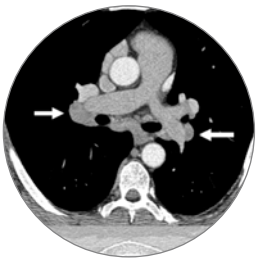

Thoracic and Cutaneous Involvement in Systemic Diseases: Clues for the General Radiologist

Manifestaciones torácicas y dermatológicas de las enfermedades sistémicas: claves para el radiólogo general

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Summary

There are many diseases with manifestations in the chest and on the skin. Within this great variety of diseases, it is important the identification of pathological patterns in Multidetector Computed Tomography (MDCT) and its correlation with cutaneous manifestations. In this article, we present a review of the main entities: infectious, inflammatory, connective tissue diseases, hereditary and acquired diseases. Information is provided on the most frequent radiological presentations of these diseases in the thorax, being one of the most frequent presentations the pulmonary interstitial disease where NSIP, UIP, and NO are the predominant patterns, whose frequency varies according to the disease and which, in turn, are different from the radiological patterns in MDCT. The importance of the Multidetector Computed Tomography in patients with dermatological pathologies is highlighted. Key dermatologic and radiologic findings to suspect the diagnosis in any of these pathologies are presented, which allows the radiologist to provide more information to define the treatment and follow-up of these patients.

Resumen

Hay una gran cantidad de enfermedades con manifestaciones en tórax y en piel. Dentro de ellas es muy importante la identificación de patrones radiológicos en tomografía computarizada multidetector (TCMD) y su correlación con la clínica, con énfasis en las manifestaciones cutáneas. En este artículo se hace una revisión de las principales entidades infecciosas, inflamatorias, enfermedades de tejido conjuntivo, enfermedades hereditarias y adquiridas. Se brinda información sobre las presentaciones radiológicas más frecuentes en el tórax, como la enfermedad intersticial pulmonar en la que predominan los patrones NINE, NIU y NO, cuya frecuencia varía según la enfermedad y que, a su vez, son diferentes de los patrones radiológicos en TCMD. Se destaca su importancia en pacientes con patologías dermatológicas. Se plantean hallazgos dermatológicos y radiológicos claves para sospechar el diagnóstico de estas patologías, lo que permite al radiólogo entregar una mayor información para definir el tratamiento y seguimiento de dichos pacientes.

Introduction

A considerable number of pathologies concomitantly affect the skin and lung, with different types of radiological manifestations for each entity both in their temporality and in the imaging characteristics that will be addressed individually in each section. Within this variety of entities can be found infectious etiology (infective endocarditis and SAPHO syndrome), inflammatory disease (sarcoidosis), connective tissue disease (polymyositis and dermatomyositis, systemic sclerosis, Sjögren›s syndrome, systemic lupus erythematosus and rheumatoid arthritis), hereditary (neurofibromatosis type 1) and acquired (Kaposi›s sarcoma).

The aim of this article is to provide the general radiologist with the tools to identify pathologic patterns in high-resolution chest tomography (HRCT) or multidetector computed tomography with chest contrast medium (MDCT) and their correlation with the cutaneous manifestations of different systemic entities that affect the skin and chest simultaneously, as well as a review of the main entities of each group of pathologies that generate both cutaneous and pulmonary manifestations, with emphasis on those that are frequently found in daily radiological practice, are also reviewed.

1. Radiological patterns associated with dermatological diseases

It is necessary to make a brief introduction to some concepts, which are important for understanding the

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thoracic involvement of dermatologic diseases. The thoracic manifestations of dermatological diseases are varied; however, the most frequent are: pulmonary arterial hypertension and interstitial lung disease (ILD) (1). ILD occurs mainly in older adults and is defined by the radiological pattern present in MDCT and tissue histopathology, a diagnosis that may or may not be accompanied by symptoms and signs; the most frequent clinical presentation is with dyspnea, chronic cough and bibasal rales, a clinical presentation that does not correlate with constitutional symptoms suggesting multisystemic disease (2). Within the different radiological patterns that form ILD, non-specific interstitial pneumonia (NSIP), usual interstitial pneumonia (UIP), organizing pneumonia (OP) and lymphoid interstitial pneumonia (LIP) should be considered (1). In dermatologic diseases, NSIP, UIN and OP patterns predominate (2-8); however, other causes -pharmacologic, expositional or risk factors associated with ILD, such as smoking, gastroesophageal reflux, viral infections (Epstein Barr and hepatitis C) and family history of ILD (2)- should be considered.

Within the pulmonary involvement of dermatologic diseases, NSIP is the most frequent pattern of ILD and occurs especially in systemic sclerosis and polymyositis/dermatomyositis (1). This pattern presents with areas of alteration of the pulmonary architecture: reticulation and predominance of "ground glass" areas, homogeneous involvement in both lungs, traction bronchiectasis in lower lobes, and with a characteristic respect for the subpleural space (1). NSIP has a cellular phase, in which pulmonary involvement begins, and a fibrotic phase, in which the findings are more severe, with "honeycomb" formation, sometimes impossible to differentiate from the UIP pattern (1). The "honeycomb" pattern refers to cystic air spaces of 3 to 10 mm in diameter, with thick and well-defined walls, accompanied by reticular opacities with traction bronchiectasis and bronchioloectasis (2). It gives the appearance of a honeycomb due to the multiple layers of subpleural cysts that are located one on top of the other; however, in some cases it can be only one layer, which makes the differential diagnosis with paraseptal emphysema or traction bronchiectasis difficult (2) (figure 1).

UIN is the second most frequent pattern in dermatologic entities, predominating in patients with pulmonary involvement due to rheumatoid arthritis (1). This pattern is characterized by alteration of the pulmonary architecture, scarce "ground glass" opacities, reticular opacities, traction bronchiectasis and "honeycomb" formation predominantly in lower lobes, with a characteristic of temporal heterogeneity (1, 2) (figure 2). The difference between the typical "ground-glass" pattern of UIN - which consists of opacities superimposed on a reticular pattern - and a "pure ground-glass" opacity - which would be indicative of an acute exacerbation in a patient with ILD - should be clarified, and is more suggestive of exacerbation if accompanied by bilateral "ground-glass" with or without consolidation and pulmonary fibrosis in the background (2). The most recent guidelines (2) recommend classifying ILD into four categories according to MDCT findings:

- **UIN pattern:** "honeycombing" is observed, which may or may not be accompanied by bronchiectasis and bronchioloectasis. The typical distribution is usually subpleural with basal predominance, usually heterogeneous.
- **Probable pattern of UIN:** Subpleural reticular opacities would be evident, with basal predominance and heterogeneous. It may be accompanied by "ground-glass" opacities, bronchiectasis and bronchioloectasis.
- **Indeterminate pattern of UIN:** It is characterized by a pulmonary fibrosis pattern, not consistent with a pattern of UIN and not consistent with a probable pattern of UIN. Other diagnostic alternatives: Propose alternative diagnoses according to the predominant findings.

Organizing pneumonia (OP) is rare as a thoracic manifestation; however, it has been described in patients with polymyositis/dermatomyositis (1). It is characterized by areas of consolidation of peripheral or peribronchial distribution predominantly in the lower lobes and polygonal or geographic consolidations, which may be surrounded by areas of "ground glass", called the "reverse halo" sign (1). Its diagnosis is important since OP is characterized by a good response to management with corticosteroids (1).

2. Infectious etiology

2.1 Bacterial endocarditis

Bacterial endocarditis is defined as infection of the inner lining of the cardiac valves and chambers (9). The most common causative microorganism is Staphylococcus aureus (10). Predisposing conditions have been described, such as calcified aortic stenosis, congenital heart disease, previous episodes of endocarditis, prosthetic valves -most commonly in the mitral valve-, infected central venous catheters, periodontal disease, or in patients using intravenous drugs (9, 11).

Dermatological manifestations are very suggestive for its diagnosis; however, they tend to be uncommon, with a prevalence of approximately 11.9%, according to the literature (12). Peripheral embolism is the symptom that most frequently affects the extremities, especially the fingers or toes (9). Osler nodules, Janeway lesions and subungual hemorrhage, which is characterized by being linear or "splinter", are other findings of this type of entities (9, 12).

However, the diagnostic approach usually begins with an echocardiogram to clarify the diagnosis, or to suspect it, due to the finding of vegetations in cardiac valves (13). There are other imaging modalities, such as chest X-ray, CT or MDCT and magnetic resonance imaging (MRI), in which useful diagnostic findings can be identified. In chest X-ray, HRCT and MDCT it is characteristic the appearance of multiple pulmonary nodules, solid, of ill-defined margins, with peripheral predominance, which can cavitate according to the time of evolution of the disease and with a greater profusion towards the subpleural or basal region (9) (figure 3). These nodules have a sign called "nutrient vessel", which consists of a vessel that goes directly to the nodule, a finding that has been described in up to 100% of patients with septic embolism (11). In these cases, the vessel does not always correspond to pulmonary arterial circulation; it may also correspond to pulmonary veins (11). Wedge-shaped subpleural opacities have also been described (11).

2.2. SAPHO syndrome

The acronym SAPHO refers to the description given by Chamot and collaborators in 1987 to the relationship between musculoskeletal lesions, specifically synovitis, hyperostosis, osteitis and skin lesions: pustulosis and severe acne, described in French as le syndrome acne-pustulose-hyperostose-osteite (14). SAPHO syndro-

me is characterized by an exaggerated immunological reaction to bacterial infection by Propionibacterium acnes (15). Its prevalence is equal in men and women, and it debuts at an average age of 30 to 55 years (16).

