Learning objectives

1) to review the wide spectrum of HRCT presentation of pulmonary sarcoidosis.

2) to discuss HRCT findings useful to differentiate sarcoidosis from other diseases.

Background

Sarcoidosis is an inflammatory, multisystemic, disease of unknown etiology, characterized pathologically by the presence of non-caseating granulomas.

Pulmonary involvement in sarcoidosis is reported in up to 90% of patients. It resolves spontaneously in the majority of cases, but fibrosis causing permanent functional impairment develops in 20 to 25% of patients, resulting in death in 5-10% of them.

Sarcoidosis is the most frequent among the interstitial lung diseases, showing a higher incidence in women than in men and begins most often between 20 and 40 years of age. The extrapulmonary involvement, particularly skin and eyes, is present in 25% of cases, while more rare is the involvement of central nervous system, heart and kidneys.

There are multiple clinical and radiological appearances: half of patients is asymptomatic at the time of diagnosis and the involvement of various organs can vary significantly from patient to patient.

Chest X-ray has been widely used in the past in the diagnosis and staging of the disease. The use of high-resolution computed tomography (HRCT) provides detailed information on the wide spectrum of radiological presentation of sarcoidosis.

In some cases the definitive diagnosis of sarcoidosis needs transbronchial biopsy or broncho-alveolar lavage especially in clinical or radiological atypical cases.

Imaging findings OR Procedure details

The precise role of imaging in the diagnosis of sarcoidosis is not yet defined. In the past, the chest X-ray was widely used defining 5 stages: stage 0 (normal appearances), stage I (bilateral hilar lymphadenopathy), stage II (bilateral hilar lymphadenopathy with pulmonary infiltrates), stage III (parenchymal infiltrates) and stage IV (irreversible fibrosis with parenchymal distortion and bullae). All patients should have a chest radiograph and,
occasionally, in the correct clinical and laboratory context, this can be sufficient for the diagnosis.

HRCT plays a diagnostic role in patients with atypical clinical or radiographic findings, or in patients with a normal chest radiograph but clinical suspicion of sarcoidosis; it is also important for the detection of complications. Besides, CT plays a key role in identification of high-yield sites for transbronchial or surgical lung biopsy, when patients require tissue confirmation.

Sarcoidosis can be called the "great mimicker" because of its ability to mimic other disease (Tab.1).

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**Table 1**: Sarcoidosis: common and uncommon HRCT findings

**References**: RADIOLOGIA, OSPEDALE SS. ANNUNZIATA - Chieti/IT
PERILYMPHATIC NODULES

The most characteristic HRCT abnormality in patients with sarcoidosis consists of small nodules ranging from 2 to 5 mm in diameter. Nodules have a perilymphatic distribution, so they are mainly clustered along the bronchovascular bundles, interlobular septa, interlobar fissures, subpleural zones and centrilobular regions (fig 1). An upper lobe predominance is very common. Mediastinal lymphadenopathies, often bilateral and symmetric, are observed in 70-90% of cases with a prevalence of the hilar, subcarinal and right paratracheal regions. Involvement of hilar stations is so typical in patients with sarcoidosis that the presence of mediastinal lymphadenopathy without a hilar involvement, raises doubts about the diagnosis of sarcoidosis (fig.2). Patients with sarcoidosis can present mediastinal lymph nodes with no or minimal a parenchymal involvement. A cloud-like or "icing -sugar" calcification of lymphonodes is also typical of sarcoidosis.

Differential diagnosis: conditions that can closely mimic the HRCT appearance of sarcoidosis with nodules in a perilymphatic distribution are pulmonary lymphangitic carcinomatosis and silicosis or coal worker's pneumoconiosis (CWP).

In lymphangitis carcinomatosis nodules are most frequently septal and peribronchovascular (fig. 3); lung involvement can be unilateral or bilateral and mediastinal lymph nodes are involved in 25% of cases. In sarcoidosis nodules are peribronchovascular and subpleural; septal thickening is a limited finding, less extensive and does not outline the secondary pulmonary lobule forming polygonal structure as in lymphangitis. Anyway lymph node involvement is almost always present in sarcoidosis.

In silicosis and CWP nodules are frequently centrilobular and subpleural ranging from 2 to 10 mm in diameter, located predominantly in the posterior segments of the upper lobes. Nodules's profusion is less extensive than sarcoidosis (fig. 4). Hilar and mediastinal lymph node involvement is present in 35-40% of patients with silicosis and almost always present in sarcoidosis.

MILIARY NODULES

Uncommonly, sarcoïd granulomas can be located in a random distribution instead of the classic perilymphatic location. This is the miliary pattern of sarcoidosis (fig. 5), which is seen as tiny, innumerable nodules distributed diffusely in the lung parenchyma.

