PICTORIAL REVIEW

THORACIC INVOLVEMENT IN CONNECTIVE TISSUE DISEASES: RADIOLOGICAL PATTERNS AND FOLLOW-UP

G. Serra1, A.-L. Brun1, P. Ialongo2, M.-L. Chabi1, P.A. Grenier1

Connective tissue diseases (CTDs) are a heterogeneous group of idiopathic inflammatory diseases involving various organs. A thoracic involvement is frequent, and chest CT represents the imaging technique of reference in its assessment. Pulmonary abnormalities related to CTDs are various; although several disease-specific aspects have been described, the two most clinically relevant complications are represented by interstitial lung disease and pulmonary arterial hypertension. The early identification of a thoracic involvement, with the adoption of specific therapies, can significantly change patient’s prognosis. The aim of this article is to review the most common typical and atypical CT features of thoracic involvement occurring in CT, especially focusing on interstitial lung disease.

Key-word: Connective tissue, diseases – Lung, interstitial disease – Hypertension, pulmonary.

Connective tissue diseases (CTDs) are a heterogeneous group of inflammatory diseases derived from an immunologic deregulation affecting various organs. A thoracic involvement (pulmonary, pleural or mediastinal) can be frequently found; its frequency and expression depends on the type of disease, and may induce an extremely wide range of abnormalities (1-3).

All CTDs can present a pulmonary involvement: rheumatoid arthritis (RA), progressive systemic sclerosis (PSS), systemic lupus erythematosus (SLE), polymyositis and dermatomyositis (PM/DM), mixed connective tissue disease (MCTD), Sjögren syndrome (SJOS), and relapsing polychondritis (RP). The identification of a pulmonary involvement at its initial stage is crucial, as an early treatment can often improve patients’ prognosis. Interstitial lung disease and pulmonary arterial hypertension, both significantly affecting morbidity and mortality in these patients, represent the two most clinically relevant complications in CTD, particularly PSS, PM/DM and MCTD. It is characterized histologically by relatively homogeneous expansion of the alveolar walls by inflammation, fibrosis or both. UIP is the second most commonly pattern of chronic ILD and seen most frequently in patients with PSS and RA. The pathologic findings of UIP consist of patchy heterogeneous pattern with foci of normal lung, interstitial inflammation, fibrosis and honeycombing. Fibroplastic foci are present but less extensive in CTD than in idiopathic pulmonary fibrosis, and this feature probably accounts for the better prognosis in these patients (5, 7).

The most common CTD associated with OP is PM/DM. OP also occurs in increased frequency in RA and has been described in SLE and SJOS. The histologic pattern of OP is made of intraluminal plugs of granulation tissue within alveolar ducts and surrounding alveoli associated with chronic inflammation in the alveolar walls. The patients usually respond well to corticosteroid therapy and have a good prognosis. However patients with OP associated with CTD seem to have a greater tendency to develop fibrosis and a higher mortality than patients with cryptogenic OP (5, 6). The CTD, typically associated with LIP, is SJOS; however LIP may also occasionally be seen in SLE and RA (Table I).

Patients with CTD and chronic ILD similar to those with idiopathic ILD, may develop acute exacerbation. Such acute exacerbation is most common in chronic ILD associated with RA but may be seen in PSS, PM/DM and SJOS. Despite intensive anti-inflammatory immunosuppressive therapy, the prognosis of acute exacerbation of CTD associated with ILD is poor, with high mortality rate (5). Occasionally, patients with CTD without evidence of prior ILD may present with acute respiratory distress syndrome due to DAD (8). This pattern may be the initial manifestation of lung involvement in these patients with rapid progression to respiratory failure. This presentation has been described most commonly in patients with SLE and PM/DM.

