

# Intrathoracic manifestations of collagen vascular diseases on high-resolution chest computed tomography\*

*Manifestações intratorácicas das doenças do colágeno na tomografia computadorizada de alta resolução do tórax*

C. Isabela S. Silva<sup>1</sup>, Nestor L. Müller<sup>2</sup>

**Abstract** Intrathoracic manifestations of collagen vascular diseases are very common. The frequency of intrathoracic manifestations and the patterns of abnormality are variable depending on the type of collagen vascular disease and may simultaneously involve one or more of the following: lung parenchyma, airways, pulmonary vessels, pericardium, and pleura. The most common pulmonary manifestations are diffuse interstitial pneumonia and pulmonary hypertension which together represent the main causes of morbidity and mortality of these patients. Pulmonary, airway and pleural involvement may also be secondary to the disease therapy, or result from bacterial pneumonia or opportunistic infection. In the present review, the authors summarize the main intrathoracic manifestations of collagen vascular diseases and the differential diagnosis on high-resolution chest computed tomography.

**Keywords:** Lung; Collagen vascular disease; Interstitial pneumonia; Pulmonary hypertension; Computed tomography.

**Resumo** As manifestações intratorácicas das doenças do colágeno são bastante comuns. O padrão e a freqüência de comprometimento dependem do tipo específico de doença do colágeno, que pode envolver um ou vários compartimentos simultaneamente, tais como parênquima, vias aéreas, artérias pulmonares, pleura, e pericárdio. As manifestações mais importantes incluem as pneumonias intersticiais difusas e a hipertensão pulmonar, que em conjunto representam as principais causas de mortalidade e morbidade nesses pacientes. O acometimento pulmonar, pleural e de via aérea pode ser também secundário a terapêutica instituída ou ser decorrente de processos infecciosos bacterianos ou por germes oportunistas, por causa da imunossupressão. Nesta revisão os autores sumarizam as manifestações intratorácicas e o diagnóstico diferencial das principais doenças do colágeno na tomografia computadorizada de alta resolução do tórax.

**Unitermos:** Pulmão; Doença do colágeno; Pneumonia intersticial; Hipertensão pulmonar; Tomografia computadorizada.

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## INTRODUCTION

Collagen vascular diseases are a group of diseases with specific autoimmune characteristics that affect several organs including the lungs<sup>(1,2)</sup>. Intrathoracic manifestations are frequent and may be asymptomatic or symptomatic, with varied degrees of severity. The pattern and frequency of the intrathoracic involvement depend on the

specific type of collagen vascular disease and may include one or more pulmonary compartments such as alveolus, interstitium, vessels, lymphatic tissue, airways and pleura<sup>(1–7)</sup>. The most frequent pulmonary manifestations are diffuse interstitial pneumonias<sup>(1,2,6)</sup> and pulmonary hypertension<sup>(1,2,8)</sup> which as a whole represent the main causes of mortality and morbidity in these patients<sup>(1,2)</sup>. It is important to note that pulmonary abnormalities in patients with collagen vascular disease may be due not only to the underlying disease, but also result from its treatment, and include drug reaction and infection by bacteria or opportunistic organisms, such as *Pneumocystis jiroveci*, and atypical mycobacteria as a result of immunosuppression<sup>(1,2)</sup>. The collagen vascular diseases that most commonly result in interstitial lung disease are

rheumatoid arthritis, progressive systemic sclerosis, systemic lupus erythematosus, dermatopolymyositis, mixed connective tissue disease and Sjögren's syndrome<sup>(1,2,6)</sup>. Chest radiography represents the imaging method most frequently utilized in the initial evaluation of intrathoracic manifestations of collagen vascular diseases. Chest radiography, however, has low sensitivity and specificity. High-resolution computed tomography (HRCT) is the method of choice for assessment of pulmonary abnormalities in collagen vascular diseases, offering the best correlation with histologic findings, disease severity, prognosis, evaluation of disease progression, and differential diagnosis<sup>(1)</sup>. The aim of this manuscript is to review the main intrathoracic manifestations of collagen vascular diseases on HRCT.

\* From the Department of Radiology, University of British Columbia, Vancouver General Hospital, Vancouver, Canada.

1. MD, PhD, Research Associate, University of British Columbia, Vancouver General Hospital, Vancouver, Canada.

2. Professor and Chairman, Department of Radiology at University of British Columbia, Vancouver General Hospital, Vancouver, Canada.

