Contribution of high resolution computed tomography (HRCT) imaging in positive and differential diagnosis of pulmonary sarcoidosis.

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Learning objectives

The main aims of this exhibit are first to describe the elementary signs and the imaging features of thoracic sarcoidosis and second, based on these signs, to identify differential diagnoses that can give imitating images.
Background

Sarcoidosis is a systemic granulomatosis of unknown origin. It affects mostly patients less than 40 years old and has a feminine predilection. It has various clinical features and manifests often with respiratory symptoms. Pathologically, it is characterized by the presence of non-caseating granulomas (1). Although different organs might be affected by this disease, the most frequent site remains thoracic.
Findings and procedure details

The diagnosis of sarcoidosis, clinically suspected, can be established and staging made on the basis of chest radiographic findings Table 1 on page 9. Chest high resolution computed tomography (HRCT) is nowadays an increasingly used technique for identifying and managing sarcoidosis (2). HRCT uses high spatial frequency reconstructions and thin-section collimation. It allows detection of subtle parenchymal changes such as faint ground glass, interlobular septal thickening and nodular and reticular opacities.

While, the diagnosis of sarcoidosis can be suspected upon features detected on chest radiography, pulmonary infiltrates and their distribution are better appreciated on a CT examination (3). A detailed analysis of lung parenchyma changes can be made on HRCT. This imaging technique allows also the detection of vascular, airway or lymphatic involvement and helps analyze the interstitial tissue. Subtle mediastinal adenopathy hardly visible in chest radiography can also be demonstrated.

1-Imaging features

The imaging features of pulmonary parenchymal involvement in sarcoidosis depend upon the chronicity and the stage of the disease.

CT findings can be devided into:

Reversible pulmonary lesions

1-Nodular opacities with a perilymphatic distibution Fig. 1 on page 9 Fig. 2 on page 10: They are typically sharply defined but may have irregular or smooth margins. They are predominantly located is in the mid or upper lung zones. They also have a lymphatic predilection and are thus clustered along the peribronchovascular interstitium Fig. 3 on page 10, in the interlobular septa, in the interlobar fissures and in the pleural surfaces (4). They commonly measure between 2 and 5 mm (5).

2-Large nodules, lung consolidations and conglomerate masses: confluent nodular opacities may present as areas of parenchymal consolidation with air bronchograms. The distribution is in general bilateral and symmetrical with a mid and upper lung distribution (6). These masses can be surrounded by small satellite nodules realizing an appearance termed "the galaxy sign".

3-Ground glass opacities Fig. 4 on page 11: it has been suggested that ground glass may correspond to innumerable small interstitial granulomas beyond the resolution of HRCT (7). Another hypothesis supposes that it is related to an active alveolitis (8).

4-Mosaic attenuation and air trapping: a mosaic pattern can be caused by an increased perfusion secondary to vascular distribution. This vascular distribution is a
result of a hypoperfusion in the surrounding areas and a hypoventilation caused by bronchiolar narrowing (3).

The appreciation of air trapping can only be done on expiratory acquisitions. It appears as multiple patchy areas of decreased attenuation that decrease in size but increase in density after expiration.

5-Mediastinal and hilar lymph node enlargement usually symmetrical Fig. 5 on page 12 Fig. 6 on page 13: lymphadenopathy are present in 80% of the cases of thoracic sarcoidosis (9) and are typically well-defined and non-compressive. Lymph node enlargement is seen in the aortopulmonary, tracheobronchial and subcarinal regions. Icing sugar and cloud like calcification are typical of sarcoidosis (10).

Irreversible pulmonary lesions:(11)

Findings of fibrosis are more frequent in the upper lobes and have a perihilar distribution. This distribution is specific and should suggest the diagnosis of sarcoidosis Fig. 7 on page 15.

The most common features are:

1-Septa thickening Fig. 8 on page 14: irregular hilar-peripheral linear opacities might be noted and have a diffuse distribution. These lines are obviously fibrotic because of their angulation and their association with signs of fissural and bronchial distortion.

2-Traction bronchiectasis is shown by posterior displacement of the main or upper lobe bronchus. It might also be composed of central bronchial deformation, angulated or crossed bronchis. It occurs in the middle and upper lung zones.

3-Honeycombing is a less common feature represented by clustered cystic air spaces with diameters of 0.3 to 1 cm that have often well-defined and thick walls and are mostly located in the subpleural and upper zones.

In more advanced cases upper lobes volume loss and retraction of hila might be noted.