CT is commonly used in the initial evaluation and follow-up of patients with CTD and clinically suspected or proven ILD. The CT findings of chronic ILD seen in patients with CTD are similar to those seen in idiopathic interstitial pneumonia (9). In the context of ILD occurring in a patient having a CTD, CT is particularly helpful at it often shows more than one pulmonary disease. Diagnostic precision in CTD-ILD is challenging because of a wide range of potential simultaneous pathologies and the possibility of concurrent CTD (i.e.
rheumatoid arthritis and Sjögren syndrome). In addition further possible confounders include the presence of smoking or drug-related abnormalities and immunosuppression related infection (1). Actually ILD, particularly NSIP, OP and DAD may also be a reaction pattern to many drugs. Because most patients with CTD are treated with anti-inflammatory or immunosuppressive medication, drug-induced lung disease should always be considered in the differential diagnosis, or a potential cause of the lung abnormalities (10). Patients with drug-induced pulmonary toxicity usually present subacute clinical symptoms (fever, dyspnea, cough) progressing over many weeks. The identification of a drug-induced pulmonary involvement is based on an exclusion diagnosis: pulmonary infection or acute exacerbation of interstitial pneumonia should always be considered in the first consideration (5).

Because patients with CTD are treated with steroids or other immunosuppressive drugs, they are at risk of bacterial pneumonia and opportunistic infections. The prevalence of *Pneumocystis Jiroveci* pneumonia seems to be particularly increased in patients with CTD and ILD who are being treated with corticosteroids (11). As a result, *Pneumocystis Jiroveci* pneumonia should be the differential diagnosis of new extensive ground glass opacity on CT in these patients.

**Pulmonary arterial hypertension (PAH)**

PAH is defined as mean resting pulmonary artery pressure higher or equal to 25 mmHg and a pulmonary capillary wedge pressure lower than 15 mmHg. Patients with CTD present a higher risk to develop PAH, with or without the association with pulmonary interstitial involvement (1, 4). Clinical presentation, symptoms and therapeutic approach are the same of those of a primary pulmonary hypertension. PSS and MCTD are the two entities more frequently associated with PAH (12); it is less frequent in case of SLE and unusual in patients with RA and PM/DM (Table I). The histopathologic features resemble those of a primary pulmonary hypertension. A thromboembolic origin could be suggested in patients with SLE with antiphospholipid syndrome. Screening echocardiography is indicated in all patients affected by PSS or MCTD. In selected cases, right catheterism (gold standard) is necessary for a definitive diagnosis.

**Other thoracic manifestations (3, 4)**

Follicular bronchiolitis is characterized histologically by a peribronchial lymphocytic follicular hyperplasia of bronchus-associated lymphoid tissue (BALT) with the follicles distributed along the bronchioles. Follicular bronchiolitis is part of the spectrum of lymphoproliferative disease and may be sometimes overlap with LIP. Most cases of follicular bronchiolitis or lymphocytic bronchiolitis are associated with CTD, especially RA, SJOS and PSS.

Bronchial inflammation (follicular bronchitis) may result in bronchiectasis unrelated to interstitial lung fibrosis. Bronchiectasis and/or associated obliterative bronchiolitis occur relatively frequently in patients with RA, SJOS and SLE.

Airway wall thickening and luminal narrowing due to inflammatory and fibrotic changes in cartilage are characteristic of RP.

Alveolar hemorrhage due to capillaritis is a well-known complication of SLE, and may also occur in patients with RA, PSS, PM/DM or MCTD.

Other extrapulmonary thoracic abnormalities, such as esophageal dilatation, pleuro-pericardial effusion/thickening or an osteoarticular involvement can suggest an underlying CTD. Mediastinal lymphadenopathies are another frequent finding in this group of patients, with or without the association with ILD.

**Rheumatoid Arthritis (RA)**

RA is a relatively frequent disease (1-2% of the adult population worldwide...
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Its incidence is higher in women (age: 25-50 years). It is characterized by bilateral and symmetric arthritis, morning stiffness, and the presence of rheumatoid factor. Extra-articular manifestations are observed in half of the patients and occur more frequently in men. Pulmonary involvement is the second cause of death after infections. By contrast, in individuals with no symptoms of respiratory disease, up to half have lung parenchymal abnormalities on CT. Cigarette smoking has a synergistic effect on the pulmonary manifestations of RA, and smoking is the most consistent independent predictor of ILD in RA.

Radiological manifestations of disease (1, 4, 14)

Pleural thickening (probably secondary to previous effusions) represents the most frequent thoracic abnormality. Effusions are less frequent, usually unilateral, containing small amounts of liquid and often self-resolving over a period of weeks to months; in some patients they can persist over years.

