Typical and atypical findings of pulmonary sarcoidosis at high resolution CT

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Learning objectives

To describe typical and atypical HRCT findings that suggest pulmonary sarcoidosis and the differential diagnosis of this disorder.

Background

Sarcoidosis is a chronic inflammatory disease of unknown etiology. It is characterized by the presence of noncaseating epithelioid cell granulomas in almost any organ of the body.

The disease most commonly affects lungs and hilar and lymph nodes (90% of cases), being this the main cause of morbidity and mortality associated with this condition.

• CLINICAL FEATURES

The most common clinical features are respiratory symptoms (cough, dyspnoea, bronchial hyper-reactivity), fatigue, night sweats, weight loss and erythema nodosum. However, up to 50% of cases of sarcoidosis are asymptomatic and abnormalities are identified incidentally on the chest radiograph.

Pulmonary function tests typically show a restrictive ventilatory pattern with decreased lung volumes and reduced carbon monoxide diffusion.

In presence of endobronchial involvement, an obstructive ventilatory pattern may occur.

The progression of the disease varies. Approximately two-thirds of patients with sarcoidosis remain stable or show remission within 10 years after diagnosis. About 20% of patients develop a chronic condition that leads to pulmonary fibrosis and less than a 5% of patients die as a result of the disease. Death from sarcoidosis is commonly related to an extensive and irreversible pulmonary fibrosis associated with respiratory failure or cardiac or neurologic involvement.

• PHATOGENESIS AND HISTOLOGY

Sarcoidosis is an immune-mediated multisystem disease. The most widely accepted explanation of the pathogenesis of this disorder is that one or more specific environmental agents trigger an immune system response mediated by activated alveolar macrophages and T cells.

The disease is characterised by noncaseating granulomas composed of a central core of histiocytes, epithelioid cells and multinucleated giant cells surrounded by
lymphocytes, plasma cells and varying quantities of fibroblasts and collagen in the periphery.

Granulomas in the lung parenchyma show a characteristic distribution, being related to lymphatic vessels in the peribronchovascular interstitial space and, to a lesser extent, in the interlobular septa (i.e., a lymphangitic distribution).

The upper lung lobes are most severely affected.

  • SILTZBACH STAGING

Siltzbach defines 5 stages of sarcoidosis:

  • stage 0: normal chest radiograph
  • stage I: lymph node enlargement
  • stage II: lymph node enlargement and pulmonary opacities
  • stage III: pulmonary opacities
  • stage IV: pulmonary fibrosis

  • DIAGNOSIS

The diagnosis of sarcoidosis is established on the basis of clinical and imaging findings as well as histologic evidence of noncaseating granulomas in one or more organs in the absence of any other possible causative organism. Granulomas with a known cause and sarcoid-like reactions must be excluded.

Imaging findings OR Procedure details

USE OF HIGH-RESOLUTION CT

High-resolution CT may be particularly useful to distinguish active inflammation from irreversible fibrosis in those patients with stage 2 or 3 sarcoidosis.

Nodules, ground-glass opacities and alveolar opacities suggest granulomatous inflammation that may be reversed with treatment.

On the other hand, honeycomb-like cysts, bullae and septal bands, architectural distortion, volume loss and traction bronchiectasis are indicative of irreversible fibrosis

HRCT may be useful to confirm the diagnosis of sarcoidosis in those patients with atypical clinical manifestations or unusual radiographic features.
Within an appropriate clinical context, observation of typical imaging features of sarcoidosis and the anatomic distribution of those abnormalities may point to a highly specific diagnosis. However, presence of atypical manifestations will require a broader differential diagnosis including tuberculosis, granulomatous infections, silicosis, malignancies and pneumoconiosis.

• **RADIOLOGIC-PATHOLOGIC CORRELATION**

Perivascular nodules and thickened peribronchovascular interstitium correspond to granulomas.

Pleural or subpleural nodules are correlated with granulomas adjacent to the visceral pleura.

Ground-glass opacities represent collections of several granulomas, with or without fibrosis, around the small vessels in the alveolar septa.

Large parenchymal nodules (>1 cm in diameter) represent coalescent granulomas.