Differential diagnosis: the military pattern is very rare and should be differentiated from miliary tuberculosis (TB) and from metastatic lesions. The differential diagnosis of these three entities, based only on radiologic findings, can be sometimes very difficult.

Miliary TB usually manifests with nodules of 1-2 mm in diameter diffusely distributed in the lungs. Sometimes nodules may coalesce and become larger. Distribution depends on hematogenous dissemination (fig.6).
Lung metastases occur more frequently as well-defined nodules, usually in the lower lobes (fig.7); they are often located at the end of the arteries due to their hematogenous spread ("feeding vessel sign").

LARGE OPACITIES/CONSOLIDATION

Nodules may confluence resulting in large opacities/nodules (1-3 cm in diameter) or in frank area of consolidation both with ill-defined contours. Large nodules were seen in 15-25% of patients and they are most often located in the upper lobes and perihilar zone. Air bronchograms can be seen within large nodules, but cavitation is rare. Small satellite nodules may be present at the periphery of these large nodules or areas of consolidation: this radiological finding is termed "galaxy sign" (figg. 8-10).

Differential diagnosis: this presentation of sarcoidosis as large nodules or consolidation should be differentiate from tuberculosis, metastasis, organizing pneumonia and lung cancer.

Tuberculosis on HRCT shows unilateral or bilateral airspace consolidation, frequently peribronchial in distribution with possibile cavitation. Nodules with centrilobular distribution and a "tree in bud " appearance are also present; sometimes there is also a "galaxy sign" (fig.11). Hilar and mediastinaal lymph node enlargement is commonly seen in patients with TB. Nodes larger than 2 cm in diameter invariably showed central areas of low-attenuation on contrast-enhanced CT with a peripheral rim enhancement. Lymph nodes calcifications in tuberculosis are more dense and unilateral than sarcoidosis. However, sarcoidosis and tuberculosis can co-exist in the same patient.

Organizing pneumonia (OP) is a clinical-pathological entity that can be idiopathic (50% of cases ) or secondary, representing one modality of response of the lung to various forms of injury. Typical HRCT pattern consists of peripheral parenchymal consolidations (80%) with air bronchogram with or without surrounding ground-glass-like opacities (60%) (fig.12). OP may present as a single parenchymal lesion, frequently located in the upper lobes in contact with the pleura and fissures or along the bronchovascular bundles. OP can also manifest in the form of bilateral nodules or multiple masses measuring 0.8-5 cm in diameter, with ill-defined spiculated margins and peripheral location. Moreover, OP can manifest as areas of ground glass surrounded by consolidation, the so called "reverse halo sign" that is quite typical of OP, helping in the differential diagnosis.

Peripheral lung cancers can be located everywhere in the lung. Tipically they are oval or spheric in shape, with smooth or irregular margins (fig.13). Sometimes the neoplastic mass shows one or more strands radiating into the surrounding lung, an appearance often described as spiculated. A single linear or band like area can connect the tumor with the pleura. They can show calcification or cavitation in their context. Mediastinal lymph nodes can be involved or not, depending on the stage of the tumor.
CONGLOMERATE PERIHILAR MASSES

Over time the confluence of small nodules can lead to the formation of perihilar conglomerate masses (fig.14), frequently associated with traction bronchiectasis and lung distortion with a posterior displacement of the main and upper bronchi.

**Differential diagnosis:** The disease that commonly result in conglomerate massive fibrosis are silicosis or CPW, talcosis and TB.

Silicosis or CPW show oval perihilar masses, with irregular borders and sometimes calcification within; the long axis of the mass tend to be parallel to the chest wall, often associated with paracicatritical emphysema (fig.15). In sarcoidosis perihilar masses seem to derive directly from the hila region. In both cases, the masses can excavate and it is required the differential diagnosis with bronchogenic carcinoma (fig.16).

FIBROSIS

Approximately 20-25% of patients with sarcoidosis develops fibrosis in few years. The distribution reflects the predilection of the disease for the upper lobes and perihilar regions (fig.17). Patients who have sarcoidosis sometimes show patchy areas of ground glass opacities superimposed on a background of fibrosis or interstitial nodules. Volume reduction is common in the upper lobes, with posterior and cranial dislocation of the pulmonary hila. Honeycombing involves mainly the middle and upper lung zone, with relative sparing of the lung bases.

**Differential diagnosis:** In these cases, sarcoidosis should be distinguished from idiopathic pulmonary fibrosis (IPF) and other fibrotic diseases with fibrotic involvement.

UIP (Usual Interstitial Pneumonia) characterized by honeycombing, traction bronchiectasis and bronchiolectasis, irregular septal thickening, intralobular septal thickening with a basal and subpleural distribution (fig.18). The distribution of the abnormalities is the most important discriminating feature between the two conditions.

