Thoracic Sarcoidosis and Sarcoid Reactions: Typical and Atypical Manifestations

Poster No.: C-1356
Congress: ECR 2016
Type: Educational Exhibit
Authors: I. Sánchez Paniagua¹, A. Martínez de Alegría¹, S. Baleato González², R. García Figueiras¹, A. L. Carballoira³, A. Arango¹; ¹Santiago de Compostela/ES, ²SANTIAGO DE COMPOSTELA, A CORUÑA/ES, ³15705, Co/ES
Keywords: Tissue characterisation, Contrast agent-intravenous, MR, CT-High Resolution, Conventional radiography, Thorax, Lung, Cardiac
DOI: 10.1594/ecr2016/C-1356

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method ist strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Learning objectives

1. To describe the epidemiology, clinical manifestations, staging and prognosis of sarcoidosis.

2. To recognize the typical and atypical radiologic features of thoracic sarcoidosis.

3. To discuss the role of the different imaging techniques, especially high resolution computed tomography (HRCT), in its diagnosis and management.

4. To review the coexistence of sarcoidosis and sarcoid reactions in cancer patients.

Background

Sarcoidosis is a multisystem chronic inflammatory disorder of unknown cause. It may affect almost any organ (skin, eyes, liver, spleen, central nervous system (CNS), genitourinary system, musculoskeletal system), but thoracic involvement (lung, mediastinal and hilar lymph nodes) is most common (90%) with high morbidity and mortality. Fig. 2.

The diagnosis is established on the basis of compatible clinical and radiological findings and evidence of noncaseous epithelioid cell granulomas. This histology may also be detected in patients with malignant tumors, representing true sarcoidosis or sarcoid-like reaction.

Images for this section:
Fig. 2: The organs affected by sarcoidosis.

Findings and procedure details

Based on our last 10 years of experience, the clinical and radiologic appearance of thoracic sarcoidosis and sarcoid reactions is reviewed, with the intention to present the typical and atypical manifestations and the intriguing relationship between sarcoidosis and cancer.

1. EPIDEMIOLOGY:

The incidence of sarcoidosis is variable and is affected by demographic factors such as race, ethnicity, age, sex and familial history:

- Typically affects adults less than 40 years old, with peak of incidence in the 3rd decade of life.
- Sarcoidosis is slightly more common in women.
- The prevalence of sarcoidosis is higher in black Americans, Swedes and Danes. Still rare in Saudi Arabia, Portugal, India, Spain and South America, probably because here granulomatous diseases are tuberculosis, leprosy and fungal infections.
- The manifestations and natural history of sarcoidosis are influenced by epidemiologic factors. For example, whites often present asymptomatic, whereas blacks present with severe multisystem disease and mortality in blacks is higher, probably by differences in access to health care.

2. CLINICAL FEATURES:

- The most frequent clinical features at presentation are:
  - Respiratory symptoms: cough, dyspnea, bronchial hyperreactivity
  - Fatigue
  - Night sweats
  - Weight loss
  - Erythema nodosum

- But as many as 50% of cases of sarcoidosis are asymptomatic, with abnormalities detected only at chest radiography.

- Pulmonary function tests show a restrictive ventilatory defect with decreased lung volumes and decreased carbon monoxide diffusing capacity, which become more frequent and marked from stage 1 to stage 4.
- The 5.7% of cases of sarcoidosis present obstructive ventilatory defect (endobronchial sarcoidosis). They have increased morbidity, greater frequency of respiratory symptoms and radiographic stage 4 disease which represent a poor prognosis.

- The clinical course varies:
  
  • 2/3 of patients with sarcoidosis are stable or in remission within 10 years.
  • 20% of patients develop chronic disease with pulmonary fibrosis.
  • Recurrence after a remission lasting 1 year or more is rare (<5% of patients), but may occur at any age and any organ.
  • Less than 5% of patients die of sarcoidosis as a result of extensive and irreversible lung fibrosis with respiratory failure or cardiac or neurologic involvement.

3. PATHOGENESIS:

Sarcoidosis is an immune-mediated multisystem disease. One or more specific enviromental agents trigger an inflammatory response in the immune system of a genetically susceptible host. Epithelioid cell granulomas are a result of stimulation of cell-mediated immunity with the activation of T cells and alveolar macrophages that release interleukin, fibronectin and growth factors. The process may resolve spontaneously, or it may progress to extensive formation of noncaseous granulomas and fibrosis.

