VOLUME 2 | ISSUE 4

HJR

Chest Imaging REVIEW ARTICLE

Pulmonary Sarcoidosis: Spectrum of imaging findings

Irini Blana, Demosthenes D Cokkinos, Maria Skilakaki
Department of Radiology, Evangelismos Hospital, Athens, Greece

SUBMISSION: 19/3/2017 | ACCEPTANCE: 3/12/2017

ABSTRACT

Sarcoidosis is a systemic chronic inflammatory disorder of unknown aetiology, characterised by non-caseating epithelioid cell granulomas. A diagnosis of the disease requires compatible clinical and imaging findings, supported by the identification of typical lesions in at least one organ system, and the exclusion of other causes of granulomatous diseases. It has a wide spectrum of clinical and radiological manifestations; however the lung as well as mediastinal and hilar lymph nodes are involved in more than 90% of cases. For the evaluation of pulmonary sarcoidosis conventional chest radiograph remains the first imaging modality of choice and may often be sufficient to establish the diagnosis. However, the protean radiological appearance of the disorder, its ability to mimic other lung diseases as well as its complications, have rendered the use of chest CT crucial in several clinical settings. In this review we discuss the variety of chest radiography and CT findings in pulmonary sarcoidosis, typical and atypical, involving the lung parenchyma, the mediastinum, small and large airways and the pleura.

KEY WORDS

sarcoidosis; lung; chest radiography; computed tomography; differential diagnosis

Introduction

Sarcoidosis is a global disease of unknown aetiology that has the highest incidence among chronic interstitial lung diseases, representing 23-38% of them [1]. Although the disease may occur at any age, it is recognised up to 70% in patients between the ages of 25 and 45 years [1, 2]. Female predominance is common in all regions of the world, with a female to male ratio from 1.12 to 1.75 [1-3].

CORRESPONDING AUTHOR, GUARANTOR

Corresponding author: Irini Blana, Department of Radiology, Evangelismos Hospital, 37 Solomou, Agia Paraskevi, 15341, Athens, Greece, E-mail: irini.blana@gmail.com
Guarantor: Maria Skilakaki, Department of Radiology, Evangelismos Hospital, Athens, Greece, E-mail: skmaria@otenet.gr

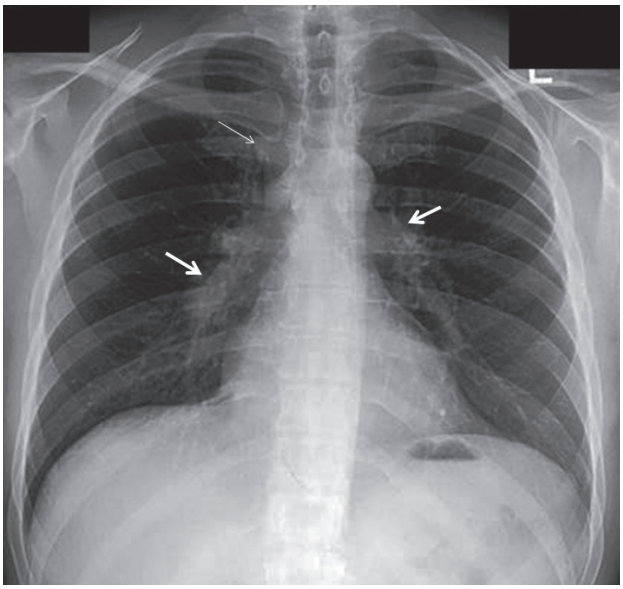

Fig. 1. *Scadding's radiographic stages of sarcoidosis: Stage 1. Posteroanterior chest radiograph with bilateral hilar (thick arrows) and right paratracheal (thin arrow) adenopathy, but no parenchymal findings*

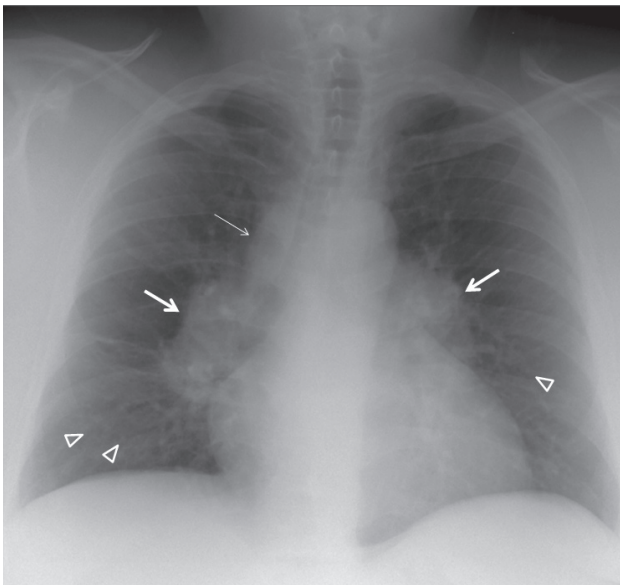

Fig. 2. *Sarcoidosis: Stage 2. Posteroanterior chest radiograph showing bilateral hilar (thick arrows) and mediastinal (thin arrow) adenopathy, as well as nodular parenchymal opacities (arrowheads)*

The pathologic hallmark of sarcoidosis is the granuloma, a more or less well-circumscribed collection of epithelioid histiocytes, multinucleated giant-cells and lymphocytes. In the more mature granulomas, fibroblasts are present in considerable numbers at the periphery. Although the majority of sarcoid granulomas are non-necrotising, a focal central coagulative necrosis has occasionally been documented [1, 3-6]. It is probable that many granulomas resolve completely over time. Yet, some undoubtedly undergo progressive fibrosis. Fibrotic changes usually begin at the periphery of the granuloma and proceed inward, until the entire granuloma is converted into a scar [1, 4-6].