Its clinical symptoms are localized inflammatory pain, soft tissue edema and limited mobility, associated with skin lesions that may occur before, during or after bone manifestations (16). Regarding cutaneous involvement, it is related to yellowish pustules and vesicles, which are limited to the palms and soles (15). In addition, outbreaks of acne - which may be of fulminans, conglobata or hidradenitis suppurativa characteristics - may be accompanied by ulcerative nodules and crusted plaques, and usually occur on the face, back and chest (15).

Radiological findings vary according to the stage of the lesion, with osteolytic involvement in early stages of the disease and osteoproliferative in late stages (14). In relation to hyperostosis and osteitis, they are characterized by an increase in bone sclerosis (14). Hyperostosis manifests with cortical and periosteal thickening, while osteitis, with trabecular changes (15). Bone involvement predominates in long bones - in the metaphysis - in children and adolescents; in adults, in the anterior wall of the thorax, particularly in the sternoclavicular and sternocostal joints (14). It is important to clarify that the manifestations can be in a single bone, in 67% of patients, and in the remaining, in multiple bones (from 2 to 6 bones) (14).

The involvement of the anterior wall of the thorax is the most frequent in this entity, affecting between 60% and 95% of patients (14). Among the most common findings there is evidence of costoclavicular enthesopathy, hyperostotic foci of about 5 mm in diameter, usually located in the proximal end of the sternum, adjacent to the first rib, findings that are considered decisive in the early diagnosis of the disease (15). Bone scintigraphy helps in the detection of lesions in asymptomatic patients, with radiotracer uptake, especially in the sternoclavicular region, forming the characteristic sign, known as bull head sign, which helps in the detection of lesions, which helps to clarify the diagnosis of this condition (15).

3. Inflammatory etiology

3.1 Sarcoidosis

Sarcoidosis is considered to be a multisystemic disease, consisting of a chronic inflammatory process with an unclear etiology, whose main characteristic is the formation of non-caseating granulomas in multiple organs; and the lung is the most commonly affected organ (9).

Between 20% and 35% of patients diagnosed with sarcoidosis will present, at some point in the course of their disease, cutaneous manifestations that can be classified into two groups: specific and non-specific (9, 17). The most common specific manifestations are maculopapular nodules, plaques and lupus pernio, and are considered specific if non-caseating granulomas are evident on histological examination (17). Among the non-specific manifestations, the most relevant is erythema nodosum (17). Cutaneous manifestations involving the nail apparatus have even been described (18).

The respiratory symptomatology of these patients is usually non-specific, most of them are asymptomatic. The initial study is a chest X-ray, whose findings can be grouped according to Siltzbach's classification (9, 19), which defines five stages of sarcoidosis:

- **Stage 0:** normal radiography.
- **Stage 1:** lymphadenopathy.
- **Stage 2:** lymphadenopathy and pulmonary disease.
- **Stage 3:** pulmonary involvement.
- **Stage 4**: pulmonary fibrosis (9).

The classification describes the range of alterations found in the radiography at the moment of diagnosis, which can be from a normal radiography; demonstrate only mediastinal and parahilar adenomegalies, in some cases calcified; show only pulmonary findings such as nodules or masses; a combination of pulmonary nodules and mediastinal adenomegalies, up to, in final stages, pulmonary fibrosis changes (9).

In MDCT bilateral mediastinal and parahilar adenomegalies will be observed, which are usually symmetrical (figure 4). Some of them may be calcified with an "eggshell" pattern, and show homogeneous enhancement after contrast medium administration. In the pulmonary parenchyma there will be micronodules of perilymphatic and subpleural distribution (figure 4). Some of these nodules may confluence forming conglomerates or masses, in addition to masses or nodules surrounded by other smaller nodules that form the so-called "galaxy" sign, perihilar opacities and pulmonary fibrosis changes that predominate in the upper lobes (figure 4) (20). There may be manifestations in the pleura - seen as pleural plaques and, less frequently, pleural effusion (21) - and in the trachea - detected as areas of stenosis due to extrinsic compression secondary to mediastinal adenomegaly and areas of nodular or smooth thickening of the bronchi that may lead to stenosis (22).

4. Connective tissue diseases

4.1 Polymyositis and dermatomyositis

Polymyositis and dermatomyositis belong to the group of connective tissue diseases. They are characterized by generating an inflammatory process of the skeletal striated muscle, which results in strength deficit in the proximal muscle groups, myalgias and elevation of creatine kinase (CK) (23). However, when there is muscle and skin involvement, specifically cutaneous eruption, it would be called dermatomyositis, with one of its most characteristic presentations: Gottron's papules. Its etiology is not well known; however, it is believed that polymyositis is related to muscular antigens, which in dermatomyositis generate damage to the microvasculature due to an immune response, which leads to hypoperfusion and the presence of inflammatory cells in the perifascicular region (9, 23).

The cutaneous manifestation has a relevant role in the diagnosis of dermatomyositis, which allows it to be classified into 7 different groups: pathognomonic, characteristic, compatible, uncommon, rare, recently described and non-specific skin manifestations (24). Within the pathognomonic group are Gottron's sign and Gottron's papules.

The sign refers to erythematous macules, in some cases desquamative, with linear characteristics, which are arranged on the sheaths of the extensor tendons of the extremities, more marked in the dorsal

and lateral areas of the hands. Gottron papules are represented as lesions on the dorsum of the metacarpals, interphalangeal joints and on the contour of the nails, they are flat, papular and violaceous in color. Finally, the other most frequent subgroup should be taken into account: the characteristic lesions, which include heliotropic rash, the "shawl" or "V" sign, periungual telangiectasias and atrophic and scaly plaques of the scalp (24).

As for the thoracic manifestations of these two entities, interstitial pneumonias, vasculitis, pulmonary hypertension and atrophy of thoracic muscles have been described. The most clinically significant finding is interstitial involvement, with a pattern of organizing pneumonia (OP) that may appear even before skin involvement (9, 25). Interstitial lung involvement is caused by myositis-associated antibody and antibodies against aminoacyl tRNA synthetase enzymes, which correlate with its clinical presentation and the risk of developing pulmonary interstitial disease (25). Another pattern described is NSIP, in up to 13.7% of patients (5). NSIP and OP are not mutually exclusive, so the same patient may have radiological and histological findings of both entities simultaneously (9). Other compromises related to these two entities are those secondary to treatment, infection or respiratory failure, such as pneumonia due to immunosuppression, aspiration pneumonia related to atrophy of the pharyngeal muscles, respiratory failure due to thinning of intercostal muscles and toxic effects of pharmacological treatment, the latter of which can also lead to a pattern of OP (9).

4.2 Systemic Sclerosis

Systemic sclerosis, or scleroderma, is an autoimmune pathology characterized by fibrosis, vascular damage and inflammation (1). At the onset of the disease, only 1% of patients have respiratory symptoms; however, 60% develop them during the course of the disease (26). This entity predominantly affects women, in a 3:1 ratio, with a peak incidence between 45 and 64 years of age (27).

The most recognized cutaneous manifestations of this disease are cutaneous thickening -which begins in the fingers of the hands-, digital ischemia due to vasculopathy, facial involvement -which leads to expressionless facies- and telangiectasias in the mouth, hands and chest wall (9). These manifestations can be divided into limited and diffuse. When they are limited, they only affect the distal zone of the extremities and the face -also called limited systemic sclerosis, whose main clinical form or manifestation is CREST syndrome (for the initials of calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly and telangiectasias) (27)-. When the manifestations are diffuse, cutaneous sclerosis is found in the trunk and in the proximal zone of the lower limbs and sclerodactyly -also called diffuse systemic sclerosis-. This division of cutaneous involvement is also related to different clinical associations and different relationship with specific serum autoantibodies (9, 28). It should be noted that, as well as this division of cutaneous involvement, there is also the subtype of sine scleroderma (SSc), which affects 5% of patients with scleroderma and is based on having suggestive clinical features: Raynaud's phenomenon, digital ulcers, arterial pulmonary hypertension and autoantibodies for systemic sclerosis, without skin involvement (28).

When evaluating thoracic involvement in this entity, it should be taken into account that these patients may develop pulmonary fibrosis, an entity that is related to the presence of antitopoisomerase I antibodies, which is found in 10 to 16% of diffuse systemic sclerosis (27, 29). The most common pattern in this class of patients is NSIP (9). When reporting the results of the studies, an attempt should be made to determine the percentage of pulmonary involvement, since one greater than 20% (considered extensive) has a higher mortality rate and a rapid deterioration of pulmonary function (1).

Another finding in MDCT is arterial pulmonary hypertension, which can be related to pulmonary involvement (group 3) or by primary vasculopathy (group 1) (figure 5); however, it has also been found to be related to the presence of anti-centromere antibodies (ACA) (9, 29). A very frequent manifestation -described in approximately 97% of patients with systemic sclerosis - is esophageal dilatation, which can predispose to aspiration pneumonitis or bronchiolitis (Figure 5) (1).