Rheumatoid pulmonary nodules (necrobiotic nodules) are more frequently observed in smokers (men > women), in association with subcutaneous nodules and significant blood elevation of the rheumatoid factor. Rheumatoid nodules can also appear before the clinical manifestations of disease and their histological characteristics (fibrinoid necrosis) resemble those of the subcutaneous nodules. Their diameter

Fig. 1. — Rheumatoid nodules in a 50 y.o. female smoker patient who have suffered from RA for many years. Axial CT images show the presence of bilateral pulmonary nodules with irregular and spiculated contours predominantly distributed in the upper lung zones. Some of these nodules are cavitated.

Fig. 2. — Typical CT pattern of UIP in a patient with RA. Axial and coronal reformat show bilateral subpleural honeycombing in the lower lobes. Associated findings include ground-glass opacities with superimposed intralobular reticulations and traction bronchiectasis.
ranges between 0.5 and 5 cm and they usually present a peripheral distribution, with middle and upper predominance (Fig. 1). These nodules, usually asymptomatic, can cavitate (50-100% of cases), grow in dimensions or spontaneously disappear over time. Rarely, a communication with the pleural surface and cavitated nodules can occur, causing pneumothorax, pleural effusions or empyemas. Because of drug-related immunosuppression, cavitated nodules may become infected. Inner calcifications are uncommon; the presence of calcifications has been associated with the Caplan-Colinet syndrome (association between rheumatoid polyarthritis and pneumoconiosis).

The most common fibrotic ILD in RA are UIP and NSIP. Unlike other CTDs, UIP is more frequent than NSIP in patients with RA.

Fig. 3. — CT pattern of fibrotic NSIP in a 48 y.o. female patient RA. Axial CT images and coronal reformatted slab on which minimal intensity projection was applied, show bilateral patchy areas of ground-glass opacities with superimposed intralobular reticulations and traction bronchiectasis. The abnormal areas have a predominant peribronchovascular distribution.

Fig. 4. — Follicular bronchiolitis in a patient with RA. Axial CT image showing multiple small ill-defined centrilobular nodular opacities with diffuse and homogeneous distribution.
The characteristic CT features of UIP are intralobular reticulations associated with honeycombing in a peripheral and basal distribution (Fig. 2). The disease tends to creep anteriorly and subpleurally in the upper lobes. Traction bronchiectasis and bronchiolectasis are frequently associated. Ground-glass opacities may be observed, but with less extent than NSIP. In advanced disease, architectural distortion and volume loss are present.

The CT pattern of NSIP is made of ground-glass opacities with underlying distortion and fine reticulation which may or may not be subpleural and basal. Traction bronchiectasis and traction bronchiolectasis may appear in case of fibrotic NSIP, and, a loss of volume and architectural distortion may be present in case of advanced fibrosis (Fig. 3).

Other lung diseases that may occur in patients with RA include OP and follicular bronchiolitis. OP is usually seen in the middle or lower zones, frequently in a peribronchovascular or peripheral distribution. The CT pattern of OP is made of bilateral areas of airspace consolidation more or less associated with air bronchogram and some areas of ground-glass opacities.

CT signs of follicular bronchiolitis include centrilobular and peribronchial nodules measuring 1 to 12 mm in diameter more or less associated with patchy areas of ground-glass opacities that are generally bilateral and diffuse in distribution (Fig. 4). The CT characteristics of LIP include ground-glass opacities, poorly defined centrilobular nodules, interlobular septal thickening and lung cysts. However most of the cases of LIP are associated with SJOS rather than RA.

There is a strong association between the duration of RA and airway disease, with obliteratorive bronchiolitis and bronchiectasis frequently coexisting (15) (Fig. 5).

Bronchiectasis may be related to autoimmune bronchial destruction, smoking or infection (16). Obliteratorive bronchiolitis is subclinical in many patients with RA. The characteristics HRCT findings consist of areas of decreased lung attenuation and vascularity with redistribution of blood flow to more normal lung resulting in a mosaic perfusion attenuation pattern with expiratory air trapping.