Chronic hypersensitivity pneumonitis (HP) is characterized on HRCT by findings of fibrosis, ground-glass areas, small nodules, areas of decreased attenuation due to mosaic perfusion (fig. 19) and air-trapping on expiratory scans. Sarcoidosis may resemble chronic HP on HRCT scans because of the presence of pulmonary distortion and fibrosis and area of mosaic attenuation.

RETICULAR PATTERN

The reticular pattern of presentation with exclusive involvement of the interlobular septa without the presence of nodules is very rare (fig.20) and must be differentiated from lymphangitis carcinomatosis (LC) and pulmonary edema.
**Differential diagnosis:** In pulmonary edema and LC HRCT scans show septal thickening with complete or almost complete outline of the second pulmonary lobule. In LC septal thickening can be nodular and monolateral or bilateral. In pulmonary edema septal thickening is almost always bilateral and there are signs of heart failure (fig.21). Pleural effusion is present in these two entities, but it is very rare in sarcoidosis.

**MEDIASTINAL INVOLVEMENT ONLY**

Possible, although rare, is an **exclusive involvement of the lymph nodes**, without parenchymal involvement.

**Differential diagnosis:** This presentation must be distinguished from a lymphoproliferative disorder or with small cell cancer. In sarcoidosis lymph node enlargement can be occasionally unilateral and asymmetrical making difficult the differential diagnosis with Lymphoma (fig.22).

Small cell carcinoma is usually hilar and/or perihilar mass, with a marked mediastinal lymphadenopathy (fig.23). Usually hilar involvement is unilateral and distant metastasis coexist. These features are important and allows to distinguish small cell lung cancer from sarcoidosis with exclusive involvement of the lymph nodes.

In patients with sarcoidosis are very frequently seen areas of **air trapping on expiratory HRCT scans**. This is due to endoluminal or submucosal sarcoid granulomas or fibrotic obstruction of small airways is more common (fig.24). However isolated air trapping, with no parenchymal involvement is a far less common finding and should be differentiated from bronchiolitis obliterans.

**Images for this section:**

![Image A](image1.png) ![Image B](image2.png) ![Image C](image3.png)

**Fig. 1:** Nodules with a typical perilymphatic distribution. Scheme of distribution (A) MIP axial planes (B) and MIP coronal planes (C) showing perilymphatic nodules in sarcoidosis with typical involvement of dorsal regions of upper lobes.
**Fig. 2:** CT scans at the level of the pulmonary trunk (A) and at the level of the left atrium (B) showing bilateral hilar and subcarinal lymphadenopathy.

**Fig. 3:** HRCT scan in a patient with sarcoidosis (A) show nodules with perilymphatic distribution. Nodules clustered along interlobular septa (arrow in A) but secondary pulmonary lobule is not outlined completely. CT scans (B,C) in patients with left lung cancer show bilateral smooth and nodular interlobular septal thickening with major involvement of the right upper and lower lobes. Bilateral pleural effusion is also present: this is a case of pulmonary lymphangitic carcinomatosis.

**Fig. 4:** HRCT scan at the level of the aortic arch (A) showing small nodules located in the upper lobes with a centrilobular (arrowheads) and subpleural distribution (arrows).
CT scan (B) and MIP axial planes (C) of another patient showing small nodules with a centrilobular distribution (yellow arrows) in the upper lobes. Nodules are better seen on MIP reconstruction (C). These two patients have history of silica exposure.

Fig. 5: CT scans (A,B) demonstrate a distribution of nodules that is quite diffuse and uniform resembling a miliary pattern. The bronchoalveolar lavage revealed sarcoidosis. Five months CT scan follow-up (C) after therapy shows a marked reduction of nodules.
Fig. 6: HRCT scans (A,B) in a 42-year-old man with fever, asthenia and weight loss show small nodules with a miliary distribution. CT scan (C) at the level of the aortic arch show low-density lymphadenoopathy. The radiological and clinical context suggest the diagnosis of miliary tuberculosis.

Fig. 7: CT scans (A,B,C) reveal multiple pulmonary nodules with a miliary distribution. Patient was a 67-year-old man with pulmonary metastases. CT scan at the level of the carina (C) show a right hydro-pneumotorax and the cranial extremity of a drainage tube.
**Fig. 8:** CT scans show the presence of consolidation, ground glass opacities and nodules in the left upper lobe. Transbronchial biopsy revealed sarcoidosis.

**Fig. 9:** HRCT scans show bilateral patchy areas of ground glass opacities in the upper lobes (yellow arrows in A). There are also evident in the apical segment of the left lower lobe (B) and in the lateral segment of the right lower lobe (C) areas of consolidation surrounded by ground glass or small nodules (galaxy sign).
**Fig. 10**: Axial HRCT images (A and B) showing multiple small nodules along the peribroncovascular interstitium and the fissures. Some nodules arise from the coalescence of small nodules, that sign is called the "galaxy sign" (arrowheads).