4.3 Sjögren's Syndrome (SJ)

SJ is an autoimmune inflammatory disease related to the infiltration of T lymphocytes in different organs, such as lung, kidneys and exocrine glands (8). The most commonly affected are the exocrine glands - lacrimal and salivary glands - which inhibits glandular secretion and thus causes dry mucous membranes (8). It has a prevalence of 3% in adults, with predominance in women in a 9:1 ratio and tends to be more common in the fourth and fifth decades of life (30). It can be divided into primary SJ - found as the only clinical presentation - and secondary SJ - related to another autoimmune disease (8).

The main symptoms of this entity are xerophthalmia (keratoconjunctivitis sicca) and xerostomia (1). Other manifestations, such as epistaxis, nasal crusts or perforation of the nasal septum are due to the involvement of the upper respiratory tract (27). If the lower airway is affected, it presents with chronic symptoms, such as dry cough, dyspnea and recurrent bronchitis (30). In these patients it is relevant to determine the presence of B symptoms, since they are at higher risk of developing lymphoma -usually B-cell non-Hodgkin's lymphoma- (1).

Interstitial lung disease affects 25% of patients with SJ (7). Such involvement is more common in patients with primary SJ, and is observed with patterns such as NSIP, UIP, OP and LIP, less common with patterns of bronchiolitis or amyloidosis (1, 26). Formerly, it was suggested that LIP was the most characteristic pattern; however, recent studies found that NSIP is the prevalent pattern (7, 8). In MDCT, ILN is described as "ground-glass" areas, thickening of interlobular septa, nodules and thin-walled cysts (1) (Figure 6). In follicular bronchiolitis there is evidence of cyst formation secondary to the infiltration of lymphocytes in the bronchial wall that generates a secondary bronchiolar dilatation and, thus, the cystic appearance (1, 27).

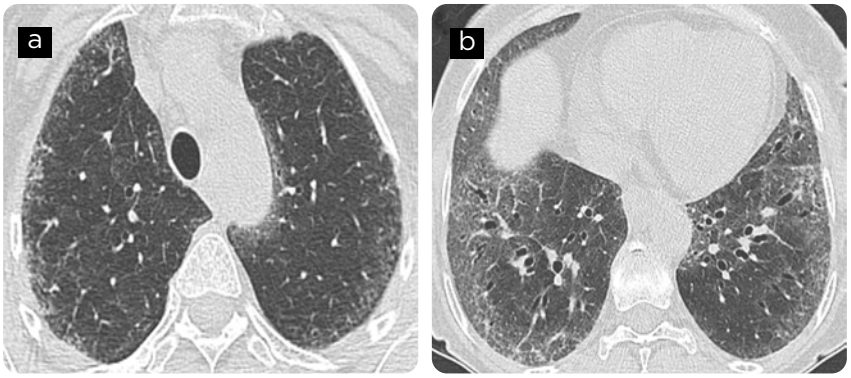

Figure 1. Patient with a diagnosis of nonspecific interstitial pneumonia (NSIP). Chest CT, lung window. a) Axial section in upper lobes and b) in lower lobes. Alteration of the pulmonary architecture with "ground-glass" opacities associated with reticulation and some traction bronchiectasis, without "honeycomb" formation; it configures an indeterminate pattern of interstitial pneumonia usual in histopathological study, which corresponds to non-specific interstitial pneumonia.

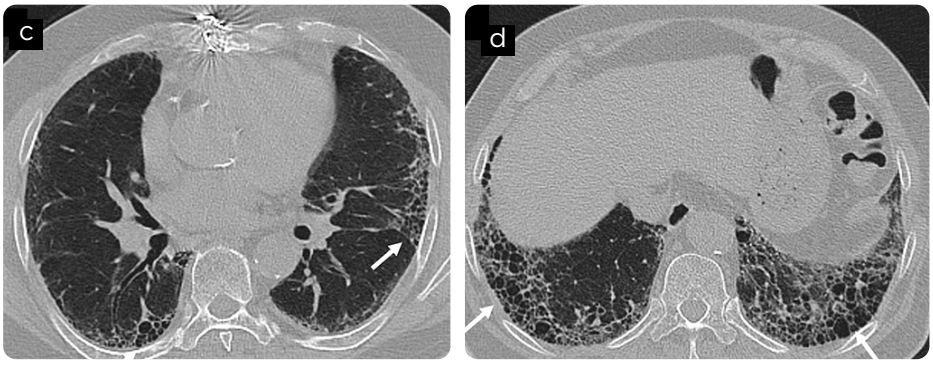

Figure 2. Patient with a diagnosis of usual interstitial pneumonia (UIP). Chest CT, lung window. a and b) Axial section in lower lobes. Alteration of the pulmonary architecture with "honeycomb" areas of subpleural predominance in lower lobes, associated with irregular thickening of interlobular septa and some traction bronchiectasis configuring a pattern of usual interstitial pneumonia..

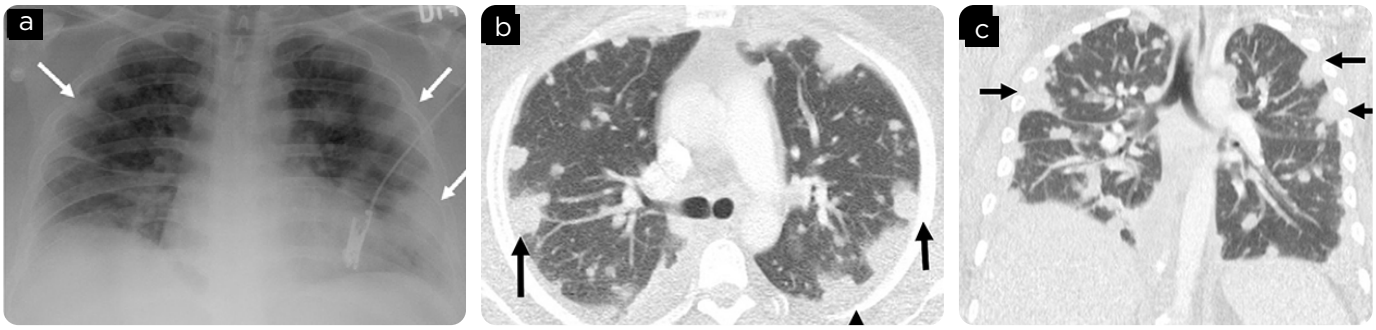

Figure 3. Patient with diagnosis of septic embolism. a) Chest X-ray with vanteroposterior projection. Multiple nodules with soft tissue density in both lungs, mostly subpleural predominance. Chest CT, b) infracarinal lung window and c) coronal reconstruction. Multiple solid nodules of subpleural predominance in the different lung segments, some of them show areas of central cavitation.

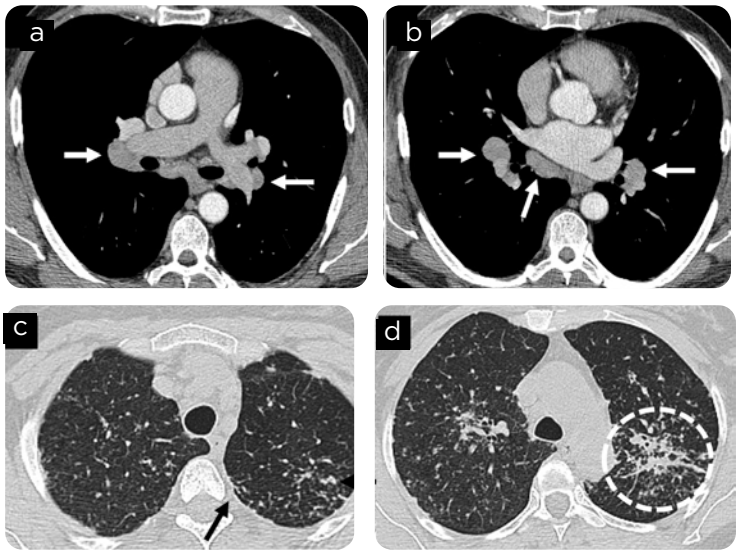

Figure 4. Patient with known diagnosis of sarcoidosis. Chest CT with contrast medium, mediastinal window. a) In the pulmonary artery and b) in lower lobes. Multiple symmetric and well-defined mediastinal adenomegalies, with homogeneous enhancement after the administration of contrast medium, predominantly in the parahilar (arrows) and infracarinal region. c and d) Simple CT of the thorax, window for lung in upper lobes. There are solid nodules with soft tissue density no larger than 5 mm, perilymphatic disposition (arrows), some of them converge forming "pseudomasses" and configured the sign of "the galaxy" (dotted line).

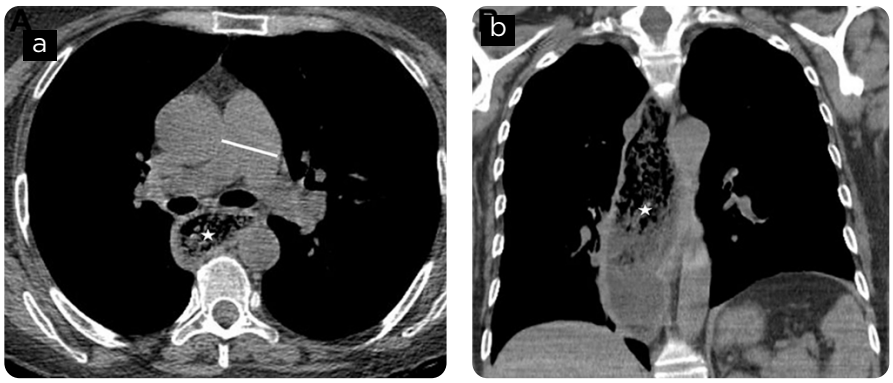

Figure 5. Patient with history of systemic sclerosis. Chest CT, mediastinal window. a) axial section in upper lobes and b) coronal reconstruction. Prominence of the main pulmonary artery due to pulmonary arterial hypertension (white line in a). There is dilatation of the esophagus in its three thirds (asterisk).