Air bronchiogram sign within regions of dense consolidation on CT images correspond to bronchiolar dilation with surrounding fibrosis.

• **LYMPHADENOPATHY**

**TYPICAL PATTERNS**

The most common pattern is a well-defined, bilateral and symmetric hilar and right paratracheal lymph nodes enlargement.

Bilateral hilar lymph nodes enlargement, alone or in combination with mediastinal lymph nodes enlargement, occurs in an estimated 95% of patients affected with sarcoidosis.

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.

Bilateral hilar lymph nodes enlargement may be a finding of infection or malignancy. However, in the absence of specific symptoms or signs, sarcoidosis is the most common cause of this feature. Although histological confirmation is not required for a diagnosis of sarcoidosis in these patients, a biopsy should be performed if the imaging findings worsen or specific signs and symptoms develop.
**Fig. 1:** HRCT. Multiple enlarged mediastinal lymph nodes in the prevascular space and pretracheal retrocaval space. References: Radiology Department, Hospital Universitario Central de Asturias - Oviedo/ES

**References:** Servicio de Radiodiagnóstico, Hospital Universitario Central de Asturias - Oviedo/ES
Fig. 2: Axial HRCT scan that shows bilateral subcarinal and hilar enlarged lymph nodes. References: Radiology Department, Hospital Universitario Central de Asturias - Oviedo/ES

References: Servicio de Radiodiagnóstico, Hospital Universitario Central de Asturias - Oviedo/ES
ATYPICAL PATTERNS

Atypical patterns of lymphadenopathy occur more frequently in patients older than 50 years.

Lymph nodes enlargement may be asymmetric or show unusual locations (i.e., internal mammary chain, paravertebral or retrocrural regions). Such findings should lead to the inclusion of entities such as lymphoma or tuberculosis in the differential diagnosis.

Isolated unilateral hilar lymph nodes enlargement, usually on the right side, is seen in less than 5% of cases.
Enlargement of mediastinal lymph nodes without hilar lymph nodes enlargement is even less common.

The enlarged nodes may occasionally become calcified, this being related to the duration of the disease (calcification occurs in 3% of patients after 5 years and in 20% after 10 years).

The calcifications in sarcoidosis may be indistinguishable from those seen in tuberculosis and histoplasmosis. Eggshell-like calcifications may also be identified in silicosis.

**Fig. 4**: HRCT. Calcified enlarged lymph nodes in the pretracheal space in a patient with sarcoidosis. Nodular pattern with peribronchovascular and subpleural distribution, where nodules show a tendency to conglomerate leading to formation of masses. References: Radiology Department, Hospital Universitario Central de Asturias - Oviedo/ES

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- **PARENCHIMAL MANIFESTATIONS**
TYPICAL PATTERNS

MICRONODULES WITH A PERILYMPHATIC DISTRIBUTION

A perilymphatic distribution of micronodular lesions is the most common pattern of parenchymal disease in patients with sarcoidosis (75-90% of cases).

![Frontal chest radiograph](image)

**Fig. 5:** Frontal chest radiograph that exhibits a sarcoidosis-related diffuse bilateral micronodular pattern, more profuse in upper lung zones. References: Radiology Department, Hospital Universitario Central de Asturias - Oviedo/ES

**References:** Servicio de Radiodiagnóstico, Hospital Universitario Central de Asturias - Oviedo/ES

HRCT shows well-defined, small (2-4 mm) and rounded nodules, usually with a bilateral and symmetric distribution, predominantly in the upper and middle lung zones. The nodules are found most often in the peribronchovascular interstitium and less often in the interlobular septa. The micronodular lesions may coalesce over time, forming larger lesions.
Sarcoid granulomas frequently cause nodular or irregular thickening of the peribronchovascular interstitium.