Sarcoidosis may involve virtually any tissue or organ. It is because of this variable location that sarcoidosis is known as "the great mimicker" [7], but the most commonly affected structures are: the mediastinal and hilar lymph nodes, the lungs, the skin and the eyes [2-4]. Intrathoracic manifestations of the disease are present in 90% of patients. Moreover, 25% of patients have respiratory symptoms at diagnosis and 20-25% will develop permanent functional impairment [4]. Therefore, imaging has an important role in the work up of patients with pulmonary sarcoidosis. Understandably, chest radiograph is the first imaging examination to be performed and is useful for initial diagnosis and staging. Computed tomography (CT) shows the various types of pulmonary lesions in detail and is useful for the quantification of disease activity and follow-up. PET/CT is useful for disease staging, occult site identification and biopsy guidance.

Radiologic Manifestations

Sarcoidosis has been described as occurring in stages based on chest radiograph findings:

Stage 0: No visible abnormalities (10% of cases).

Stage 1: Hilar or mediastinal lymph node enlargement not associated with visible lung disease (50% of cases) (**Fig. 1**).

Stage 2: Hilar or mediastinal lymph node enlargement associated with visible lung disease (30% of cases) (**Fig. 2**).

Stage 3: Diffuse lung disease without lymph node enlargement (10% of cases) (**Fig. 3**).

Stage 4: This designation is used to refer to end-stage disease [5, 6, 8].

More than 90% of patients with sarcoidosis are detected by the abnormalities noted on plain radiographs or/and CT scans of the thorax. Patients with a completely normal chest radiograph may display extrathoracic manifestations of the disease, mainly ocular or skin lesions [4, 8]. In such cases, with a clinical suspicion of sar-

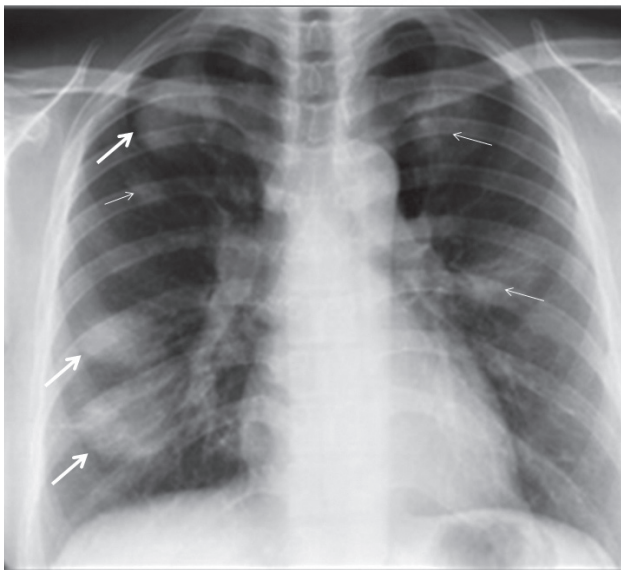

Fig. 3. *Stage 3. Posteroanterior radiograph showing bilateral large nodules (thin arrows) and masses (thick arrows), unassociated with lymph node enlargement*

coidosis, CT scans are indicated in order to demonstrate parenchymal abnormalities, or subtle or unusually located lymphadenopathy [4]. One should also keep in mind that a normal high resolution (HR) CT does not exclude the diagnosis of sarcoidosis [8].

1. Lymphadenopathy without pulmonary disease

Lymphadenopathy is the most common intrathoracic manifestation of sarcoidosis, detected in more than half of the patients at the time of the diagnosis, and occurring in the majority of them at some point in the course of the disease [9, 10].

Chest Radiograph

The most frequent abnormality seen on chest radiograph is bilateral enlarged hilar lymph nodes [6, 11]. They are often associated with enlarged right paratracheal lymph nodes (the combination is known as the "Garland triad" or the "1-2-3" sign, a pattern typical, but not specific, of sarcoidosis) and aortopulmonary window lymph nodes [6, 11-13]. Hilar lymphadenopathy is evident in more than 95% of patients who have intrathoracic lymph node enlargement, and is typically symmetrical and noncompressive. Nodal size ranges from barely detectable to massive, the latter giving the

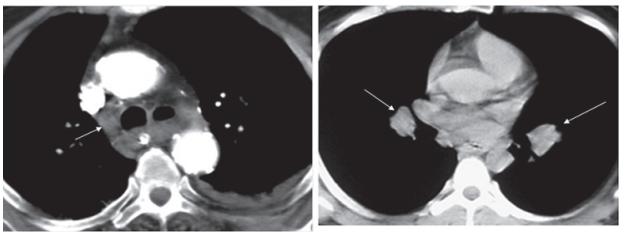

Fig. 4. *Axial CT images of different patients showing enlarged right paratracheal (arrow in left image) and bilateral hilar (arrows in right image) lymph nodes*

hila a lobulated and well-demarcated contour [11, 14, 15]. A translucent space between the enlarged lymph nodes and the cardiovascular margin (clearer on the right side) is often noted [16]. Right paratracheal adenopathy can be recognised on frontal radiographs as thickening of the right paratracheal stripe with increased regional opacity and lobularity [12, 15]. Aortopulmonary window adenopathy manifests as a convex opacity between the aortic arch and the pulmonary artery on lateral views [12, 15].