About 20% of patients with RA have mild PAH because of pulmonary vasculopathy affecting the smaller vessels. In patients with RA, PAH may also occur secondary to ILD or cardiac disease.

Radiological manifestations of complications

Amyloidosis can be difficult to identify on CT because the appearances are not specific. Irregular or amorphous calcifications are occasionally identifiable within large mediastinal or pulmonary amyloid deposits.

Several drugs employed in the medical treatment of RA can cause pulmonary toxicity: gold salts and...
penicillamine can possibly cause DAD or obliterative bronchiolitis; also methotrexate can frequently determine pulmonary damage with pneumonia (17). The most frequent CT features of a drug-induced pulmonary toxicity are multiple ground-glass opacities, centrilobular nodules and mediastinal lymphadenopathies (10, 17). A complete resolution can often be achieved by the interruption of treatment and administration of high doses of corticosteroids.

**Progressive Systemic Sclerosis (PSS)**

PSS is a multisystemic chronic autoimmune disease of unknown etiology, characterized by three pathological features: inflammation, vascular damage and fibrosis. It is a rare disease more frequent in women with a peak incidence between 45 and 64 years. Only 1% of the patients with PSS present respiratory symptoms at time of diagnosis, but about 60% of them will develop a pulmonary involvement.

CREST syndrome, a limited form of systemic sclerosis, is characterized by five main clinical features: calcinosis, Raynaud’s phenomenon, esophageal dysmotility, sclerodactyly and telangiectasia. Lung involvement occurs more frequently in the diffuse forms of PSS than in limited forms (CREST syndrome). The two main pulmonary manifestations are interstitial fibrosis and PAH (1).

Interstitial pulmonary fibrosis represents the most frequent thoracic manifestation (50% of patients) and it is associated to the presence of anti-topoisomerase antibodies (anti-Scl-70) (18). The majority of patients with pulmonary lung fibrosis and PSS have a histological pattern of NSIP rather than UIP (19).

PAH represents the most frequent cause of death. It may occur in patients with very restrictive lung disease at pulmonary function tests and is probably secondary to the presence of ILD or heart disease. Isolated PAH may occur in patients with PSS, particularly those with limited form (PAH occurs in 50% of patients with CREST) (1).

Radiological manifestations of disease

The main CT features are those of fibrotic or non fibrotic NSIP including intralobular reticulations superimposed on ground-glass opacities (Fig. 6); this is potentially associated with traction bronchiectasis and bronchiolectasis (Fig. 7). In case of advanced fibrosis a volume loss and architectural distortion can also be observed. A subpleural sparing of the parenchyma is often present (5, 20, 21) (Fig. 7). Less frequently, foci of airspace consolidation, pulmonary cysts or rare honeycombing foci can be found (Fig. 8). CT signs of PAH are primarily given by an enlarged caliber of the pulmonary trunk (> 29 mm), a dilatation of the right and left pulmonary arteries and their segmental branches. A diameter of the pulmonary arte
**Fig. 10. —** A 38 y.o. male patient with SLE. Axial CT images showing bilateral patchy areas of ground-glass opacity with superimposed reticulation and traction bronchiectasis suggesting fibrotic NSIP.

**Fig. 11. —** A 27 y.o female patient with SLE presenting with dyspnea. Absence of infection. A,B. Axial CT images (left) showing patchy areas of airspace consolidations associated with some areas of ground-glass opacity suggestive of OP pattern. C,D. CT scan performed 2 years later (right). In spite of corticosteroid and immuno-suppressive treatment there is persistence of ILD. Airspace consolidation was replaced by ground-glass opacities, linear opacities and small cysts suggestive of lung fibrosis.
nary embolism is a consideration, particularly in patients who have antiphospholipid syndrome (1). Lower respiratory tract infections are caused by both common and opportunistic pathogens because patients are frequently immunosuppressed and have altered cellular immunity. The shrinking lung syndrome is characterized by pulmonary volume loss causing dyspnea and pleural pain, associated with a restrictive syndrome at pulmonary function tests (24). Respiratory muscle weaknesses, diaphragmatic neuropathy and pleural inflammation might play a role in the genesis of this syndrome which usually shows a good response to medical treatment with good prognosis.