**Fig. 6:** Diffuse bilateral micronodular pattern showing a peribronchovascular distribution, compatible with sarcoidosis. References: Radiology Department, Hospital Universitario Central de Asturias - Oviedo/ES

**References:** Servicio de Radiodiagnóstico, Hospital Universitario Central de Asturias - Oviedo/ES
Fig. 7: HRCT. Micronodular pattern with a peribronchovascular distribution and numerous subpleural nodules showing tendency to conglomerate. Infracarinal enlarged lymph nodes. References: Radiology Department, Hospital Universitario Central de Asturias - Oviedo/ES

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FIBROTIC CHANGES

In most patients, sarcoid granulomas resolve with time without treatment. However, an estimated 20% of patients develop pulmonary fibrosis, showing linear opacities, traction bronchiectasis and architectural distortion, in a patchy distribution, usually in the upper and middle lung zones.
**Fig. 8:** Frontal chest radiograph showing pulmonary masses in middle and upper zones causing traction and pulmonary architectural distortion along with bullae formation. Findings related to fibrotic lung changes in sarcoidosis. References: Radiology Department, Hospital Universitario Central de Asturias - Oviedo/ES

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**BILATERAL PERIHILAR OPACITIES**

Areas of lung consolidation with irregular, blurred margins, radiating from the hilum toward the periphery, with or without air bronchogram. These areas of consolidation are formed by multiple confluent nodular opacities.
Fig. 9: Centrilobular and subpleural micronodular interstitial pattern accompanied by diffuse bilateral reticular areas with more extensive involvement of perihilar regions. Suggestive findings of stage III sarcoidosis. References: Radiology Department, Hospital Universitario Central de Asturias - Oviedo/ES

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ATYPICAL PATTERNS:

PULMONARY NODULES AND MASSES

Pulmonary nodules and masses are seen in 15%-25% of patients. On CT, they usually appear as ill-defined irregular opacities, measuring 1-4 cm in diameter, that represent coalescent interstitial granulomas. These lesions are typically multiple and bilateral, commonly located in perihilar or peripheral regions.
**Fig. 10:** HRCT showing an interstitial pattern with spiculated nodules in a peribronchovascular and subpleural distribution, predominantly in middle and upper lung zones. Associated to traction bronchiectasis and enlarged right hilum lymph nodes. Suggestive findings of sarcoidosis as first option. References: Radiology Department, Hospital Universitario Central de Asturias - Oviedo/ES

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**Fig. 11:** Coronal maximum-intensity projection image obtained with lung window settings that shows a diffuse bilateral micronodular pattern with a peribronchovascular distribution and larger nodules. References: Radiology Department, Hospital Universitario Central de Asturias - Oviedo/ES

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Air bronchogram may be present, but cavitation is rare.

Small satellite nodules are often identified at the periphery of these masses, giving an appearance that has been termed the "sarcoid galaxy sign". The same feature may be present in other granulomatous diseases and neoplasms.

A recently described CT sign, the "sarcoid cluster", consists of multiple micronodules spread along the subpleural lymph vessels located in peripheral regions of the upper and middle lung zones.
Occasionally, parenchymal lesions coalesce, forming masses that consist of peribronchovascular fibrous tissue surrounding abnormal conglomerations of perihilar bronchi and vessels. These masses, which are typically seen bilaterally in the upper and middle lung zones, may mimic progressive massive fibrosis. Such lesions may also be observed in silicosis, berylliosis, tuberculosis and talcosis.

Fig. 4: HRCT. Calcified enlarged lymph nodes in the pretracheal space in a patient with sarcoidosis. Nodular pattern with peribronchovascular and subpleural distribution, where nodules show a tendency to conglomerate leading to formation of masses. References: Radiology Department, Hospital Universitario Central de Asturias - Oviedo/ES

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A solitary lung mass or nodule is rarely seen in sarcoidosis.
Fig. 12: Axial HRCT scan exhibiting micronodules in both pulmonary parenchyma with an asymmetric distribution and images of larger nodules (±1 cm). Multiple calcified mediastinal enlarged lymph nodes were visible. References: Radiology Department, Hospital Universitario Central de Asturias - Oviedo/ES

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**PATCHY AIRSPACE CONSOLIDATION**

Patchy airspace consolidation is seen in 10%-20% of patients with sarcoidosis. It is usually bilateral and symmetric and predominantly affects the middle and upper lung zones.

These regions may contain air bronchograms and commonly show ill-defined margins, with a nodular pattern toward the lung periphery.