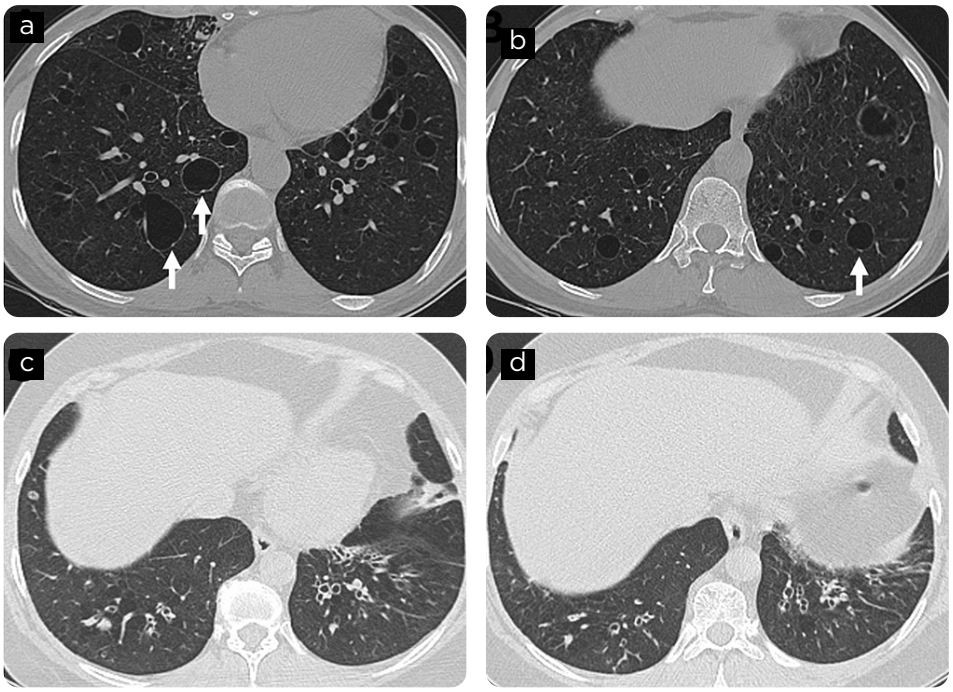

Figure 6. Two patients with known diagnosis of Sjögren's syndrome. a and b) CT window for lung, axial section in lower lobes. There are images of cystic appearance, of thin wall, predominantly in lower lobes associated with nodularity of the wall of some cysts (white arrow) in relation to lymphoid interstitial pneumonia. c and d) Chest CT, lung window, c) axial section in lower lobes d) and sagittal reconstruction. Bronchiectasis in lower lobes with bronchial wall thickening, especially in the left lower lobe, in a patient with a history of Sjögren's syndrome.

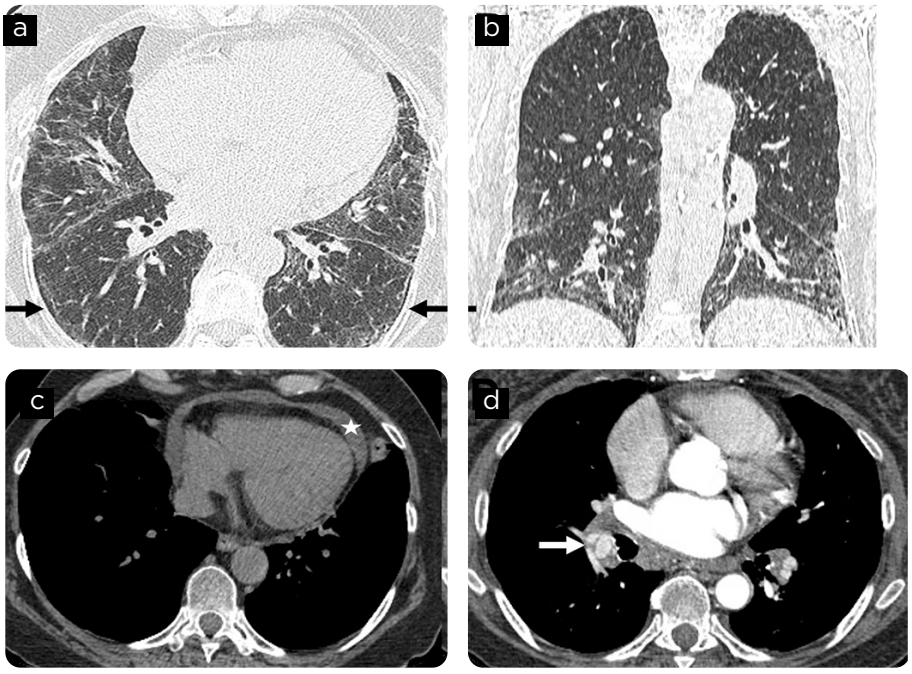

Figure 7. Patient with known diagnosis of SLE. a) High resolution CT, lung window, axial section in lower lobes and b) coronal reconstruction. Alteration of the pulmonary architecture with opacities in "ground glass" associated with reticulation and some traction bronchiectasis without "honeycomb" formation, which configures an indeterminate pattern of usual interstitial pneumonia. There are areas of subpleural compliance. These findings configure a non-specific interstitial pneumonia pattern. c) Patient with a history of SLE with chest pain. CT in mediastinal window. Low density image in the pericardium corresponding to pericardial effusion fluid (asterisk) in patient with a diagnosis of pericarditis in the context of SLE. d) Patient with a history of SLE and antiphospholipid syndrome. Chest CT with contrast medium in lower lobes. Chronic pulmonary thromboembolism is seen with a low density band, peripherally located, occupying the branch of the pulmonary artery to the right lower lobe (arrow).

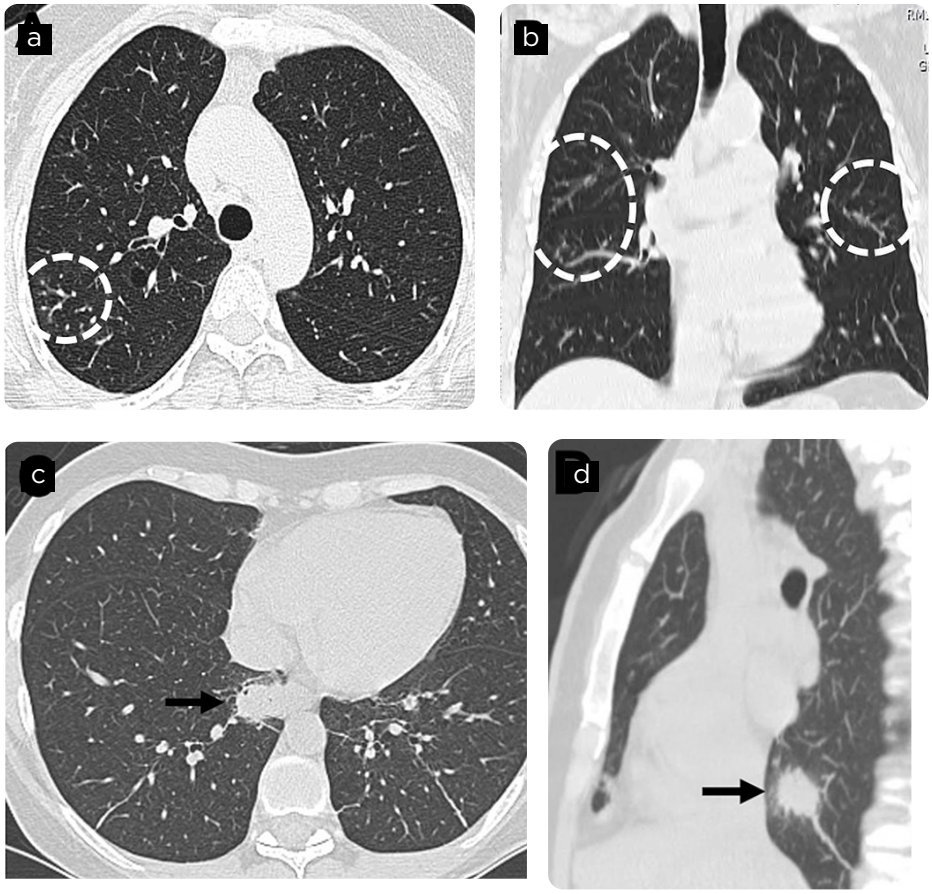

Figure 8. Two patients with known diagnosis of rheumatoid arthritis. CT, a) lung window, axial view and b) coronal reconstruction. There are non-specific areas of "tree in twinning" (dotted line), with histopathological report of follicular bronchiolitis in a patient with a history of rheumatoid arthritis. Chest CT, c) lung window, axial section in lower lobes and d) sagittal reconstruction. There is a solid, subpleural, oval nodule, with soft tissue density, partially defined contours with "ground glass" halo and small central area of low density (in a) related to rheumatoid nodule that resolved in subsequent controls.