**Fig. 11**: HRTC scan (a) and MPR coronal reconstruction (B) showing in the right upper lobe a consolidation with air bronchogram within, associated to small satellite nodules «galaxy sign», (white arrow in A) and centrilobular nodules (yellow arrow, in A). This is a case of tuberculosis.

**Fig. 12**: HRCT scans showing in the right lung subpleural areas of consolidation (arrows) surrounded by ground-glass opacities. In a patient with cough and no fever this radiological findings are suggestive of organizing pneumonia; typical aspect of organizing pneumonia.
Fig. 13: CT scan shows a right upper lobe nodule with an oval shape, spiculated margin, and bands towards the pleura. This was a peripheral lung carcinoma.
**Fig. 14:** HRCT scan at the level of the pulmonary trunk show dense conglomerate masses in the perihilar region and small satellite nodules typical of the «galaxy sign». 
Fig. 15: HRCT scans show bilateral conglomerate masses with areas of calcification within them, distortion of lung parenchyma and paracicatrizial emphysema. We also see some centrilobular small nodules (arrow). These masses are oval with long axis parallel to chest wall. In subjects with history of silica exposure, these masses should suggest a complicated silicosis.

Fig. 16: HRCT scans (A,B,C) showing cavitated masses in upper lobes that should be differentiated. The diagnosis are: end-stage complicated sarcoidosis (A), left upper lobe lung cancer (B), cavitated tuberculous mass (C). In order to make the correct diagnosis it is necessary to know the clinical context.
**Fig. 17:** HRCT scans at the level of the aortic arch (A) and the pulmonary trunk (B) showing a classic appearance of advanced fibrotic sarcoidosis. A dense conglomerate mass in the right upper lobe and bilateral traction bronchiectasis that radiate from the hilum towards the dorsal regions of upper lobes. There is also evident intralobular interstitial thickening in the upper lobes.

**Fig. 18:** HRCT scans (A,B) show diffuse sign of fibrosis at the lung bases (B) characterized by intralobular interstitial thickening, traction bronchiectasis and honeycombing, typical features of idiopathic pulmonary fibrosis.
Fig. 19: Axial thin-section CT (A,B) show bilateral patchy areas of ground glass opacity superimposed on fine reticulation (arrows in A). Note lobules of decreased attenuation reflecting small airways obliteration (B). This patient has chronic hypersensitivity pneumonitis (HP). Sarcoidosis may resemble chronic HP on HRCT scans because of the presence of pulmonary distortion, fibrosis and area of mosaic attenuation.

Fig. 20: HRCT scan at the level of the epiaortic vessels in patients who undergone a surgical right lung upper lobe biopsy (A). CT scan (A) reveals interlobular septal thickening in the upper lobes, more evident on the left. There are also seen some tiny nodules along the septa (A). Parenchimal bands in the right upper lobe are also evident. This is a case of sarcoidosis (A). CT scan in B showing smooth interlobular septal thickening involving the right upper lobe with a thick peribronchovascular thickening. This case is a pulmonary lymphangitic carcinomatosis.
Fig. 21: CT scan shows a diffuse smooth, bilateral, septal thickening at the lower lobes with bilateral pleural effusion. This is a patient with pulmonary edema.

Fig. 22: CT scans show anterior mediastinal lymphadenopathy (arrows in A, B) without involvement of the hila and the parenchyma (C). Case of lymphoproliferative disorder (lymphoma).
**Fig. 23:** CT scans show right paratracheal and periaortic lymph nodes (arrows in A) without a right hilar involvement. A left hilar mass is present. Bronchoscopy with pathologic sample revealed a small cell lung cancer.

**Fig. 24:** HRCT scans (A,D) in patient with sarcoidosis showing some subtle areas of decreased attenuation related to air trapping (yellow arrows in A,B,D). There are also small perilymphatic nodules in the apical segment of the left lower lobe (red arrow in C).
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- **Chronic hypersensitivity pneumonitis.**
- **Lymphoproliferative disorder.**
- **Microcitoma.**

**Table 1**: Sarcoidosis: common and uncommon HRCT findings
**Conclusion**

Sarcoidosis is a common disease with a wide spectrum of radiological and clinical manifestations.

The disease is also known as the "great mimicker", for its capacity to simulate other pathologies, so it's important for the radiologist to know typical and atypical patterns of presentation of sarcoidosis in order to make a correct diagnosis. Imaging plays an important role in the diagnosis of sarcoidosis, especially in typical cases, while atypical ones often require further investigation, and in this scenario CT plays a key role in identification of high-yield sites for transbronchial or surgical lung biopsy.

**References**


Personal Information

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