The major differential diagnosis of intrathoracic node enlargement includes fungal infection, tuberculosis and lymphoma [5, 6, 10, 13]. In such cases, symmetry is an important diagnostic feature of sarcoidosis [6, 10].

Computed Tomography

On chest CT, lymphadenopathy is detected in up to 98% of patients with sarcoidosis, being the most common finding, irrespective of radiographic staging [8, 11]. CT is superior to radiographs in the detection of subtly enlarged lymph nodes and of mediastinal adenopathy (in the anterior and posterior mediastinum as well as in the subcarinal region) [8, 15]. Lymph nodes are commonly bilaterally enlarged (**Fig. 4**), non-necrotic and non-compressive, but often asymmetric, with right-sided predominance [8, 11, 12]. Asymmetry on CT is more frequently encountered in the mediastinal nodes, although unilateral hilar adenopathy can occur in up to 40% of patients, almost always on the right side [8]. Enhancement and necrosis are rare findings on CT.

Lymph node calcification in sarcoidosis is usually a late manifestation, almost invariably associated with advanced disease; it has also been reported after corticosteroid therapy [6, 11, 13]. Calcification of hilar and mediastinal lymph nodes is seen more commonly on CT

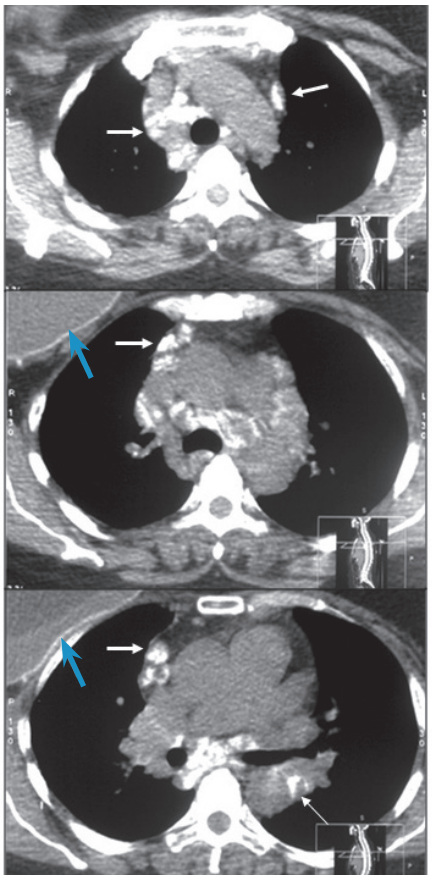

Fig. 5. *Axial CT images showing calcified mediastinal and hilar lymph nodes (white arrows). A silicone prosthesis due to right mastectomy is also noted (blue arrows)*

than on radiographs [6, 11, 13] (**Fig. 5**). It is apparent at presentation in 20% of patients and its incidence increases to 44% during the course of the disease [11, 13]. The patterns of calcification are varied and non-specific: they can be punctuate, "popcorn"-like, amorphous and "eggshell"-like [5]. The "eggshell"-like appearance needs to be differentiated from silicosis; in fact, sarcoidosis is considered to be the most common cause of circumferential or "eggshell"-like calcification in patients not exposed to silica [5, 6].

The other types of calcification may also be seen in other granulomatous disorders, like tuberculosis and histoplasmosis [5, 13]. The amorphous, "icing sugar" pattern, a cloud like appearance of calcification, is highly suggestive of sarcoidosis, since it is less frequently associated with other granulomatous diseases [17]. When comparing the pattern and distribution of calcified mediastinal lymph nodes in sarcoidosis and tuberculosis, in sarcoidosis the mean diameter of calcified nodes is significantly larger, calcium deposition is more often focal, whereas when hilar lymph nodes are calcified, the distribution is more likely to be bilateral (65%). On the contrary, in tuberculosis, the mean diameter is smaller, calcium deposition is more commonly diffuse, and bilateral hilar calcification is present in only 8% of cases [6, 11, 13].

2. Parenchymal disease with or without lymph node enlargement

Chest Radiograph

Parenchymal abnormalities are seen on chest radiographs of approximately 40% of sarcoidosis patients at presentation, and occur at some time during the course of the disease in 50-65% [6, 11, 12]. Findings are typically symmetric and bilateral, involving the middle and upper lung zones [12, 15]. They may be patchy or diffuse, with a central/perihilar rather than peripheral predilection [15, 16]. The pattern is typically nodular or reticulonodular.

Nodules are usually well defined, with irregular margins and size ranging from 1 to10 mm, although the majority measures less than 3 mm [6, 12]. They represent interstitial aggregates of granulomas and associated fibrous tissue [11, 13, 15]. They may also appear as dense, round, sharply marginated opacities, greater than 1 cm in diameter, simulating a metastatic neoplasm [6, 11, 18]. These nodules are usually seen in association with smaller nodular opacities, although they can be rarely solitary [6, 11, 19].

Air space consolidation is the predominant finding on chest radiographs of 10-20% of sarcoidosis patients [5, 6, 19]. It is typically patchy, bilateral and symmetrical, with a predilection for the middle and upper lung zones [5, 6]. The appearance may mimic pulmonary oedema. Occasionally it has lobar, or rarely, peripheral distribution, resembling chronic eosinophilic pneumonia or bronchiolitis obliterans organising pneumonia [5, 6]. If consolidation is largely confined to the upper lung zones, the pattern may mimic tuberculosis [6].