This pattern is known as the acinar or alveolar form of sarcoidosis, which may mimic pneumonia, tuberculosis, or bronchiolitis obliterans organizing pneumonia.
Fig. 13: Axial HRCT scan showing patchy bilateral lung consolidations, predominantly in hilum, with air bronchogram areas associated with small bilateral peripheral nodules. Related to distortion of the lung parenchyma. Suggestive findings of sarcoidosis. References: Radiology Department, Hospital Universitario Central de Asturias - Oviedo/ES

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PATCHY GROUND-GLASS OPACITIES

Patchy ground-glass opacities result from the confluence of multiple granulomatous nodules and fibrotic interstitial lesions, which may cause airway compression but not airspace filling like that seen in alveolitis.

These ground-glass opacities show ill-defined margins and air bronchogram may be present.

Differential diagnosis must be made with bronchoalveolar carcinoma, lymphoma, pneumoconiosis, pneumonia and bronchiolitis obliterans organizing pneumonia.
Fig. 14: Fig. 14: Axial HRCT scan in a patient with sarcoidosis showing an increased attenuation with a patchy pattern and a ground-glass appearance, predominantly in peripheral areas and upper lung zones. Interstitial thickening and some images of tree in bud nodules were also visible.

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**LINEAR RETICULAR OPACITIES**

This pattern is produced by interlobular and intralobular septal thickening and is commonly seen in the subpleural space of the upper and middle lung zones. Although this pattern may simulate lymphangitic carcinomatosis, this disorder is characterized by a more extensive and more severe involvement of the interlobular septa and subpleural space than is typical either in lymphoma or in sarcoidosis.
**Fig. 15:** HRCT. Mixed pattern with a diffuse thickening of the interstitium, with both linear and nodular characteristics, along with thickening of the peripheral septa and axial interstitium. References: Radiology Department, Hospital Universitario Central de Asturias - Oviedo/ES

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**FIBROTIC CHANGES**

Cysts, bullae and paracicatrical emphysema correspond to late stages of sarcoidosis. They typically involve the upper and middle lung zones in a perihilar distribution.

**MILIARY PATTERN**

This pattern is rare in sarcoidosis (<1% of cases) and its presence requires a wide differential diagnosis, including entities such as tuberculosis, pneumoconiosis, metastatic lesions, histoplasmosis and histiocytosis.
AIRWAY INVOLVEMENT

The most common imaging findings of airway involvement are a mosaic attenuation pattern, air trapping, tracheobronchial abnormalities and atelectasis.

Mosaic Attenuation Pattern: It refers to the presence of heterogeneous attenuation in the lung parenchyma on inspiratory CT images. In patients with sarcoidosis, this pattern results from airway involvement by granulomas or fibrosis, which may lead to obstruction.

Air trapping: It is characterized by focal areas of decreased attenuation on expiratory CT images. It is a common, albeit nonspecific, feature. There is no correlation with the stage of the disease.

Tracheobronchial Abnormalities: Stenosis, irregularity, distortion and focal areas of bronchiectasis.

Atelectasis: As a result of the obstruction of lobar or segmental bronchi by granulomas.

PLEURAL DISEASE

Pleural involvement in sarcoidosis is rare (1%-4%). Manifestations of pleural involvement include pleural exudates or transudates, chylothorax, hemothorax, pneumothorax, pleural thickening and, rarely, pleural calcification.

Pleural effusions are usually minimal and resolve within 2 to 3 months.
Fig. 16: Fig. 16: Thickening of the perivascular interstitium in both lungs associated to a slight granulation in the cisural area and paratracheal and prevascular enlarged lymph nodes in a patient with sarcoidosis. The image demonstrates a small pleural effusion on the right side. References: Radiology Department, Hospital Universitario Central de Asturias - Oviedo/ES

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Pneumothorax occurs as a complication of advanced bullous disease (in patients that exhibit fibrotic changes) or as a result of a bleb rupture or necrosis of subpleural sarcoid granulomas.

Images for this section:
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Conclusion

HRCT allows a high-certainty diagnosis of sarcoidosis in those patients with typical imaging findings and a compatible clinical context. HRCT is also useful for those patients with atypical clinical or imaging features that may require an extensive differential diagnosis, which should include silicosis and other pneumoconioses, lymphangitic carcinomatosis, tuberculosis and other infectious conditions.

References


Personal Information