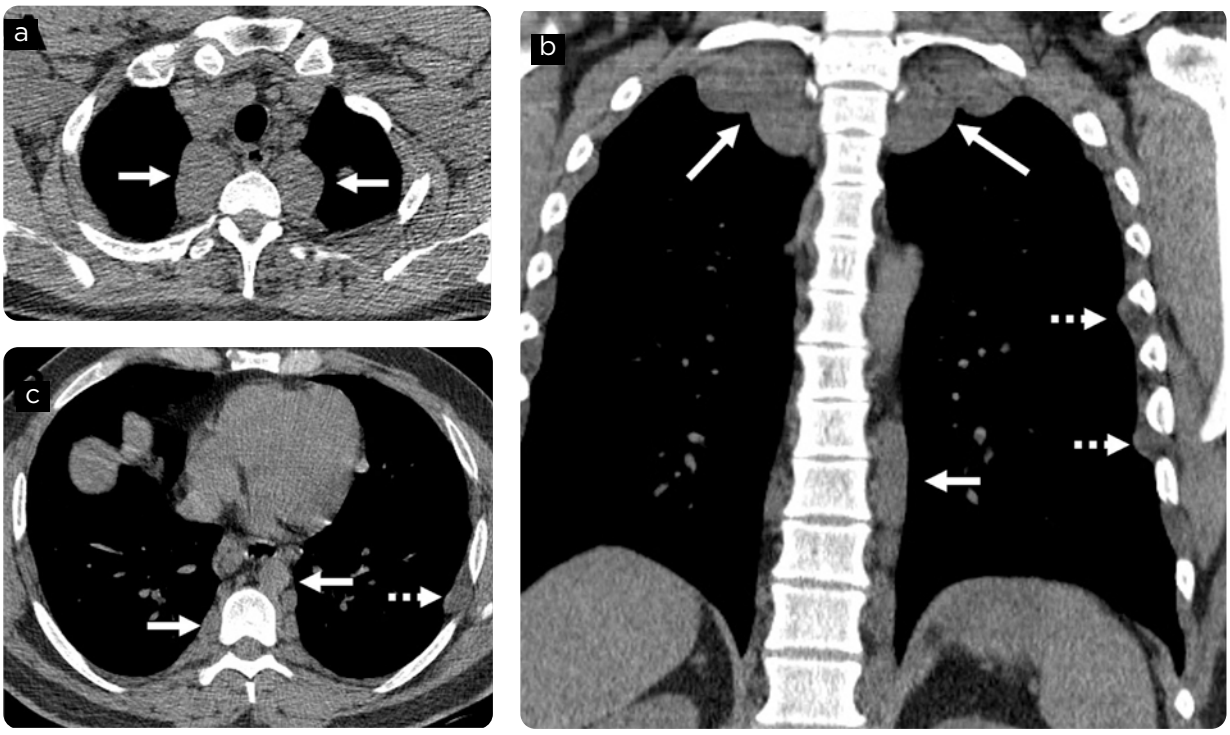

Figure 9. Patient with a history of neurofibromatosis. Simple multidetector CT of the thorax. a) Apical axial section in the upper lobes, b) caudal axial section in the upper lobes and c) coronal reconstruction. Nodular images with soft tissue density in the paravertebral mediastinal space (white arrows) and some in intercostal spaces (dotted arrow) corresponding to neurofibromas.

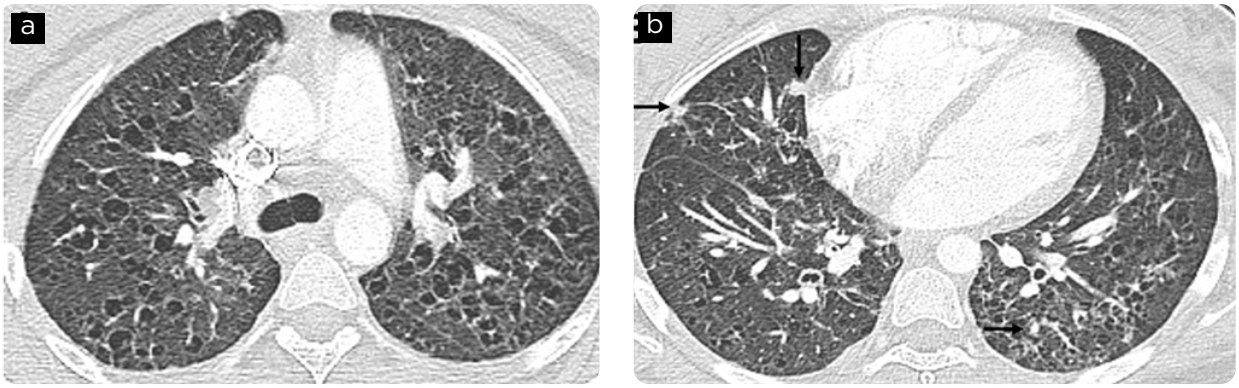

Figure 10. Patient with tuberous sclerosis and progressive respiratory symptoms. Chest CT, lung window. a) Axial section in upper lobes, b) axial section in lower lobes. Multiple areas of cystic appearance and thin wall in the four quadrants suggestive of lymphangioleiomyomatosis. There are some small nodules of random distribution (arrows).

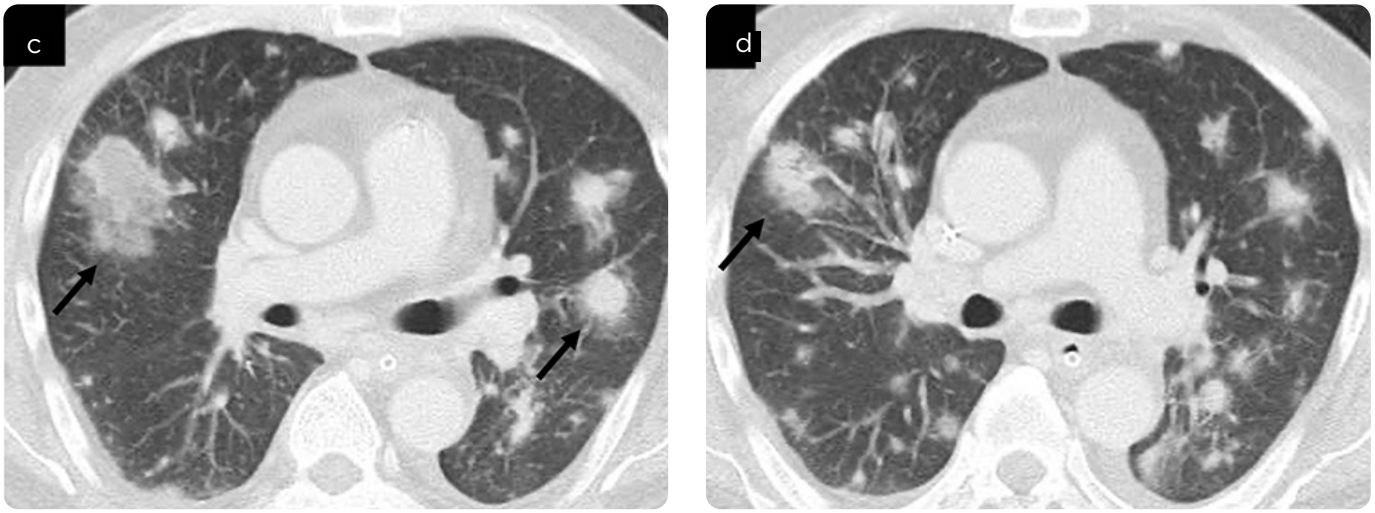

Figure 11. Patient with history of infection by human immunodeficiency virus. a and b) CT, axial section, in lung window. Some nodular opacities and masses of partially defined contours with "ground glass" halo distributed in the different pulmonary segments are observed in a patient with known diagnosis of Kaposi's sarcoma.

Other pathological findings in MDCT are airway complications, with bronchial wall thickening, bronchiectasis, bronchioloectasis and areas of air trapping (27) (figure 6). Pleural involvement or pleural effusion is rare; however, it may be related to other concomitant autoimmune diseases, such as RA or SLE (30). Finally, if consolidation, large nodules and pleural effusion are observed in MDCT, lymphoma should be ruled out (27).

4.4 Systemic lupus erythematosus (SLE)

SLE is a multisystem autoimmune disease of connective tissue that affects the skin, joints, kidneys and central nervous system (9). It has a prevalence of 20 to 70 per 100,000 people per year (27). This entity, which predominates in women during reproductive age (90%), has a peak presentation between 15 and 50 years of age (9). Apoptotic cells become antigenic due to the release of cellular debris, which generates immune complexes and complement activation, with tissue damage in the affected organ (9).

Among the most affected organs are the kidneys (lupus nephritis) and the skin (31). Dermatological involvement occurs in 75% of patients during the course of the disease, so it is important to characterize it early, since 25% of patients present skin alterations weeks or months before having systemic symptoms (31). The manifestations of cutaneous lupus erythematosus include malar erythema in "butterfly wings", subacute presentations with areas of alopecia and hypopigmentation, recurrent manifestations such as papules and non-scarring plaques related to exposure to UV rays on the face, zygomatic area and hands, as well as other variants, such as annular with erythematous plaques in the form of a ring (31).