Acute Lupus pneumonitis is a rare and severe complication (mortality 50%) caused by a DAD with necrosis, cellular infiltrations, hyaline membranes deposition, capillary inflammation and hemorrhage (not always present). It is clinically characterized by fever, dyspnea, cough, hypoxemia and pleural pain (22). Interstitial pneumonia is an unusual complication, most frequently presenting as NSIP (22); SLE-associated NSIP shows no response to medical treatment. More frequent in patients with antiphospholipid antibodies, pulmonary embolism is a consideration, particularly in patients who have antiphospholipid syndrome (1).

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Trunk being greater than that of the adjacent ascending aorta has proven to be a useful CT sign of PAH (Fig. 8). In advanced cases, a dilatation of the right cardiac cavities and the ayzygos and hemiazygos venous systems can be associated. Presence of contrast media reflux in the inferior vena cava and the hepatic veins represents another relevant radiological sign of right heart dysfunction. Pericardial effusion, an indirect sign of insufficient lymphatic and venous drainage (secondary to right heart high blood pressures), can be observed in severe cases, as indicator of poor prognosis. However a non dilated pulmonary artery does not necessary exclude PAH. Echocardiography is useful to screen for pulmonary hypertension (12).

An esophageal involvement is very common in patients with PSS (97% of cases), presenting with a lumen dilatation (Figs. 7, 8) and/or motility disorders, which can be the cause of inhalation pneumonia or bronchiolitis. CT scan will show mucus plugs, “tree-in-bud” patterns, centrilobular nodules, lobular or peribronchial airspace consolidations and bronchiectasis (4). A pleural involvement is rare, seen as pleural pseudoplaques or diffuse pleural thickening.

Few isolated cases of DAD and diffuse alveolar hemorrhage in patients with PSS have been reported. On CT scans only non specific appearances are present (widespread consolidation and ground-glass opacities).

Patients with PSS show a higher risk of developing lung cancer (usually adenocarcinoma) including non smokers. Systemic Lupus Erythematosus (SLE)

SLE is a systemic autoimmune disease more common in women in reproductive age principally affecting skin, articulations, kidneys, blood cells and the nervous system. SLE tissular lesions derive from an immune-complex deposition with complement activation. The presence of anti-DNA and anti-smooth muscle antibodies is highly specific for SLE. A thoracic involvement is observed in a high percentage of patients (50-100%), most frequently represented by pleural disease and infectious pneumonia (22, 23). Most of the patients with SLE usually present minor respiratory symptoms or no symptoms at all.

Pulmonary involvement is not necessary associated with significant morbidity and may be asymptomatic. Pleural effusions are usually small, bilateral, protein-rich exudates. Although pleuritic symptoms may express active lupus, pulmonary embolism is a consideration, particularly in patients who have antiphospholipid syndrome (1).

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Fig. 12. — Airway disease occurring in a 37 y.o. female patient with SLE.
Axial CT image showing bilateral cylindrical bronchiectasis in the lower lobes, associated with oblitative bronchiolitis (decreased lung attenuation and vascularity).

Fig. 13. — Diffuse pulmonary hemorrhage occurring in a 42 y.o. male patient with SLE and antiphospholipid syndrome.
Axial CT image showing bilateral patchy areas of ground-glass opacities and airspace consolidation.

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Fig. 14. — Severe PAH in a 28 y.o. female patient with SLE.
A. Post-contrast CT scan (axial and sagittal MIP reformatted images) showing dilatation of the trunk and main branches of the pulmonary artery without any arterial thrombosis.
B. Coronal reformatted CT images, targeted on the right lung, showing the presence of small ill-defined centrilobular nodular opacities [arrows].
nary embolism is a complication possibly leading to chronic pulmonary thromboembolic disease. Pulmonary arterial hypertension (PAH) can be secondary to thrombosis, ILD, valvular disease, or may occasionally be primary and results from unexplained pleuropulmonary lesions in the pre-capillary vasculature (22).

Diffuse alveolar hemorrhage is a rare and severe complication (2-5% of cases), not always presenting with hemoptysis, associated with a high rate of mortality.