At presentation, 5% of sarcoidosis patients have fibrotic changes on chest radiographs, whereas in 10-20% of patients, fibrosis develops during the course of the disease [13]. On chest radiographs these changes are marked by: reticular pattern with a central and upper- lung zone predominance, architectural distortion involving vessels and fissures, presence of perihilar masses, coarse linear bands

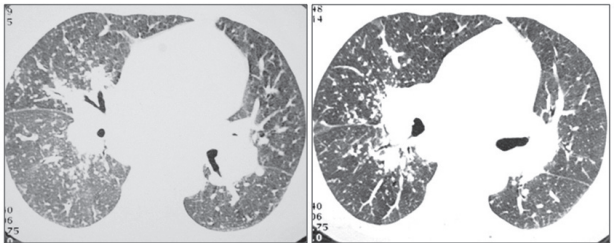

Fig. 6. *Axial CT images of the upper lobes demonstrating innumerable small nodules located mainly along the bronchi, the pulmonary vessels and the subpleural lung regions*

and linear opacities radiating from the hilum into the middle and upper zones, upper-lobe volume loss with hilar retraction, bullae formation, traction bronchiectasis and areas of paracicatricial emphysema, including compensatory overinflation of the lower lobes [6, 11, 13, 16, 18].

Computed Tomography

Micronodules with a perilymphatic distribution

In patients with parenchymal lung involvement, small nodules are evident on HRCT in 80-100% of cases, thus being the most frequently seen abnormality [6, 8, 11, 13]. They are typically well defined, measuring 1-5 mm in diameter and they predominate, though not invariably, in the middle and upper lung zones [5, 17]. Nodules are usually found bilaterally and symmetrically, following a perilymphatic pattern of distribution [5, 8, 13].

Nodules in sarcoidosis tend to be more abundant around bronchovascular bundles and subpleurally, and to a lesser extent along the interlobular septa [5, 18]. Their presence often gives these structures a thickened appearance, which is usually irregular or beaded, but can also be smooth [5, 11, 19]. The "pipe-cleaner" sign describes this beaded appearance of bronchovascular bundles, resembling the brush originally used to clean smoking pipes [20]. Peribronchovascular thickening often emanates from the hila in an axial fashion and is occasionally accompanied by airway luminal stenosis [11]. Peribronchovascular and fissural nodularity on HRCT is highly suggestive of sarcoidosis [5, 11, 13] **(Figs. 6, 7)**. Rarely, micronodules may adopt a miliary pattern, seen in less than 1% of patients [5, 15].

The differential diagnosis of diseases with perilymphatic micronodules predominance includes: pulmonary lymphangitic carcinomatosis (most commonly due to adenocarcinomas of the lung, breast, gastrointestinal system,

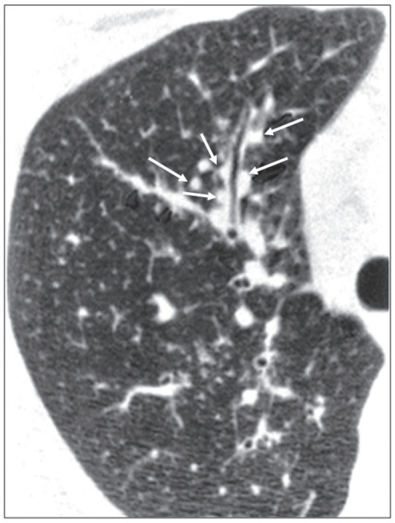

Fig. 7. *Axial CT image at the level of the right upper lobe showing nodules with irregular margins located at the periphery of the lung, accompanied by micronodules with bronchiolar involvement (arrows)*

prostate and kidney), lymphoma, silicosis, coal worker's pneumoconiosis and amyloidosis [11, 12,15, 20-22].

Large nodules and consolidation

(Nodular and alveolar sarcoidosis)

Confluence of numerous interstitial granulomas can result in large nodules and masses, seen in 15-25% of sarcoidosis patients [5, 6, 12,18]. These nodules usually appear as dense opacities with irregular margins, sometimes spiculated, ranging from 1 to 4 cm, and are typically multiple and bilateral [5, 18, 23]. Satellite nodules are often visible in the periphery of these lesions, a finding known as the "galaxy sign" [5, 8, 10-13, 18, 19].

Compression of alveolar airspaces by confluent interstitial granulomas and loss of the alveolar air is responsible for the alveolar or pseudoalveolar consolidation seen in 10-20% of patients [5, 13, 19]. This appearance has been termed as alveolar sarcoidosis and is characterised by bilateral, multifocal, poorly defined parenchymal opacities measuring from 1 to 10 cm [5, 18, 19].

Nodules, masses and consolidations are usually located in the mid and upper lung zones, along the bronchovascular bundles or sub-pleurally, typically sparing the costophrenic angles [8, 10, 11, 12, 15, 23]. Central air bronchograms may or may not be seen within these lesions [5, 11-13, 15]. Pathologically, air bronchograms correspond

to bronchiolar dilation with surrounding fibrosis and microscopic honeycombing [12, 15]. Cavitation of large nodules and consolidations are very rare, occurring in less than 1% of cases, and are usually benign. However haemoptysis can occur [8, 12, 13]. Patients with an initial presentation after the age of 50 years have a higher prevalence of solitary and multiple mass-like opacities in the lung.

The radiologic signs in nodular and alveolar sarcoidosis are not specific and resemble other diseases. Differential diagnosis includes: malignancy, both pulmonary primary neoplasms and metastatic lesions, pneumonia, mycobacterial and fungal infections and bronchiolitis obliterans organising pneumonia [5, 11, 21, 23].