Regarding thoracic involvement, it is important to point out that respiratory symptomatology is null or mild; however, pleuritic pain is the main symptom, and it is related to the imaging finding of bilateral pleural effusion and pleural thickening, which are considered manifestations of serositis (9). These findings have been described in 61% of patients and as a consequence, a small percentage may develop fibrothorax, a complication in which smooth pleural thickening, non-free pleural effusion or pleural collections and underlying atelectasis are evidenced (27, 32).

Infectious complications secondary to alterations (primary or secondary) of the immune system of these patients may be other ma-

nifestations found, especially those under immunomodulator management (27). The finding of community-acquired pneumonia is the most common; however, atypical microorganisms such as tuberculous and non-tuberculous mycobacteria, Pneumocystis jirovecii, Cytomegalovirus and Aspergillus should also be taken into account (33).

Interstitial involvement in SLE is uncommon, affecting between 3% and 8% of patients (34). The most frequent pattern is NSIP (1, 27) (figure 7). Chest radiography tends to be of little significance, since in mild to moderate stages the findings are usually subtle (32). The HRCT is of great importance, since it allows assessing the areas of "ground glass" in early interstitial involvement (34).

Other manifestations, such as diffuse consolidations, should suggest uncommon entities, but which put the patient's life at risk, such as alveolar hemorrhage or pneumonitis, which appear in less than 2% and 1.4% to 4% of patients, respectively (9, 34). Another entity to look for, taking into account the relationship of SLE with antiphospholipid syndrome, is pulmonary thromboembolism (Figure 7), which should be ruled out in patients with acute dyspnea with associated pleuritic pain (35). However, there are very rare manifestations, such as the "shrinking lung syndrome", described in 1965 as a progressive decrease in lung volume associated with dyspnea and pleuritic pain (36). Chest radiographic and MDCT findings, such as unilateral or bilateral elevation of the diaphragm, basal atelectasis and no evidence of parenchymal involvement, give the appearance of volume loss or atelectasis (36, 37).

In 58% to 77% of cases there are cardiovascular manifestations, the most frequent is pericarditis which debuts as pericardial effusion (32) (figure 7). Other cardiac conditions related to SLE are: myocarditis, valvular alterations - such as Libman-Sacks endocarditis - and premature atherosclerosis of the coronary arteries (32).

4.5 Rheumatoid arthritis

Rheumatoid arthritis (RA) is the most common connective tissue disease, affecting 1% of the world's population, mostly women between 25 and 50 years of age (27). It is an inflammatory, symmetrical polyarthropathy involving the hands and feet; it can also cause involvement of other organs (e.g. pericarditis, splenomegaly, ocular inflammation and subcutaneous nodules) (38).

Extra-articular manifestations occur in 40% of patients diagnosed with RA (39). They are more frequent in men and are related to a higher elevation of rheumatoid factor and anti-cyclic citrullinated peptide antibody (anti-CCP) titers (40). Cutaneous involvement is one of the most frequent forms, and includes clinical presentations such as rheumatoid nodules, rheumatoid nodulosis, Felty syndrome, rheumatoid vasculitis, pyoderma gangrenosum, among others, without forgetting the cutaneous involvement related to RA treatment (41).

In patients with RA there is a relationship between smoking and the appearance of more severe pulmonary manifestations (38). Between 38% to 73% of patients with RA present pleural involvement, mainly pleural effusion, findings that are not necessarily related to lung parenchymal disease (27). Pleural involvement can trigger complications such as pleural thickening that generates a pulmonary restrictive effect (38). In addition, there may be much rarer complications, such as a pseudocychothorax, in which the pleural effusion is cholesterol-rich, although the pathophysiologic mechanism of this complication is unclear (38).

Among the airway conditions of RA, cricoarytenoid arthritis, vocal cord paresis and bronchiectasis are described, the latter found in a HRCT in 30% of patients, without association with pulmonary fibrosis (38, 42). Among the complications related to the airway in RA are bronchiolitis obliterans -characterized by reduction in the bronchial lumen due to infiltration of mononuclear cells-, which appears in HRCT with an "attenuation mosaic" pattern with air trapping in images obtained in expiration (1). Another complication is follicular bronchiolitis, also called lymphoid pulmonary hyperplasia, which is found within the spectrum of lymphoid interstitial pneumonia (LIP) with areas of "twinning tree" and occasionally associated bronchiectasis (38) (figure 8). LIP involvement may be evident on chest radiograph as nodular or reticulonodular opacities; however, in some cases the radiograph is normal (38). In a HRCT, centrolobulillary nodules with measures of 1 to 12 mm in diameter and with halo in "ground glass" are evidenced, in addition, in the parenchyma there are patches of opacities in "ground glass", bronchiectasis and "tree in gemmation" (38).

On the other hand, rheumatoid pulmonary nodules are found in 20% of patients diagnosed with RA (43) (Figure 8). These nodules are related to the appearance of subcutaneous nodules and are evident during advanced stages of the disease; however, their presence does not reflect disease activity (38). In MDCT, solid nodules with well-defined borders, no larger than 5 cm, located in the periphery and cavitated are observed in 50% of the cases (38). If the nodules have calcifications, they could indicate Caplan's syndrome, which is related to occupational disease -such as silicosis, which is the most frequent one (1)-.

Interstitial involvement occurs in 20-30% of patients, mainly with UIP, and OP patterns, with predominance of UIP, and is accompanied by other concomitant findings, such as pleural involvement, suggesting a diagnosis of RA (38).

Other side effects result from RA treatment. Pulmonary toxicity may occur with methotrexate use in 5% to 10% of cases; however, no relationship has been found between specific doses or duration of time to present pulmonary toxicity (43, 44). On the other hand, the use of tumor necrosis factor (TNF) antagonists, such as infliximab, can be related to the appearance of granulomatous infections in approximately 239 out of every 100,000 patients; of these, the most frequent is infection by Mycobacterium tuberculosis, for which reason the British Thorax Society (BTS) recommends taking a chest X-ray before initiating this therapy (45, 46).

5. Hereditary etiology

5.1 Neurofibromatosis type 1

Neurofibromatosis type 1 (NF-1), also called Von Recklinghausen's disease, is a neurocutaneous syndrome with autosomal dominant inheritance pattern caused by mutation of the NF1 gene, located on chromosome 17 (9). However, in up to 50% of cases it can occur by spontaneous mutation (47). NF1 is the most common disease of the phakomatosis group, occurring in 1 out of every 2,000 live births (47). The most frequently affected organs include the skin, central nervous system, bones, and endocrine glands (47).

The cutaneous involvement is characterized by "café au lait" spots, neurofibromas and hamartomas in the iris called "Lisch nodules" (9). These neurofibromas are produced from Schwann cells and fibroblasts

in any peripheral nerve, most frequently in the V cranial nerve, and usually in 30% of patients it is found as the only clinical presentation (48). However, the typical clinical manifestation of NF1 consists of circumscribed areas of skin with increased "café-au-lait" spots and cutaneous or subcutaneous tumors (49). There may also be other findings, such as axillary freckling, Lisch nodules, bone dysplasias and multiple CNS tumors (gliomas in optic nerves) (48, 49).

In the thorax, NF1 tends to appear more in soft tissues, due to the distribution of peripheral nerves on its surface (9). The main findings are: well-defined subcutaneous neurofibromas, thoracic scoliosis, alteration in the morphology of the vertebral bodies, mediastinal involvement by neurogenic tumors (neurofibromas and schwannomas) (Figure 9) and abnormalities in the configuration of the ribs due to bone dysplasia or erosion by adjacent neurofibromas (47). Subcutaneous neurofibromas are nodules with soft tissue density, they are usually multiple and well defined, they do not have significant contrast enhancement. The differential diagnosis should include primary and secondary cutaneous neoplasms, sebaceous cysts or epidermal cysts (seen, for example, in Gardner's syndrome) (47).

However, within the uncommon involvement of the lung by NF1, areas of cystic appearance or bullae can be found, predominantly in the upper lobes and subpleural location simulating a paraseptal emphysema (9). In addition, the lung bases may be involved by interstitial pulmonary abnormalities, with subpleural bands and reticulation suggestive of pulmonary fibrosis (9).

5.2 Tuberous sclerosis

Tuberous sclerosis is an autosomal dominant disease related to the mutation of the tumor suppressor gene TSC1 on chromosome 9 and TSC2 on chromosome 16 (50). These mutations predispose to the generation of benign, circumscribed, non-invasive lesions that can originate in any organ (50). This entity occurs in approximately 1 in 6,000 live births (51). Prenatal diagnosis by ultrasound and MRI has been described, with the identification of cardiac and cerebral lesions (50).

Ninety percent of patients develop skin manifestations (9, 50). Other frequently affected organs include the brain in 90%, the kidneys in 70% to 90%, and the retina in 40% to 50% of patients (50). Cutaneous manifestations include sebaceous adenomas and periungual fibromas, also called Koenen's tumors, in 25% of patients with tuberous sclerosis (9, 50). Other manifestations described, but less specific, are Fitzpatrick's patches, hypomelanotic lesions and orange peel lesions on the dorsum that usually represent hamartomas (9, 50).