Uncommon features:

- Confluent granulomas can be the site of central necrosis resulting in cavitation. It is a rare complication that can happen in less than 2% of the case and should suggest the diagnosis of a surimposed infection (12).

- Pleural involvement includes either pleural effusion or pleural thickening. Pleural thickening is a result of extra-thoracic soft tissue and fat fibrotic retraction.

- Air trapping and alveolar distension due to bronchiolar narrowing may result in the formation of large bullae.
- A solitary pulmonary nodule is a rare presentation.

- Mycetomas can develop in cystic spaces and are seen in 1 to 3% of patients they should be suspected when a new pleural thickening adjacent to a known cyst appears (1).

2-Differential diagnoses:

For its imaging feature variety and it capacity to simulate a multitude of other disease, sarcoidosis is denominated "the great mimicker".

Nodular opacities:

Nodular opacities with a peribronchovascular distribution may also be seen in tuberculosis. The key features that suggest the diagnosis of tuberculosis are exsudate, parenchymal consolidation, acinar nodules or a tree-in-budd pattern.

In lymphangitis carcinomatosis Fig. 9 on page 16: nodules have a septal and peribronchovascular distribution. They are more extensive and outline the secondary pulmonary lobule. Lung involvement can be unilateral or bilateral.

In silicosis Fig. 10 on page 15 and pneumoconiosis: nodules are less extensive than those of sarcoidosis, often centrolobular and located in the subpleural space. The posterior segments of the upper lobes are the most affected sites.

Granulomas may also be observed in infections caused by Nocardia, Histoplasma, Cryptococcus, Aspergillosis and actinomycosis.

Miliary opacities are rare in sarcoidosis and may suggest the diagnosis of tuberculosis, pneumoconiosis or metastatic lesions if the distribution is random suggesting their hematogeneous dissimination (5) Fig. 11 on page 18.

Interlobular septal thickening and linear reticular opacities:

Lymphangitis carcinomatosis Fig. 9 on page 16:

In sarcoidosis septal thickening is due to the presence of granulomas in the lymphatics of the interlobular septa and is thus usually beaded and nodular. In lymphangitis carcinomatosis thickening is caused by the accumulation of cells and fluid in the interlobular septas and is usually extensive with marked outlining (polygonal pattern) of the secondary pulmonary lobules (13).

In lymphoma Fig. 12 on page 17 a severe involvement of the subpleural space and of the intralobular septa is noted.

In pulmonary edema Fig. 13 on page 19 there is regular and bilateral septal thickening outlining the second pulmonary lobule associated with signs of heart failure.
Large consolidation:

The confluence of numerous acinar and interstitial micronodules results in the formation of central consolidation with ill-defined margins and surrounded by a nodular pattern. Pneumonia, tuberculosis and bronchiolitis obliterans organizing pneumonia.

In tuberculosis: Air space consolidation can be uni or bilateral. It has a peribronchovascular distribution and can cavitate. Centrolobular nodules and tree-in-bud appearance may also be noted.

In organizing pneumonia: there is typically peripheral parenchymal consolidation with air bronchogram that can be surrounded by ground-glass-like opacities. It is mostly located in the upper lobes along fissures or the pleura.

Lung cancer: It has a round or oval shape with smooth, irregular or spiculated margins and can be located at any lobe. Bands connecting the mass to the pleura may also be seen.

Conglomerate parahilar masses:

In sarcoidosis fibrosis occurs in 20 to 25% of the patients. It can be so marked that parahilar conglomerate opacities develop.

Similar patterns also called progressive massive fibrosis can be seen in silicosis, coal worker pneumoconiosis and pulmonary talcosis. In all cases history of specific exposure suggests the diagnosis (14). The main imaging feature consists in lung consolidations with radiating strand located predominantly in the upper lobes. These regions can contain air bronchograms or calcifications.

Pleural plaque-like opacities:

In sarcoidosis: they are formed by coalescing granulomas and have well defined and irregular margins. They are associated in most cases with pleural effusion (15).

Similar patterns can be seen in pneumoconiosis and coal worker’s pneumoconiosis.

The patchy ground-glass opacities:

In sarcoidosis, they are superimposed on a background of interstitial nodules and are usually accompanied by other abnormalities.

An isolated and bilateral ground glass pattern can be seen in bronchoalveolar cell carcinoma, lymphoma, in pneumonia, in pneumoconiosis and in bronchiolitis obliterans organizing pneumonia (5).