**Radiological manifestations of disease**

The most common CT abnormalities are bilateral pleural effusion, pleural thickening, pericardial effusion and infectious pneumonia (Fig. 9). Infectious pneumonia can be community-acquired pneumonias or be caused by atypical germs, such as *mycobacteria, pneumocystis j., CMV, aspergillus or nocardia*. Pulmonary tuberculosis should always be screened during high-dose corticosteroids and immunosuppressive drugs administration.

Several CT abnormalities may be observed in patients with SLE who did not have respiratory symptoms (22, 23). They include a) CT findings of ILD, more often taking the appearance of fibrotic or non-fibrotic NSIP, and less frequently those of UIP or OP (Fig. 10, 11); b) bronchiectasis made mainly of mild dilatation, more or less associated with obliterator bronchiolitis (decreased lung attenuation, decreased vascularity and expiratory air trapping) (Fig. 12); c) axillary and mediastinal lymphadenopathies, d) pleuropericardial abnormalities and pleural irregularities. In case of diffuse alveolar hemorrhage, the CT appearances are not specific, made of widespread ground-glass opacities and airspace consolidation (Fig. 13). The CT features of diffuse alveolar hemorrhage may be indistinguishable from those of infectious pneumonia or DAD (5).

In case of shrinking lung syndrome CT scans or chest radiographs can show unilateral or bilateral diaphragmatic elevation with or without parenchymal involvement, made of passive atelectasis in the subpleural area along the diaphragm and associated with some parenchymal bands in the lung bases (24).

When PAH is present CT scan may show small ill-defined centrilobular nodules varied in numbers and conspicuity and having no lung zone predominance (Fig. 14). These small nodular opacities may reflect the presence of cholesterol granulomas resulting from pulmonary hemorrhage (25).

**Polymyositis and dermatomyositis (PM/DM)**

PM and DM are idiopathic inflammatory myopathies with an autoimmune pathogenesis. They are more frequent in women (40-50 y.o.). Typical features are subacute onset, proximal symmetric muscle weakness, elevated serum creatine kinase activity, and mononuclear cell infiltrates in the muscle biopsy. In addition patients with DM have characteristics skin abnormalities. PM/DM occur isolated or in connection with another CTD.

Since the results of auto-antibodies were available, patients with idiopathic inflammatory myopathies have been classified according to the clinico-serologic classification. This includes pure polymyositis, pure dermatomyositis, overlap myositis, and cancer associated myositis (26).

Overlap myositis is defined as myositis with at least one clinical overlap feature and/or an overlap auto-antibody. Cancer associated myositis is defined by the presence of clinical paraneoplastic features and without an overlap auto-antibody or anti-MI-2.

ILD is frequent in overlap myositis and seems to be associated with the presence of autoantibodies tRNA synthetase. The antisynthetase syndrome features include arthritis, ILD, fever, Raynaud’s phenomenon, and mechanic hand. ILD is particularly common in the antisynthetase syndrome occurring up to 80%. Anti-JO-1 is the most common overlap autoantibody. Antibodies to other synthetases also exist (anti-PL-7, anti-PL-12, anti-OJ, anti-KU) which seem to preferentially identified individuals with amyopathic lung disease. Antisynthetase predicts more severe ILD, and ILD progression is associated with acute onset (27). In addition, pulmonary involvement

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**Fig. 15.** — Association of OP and NSIP in a 40 y.o. female patient with dermatomyositis.
A. Bilateral subpleural and perilobar areas of airspace consolidation and ground-glass opacities.
B. Follow-up CT scan performed 18 months later showing the disappearance of airspace consolidation, replaced by subtle ground-glass opacities in the periphery of the lungs.
in patients with antisynthetase syndrome (anti JO1) predicts disease-modifying antirheumatic drug use (28).

The main clinical manifestations of pulmonary involvement in PM/DM are represented by hypoventilation with secondary respiratory insufficiency, which can be determined by respiratory muscles functional defects, ILD or aspiration pneumonia or diffuse bronchiolitis (caused by pharyngeal muscles dysfunction) (29).