4. HISTOLOGIC FINDINGS:

The characteristic histologic feature of sarcoidosis is noncaseous 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. The giant cells may contain cytoplasmic inclusions such as asteroid bodies and Schaumann bodies. The central portion of the granuloma contains lymphocytes CD4 whereas lymphocytes CD8 are in the peripheral zone. Fibroblasts, mast cells, collagen and proteoglycans may encase the granuloma and lead to fibrosis and irreversible organ dysfunction. These fibrotic changes begin at the periphery of the granuloma. (Fig. 3).

Granulomas in the lung parenchyma have a distribution in relation to lymphatics through the peribronchovascular and subpleural interstitial spaces, as well as the interlobular septa. The upper lobes are most severely affected and vascular involvement is observed in more than 50% of patients.

5. STAGING AND PROGNOSIS:
The Siltzbach Classification based on the pattern of chest radiographic findings defines five stages of sarcoidosis. (Fig. 4. Table 1):

- Stage 0: normal appearance at chest radiography (5-10% of patients at presentation of disease)
- Stage 1: lymphadenopathy (50%)
- Stage 2: lymphadenopathy and parenchymal lung disease (25-30%)
- Stage 3: parenchymal lung disease (10-12%)
- Stage 4: pulmonary fibrosis (5% at presentation, up to 25% during the course of the disease)

Pulmonary function worsens with more advanced disease stage, but the radiographic stage does not correlate well with the severity of pulmonary function abnormalities. A case of spontaneous remission is shown in Table 2.

It is necessary to keep in mind that these stages and the prognosis are based on findings at chest radiograph, not in CT findings. High resolution CT (HRCT) is more sensitive to find subtle parenchymal changes in early stages of sarcoidosis, even in stage 1, which is associated with a good prognosis.

There are some factors associated with a poor or a good prognosis:

a) Poor prognostic factors:

- Stage 2 or 3 at the time of diagnosis
- Beginning after 40 years old
- Black race
- Hypercalcemia
- Splenomegaly
- Bone involvement
- Chronic uveitis
- Lupus pernio

b) Good prognostic factors: (early stage with a spontaneous remission rate of >85%). Löfgren syndrome:

- Fever
- Polyarthritis
- Erythema nodosum
- Bilateral hilar lymphadenopathy

6. DIAGNOSIS OF PULMONARY SARCOIDOSIS:
A diagnosis of sarcoidosis is established on the basis of compatible clinical and radiologic findings and evidence of noncaseous epithelioid cell granulomas with no causative agents.

It is necessary to rule granulomas of known causes such as tuberculosis, hypersensitivity pneumonitis, Crohn's disease or fungal disease and sarcoidlike reactions (this will be further explained in section 8). If a biopsy is needed for diagnosis, it may be a transbronchial, CT-guided or surgical biopsy.

When pulmonary sarcoidosis is suspected, diagnostic procedures should allow:

- Histologic verification
- Assessment of the severity and extent of organ involvement
- Assess whether the disease is stable or progressive
- Determine whether a patient might benefit from treatment

Laboratory parameters that help in the diagnosis are: an elevated levels of angiotensin-converting enzyme (ACE), a decrease of rate CD4:CD8 and hypercalcemia.

To establish the radiologic features, high-resolution CT (HRCT) is superior to conventional CT for assessing subtle parenchymal details. It allows thin-section collimation (1-1.5 mm section thickness) with multiplanar reconstructions that improve detection of the different patterns of sarcoidosis. Moreover, it is useful in distinguishing active inflammation from irreversible fibrosis in patients with stage 2 or 3 of sarcoidosis. (Table 3).

While typical findings, such as bilateral hilar lymphadenopathy with a perilymphatic micronodular pattern in upper lobe predominance, are highly specific of sarcoidosis, atypical manifestations require to establish a differential diagnosis with TB, silicosis, pneumoconiosis and malignancies.

The specific characteristics of each pulmonary sarcoidosis finding are described next. (Table 4).