Ground glass opacities

In patients with sarcoidosis the prevalence of ground glass opacities is estimated at 40%, ranging from 16% to 83% [5, 8, 13, 17]. Ground glass opacities are believed to result from the confluence of innumerable interstitial granulomas and/or fibrotic interstitial lesions beyond the resolution of HRCT [13, 14, 17, 21].

Ground glass opacities represent hazy areas of increased attenuation with ill-defined borders, which allow the preservation of bronchial and vascular margins [5, 13]. They are seldom the predominant finding on HRCT, usually being accompanied by other abnormalities, such as lymphadenopathy and small nodules [5, 11]. In fact, ground glass opacities are frequently overlaid on a background of subtle micronodularity or fibrosis [5, 11, 13]. They are usually patchy and multifocal, and very rarely extensive [5, 11]. Furthermore, they seem to be more common at presentation than later in the disease course [11, 13].

Fibrotic changes

In 50-70% of patients with Stage 2 disease and 20-40% with Stage 3, radiological abnormalities eventually resolve [6, 24]. Many patients with persistent radiographic abnormalities improve clinically; an estimated 20% develop pulmonary fibrosis [5, 6, 8, 25]. Compared to non-fibrotic chronically active disease, fibrotic sarcoidosis has worse potential complications and outcome [24].

In sarcoidosis, HRCT manifestations of fibrosis are highly variable, varying from ground-glass attenuation (representing fine fibrosis) to a coarse reticular pattern with or without honeycombing, or from mild architectural distortion, with linear opacities and irregular undulation of fissures and bronchi to severe upper lobe volume loss, with upward hilar retraction, bronchial clumping and distortion [8, 24, 26].

As fibrosis progresses, it may result in central conglomeration of ectatic perihilar bronchi and vessels, associated or not with masses of fibrous tissue [6, 26]. These conglomerate masses are a frequent finding in Stage 4 disease (60% of cases), typically bilateral, with a predominance in the upper and middle lung zones, and they may mimic progressive massive fibrosis [5, 6, 11, 13, 24].

Structural changes in the lungs are another constant finding in Stage 4 sarcoidosis, and overall present in 20-50% of patients [11]. They include upward retraction of the hila, abnormal displacement of fissures and distortion of the secondary lobules [11]. Other characteristic findings are bronchiectasis, bulla formation and paracicatricial emphysema, mainly in the upper and middle zones, compensatory overinflation of the lower lobes, and honeycombing [5, 6, 11, 13].

Patients with extensive fibrosis usually develop pulmonary arterial hypertension (cor pulmonale) and respiratory failure [2, 8, 11, 13]. Another major complication of sarcoidosis in patients with parenchymal destruction and bullae, is mycetoma formation and haemorrhage [11, 13-15, 17]. Rarely, giant bullous changes cause the Vanishing Lung Syndrome, characterised by marked parenchymal destruction and the development of large air spaces [19, 27]. Exceptionally, a usual interstitial pneumonia (UIP)-like distribution in the lower lobes with a peripheral and subpleural predominance of cystic changes can also be seen [5, 11, 13, 17].

Necrotising sarcoid granulomatosis

This rare entity, first described in 1973, has raised a lot of debate during the past decades, as to whether it is a manifestation of systemic sarcoidosis with necrotising granulomas or a form of necrotising angiitis with sarcoid-like reaction [8, 13]. Recent data however favour the former, providing evidence that it is a variant of nodular sarcoidosis [13]. Necrotising sarcoid granulomatosis is characterised by an extensive non-necrotising granulomatous inflammation with areas of parenchymal infarct-like necrosis and various degrees of fibrosis, in addition to a marked vasculitis [1, 8, 11, 13, 19]. It involves both arteries and veins, most commonly in the lungs, although, being a systemic disor-

der, it may have extrapulmonary manifestations as well [7, 11, 19, 28]. It is more frequent in women, and it usually leads a benign clinical course [7], cough being the typical presenting symptom. In 40% of cases it is asymptomatic and it may be detected incidentally [7, 18]. Radiographic findings in necrotising sarcoid granulomatosis include multiple, bilateral, often confluent, lung nodules up to 4 cm, which can cavitate [8, 12, 18, 19]. Another common feature is consolidation, often subpleural, with air bronchograms [8, 18]. Occasionally, it may present as a solitary mass [8].

3. Bronchial and bronchiolar abnormalities

Bronchial abnormalities have been reported in 65% of patients, primarily consisting of nodular bronchial wall thickening or small endobronchial lesions [5, 8, 9, 11, 12, 29, 30]. Obstruction of lobar or segmental bronchi by granulomas may result in atelectasis, whereas obstruction of small airways by granulomas or fibrosis may result in a mosaic perfusion pattern on inspiratory HRCT scans, and air trapping on expiratory scans [5, 8, 11, 12, 29, 30]. Since air trapping in expiratory scans may be the only abnormal imaging finding, even in patients without inspiratory findings and with normal pulmonary function tests [31], it is important that expiratory scans are included in the diagnostic CT protocol of patients with suspected or diagnosed pulmonary sarcoidosis.

4. Pleural disease

Pleural involvement in sarcoidosis may present as pleural effusion, pneumothorax, chylothorax, pleural thickening, pleural nodules and pleural calcification [5, 6, 11, 13, 15, 16]. All these findings represent unusual manifestations of sarcoidosis, may arise at any stage of the disease and do not seem to have any clear prognostic value [16].