Mailing address: Dr C. Isabela S. Silva. Department of Radiology, University of British Columbia, Vancouver General Hospital, 3350-950 West 10th Avenue, Vancouver, BC V5Z 4E3 Canada. E-mail: isabela.silva@vch.ca

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## MAIN INTRATHORACIC MANIFESTATIONS OF COLLAGEN VASCULAR DISEASES

### 1. Diffuse interstitial pneumonias

Interstitial pneumonias represent the most common intrathoracic manifestations of collagen vascular disease<sup>(1,2)</sup>. Collagen vascular diseases may be associated with virtually all patterns of diffuse interstitial pneumonia and may progress to pulmonary fibrosis<sup>(1-3,6)</sup>. The histological classification is similar to that of idiopathic interstitial pneumonias including: *a) patterns of chronic progression* – usual interstitial pneumonia, non-specific interstitial pneumonia and lymphocytic interstitial pneumonia; *b) pattern of subacute progression* – organizing pneumonia (also known as bronchiolitis obliterans organizing pneumonia —BOOP); *c) pattern of acute pro-*

*gression of pulmonary injury* – diffuse alveolar damage<sup>(3,9,10)</sup>.

High-resolution CT manifestations of interstitial pneumonias in patients with collagen vascular diseases also are similar to the ones described for patients with idiopathic disease (Table 1)<sup>(1-3,9,11)</sup>. Collagen vascular diseases most frequently associated with interstitial pneumonia are: rheumatoid arthritis, progressive systemic sclerosis (scleroderma) and dermatopolymyositis. In general, non-specific interstitial pneumonia is the most common pattern of interstitial pneumonia in patients with collagen vascular diseases (Figure 1)<sup>(1,2)</sup>. In patients with rheumatoid arthritis, however, it seems that the pattern of usual interstitial pneumonia (Figure 2) is the most frequent one<sup>(1,7)</sup>. On the other hand, lymphocytic interstitial pneumonia, although rare, is most common in patients with Sjögren's

syndrome (Figure 3)<sup>(1,2,12)</sup>, while the diffuse alveolar damage pattern is more frequent in patients with dermatopolymyositis and systemic lupus erythematosus. Table 2 shows the frequency of each interstitial pneumonia pattern found in the main collagen vascular diseases discussed in the present review.

In general, chronic progressive interstitial pneumonias in collagen vascular diseases have a better prognosis than those of idiopathic nature, with a better five year survival rate (Figure 4)<sup>(13)</sup>. However, cases of unfavorable progression in patients with collagen vascular disease and interstitial pulmonary involvement with no response to the therapy are not infrequent. Similarly to the idiopathic form of disease, the non-specific interstitial pneumonia pattern in collagen vascular disease has a better prognosis than the pattern of usual interstitial

**Table 1** HRCT findings in interstitial pneumonias.

Pattern	Typical findings	Typical distribution	Unusual findings
Usual interstitial pneumonia	Reticular pattern, bronchiectasis and traction bronchiectasis, honeycombing, absent or minimal ground-glass opacities	Peripheral, basal and posterior predominance	Asymmetrical distribution, major involvement of upper lobes
Non-specific interstitial pneumonia	Ground-glass opacities, mild reticulation, traction bronchiectasis and bronchiolectasis, absent honeycombing in the early stages	Lower lobes and peripheral regions. Findings may be diffuse. 20–50% of patients show less severe involvement of the pulmonary parenchyma immediately adjacent to the pleural surface ( <i>subpleural sparing</i> )	Extensive reticular pattern, consolidation (may represent areas of co-existing organizing pneumonia – BOOP), peribronchovascular distribution
Organizing pneumonia (BOOP)	Consolidation is the typical finding, ground-glass opacity usually is associated with areas of consolidation, perilobular pattern or reversed halo sign may be found	Bilateral symmetrical or asymmetrical, peripheral and/or peribronchovascular in 60–80% of cases, predominance in lower lobes	Focal consolidation mimicking mass may progress to fibrosis
Lymphocytic interstitial pneumonia	Ground-glass opacities associated with sparse cysts ranging from 1–3 cm in diameter	May be diffuse or predominate in the lower lobes; cysts may have subpleural and peripheral distribution	Isolated pulmonary cysts, ground-glass opacity as an isolated finding, septal thickening, and centrilobular nodules
Diffuse alveolar damage	Ground-glass opacity, “crazy paving” pattern, bilateral areas of consolidation may be present mainly in dependent regions	Bilateral and diffuse, rarely multifocal	May progress to pulmonary fibrosis. Patients who survive may have HRCT pattern similar to non-specific interstitial pneumonia

**Table 2** Frequency of interstitial pneumonias in collagen vascular diseases.

Pattern	Rheumatoid arthritis	Progressive systemic sclerosis	Dermatopolymyositis	Sjögren's syndrome	Mixed connective tissue disease	Systemic lupus erythematosus
Usual interstitial pneumonia	+++	+	+	+	+	+
Non-specific interstitial pneumonia	++	+++	+++	++	++	++
Organizing pneumonia (BOOP)	++	+	+++	-	+	+
Lymphocytic interstitial pneumonia	+	-	-	++	-	+
Diffuse alveolar damage	+	+	++	+	-	++