A. TYPICAL PATTERN OF LYMPHADENOPATHY

• Well-defined, bilateral, symmetric hilar and right paratracheal lymph node enlargement (95% of patients). (Fig. 5).
• Middle mediastinum lymph nodes and/or prevascular nodes are involved in 50% of patients.
• Differential diagnosis (DD): infections and malignancy (in the absence of specific symptoms, sarcoidosis is more common).

B. ATYPICAL PATTERN OF LYMPHADENOPATHY
• Asymmetric or atypical locations (eg, internal mammary, paravertebral region).
• More common in patients older than 50 years.
• Lymph node calcification (related to disease duration): 3% of patients after 5 years, 20% after 10 years. (Fig. 6).
• Morphology of calcifications varies (amorphous, punctate, popcornlike, eggshell-like).
• DD: lymphoma, TBC.

C. TYPICAL PARENCHYMAL MANIFESTATIONS

Micronodules with a perilymphatic distribution
• A perilymphatic distribution of micronodular lesions is seen in 75%-90% of patients with sarcoidosis. (Fig. 7).
• Sharply defined, small (2-4 mms), rounded nodules.
• Bilateral and symmetric distribution, predominantly in the upper and middle lung zones (U&MLZ).
• More common in the subpleural peribronchovascular interstitium and less often in the interlobular septa.
• Micronodules can coalesce over time forming macronodules.
• Nodular or irregular thickening of the peribronchovascular interstitium is common.

Fibrotic changes
• 20% of patients with sarcoidosis develop fibrosis over time.
• The radiologic findings are linear opacities, traction bronchiectasis and architectural distortion (displacement of fissures and bronchovascular bundles). (Fig. 8 and fig. 9).
• Fibrosis has a peribronchial patchy distribution in the U&MLZ and induce lung volume loss and interlobular septal thickening.
• Extensive interstitial fibrosis can cause pulmonary arterial hypertension and resultant right heart failure with imaging findings such as:

- Prominent main pulmonary artery
- Enlarged right and left pulmonary arteries
- Right ventricular enlargement
- Attenuation of peripheral vessels

**Bilateral perihilar opacities**

- Confluent nodular opacities that appear on HRCT as bilateral areas of consolidation with irregular edges and blurred margins radiating from the hilum toward the periphery. (Fig. 10).
- These consolidations can be seen with or without air bronchograms.
- They are less homogeneous peripherally and are usually accompanied by micronodules.

**D. ATYPICAL PARENCHYMAL MANIFESTATIONS:**

**Pulmonary nodules and masses**

- These lesions are seen in 15%-25% of patients with parenchimal opacities
- At CT they appear as ill-defined irregular opacities measuring 1-4 cms (coalescent interstitial granulomas). (Fig. 11).
- They are multiple and bilateral, located in perihilar or peripheral regions.
- They may or may not manifest with air bronchograms but rarely with cavitation (<3%).
- "Galaxy sign": small satellite nodules visible at the periphery of these masses (it is not specific for sarcoidosis). (Fig. 12).
- "Sarcoid cluster sign": multiple micronodules distributed along the lymph vessels on HRCT. They are rounded and are found in peripheral subpleural locations. (Fig. 13)
- Coalescing masses typically seen bilaterally in the U&MLZ may mimic progressive massive fibrosis, but they are more common in silicosis.
- A solitary lung mass or nodule is rarely seen in sarcoidosis.
- Multiple, well-defined rounded macronodules (> 5 mm) might mimic metastases.

**Patchy airspace consolidation**

- It is seen in 10%-20% of patients with sarcoidosis and reflects the confluence of multiple micronodules (acinar and interstitial) that encroach on the alveolar space. (Fig. 14).
- Airspace opacification is usually bilateral and symmetric in the peribronchovascular regions of the U&MLZ.
- The central regions of consolidation may contain air bronchograms and it has ill-defined margins with a nodular pattern in the periphery.
- DD: pneumonia, tuberculosis or bronchiolitis obliterans organizing pneumonia.

**Patchy ground-glass opacities**
• These lesions are seen in 40% of patients with pulmonary sarcoidosis.
• They result from the confluence of multiple micronodular and fibrotic interstitial lesions that cause airway compression without alveolar occupation. (Fig. 15 and fig 16).
• These opacities have ill-defined margins with bronchoalveolar structures within them (air bronchograms).
• The ground-glass opacities are always accompanied by other abnormalities and often are superimposed on a background of interstitial nodules, but it is not specific of sarcoidosis and this pattern can be seen in bronchoalveolar cell carcinoma, lymphoma, pneumoconiosis or pneumonia.