Pleural effusion

Sarcoidosis related pleural effusions are slightly more common in the right lung (45%) than in the left lung (33%), the reason for this being unclear [13, 16]. Approximately one fourth of cases are bilateral [6, 16]. Although generally small to medium, occasionally effusions can be massive, and rarely loculated [5, 16]. They have been described as exudates or transudates, with the typical finding being a paucicellular, lymphocyte-predominant exudate [5, 16]. Most of these effusions resolve spontaneously within 2-3 months [5, 13, 16]. If they are symptomatic or recurrent, steroid therapy is recommended [16]. Incomplete resolution occurs in some cases, with eventual progression to chronic pleural thickening or a trapped lung [6, 13, 16].

Because sarcoidosis-related pleural effusions are rare, it should not be assumed that an effusion occurring in a patient with sarcoidosis is due to the disease [16]. A definite diagnosis requires a biopsy, with the exclusion of other granulomatous diseases [16].

Pleural thickening

Pleural thickening and fibrothorax are undoubtedly much more common in sarcoidosis than has been emphasised in the literature in the past, having been identified increasingly on CT images [6, 12 ,16]. Studies have shown an incidence of 11-33% of pleural thickening on CT scanning in sarcoidosis patients [11, 16]. The prevalence is higher in chronic fibrocystic sarcoidosis [6]. Such thickening may be seen after or in association with pleural effusion, or it can occur independently [6, 12, 15, 16]. It may be unilateral or bilateral and is usually confined to the lower lobes [6, 15, 16].

Pleural nodules and masses

Pleural nodules may be present on HRCT in 22-75% of cases [16]. They rarely cause symptoms, may be associated with pleural thickening, and correspond to nodules seen on visceral and parietal pleura at thoracotomy and autopsy [16].

Rarely, sarcoidosis presents as a discrete pleural mass [6, 16].

Pneumothorax

Spontaneous pneumothorax has been estimated to occur in 2-3% of cases [6, 13, 15, 16]. The accountable mechanism seems to be the rupture of a subpleural bullae or the necrosis of a subpleural granuloma, especially in advanced fibrotic disease [5, 6, 11, 13, 16]. Nonetheless, pneumothorax may also occur in the early stages of sarcoidosis [6, 16]. In the absence of bullae, it probably represents a coincidental finding and it is of the same aetiology as with pneumothorax which occurs spontaneously in a susceptible young male population [6]. It may be recurrent and rarely bilateral [6, 13, 16]. There seems to be no preference as to the side of the thorax on which pneumothorax presents [16].

Chylothorax

Chylothorax is an exceptionally rare complication of sarcoidosis, caused by mediastinal lymph nodes or thoracic duct involvement [5, 13, 16, 19]. This type of effusion tends to be large and sometimes recurrent [16].

5. CT as a prognostic factor for quantifying disease activity

Besides its diagnostic value, CT also has a role in patient follow up and monitoring disease activity. This is important, since the disease's clinical course is variable [32]: lung involvement may resolve spontaneously in most cases, but permanent fibrosis with related functional impairment can develop in up to 25% of patients, with death in up to 10% of these cases [33]. HRCT can be useful in following the different types and extent of the disease's manifestation over time, thus aiding in prognosis prediction. Predominant patterns on the initial HRCT scan have been related with prediction of patient outcome.

Different types of lesions follow different courses [34-36]: nodular opacities may be reversible, contrary to cystic air spaces and architectural distortion, which are irreversible, irrespective of therapy. Ground-glass and linear opacity patterns may be either reversible or irreversible. Follow up CT scans may also reveal honeycombing, emphysema, parenchymal bands, traction bronchiectasis and bronchial distortion along the course of the disease. Fibrosis is noted only when ground-glass and linear opacities are associated with architectural distortion of secondary lung lobules, hilar and fissure retraction, formation of cysts and traction bronchiectases.

Three main fibrosis patterns have been described on CT [37]: Central bronchial distortion (47%), peripheral honeycombing (29%), and diffuse linear fibrosis (24%). In particular, honeycombing has been commonly associated with decreased lung diffusing capacity for carbon monoxide. Patients with bronchial distortion have experienced lower expiratory airflow rates, while in cases with linear lesions the least functional impairment has been noted. Airflow obstruction has been more often related with a reticular pattern on CT [29], whereas in patients with advanced disease, small airway abnormal findings were common but contributed little to airflow obstruction.

Altogether, in patients with nodular patterns on the initial CT scan prognosis was better, while in patients with ground-glass opacity and consolidation prognosis was worse, with more often severe respiratory insufficiency development. Shrinkage of conglomeration patterns resulted into bronchial distortion with or without irreversible functional damage.

6. Nuclear medicine methods

Gallium-67 Scanning

Gallium-67 scanning (Ga-67) is one of the early studies used for the diagnosis and management of sarcoidosis. This radiotracer localises at the inflammatory sites in the lung, but not at the normal parenchyma. Whole-body Ga-67 scanning has been used as a sensitive but nonspecific indicator of disease activity. It is very useful for the diagnosis of sarcoidosis in patients with atypical presentations, and may guide the clinician to the appropriate biopsy sites. It may help to determine whether radiologic densities represent reversible inflammation or fibrosis. Ga-67 scanning has been accepted as a tool for monitoring response to therapy in patients with positive baseline examinations [38].

Patterns of symmetrically increased uptake in the mediastinal and hilar nodes and in the lacrimal, parotid and salivary glands (panda sign) are considered pathognomonic for sarcoidosis. Sometimes the study is difficult to interpret, the findings are not specific, and a negative scan does not exclude the disease [38].