Lymphangioleiomyomatosis (LAM) is part of the spectrum of thoracic involvement in patients with tuberous sclerosis, affecting premenopausal women, and very occasionally men (50). LAM can be sporadic or related to tuberous sclerosis, the latter with an estimated frequency of 1% to 3% of patients with tuberous sclerosis (50, 52). LAM is characterized by a replacement of the pulmonary parenchyma by cystic lesions, due to a proliferation of cells similar to those of the alveolar smooth muscle, but with receptors for progesterone, estrogens and melanin-related proteins (53). Chest radiography may show increased pulmonary volumes with diaphragmatic flattening, increased retrosternal space and reticular opacities, although it should be noted that chest radiography is considered normal in up to 26% of patients (54). Diffuse cysts with thin walls, usually no larger than 20 mm, and associated pulmonary nodules appear in the HRCT (figure 10). If the nodules are larger, pulmonary angiomyolipomas may be considered as a differential diagnosis (9).

6. Acquired etiology

6.1 Kaposi's sarcoma

Kaposi's sarcoma consists of multisystemic mesenchymal lesions involving blood vessels and lymphatic vessels (9). Its etiology is related to latent infection by herpes virus 8, which is a reactive process and not a neoplastic process as previously considered (9). This entity is clearly associated with AIDS, with a CD4 count of less than 100 cells per milliliter; however, the prevalence of the disease has decreased considerably thanks to timely antiretroviral therapy (55).

One of the most affected organs is the skin; however, it can also affect the gastrointestinal tract, lymph nodes and lung (9). Dermatologic involvement is important, as it may precede systemic involvement (56). Small pink and later violaceous skin lesions are the main cutaneous finding (9).

Pulmonary involvement occurs in 45% of cases, 15% of them without associated cutaneous effect (56). Thoracic involvement may involve the lung, trachea, pleura or chest wall (9, 56). The initial study with chest radiography may reveal primary disease or infections by opportunistic germs (56). When the chest radiograph shows reticular opacities, associated with pulmonary nodules and thickening of the peribronchovascular interstitium that predominates in the middle lobe and lower lobes, it suggests primary disease due to Kaposi's sarcoma (56). In some cases the chest radiograph may be normal (9, 57). The HRCT shows ill-defined, bilateral nodules, with peribronchovascular distribution, usually with a diameter greater than 1 cm, in some cases with a "halo" sign (56) (figure 11). Mediastinal adenomegaly can be found in up to 50% of patients (9). On the other hand, cutaneous and subcutaneous masses or lytic lesions of the sternum or in the thoracic spine are the characteristics of the involvement of the thoracic wall (56, 58).

The relevant radiological findings in each of the aforementioned entities are summarized in Table 1.

Table 1. Summary of radiologic findings of systemic diseases with thoracic and dermatologic involvement

Entity	Main radiological findings	Complementary radiological findings
Septic embolism	Pulmonary nodules with ill-defined margins, cavitated.	Pleural effusion, empyema.
SAPHO syndrome	Hyperostosis in the anterior chest wall, especially in the sternoclavicular and sternocostal junction.	*Bull head* sign in the sternoclavicular region on bone scan.
Sarcoidosis	Mediastinal and parahilar adenomegalies and nodules of perilymphatic and subpleural distribution.	Pleural plaques, pleural effusion, tracheal stenosis or nodular thickening of bronchial walls.
Polymyositis/ dermatomyositis	Interstitial disease (78 %): predominantly OP (44 %), UIP (37 %) and (13.7 %).	Aspiration pneumonia, intercostal muscle thinning.
Systemic sclerosis	Interstitial disease (70-90 %): (70 %), UIP (26 %).	Pulmonary arterial hypertension, esophageal dilatation.
Sjögren's syndrome	Interstitial disease (25 %): (45 %), UIP (13 %), OP (10 %), LIP (3 %).	Bronchial wall thickening, bronchiectasis, bronchioloectasis.
Systemic lupus erythematosus	Bilateral pleural effusion and pleural thickening, pericardial effusion, pulmonary thromboembolism.	Bacterial pneumonia due to common germs, alveolar hemorrhage.
Rheumatoid arthritis	Interstitial disease (5-58 %): UIP (41 %), (30 %) and OP (8 %).	Rheumatoid pulmonary nodules, drug-induced pneumonitis, pleural effusion.
Neurofibromatosis type 1	Neurogenic tumors (neurofibromas and schwannomas), subcutaneous neurofibromas.	Areas of cystic appearance or bullae predominantly in upper lobes.
Kaposi's sarcoma	Pulmonary nodules of peribronchovascular distribution with "halo" sign.	Mediastinal adenomegalies.

Conclusions

In radiological practice it is very valuable to recognize cutaneous manifestations when approaching a group of differential diagnoses whose pathophysiology affects lung tissue and skin. The recognition of these findings and their relationship with the different entities increases the diagnostic certainty and allows a timely diagnosis to establish an appropriate management.

References

1. Aluja-Jaramillo F, Acosta L Gutiérrez FR. Neumonitis por hipersensibilidad y enfermedades del tejido conjuntivo. En: Criales Cortes JL y Gutiérrez FR. Avances en diagnóstico por imágenes: Tórax 2. 2 ed. Buenos Aires: Ediciones Journal; 2019. pp 29-43.
2. Raghu G, Remy-Jardin M, Myers JL, Richeldi L, Ryerson CJ, Lederer DJ, et al. Diagnosis of idiopathic pulmonary fibrosis. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. Am J Respir Crit Care Med. 2018;198(5):e44-e68. doi:10.1164/rccm.201807-1255ST
3. Kim DS, Yoo B, Lee JS, Kim EK, Lim CM, Lee SD, et al. The major histopathologic pattern of pulmonary fibrosis in scleroderma is nonspecific interstitial pneumonia. Sarcoidosis Vasc Diffuse Lung Dis. 2002;19(2):121-7.
4. De Lauretis A, Veeraraghavan S, Renzoni E. Review series: Aspects of interstitial lung disease: connective tissue disease-associated interstitial lung disease: how does it differ from IPF? How should the clinical approach differ? Chron Respir Dis. 2011;8(1):53-82. doi:10.1177/1479972310393758
5. Kang EH, Lee EB, Shin KC, Im CH, Chung DH, Han SK, et al. Interstitial lung disease in patients with polymyositis, dermatomyositis and amyopathic dermatomyositis. Rheumatology (Oxford). 2005;44(10):1282-6. doi:10.1093/rheumatology/keh723
6. Tanaka N, Kim JS, Newell JD, Brown KK, Cool CD, Meehan R, et al. Rheumatoid arthritis-related lung diseases: CT findings. Radiology 2004,232:81-91. doi: 10.1148/radiol.2321030174
7. Castelino FV, Varga J. Interstitial lung disease in connective tissue diseases: evolving concepts of pathogenesis and management. Arthritis Res Ther. 2010;12(4):213. doi:10.1186/ar3097
8. Ito I, Nagai S, Kitaichi M, Nicholson AG, Johkoh T, Noma S, et al. Pulmonary manifestations of primary Sjogren's syndrome: a clinical, radiologic, and pathologic study. Am J Respir Crit Care Med. 2005;171(6):632-8. doi:10.1164/rccm.200403-417OC
9. Kanne JP, Yandow DR, Haemel AK, Mayer CA. Beyond skin deep: Thoracic manifestations of systemic disorders affecting the skin. Radiographics 2011;31(6):1651-68. doi: 10.1148/rg.316115516
10. Murdoch DR, Corey GR, Hoen B, Miró JM, Fowler VG Jr, Bayer AS, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis–Prospective Cohort Study. Arch Intern Med. 2009;169(5):463-73. doi: 10.1001/archinternmed.2008.603
11. Dodd, JD, Souza C, Müller NL. High-Resolution MDCT of pulmonary septic embolism: Evaluation of the feeding vessel sign. Am J Roentgenol. 2006;187(3):623-9. doi:10.2214/ajr.05.0681
12. Servy A, Valeyrie-Allanore L, Alla F, Lechiche K, Nazeyrollas P, Chidiac C, et al. Prognostic value of skin manifestations of infective endocarditis. JAMA Dermatol. 2014;150:494-500. doi: 10.1001/jamadermatol.2013.8727
13. Evangelista A. Echocardiography in infective endocarditis. Heart. 2004;90(6):614-7. doi: 10.1136/hrt.2003.029868
14. Depasquale R, Kumar N, Lalam RK, Tins BJ, Tyrrell PNM, Singh J, Cassar-Pullicino VN. SAPHO: What radiologists should know. Clin Radiol. 2012;67(3):195–206. doi:10.1016/j.crad.2011.08.014
15. Lew PP, Ngai SS, Hamidi R, Cho JK, Birnbaum RA, Peng DH, Varma RK. Imaging of disorders affecting the bone and skin. RadioGraphics. 2014;34(1):197-216. doi:10.1148/rg.341125112
16. Hotta M, Minamimoto R, Kaneko H, Yamashita H. Fluorodeoxyglucose PET/CT of arthritis in rheumatic diseases: A pictorial review. RadioGraphics. 2020;40(1):223-40. doi:10.1148/rg.2020190047
17. Fernández-Faith E, McDonnell J. Cutaneous sarcoidosis: differential diagnosis. Clin Dermatol. 2007;25(3):276-87. doi: 10.1016/j.clindermatol.2007.03.004
18. Aluja-Jaramillo F, Quiasúa-Mejía DC, Martínez-Ordúz HM, González-Ardila C. Nail unit ultrasound: a complete guide of the nail diseases. J Ultrasound. 2017;20(3):181-92. doi:10.1007/s40477-017-0253-6
19. Siltzbach LE. Sarcoidosis: Clinical features and management. Med Clin North Am. 1967;51(2):483-502. doi:10.1016/s0025
20. Nakatsu M, Hatabu H, Morikawa K, Uematsu H, Ohno Y, Nishimura K, et al. Large coalescent parenchymal nodules in pulmonary sarcoidosis: "sarcoid galaxy" sign. AJR Am J Roentgenol. 2002;178(6):1389-93. doi: 10.2214/ajr.178.6.1781389
21. Reddy G, Ahuja J. Thoracic sarcoidosis: Imaging patterns. Sem Roentgenol. 2018:54(1):59-65. doi: https://doi.org/10.1053/j.ro.2018.12.008
22. Aluja-Jaramillo F, Gutiérrez FR, Rossi S, Bhalla S. Nonneoplastic tracheal abnormalities on CT. CDR. 2020;43(13):1-8. doi: 10.1097/01.CDR.0000668644.62958.46
23. Dalakas MC. Inflammatory muscle diseases: a critical review on pathogenesis and therapies. Curr Opin Pharmacol. 2010;10(3):346-52. DOI: 10.1016/j.coph.2010.03.001
24. Mainetti C, Terziroli Beretta-Piccoli B, Selmi C. Cutaneous manifestations of dermatomyositis: A comprehensive review. Clin Rev. 2017;53(3):337-56. doi: 10.1007/s12016-017-8652-1
25. Hallowell R, Ascherman D, Danoff S. Pulmonary manifestations of polymyositis/dermatomyositis. Sem Respir Crit Care Med. 2014;35(2):239-48. doi: 10.1055/s-0034-1371528.
26. Owens GR, Follansbee WP. Cardiopulmonary manifestations of systemic sclerosis. Chest. 1987;91(1):118-27. doi: 10.1378/chest.91.1.118
27. Copobianco J, Grimberg A, Thompson BM, Antunes VB, Jasinowodolinski D, Meirelles GS. Thoracic manifestations of collagen vascular diseases. Radiographics 2012;32:33-50. doi: 10.1148/rg.321105058
28. Denton CP, Khanna D. Systemic sclerosis. The Lancet. 2017;390(10103):1685-99. doi: 10.1016/S0140-6736(17)30933-9.
29. Hamaguchi Y. Autoantibody profiles in systemic sclerosis: predictive value for clinical evaluation and prognosis. J Dermatol. 2010;37(1):42-53. doi: 10.1111/j.1346-8138.2009.00762.x
30. Stojan G, Baer AN, Danoff SK. Pulmonary manifestations of Sjögren's syndrome. Curr Allergy Asthma Rep. 2013;13(4):354-60. doi:10.1007/s11882-013-0357-9