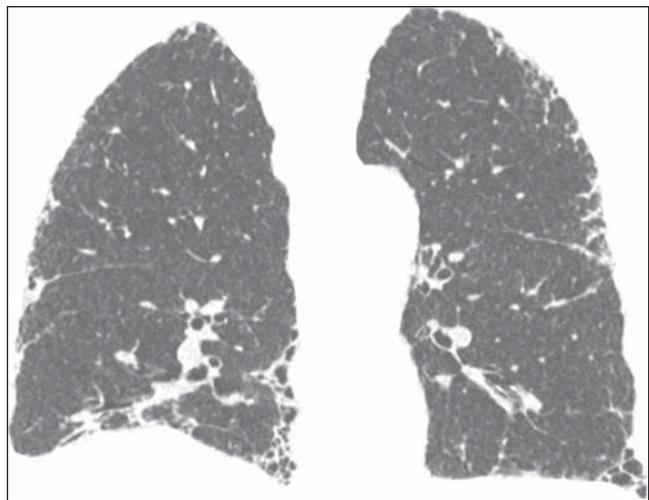
+++ represents a quite common association; ++ represents a relatively common pattern; + indicates a relatively uncommon pattern; – indicates a rare or still-to-be-described pattern for collagen vascular disease.



**Figure 1.** Pattern of non-specific interstitial pneumonia in a patient with progressive systemic sclerosis. HRCT demonstrates diffuse ground-glass opacities in the lower lobes and minimal reticulation, particularly in the middle lobe and lingula.

pneumonia<sup>(13)</sup>. The concomitant presence of more than one pattern of interstitial pneumonia, particularly the association between non-specific interstitial pneumonia and organizing pneumonia (BOOP) is not rare in collagen vascular disease, and is most common in patients with dermatopolymyositis and mixed connective tissue disease (Figure 5). Generally, the pattern of diffuse alveolar damage is associated with poor prognosis, both in patients with idiopathic disease and patients with collagen vascular disease<sup>(10)</sup>.

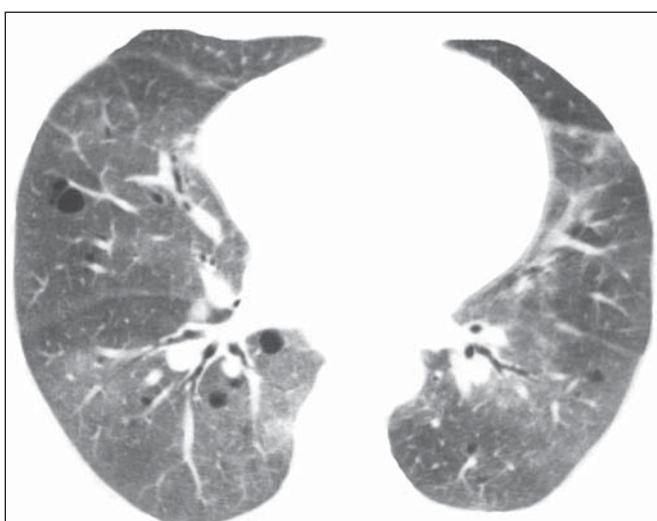
Interstitial pneumonias may precede the clinical onset of the collagen vascular disease for a period of three months up to five