18F FDG-PET/CT

In recent years the role of FDG imaging in the evaluation of inflammatory and infectious processes has been widely explored and is still under investigation. Most articles indicate that PET may not be a major tool for the initial diagnosis of sarcoidosis, but that it may play a role in the management of patients with this disorder. FDG-PET/CT is superior to Ga-67 scanning for the detection of pulmonary and extrapulmonary sarcoidosis, and is quite valuable in monitoring treatment response [39-42].

Sarcoidosis usually shows high metabolic activity at different stages of the disease (**Fig. 8**). It can mimic malignant disorders (lymphoma, metastatic disease) and has been a source of false-positive findings. Other PET tracers – in addition to FDG – are currently under investigation for the evaluation of sarcoidosis and other granulomatous diseases [43, 44].

FDG-PET/CT also has an important role for disease

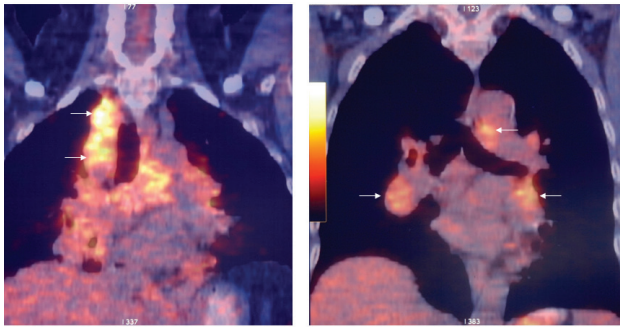

Fig. 8. *Coronal PET/CT images showing increased metabolic activity in mediastinal and hilar lymph nodes (arrows)*

staging, as well as for depicting occult sites. It is also useful for locating sites that are amenable to biopsy and for assessing inflammatory active disease, especially when other markers are normal. Thus, FDG-PET/CT is crucial for the clinical management of patients with chronic persistent sarcoidosis, by aiding in treatment planning, response monitoring and follow-up [45].

Conclusions

Sarcoidosis has many manifestations, its evolution and severity vary remarkably from case to case, and its prognosis is difficult to predict. Radiologists can play an important role in the early diagnosis and management of the disease, recognising the typical and atypical imaging patterns and its potential complications, and thus helping to prevent quality-of-life impairment. R

Conflict of interest:
The authors declared no conflicts of interest.

References

1. Valeyre D, Bernaudin J-F, Florence J, et al. Pulmonary sarcoidosis. *Clin Chest Med* 2015; 36(4): 631-641.
2. Valeyre D, Prasse A, Nunes H, et al. Sarcoidosis. *Lancet* 2014; 383(9923): 1155-1167.
3. Hamzeh N. Sarcoidosis. *Med Clin N Am* 2011; 95(6): 1223-1234.
4. Statement on sarcoidosis. Joint statement of the American Thoracic Society (ATS), the European Respiratory Society (ERS) and the World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) adopted by the ATS Board of Directors and by the ESR Executive Committee, February 1999. *Am J Respir Crit Care Med* 1999; 160(2): 736-755.
5. Criado E, Sanchez M, Ramirez J, et al. Pulmonary Sarcoidosis: Typical and atypical manifestations at high-resolution CT with pathologic correlation. *Radiographics* 2010; 30(6): 1567-1586.
6. Fraser R, Muller N, Colman N, et al. Sarcoidosis. In: Bralow L (ed). Diagnosis of diseases of the CHEST. Fourth Edition. Philadelphia, Pennsylvania, United States of America. *W.B.Saunders Company* 1999, pp 1542-1563.
7. Shadid S, ter Maaten JC. Sarcoidosis-a great mimicker. *J Intern Med* 2002; 251(2): 174-176.
8. Little B. Sarcoidosis: Overview of pulmonary manifestations and imaging. *Semin Roentgenol* 2015; 50(1): 52-64.
9. Baughman R, Lower E, Gibson K. Pulmonary manifestations of sarcoidosis. *Presse Med* 2012; 41(6 Pt 2): e289-302.
10. Nishino M, Lee K, Itoh H, et al. The spectrum of pulmonary sarcoidosis: Variations of high-resolution CT findings and clues for specific diagnosis. *Eur J Radiol* 2010; 73(1): 66-73.
11. Nunes H, Uzunhan Y, Gille T, et al. Imaging of sarcoidosis of the airways and lung parenchyma and correlation with lung function. *Eur Respir J* 2012; 40(3): 750-765.
12. Akbar J, Meyer C, Shipley R, et al. Cardiopulmonary imaging in sarcoidosis. *Clin Chest Med* 2008; 29(3): 429-443.
13. Keijsers R, Veltkamp M, Grutters J. Chest imaging. *Clin Chest Med* 2015; 36(4): 603-619.
14. Silva M, Nunes H, Valeyre D, et al. Imaging of sarcoidosis. *Clin Rev Allerg Immunol* 2015; 49(1): 45-53.
15. Vagal A, Shipley R, Meyer C. Radiological manifestations of sarcoidosis. *Clin Dermatol* 2007; 25(3): 312-25.
16. Mihailovic-Vucinic V, Jovanovic D. Pulmonary sarcoidosis. *Clin Chest Med* 2008; 29(3): 459-473.
17. Spagnolo P, Sverzellati N, Wells A, et al. Imaging aspects of the diagnosis of sarcoidosis. *Eur Radiol* 2014; 24(4): 807-816.
18. Hoang D, Nguyen E. Sarcoidosis. *Semin Roentgenol* 2010; 45(1): 36-42.
19. Hawtin K, Roddie M, Mauri F, et al. Pulmonary sarcoidosis: the 'Great Pretender'. *Clin Radiol* 2010; 65(8): 642-650.
20. Shroff G, Guirguis M, Ocazionez D, et al. Beyond metastatic disease: A pictorial review of multinodular lung