The presence of an interstitial involvement significantly affects the morbidity and mortality of patients with PM/DM. Its onset can precede the appearance of cutaneous and muscular abnormalities in 20-50% of cases; otherwise, it can be identified at time of diagnosis or during follow-up (30). The most common pathologic findings include NSIP and OP often occurring in combination (31). A rapidly progressive form of lung disease may occur, reflecting DAD.

Radiological manifestations of the disease

The characteristic CT appearance consists of patchy bilateral airspace consolidation which has a subpleural and/or peribronchial distribution in the majority of cases (Fig. 15). It most commonly involves the lower lung zones to a greater degree than the upper lung zones. This pattern reflects the presence of OP (5). Poorly defined band-like opacities that have an arcade-like or polygonal appearance (perilobular pattern) are also common. Other findings include

Fig. 16. — Association of OP and fibrotic NSIP in a 53-yo-female patient with polymyositis and antisynthetase syndrome (anti-JO1).
A. Initial CT scan showing airspace consolidation with air bronchogram made of traction bronchiectasis.
B. The CT scan performed after 3 years of treatment shows the disappearance of airspace consolidation replaced by ground-glass opacities with superimposed traction bronchiectasis and some small lung cysts.

Fig. 17. — UIP pattern in a 57 y.o. female patient with anti-synthetase syndrome (anti-JO1).
Axial and coronal CT images showing bi-basal and peripheral honeycombing associated with reticulations superimposed to ground-glass opacities, and some traction bronchiectasia.
The most serious complication of MCTD, and infection secondary to immunosuppression in the other frequent cause of death. Most patients with MCTD present with one of the following clinical features: Raynaud’s phenomenon, arthralgia, arthritis, swollen hands, sclerodactyly or acrosclerosis and myositis. Esophageal dysmotility and reflex are frequently reported. Generalized lymphadenopathy is also a frequent manifestation and secondary Sjögren syndrome is relatively common. Thoracic involvement is quite common. Cardiac abnormalities include pericarditis, myocarditis, and complete heart block. Pleural effusion is one of the most common clinical manifestations usually small and resolving spontaneously. Pulmonary hemorrhage, diffuse alveolar damage, organizing pneumonia, NSIP, UIP, airway disease may be seen in these patients. This is consistent with the other manifestations of MCTD which have features of PSS, SLE or PM/DM. A
Patients with SJOS have a higher risk of developing a lymphomatous disease (most commonly B type, non-Hodgkin), arising from the salivary glands with possible pulmonary or gastric involvement.

Global prognosis for patients affected by SJOS is relatively good; it gets worse in case of secondary forms or in patients developing a lymphomatous disease.

**Radiological manifestations of disease**

CT provides substantial information regarding the panel of pulmonary involvement in SJOS. The patterns include ILD, PAH and patterns suggestive of LIP.

Airway related abnormalities are frequent and consist of bronchial wall thickening, bronchiectasis, tree-in-bud sign and mosaic attenuation pattern with expiratory air trapping reflecting obliterative bronchiolitis (Fig. 19).

The spectrum of lymphoproliferative diseases in SJOS includes follicular bronchiolitis, LIP, nodular lymphoid hyperplasia, mucosa-associated lymphoid tissue (MALT) lymphoma, and lymphoma (38). Follicular bronchiolitis is the most common form of bronchiolitis occurring in patients with SJOS; lymphocytic bronchiolitis (lymphocytic infiltration without follicles) and infectious bronchiolitis represent the main differential diagnosis.

Patients with SJOS have a higher risk of developing a lymphomatous disease (most commonly B type, non-Hodgkin), arising from the salivary glands with possible pulmonary or gastric involvement.

**Radiological manifestations of disease**

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Airway related abnormalities are frequent and consist of bronchial wall thickening, bronchiectasis, tree-in-bud sign and mosaic attenuation pattern with expiratory air trapping reflecting obliterative bronchiolitis (Fig. 19).

The main CT abnormalities of LIP consist of patchy or confluent bilateral ground-glass opacity and poorly defined centrilobular nodules. Thin-walled cysts, usually few in number are seen in 60-80% of patients usually associated with ground-glass opacities, but occasionally as an isolated finding (42) (Fig. 20).