31. Obermoser G, Sontheimer RD, Zelger B. Overview of common, rare and atypical manifestations of cutaneous lupus erythematosus and histopathological correlates. Lupus. 2010;19(9):1050-70. doi: 10.1177/0961203310370048
32. Goh YP, Naidoo P, Ngian GS. Imaging of systemic lupus erythematosus. Part I: CNS, cardiovascular, and thoracic manifestations. Clin Radiol. 2013;68(2):181-91. doi:10.1016/j.crad.2012.06.110
33. Kinder BW, Freemer MM, King TE Jr, Lum RF, Nitiham J, Taylor K, et al. Clinical and genetic risk factors for pneumonia in systemic lupus erythematosus. Arthritis Rheum. 2007;56(8):2679-86. doi: 10.1002/art.22804
34. Paran D, Fireman E, Elkayam O. Pulmonary disease in systemic lupus erythematosus and the antiphospholipid syndrome. Autoimmun Rev. 2004;3(1):70-5. doi: 10.1016/S1568-9972(03)00090-9.
35. Wahl DG, Guillemin F, de Maistre E, Perret C, Lecompte T, Thibaut G. Risk for venous thrombosis related to antiphospholipid antibodies in systemic lupus erythematosus a meta analysis. Lupus. 1997;6(5):467-73. doi: 10.1177/096120339700600510.
36. Hoffbrand BI, Beck ER. "Unexplained" dyspnoea and shrinking lungs in systemic lupus erythematosus. BMJ. 1965;1(5445):1273-7. doi: 10.1136/bmj.1.5445.1273
37. Warrington KJ, Moder KG, Brutinel WM. The shrinking lungs syndrome in systemic lupus erythematosus. Mayo Clin Proc. 2000;75(5):467-72. doi: https://doi.org/10.4065/75.5.467
38. Massey H, Darby M, Edey A. Thoracic complications of rheumatoid disease. Clin Radiol. 2013;68(3):293-301. doi:10.1016/j.crad.2012.07.007.
39. Turesson C, Fallon WM, Crowson CS, Gabriel SE, Matteson EL. Extraarticular disease manifestations in rheumatoid arthritis: incidence trends and risk factors over 46 years. Ann Rheum Dis. 2003:62(8):722-7. doi: 10.1136/ard.62.8.722.
40. Prete M, Racanelli V, Digiglio L, Vacca A, Dammacco F, Perosa F. Extra-articular manifestations of rheumatoid arthritis: An update. Autoimmunity Reviews. 2011;11(2):123-31. doi:10.1016/j.autrev.2011.09.001
41. Lora V, Cerroni L, Cota C. Skin manifestations of rheumatoid arthritis. G Ital Dermatol Venereol. 2018;153(2):243-55. doi: 10.23736/S0392-0488.18.05872-8
42. Lieberman-Maran L, Orzano IM, Passero MA, Lally EV. Bronchiectasis in rheumatoid arthritis: Report of four cases and a review of the literature implications for management with biologic response modifiers. Sem Arthr Rheumat. 2006;35(6):379-87. doi:10.1016/j.semarthrit.
43. Franquet, T. High-resolution CT of lung disease related to collagen vascular disease. Radiol Clin North America. 2001;39(6):1171-87. doi:10.1016/s0033-8389(05)70337-7.
44. Rossi SE, Erasmus JJ, McAdams HP, Sporn TA, Goodman PC. Pulmonary drug toxicity: Radiologic and pathologic manifestations. RadioGraphics. 2000;20(5):1245-59. doi:10.1148/radiographics.20.5.g00se081245
45. Wallis RS, Broder MS, Wong JY, Hanson ME, Beenhouwer DO. Granulomatous infectious diseases associated with tumor necrosis factor antagonists. Clin Infect Dis. 2004;38(9):1261-5. doi:10.1086/383317
46. British Thoracic Society Standards of Care Committee. BTS recommendations for assessing risk and for managing Mycobacterium tuberculosis infection and disease in patients due to start anti-TNF- treatment, Thorax. 2005;60(10):800-5. doi:10.1136/thx.2005.046797
47. Fortman BJ, Kuszyk BS, Urban BA, Fishman EK. Neurofibromatosis Type 1: A diagnostic mimicker at CT. RadioGraphics. 2001;21(3):601-12. doi:10.1148/radiographics.21.3.g01ma05601
48. Boley S, Sloan JL, Pemov A, Stewart DR. A quantitative assessment of the burden and distribution of lisch nodules in adults with neurofibromatosis type 1. Investigative Opthalmology & Visual Science. 2009;50(11):5035. doi:10.1167/iovs.09-3650
49. Williams M, Verity CM. Optic nerve gliomas in children with neurofibromatosis. Lancet. 1987;1:1318-9.
50. Curatolo P, Bombardieri R, Jozwiak S. Tuberous sclerosis. The Lancet. 2008;372(9639):657-68. doi:10.1016/s0140-6736(08)61279-9
51. Osborne JP, Fryer A, Webb D. Epidemiology of tuberous sclerosis. Ann N Y Academy Sciences. 1991;615:125-7. doi: https://doi.org/10.1111/j.1749-6632.1991.tb37754.x
52. Hancock E, Osborne J. Lymphangioleiomyomatosis: a review of the literature. Respir. Med. 2002;96:1-6. doi: 10.1053/rmed.2001.1207.
53. Ferrans VJ, Yu ZX, Nelson WK, et al. Lymphangioleiomyomatosis (LAM): a review of clinical and morphological features. J Nippon Med Sch. 2000;67(5):311-29. doi: 10.1272/jnms.67.311.
54. Chu SC, Horiba K, Usuki J, Avila NA, Chen CC, Travis WD, et al. Comprehensive evaluation of 35 patients with lymphangioleiomyomatosis. Chest. 1999;115(4):1041-52. doi:10.1378/chest.115.4.1041
55. Bower M, Palmieri C, Dhillon T. AIDS-related malignancies: changing epidemiology and the impact of highly active antiretroviral therapy. Curr Opin Infect Dis. 2006;19(1):14-9. doi: 10.1097/01.qco.0000200295.30285.13.
56. Restrepo CS, Martínez S, Lemos JA, Carrillo JA, Lemos DF, Ojeda P, Koshy P. Imaging manifestations of Kaposi sarcoma. Radiographics. 2006;26(4):1169-85. doi: 10.1148/rg.264055129.
57. Willatt HJ, Moyano NC, Apey RC, Lidid AL. Sarcoma de Kaposi extratorácico: evidencias de una enfermedad multisistémica. Rev. chil. radiol. 2010;16(2):80-5. http://dx.doi.org/10.4067/S0717-93082010000200008
58. Wolff SD, Kuhlman JE, Fishman EK. Thoracic Kaposi sarcoma in AIDS: CT findings. J Comput Assist Tomogr. 1993;17(1):60-2. doi: 10.1097/00004728-199301000-00010.

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