disease with computed tomographic pathologic correlation. *Can Assoc Radiol J* 2015; 66(1): 16-23.
21. Ors F, Gumus S, Aydogan M, et al. HRCT findings of pulmonary sarcoidosis: relation to pulmonary function tests. *Multidiscip Respir Med* 2013; 8(1): 8.
22. Jain V, Hasselquist S, Delaney M. PET scanning in sarcoidosis. *Ann.NY. Acad.Sci* 2011; 1228: 46-58.
23. Shahzad H, Ur-Rehman S, Fatima K, et al. Case series and literature review of multiple nodular sarcoidosis. *BMC Res Notes* 2013; 6: 394.
24. Patterson K, Strek M. Pulmonary fibrosis in sarcoidosis. Clinical features and outcomes. *Ann Am Thorac Soc* 2013; 10(4): 362-370.
25. Jeong Y, Lee K, Chung M, et al. Chronic hypersensitivity pneumonitis and pulmonary sarcoidosis: Differentiation from usual interstitial pneumonia using high-resolution computed tomography. *Semin Ultrasound* CT MR 2014; 35(1): 47-58.
26. Kouranos V, Jacob J, Wells A. Severe sarcoidosis. *Clin Chest Med* 2015; 36(4): 715-726.
27. Morgenthau A, Teirstein A. Sarcoidosis of the upper and lower airways. *Expert Rev Respir Med* 2011; 5(6): 823-833.
28. Judson M. The Diagnosis of sarcoidosis. *Clin Chest Med* 2008; 29(3): 415-427.
29. Trail Z, Maskell G, Gleeson F. High-resolution CT findings of pulmonary sarcoidosis. *AJR Am J Roentgenol* 1997; 168(6): 1557-1560.
30. Hansell D, Milne D, Wilsher M, et al. Pulmonary sarcoidosis: morphologic associations of airflow obstruction at thin-section CT. *Radiology* 1998; 209(3): 697-704.
31. Magkanas E, Voloudaki A, Bouros D, et al. Pulmonary sarcoidosis. Correlation of expiratory high-resolution CT findings with inspiratory patterns and pulmonary function tests. *Acta Radiol* 2001; 42(5): 494-501.
32. Akira M, Kozuka T, Inoue Y. Long-term follow-up CT scan evaluation in patients with pulmonary sarcoidosis. *Chest* 2005; 127: 185-191.
33. Crystal RG, Roberts WC, Hunninghake GW, et al. Pulmonary sarcoidosis: A disease characterized and perpetuated by activated lung T-lymphocytes. *Ann Intern Med* 1981; 94: 73–94.
34. Nishimura K, Itoh H, Kitaichi M, et al. Pulmonary sarcoidosis: Correlation of CT and histopathologic findings. *Radiology* 1993; 189: 105–109.
35. Murdoch J, Muller NL. Pulmonary sarcoidosis: Changes on follow-up CT examination. *AJR Am J Roentgenol* 1992; 159: 473–477.
36. Saito W, Kobayashi H, Shinkai M, et al. Pulmonary involvement in sarcoidosis: CT findings at diagnosis and their changes at follow-up in cases without corticosteroid treatment. *Nihon Kokyuki Gakkai Zasshi* 2002; 40: 210–214.
37. Abehsera M, Valeyre D, Grenier P, et al. Sarcoidosis with pulmonary fibrosis: CT patterns and correlation with pulmonary function. *AJR Am J Roentgenol* 2000; 174: 1751–1757.
38. Schuster D, Alazraki N. Gallium and other agents in diseases of the lung. *Semin Nucl Med* 2002; 32(3): 193-211.
39. Alavi A, Buchpiguel C, Loessner A. Is there a role for FDG PET imaging in the management of patients with sarcoidosis? *J Nucl Med* 1994; 35(10): 1650-1652.
40. Larson S. Cancer or Inflammation? A holy grail for nuclear medicine. *J Nucl Med* 1994; 35(10): 1653-1655.
41. Hubner K, Buonocore E, Gould H, et al. Differentiating benign from malignant lung lesions using "Quantitative" FDG PET images. *Clin Nucl Med* 1996; 21(12): 983-984.
42. Xiu Y, Yu J, Cheng E, et al. Sarcoidosis demonstrated by FDG PET imaging with negative findings on gallium scintigraphy. *Clin Nucl Med* 2005; 30(3): 193-195.
43. Kazuo K, Masatoshi I, Kaoru O, et al. Advantage of delayed whole-body FDG-PET imaging for tumour detection. *EurJ Nucl Med* 2001; 28(6): 696-703.
44. Ludwig V, Fordice S, Lamar R, et al. Unsuspected skeletal sarcoidosis mimicking metastatic disease on FDG positron emission tomography and bone scintigraphy. *Clin Nucl Med* 2003; 28(3): 176-179.
45. Sobic-Saranovic D, Artiko V, Obradovic V. FDG PET imaging in sarcoidosis. *Semin Nucl Med* 2013; 43(6): 404-411.

READY - MADE CITATION

Blana I, Cokkinos DD, Skilakaki M. Pulmonary Sarcoidosis: Spectrum of imaging findings. *Hell J Radiol* 2017; 2(4): 45-54.