Air trapping on expiratory HRCT scans:
The diagnosis of bronchiolitis obliterans should be suggested when air trapping is isolated with no other parenchymal involvement.

**Fibrocystic changes:**

In sarcoidosis, honeycomb like cysts are most commonly distributed in the subpleural regions of the middle or upper lobes sparing the lung bases (17). Reticular abnormalities and traction bronchitis extend dorsolaterally.

The diagnosis of usual interstitial pneumonia or idiopathic pulmonary fibrosis Fig. 14 on page 20 may be suggested if fibrocystic changes are seen in the lower lobes and have a subpleural distribution.

**Hypersensitivity pneumonitis** is characterized by the combination of lobules of decreased attenuation and interstitial fibrosis (14).

**Lymphadenopathy:**

In sarcoidosis: lymph nodes are bilateral and symmetrical and commonly with calcification.

In tuberculosis the calcification tend to be unilateral and dense (10).

Lymph node calcifications may also be seen in silicosis (16).

An exclusive involvement of lymph nodes in sarcoidosis is rare but possible. It might suggest the diagnoses of

**Small cell carcinoma** : There is usually a hilar or perihilar mass with marked lymphadenopathy that is usually unilateral.

**Lymphoma:** lymph node enlargement can be asymmetrical and unilateral
Table 1: Staging of sarcoidosis on the basis on chest radiograph


Fig. 1: Coronal high CT scan of a patient with thoracic sarcoidosis showing micronodules (red arrows), septal thickening (yellow arrow), hilar enlargement (blue stars).
Fig. 2: Axial HRCT showing a pulmonary sarcoidosis manifesting in a multitude of micronodules with a perilymphatic distribution (red arrows) and fissures involvement.
**Fig. 3:** Axial high resolution CT scan of a patient with pulmonary sarcoidosis showing thickening of the peribronchovascular interstitium in the mid lobe (red arrow) and micronodules with lymphatic distribution in the apical segment of the low left lobe (yellow arrow).

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Fig. 4: Axial high resolution CT scan of a patient with pulmonary sarcoidosis showing ground-glass opacities (red arrows) and thickening of the interlobular septa (yellow arrow).

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Fig. 5: Axial section of an enhanced CT scan showing bilateral, symmetrical and non-compressive mediastinal and hilar lymphadenopathy (red arrows).

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**Fig. 6:** Axial non-enhanced CT scan showing hilar enlarged lymph nodes containing icing sugar calcifications (red arrows)

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**Fig. 8:** Axial CT scan showing an important thickening of the interlobular septa in the mid regions of the lungs (red arrows), and of the peribronchovascular interstitium (yellow arrow), and nodular opacities of the mid lobe (green arrows).

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**Fig. 7:** Axial HRCT showing findings of fibrosis including linear opacities (red arrows), bronchovascular distorsions (yellow arrows) and honeycombing cystic changes (green arrows) in a patient with pulmonary sarcoidosis.

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**Fig. 10:** CT scan showing features of silicosis manifesting in mediastinal and hilar calcified lymph nodes (red arrows) associated with centrolobuar nodules located in the posterior segments of the upper lobes (green arrows).

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Fig. 9: Contrast material enhanced HRCT showing a mediastinohilar speculated mass (red arrows). There is also an important thickening of the interlobular septa (green arrows) associated with parenchymal consolidations related to carcinomatosis lymphangitis.
Fig. 12: Contrast material enhanced CT scan showing unilateral features including parenchymal consolidations and important thickening of the interlobular septa in a patient with a history of lymphadenopathy. These patterns are related to lung involvement in lymphoma.

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**Fig. 11:** axial CT scan showing small pulmonary nodules of homogenous size and without any perilymphatic distribution in a patient with miliary tuberculosis.

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**Fig. 13:** Axial CT scan showing parahilar alveolar consolidations associated with a thickening of the interlobular septa. There is also bilateral pleural effusion. These features are related to pulmonary edema.

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**Fig. 14:** Axial HRCT scan showing extensive fibrosis in patient with the diagnosis of UIP: thickening of the interlobular septa (green arrow), honeycomb like cysts (yellow arrow) and ground-glass opacities (red arrows).

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Conclusion

Thoracic sarcoidosis manifest with various imaging pattern and is thus called "the great pretender", for its capacity to simulate other pathologies. HRCT helps make the positive diagnosis when clinically suspected and helps improve the detection of subtle parenchymal lesions. It also allows making the differential diagnosis with other pulmonary affections and leads the treatment and follow-up scheme.
References