The association of nodules and lung cysts should raise the diagnosis of amyloidosis associated with LIP.
Fig. 20. — A 64 y.o. female patient with SJOS. CT images showing the presence of several thin-walled lung cysts having a predominant subpleural and peribronchiolar distribution.

Fig. 21. — SJOS in a 52 y.o. male patient. Axial CT images showing a focal area of airspace consolidation within the left lower lobe surrounded by ground-glass opacity revealing a low grade B-lymphoma. Presence of several thin-walled cysts with peribronchovascular and subpleural distribution very suggestive of LIP.

Fig. 22. — Airway disease in a 69 y.o. male patient who has suffered from RP from many years. A., B. Axial CT images targeted on the trachea and main stem bronchi showing thickened and partly calcified anterior and lateral walls of the trachea and main stem bronchi (arrow heads). B. There is also a large thickening with calcifications of costal cartilages (arrows).
including the ears, nose, joints and tracheobronchial tree. Histologically, the acute inflammatory infiltrates present in the cartilages and perichondrial tissue induces progressive dissolution and fragmentation of the cartilage followed by fibrosis.

The mean age at diagnosis is the fifth decade with an almost equal sex ratio and more severe airway disease in female patients. About 50% of patients will develop laryngeal, tracheal or bronchial involvement. One third of patients have an associated autoimmune disease, most

**Relapsing polychondritis (RP)**

RP is a rare autoimmune disease of unknown aetiology characterized by recurrent inflammatory episodes that affects cartilage at various sites, including the ears, nose, joints and tracheobronchial tree. Histologically, the acute inflammatory infiltrates present in the cartilages and perichondrial tissue induces progressive dissolution and fragmentation of the cartilage followed by fibrosis.

The mean age at diagnosis is the fifth decade with an almost equal sex ratio and more severe airway disease in female patients. About 50% of patients will develop laryngeal, tracheal or bronchial involvement. One third of patients have an associated autoimmune disease, most
commonly systemic vasculitis or RA. The prognosis of patients who have both systemic vasculitis and RP is worse than of patients with only RP (43).

The respiratory tract symptoms are usually the results of laryngotracheal chondritis and include hoarseness, breathlessness, cough, stridor, wheezing and tenderness over the laryngotracheal cartilage. At disease onset, approximately a quarter of patients have respiratory symptoms. Airway involvement is the most cause of death in patients with RP.

Radiological manifestations of disease (44, 45)

The larynx and trachea are most commonly affected. The disease may also involve the airways more distally to the level of subsegmental bronchi.

At the early stage of disease, CT shows smooth anterior and lateral airway wall thickening with sparing of the posterior membranous wall. There is also often an increased attenuation of the cartilages (ranging from subtle to frankly calcify) (Fig. 22). In more advanced disease, thickening of airway walls become circumferential because the posterior (non cartilaginous) wall of the trachea and main bronchi appears thickened. At this stage, luminal narrowing of the trachea and bronchi may occur resulting from fibrosis following cartilaginous destruction (Fig. 23A,B). Focal narrowing of the trachea and bronchi may be present.

Loss of cartilaginous support due to cartilaginous inflammation and destruction may result in excessive dynamic expiratory collapsibility (tracheomalacia and bronchomalacia). Expiratory air trapping is frequently observed involving one lung, lobes, segments or lobules (46) (Fig. 23C).

Conclusion

A thoracic involvement can be frequently found in patients affected by CTDs; it is usually identified after or at the time of diagnosis, but even precedes other systemic signs. A wide spectrum of pulmonary abnormalities has been described, and each CTD may present characteristic CT features; nevertheless, possible complications due to superinfections or drug toxicity should be taken in account in suggestive clinical contexts. Although ILD and airways disease represent the most common abnormalities, all thoracic structures can be implied, and should always be attentively assessed. Moreover, compared to idiopathic forms, ILD occurring in CTD patients may present with some particular characteristics of patterns, evolution over time and prognosis. The role of the radiologist, with a complete knowledge of the main CT findings related to each type of CTD and the familiarity with the most frequent complications, is crucial for an adequate clinical management.

References