**Linear reticular opacities**

• Is the predominant radiologic feature in 15%-20% of patients with sarcoidosis.
• It is produced by interlobular and intralobular septal thickening and is seen in the subpleural space of the U&MLZ. (Fig. 17).
• DD: lymphangitic carcinomatosis (more extensive and severe involvement).

**Fibrocystic changes**

• Fibrotic cysts, bullae and paracaticrical emphysema represent advanced-stage sarcoidosis.
• These lesions involve the upper and middle lung zones with perihilar distribution and cause posterior bronchial displacement and volumen loss.
• There are 3 patterns of presentation:

1. *Honeycomb-like cysts:*

   - In the subpleural regions of the U&MLZ. (Fig. 18).

   - Occasionally is seen in the lower lung zones and can be mistaken for idiopathic pulmonary fibrosis.

2. *Cavitation of parenchymal lesions:*

   - It is a rare finding seen in a 10% of patients with end-stage sarcoidosis.

   - Most apparent cavities seen are bullae, blebs or cysts ( in fact pseudocavities because are lined by fibrous tissue and not by granulomas). (Fig. 19).

3. *Mycetoma formation:*

   - It is a complication seen in 1%-3% of patients of stage 4 cystic sarcoidosis.
- Preexisting cysts or bullae are colonized by saprophytic fungi, usually Aspergillus. (Fig. 20).

- Air-fluid levels within sarcoid pseudocavities are one of the first signs.

-"Air crescent or Monod sign": is the appearance of pulmonary aspergilloma and consists of a mobile opacity in a cavity bordered by a peripheral sliver of air.

- Aspergilloma is associated with hemoptysis, sometimes fatal (2nd cause of death in sarcoidosis).

**Miliary opacities**

- This pattern is rare, <1% of patients with sarcoidosis. (Fig. 21).
- In the differential diagnosis might be included tuberculosis, pneumoconiosis, metastasis.

**Reversed halo sign**

- It is a round, focal area of ground-glass attenuation surrounded by a partial or complete rim of consolidation. (Fig. 22).
- Its nodular aspect relates to the presence of granulomas in active pulmonary sarcoidosis excluding infectious causes such as tuberculosis or fungal disease or non-infectious conditions such as Wegener’s granulomatosis.

**Airway involvement**

1. **Mosaic attenuation pattern:**

- May be described as inhomogeneous attenuation seen at inspiratory CT. (Fig. 23).

- In sarcoidosis this pattern represent small airways involvement by granulomas or fibrosis.

2. **Air trapping:**

- This pattern is characterized by focal areas of decreased attenuation on expiratory CT, and is seen in 95% of patients with sarcoidosis.

- It affects a small airway but also secondary lobule.

3. **Tracheobronchial abnormalities:**
- Symptomatic bronchial stenosis or focal areas of bronchiectasis occur in only 2%-8% and result from accumulation of endobronchial granulomas within the bronchial wall, extrinsic compression or distortion by end-stage parenchymal sarcoidosis.

4. **Atelectasis**: 
- They result from bronchial obstruction by endobronchial granulomas or peribronchial lymph nodes.

**Pleural disease**

- Pleural effusion, pneumothorax, pleural thickening or calcification, are rare in sarcoidosis, with only 1%-4% of patients affected.

7. **CARDIAC SARCOIDOSIS**: 
   - Cardiac involvement is symptomatic in 5% of patients with sarcoidosis, such as with ventricular arrhythmias, heart block, dilated cardiomyopathy, congestive heart failure and even sudden death.
   - It has three separate histopathologic stages: initial edema is followed by granulomatous infiltration, with eventual progression to postinflammatory scarring and fibrosis.
   - Involvement is more commonly myocardial than pericardial with a predisposition for the left ventricular lateral wall, basal septum and right ventricular free wall. There is relative sparing of the endocardium.
   - Cardiac MR imaging is a useful noninvasive method for the early diagnosis and follow-up of cardiac sarcoidosis: (Fig. 24).

- Edema is demonstrated on T2-weighted images as areas of high signal intensity within the myocardium and early enhancement on T1-weighted images because of inflammation.

