within the connective tissue sheath surrounding pulmonary airways and vessels. The pleural or subpleural nodules are correlated with granulomas adjacent to the visceral pleura. Ground-glass opacities represent an accumulation of many granulomatous lesions, with or without fibrosis, in the alveolar septa and around the small vessels. The large parenchymal nodules (>1 cm in diameter) represent coalescent granulomas; and the air bronchiolograms within regions of dense
consolidation on CT images correspond to bronchiolar dilatation with surrounding fibrosis [2].
Images for this section:

Fig. 1: Hilar adenopathy in a 27-year-old man. Chest radiograph demonstrates typical bilateral hilar adenopathy.

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Fig. 2: Chest radiograph demonstrates pulmonary fibrosis

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**Fig. 3:** Axial contrast-enhanced CT scan (parenchymal window) shows micronodular lesions, along subpleural and scissural regions and coalescing over time, forming larger lesion

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**Fig. 4:** Axial contrast-enhanced CT scan (parenchymal window) shows peribronchovascular interstitium thickening

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**Fig. 5:** Axial high-resolution CT scans obtained at the carina (A) and the upper lobes (B) in a patient with pulmonary sarcoidosis show a fibrotic-cicatricial pattern of disease, with multiple lesions in a peribronchovascular distribution (curved arrow). Features of chronic disease are depicted, including traction bronchiectasis, severe architectural distortion and volume loss. Coalescent irregular masslike opacities (arrows)

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Fig. 6: Atypical radiologic findings of lymphadenopathy in 30-year-old man with sarcoidosis. Axial contrast material-enhanced CT scan (mediastinal window) shows atypical unilateral hilar (arrow) lymphadenopathy.

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**Fig. 7:** Axial contrast-enhanced CT scan (parenchymal window) obtained at the level of the upper left lobe. Cavity developed in the advanced fibrocystic stage of sarcoidosis

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**Fig. 8:** Axial contrast-enhanced CT scan (parenchymal window) obtained at the level of basal segmental lower lobe bronchi shows that part of the mass encases and occupies the right lower lobe bronchi, causing partial atelectasis. At diagnostic thoracotomy, sarcoidosis with tracheobronchial and pulmonary involvement was found.

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Imaging findings OR Procedure details

Chest radiography and high resolution computed tomography (HRCT) with multiplanar reconstructions are used to perform exams.
Conclusion

Sarcoidosis is a relatively common disease with characteristic imaging findings. However, a diagnosis might be difficult for several reasons, including nonspecific clinical features and difficulty in the histopathological differentiation from granulomatous infections. In addition, atypical manifestations on radiological images can make diagnosis difficult. Recognizing the various chest radiographic manifestations of pulmonary sarcoidosis plays an important role in diagnosis, which can be inconclusive or confusing in the first instance. Familiarity with chest radiographic and HRCT appearances of pulmonary sarcoidosis will help the radiologist and chest physicians in making a speedy and accurate diagnosis.
References