- Active granuloma can manifest as focal nodular areas on cine images appear bright on T2-weighted images and show delayed enhancement on T1-weighted images after contrast. (Fig 25).

- Scarring and fibrosis appear as focal areas of thinning with hypokinesia and delayed enhancement affecting the subepicardial layer, typically the basal and lateral left ventricular segments.

8. **SARCOID-LIKE REACTIONS**: 
Sarcoidosis has been reported to occur in association with malignant tumour, either preceding or following malignancy after therapy. Nonnecrotizing granulomas have been described in patients with many types of malignancy (e.g., lymphoma, testicular cancer, head and neck cancer, gastric cancer, renal cancer, and breast cancer).

Raising the question of causality and secondarily, of cause vs effect, two theories are postulated:

1. The Ptolemaic (sarcocentric) viewpoint, that posits that the disease sarcoidosis can induce the development of solid neoplasms by an unspecified mechanism.

2. The Copernican (oncocentric) viewpoint, that posits that sarcoidosis is an etiologically diverse syndrome and that when systemic granulomas coexist with neoplasia, they constitute an immunologic response.

The relationship between sarcoidosis and cancer is intriguing. Assuming a causal relationship, it appears more likely that systemic granulomas are a response to the pulmonary neoplasm.

Granulomas have been found surrounding the primary tumor (3 to 7% of cases) or in the draining lymph nodes (4.4% of cases) and probably reflect an immune response to tumor antigens, which is known as sarcoid reaction. (Fig. 26). It may be a marker of an immunologically mediated antitumour response and there is evidence that patients with sarcoid reactions have a better prognosis, such as in Hodgkin’s disease.

Sarcoid-like reaction is a localized reaction within tissues in the absence of any respiratory symptoms. Further confirmation of sarcoid-like reaction requires ruling out of any systemic involvement by radiographs, ACE level assessment and other investigation procedures which are specific for sarcoidosis. Sarcoid reaction is often indistinguishable from metastases on radiological studies and requires histopathological examination to avoid unnecessary chemotherapy.

9. TREATMENT:

- Corticosteroids therapy: is the cornerstone of therapy for severe or progressive sarcoidosis, and often produce dramatic resolution of disease. Relapses may occur upon taper or cessation of therapy. Responses to corticosteroids are usually evident within 4 to 8 weeks. Failure to respond to corticosteroids may reflect inadequate dose or duration of therapy, presence of irreversible fibrotic or cystic disease or intrinsic resistance. A minimum of 12 months of therapy is recommended.
- Immunosuppressive agents: are used to treat patients failing or experiencing adverse effects from corticosteroids.
• Lung transplantation: is a viable option for patients with end-stage pulmonary sarcoidosis refractory to medical therapy.

Images for this section:

**Fig. 3:** Photomicrograph (hematoxylin-eosin [H-E]stain, original magnification, x 400) of a lung biopsy shows a nonnecrotic granuloma expanding the interstitium, with multiple histiocytes (red start) and two multinucleated giant cells with an asteroid body (yellow arrow).

© Department of Pathology, University Hospital Complex of Santiago - Santiago de Compostela / ES
**Fig. 4:** Staging of pulmonary sarcoidosis based on the pattern of chest radiographic findings. Stage 1: Bilateral hilar lymphadenopathies. Stage 2: lymphadenopathies and parenchymal lung disease. Stage 3: parenchymal lung disease. Stage 4: pulmonary fibrosis.

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
**Table 1:** Staging of pulmonary sarcoidosis based on the pattern of chest radiographic findings. Percentages indicate the proportion of the population with this stage of sarcoidosis at presentation diagnosis.

© "Pulmonary Sarcoidosis: Typical and Atypical Manifestations at High-Resolution CT with Pathologic Correlation". Eva Criado, MD et al. RadioGraphics 2010; 30:1567-1586

<table>
<thead>
<tr>
<th>STAGE</th>
<th>Description</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No abnormalities</td>
<td>5%-10%</td>
</tr>
<tr>
<td>1</td>
<td>Lymphadenopathy (fig. A)</td>
<td>50%</td>
</tr>
<tr>
<td>2</td>
<td>Lymphadenopathy + pulmonary infiltration (fig. B)</td>
<td>25%-30%</td>
</tr>
<tr>
<td>3</td>
<td>Pulmonary infiltration (fig. C)</td>
<td>10%-12%</td>
</tr>
<tr>
<td>4</td>
<td>Fibrosis</td>
<td>5% (up to 25% during the course of the disease)</td>
</tr>
</tbody>
</table>
Table 2: Spontaneous remission rate of pulmonary sarcoidosis.

© "Pulmonary Sarcoidosis: Typical and Atypical Manifestations at High-Resolution CT with Pathologic Correlation". Eva Criado, MD et al. RadioGraphics 2010; 30:1567-1586

<table>
<thead>
<tr>
<th>STAGE</th>
<th>SPONTANEOUS REMISSION</th>
</tr>
</thead>
<tbody>
<tr>
<td>STAGE 1</td>
<td>60-90%</td>
</tr>
<tr>
<td>STAGE 2</td>
<td>40-70%</td>
</tr>
<tr>
<td>STAGE 3</td>
<td>10-20%</td>
</tr>
<tr>
<td>STAGE 4</td>
<td>0%</td>
</tr>
</tbody>
</table>
**Table 3:** Reversible and Irreversible Abnormalities of Pulmonary Sarcoidosis at High-Resolution CT.

© "Pulmonary Sarcoidosis: Typical and Atypical Manifestations at High-Resolution CT with Pathologic Correlation". Eva Criado, MD et al. RadioGraphics 2010; 30:1567-1586

<table>
<thead>
<tr>
<th>Reversible parenchymal abnormalities*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Micronodules, macronodules</td>
</tr>
<tr>
<td>Airspace consolidation: confluent alveolar opacities</td>
</tr>
<tr>
<td>Ground-glass opacities</td>
</tr>
<tr>
<td>Interlobular septal thickening</td>
</tr>
<tr>
<td>Intralobular linear opacities</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Irreversible parenchymal abnormalities†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Honeycomb-like opacities, cysts, bullae, emphysema</td>
</tr>
<tr>
<td>Architectural distortion</td>
</tr>
<tr>
<td>Traction bronchiectasis, bronchiolectasis</td>
</tr>
<tr>
<td>Volume loss in upper lobes, retraction of hila</td>
</tr>
<tr>
<td>Mycetoma (in 10% of patients with end-stage sarcoidosis and a preexisting cavity)</td>
</tr>
</tbody>
</table>

*These features are suggestive of granulomatous inflammation.
†These features are indicative of chronicity and fibrosis.
Table 4: Typical and atypical manifestations of pulmonary sarcoidosis.

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
Fig. 5: Left: Posteroanterior and lateral chest radiographs show hilar lymphadenopathies (red arrows). Right: Axial contrast-enhanced CT images show hilar (red arrows) and subcarinal (blue start) lymphadenopathies.

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
**Fig. 6:** Left: Posteroanterior chest radiograph shows calcified lymph nodes (red arrows). Right: Axial contrast-enhanced CT image shows calcified lymphadenopathies (red arrows).

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
**Fig. 7:** Left: Axial high-resolution CT (HRCT) images show the typical perilymphatic distribution of micronodules (red arrows), most often in the subpleural peribronchovascular interstitium. Central: Axial HRCT image shows nodular thickening of pleural fissure (blue start). Right: Axial HRCT images show larger subpleural micronodular lesions (yellow arrows).

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
TYPICAL MANIFESTATIONS: **Fibrotic Changes**

**Fig. 8:** Axial HRCT images show massive fibrosis with opacities as irregular coalescing masses (red arrows) and architectural distortion with linear tracts of scar appearance (blue arrows). Yellow arrows show macronodules formed by coalescence of micronodules.

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
Fig. 9: Coronal and axial HRCT images show extensive pulmonary disease with multiple micro and macronodular lesions in a peribronchovascular distribution, with the presence of large rounded fibrotic masses with air bronchograms in both upper lobes, probably formed by coalescence of these nodules.

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
**Fig. 10:** Axial HRCT images show perihilar opacities with air bronchograms (red arrows).

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
Fig. 11: Axial HRCT images show diffuse patchy parenchymal lung disease with peribronchovascular and peripheral involvement. There are some lesions of nodular appearance (blue arrows) and others larger as masses (red arrows). Some masses have small satellite nodules at the periphery, which is known as "Galaxy sign" (yellow arrows).

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
**Fig. 12:** "Galaxy sign": small satellite nodules visible at the periphery of these masses (yellow arrows).

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
**Fig. 13:** "Sarcoid cluster sign": multiple micronodules distributed along the lymph vessels. They are rounded and are found in peripheral subpleural locations (red arrows).

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
Fig. 14: Axial HRCT images show multiple foci of bilateral pulmonary consolidation with irregular margin and air bronchograms (red arrows).

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
**ATYPICAL MANIFESTATIONS:** Patchy Ground-Glass Opacities

**Fig. 15:** Axial HRCT images show patchy ground-glass opacities (red arrows).

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
**ATYPICAL MANIFESTATIONS:** Patchy Ground-Glass Opacities

**Fig. 16:** Axial HRCT images show patchy ground-glass opacities (red arrows) with associated fine reticular and nodular lesions.

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
**Fig. 17:** Axial HRCT images show multiple micronodules and extensive interlobular septal thickening (red arrows).

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
**Fig. 18:** Axial HRCT scan shows asymmetric subpleural honeycomb-like cysts (arrowheads) and architectural distortion associated with left fissure nodularity (arrow).

ATYPICAL MANIFESTATIONS: *Cavitation of Parenchymal lesions*

![Axial HRCT scan showing bilateral cystic spaces and cavities (arrow) and tracheal retraction, results of chronic severe fibrosis and scarring. The cystic spaces in the left perihilar region (*) correspond to dilated bronchi.](image)

**Fig. 19:** Axial HRCT scan shows bilateral cystic spaces and cavities (arrow) and tracheal retraction, results of chronic severe fibrosis and scarring. The cystic spaces in the left perihilar region (*) correspond to dilated bronchi.

**Fig. 20:** Axial HRCT scan depicts a mycetoma (aspergilloma) within a cystic space in the right upper lobe. The opaque fungal ball is bordered on one side by the air crescent or Monod sign (arrow). Retraction of the trachea and right upper lobe bronchus, caused by severe fibrosis and scarring, also are depicted.

Fig. 21: Axial HRCT scan shows countless tiny micronodules representing multiple and diffuse granulomas in a random distribution, with bronchial wall thickening.

ATYPICAL MANIFESTATIONS: **Reversed Halo Sign**

**Fig. 22:** Axial HRCT scan demonstrates two lesions that have a reversed halo sign, which is characterized by round and oval areas with central ground-glass attenuation surrounded by ring-shaped areas of consolidation (arrows).

**Fig. 23:** Axial HRCT image shows a mosaic pattern, with patchy areas of high and low attenuation.

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
Fig. 24: Delayed contrast-enhanced two-chamber short-axis (upper) and two-chamber long-axis (bottom) cardiac MRI show two nodular subepicardial foci of enhancement within the basal anteroseptal segment at the insertion of right ventricular wall and the basal anterior left ventricular wall.

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
**Fig. 25:** Chart illustrates the differential diagnosis of delayed contrast enhancement at cardiac MR imaging by location.

**Fig. 26:** Left: Axial CT images show micronodules and mediastinal bilateral hilar lymphadenopathies (red arrows) in a patient with testicular cancer (blue arrow). Right: Axial and coronal CT images show mediastinal bilateral hilar lymphadenopathies (red arrows) in a patient with rectal cancer (blue arrow).

© Department of Radiology, University Hospital Complex of Santiago - Santiago de Compostela / ES
Conclusion

• Thoracic sarcoidosis is known as the great mimicker because it manifests with multiple radiographic patterns. Although the typical manifestations are well known by the radiologists, atypical patterns may difficult the diagnosis, often necessitating differentiation from lymphoma, tuberculosis, and other causes of chronic pulmonary infiltrates.

• HRCT helps in detection and characterization of pulmonary abnormalities, being especially useful for differentiation active inflammation from fibrosis.

• Both sarcoidosis and sarcoid reaction should be taken into account in patients with cancer and nonnecrotizing granulomas at histology.

Personal information

References


• Sarcoid-Like Reactions. Nag S. Sarcoidosis Diagnosis and Management Edited by Prof. Mohammad Hosein Kalantar Motamedi. Published online 17, October, 2011.