A

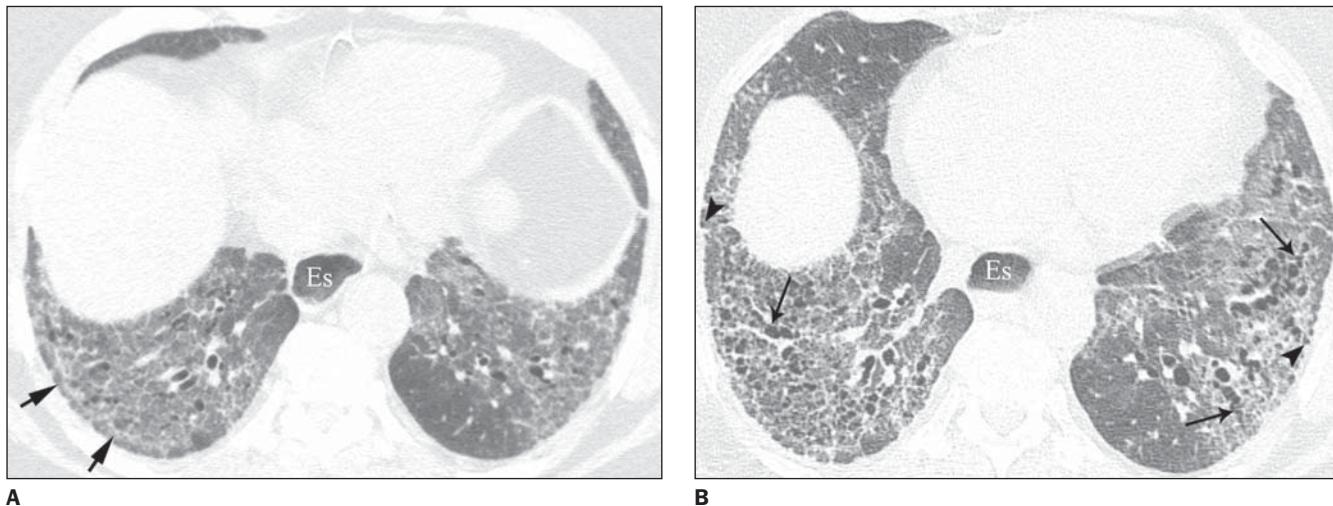
B

**Figure 2.** Pattern of usual interstitial pneumonia in a patient with rheumatoid arthritis. Axial (A) and coronal (B) HRCT images demonstrate findings of architectural distortion with peripheral reticulation and honeycombing (arrows) intermingled with relatively normal areas of pulmonary parenchyma. Note the more extensive involvement of the lung bases (B).

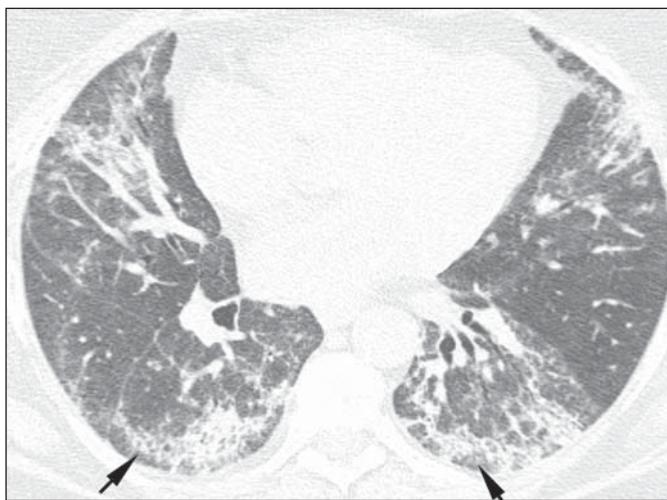


**Figure 3.** Pattern of lymphocytic interstitial pneumonia in a patient with Sjögren's syndrome. HRCT image demonstrates bilateral ground-glass opacities and a few pulmonary cysts.

years, usually with a pattern of non-specific interstitial pneumonia<sup>(14)</sup> or acutely with a pattern of diffuse alveolar damage. Patients with collagen vascular disease, especially rheumatoid arthritis, scleroderma and dermatopolymyositis, may progress with acute exacerbation of fibrotic interstitial pneumonia<sup>(15)</sup>. Most frequently, acute pulmonary injury manifests histologically as diffuse alveolar damage superimposed on underlying pulmonary fibrosis (generally usual interstitial pneumonia or non-specific interstitial pneumonia patterns)<sup>(15)</sup>. HRCT findings of acute exacerbation of chronic progressive interstitial pneumonia in patients with collagen vascular disease consist in diffuse areas of ground-glass attenuation,

**A**

**Figure 4.** High-resolution CT follow-up of non-specific interstitial pneumonia in a patient with progressive systemic sclerosis receiving corticosteroid therapy. HRCT image (**A**) demonstrates diffuse ground-glass opacities, extensive reticulation and subtle signs of fibrosis characterized by irregularities of the pleuropulmonary interface and presence of some irregular and tortuous bronchi and bronchioles in the areas of ground-glass attenuation. Note the less extensive involvement of the posterior pulmonary regions immediately adjacent to the pleural surface (arrows; *subpleural sparing*) - a typical finding of non-specific interstitial pneumonia -, as well of esophageal dilatation (Es), a common finding in patients with progressive systemic fibrosis. HRCT image (**B**) acquired two years later demonstrates, despite treatment, substantial progression of fibrosis, with extensive traction bronchiectasis (long arrows) and bronchiolectasis, and interval development of mild subpleural honeycombing (arrowheads).



**Figure 5.** Concomitant presence of non-specific interstitial pneumonia and organizing pneumonia in a patient with dermatopolymyositis. HRCT demonstrates bilateral ground-glass opacities, minimal reticulation, and focal areas of consolidation. Note the less extensive involvement of posterior pulmonary regions immediately adjacent to the pleural surface (arrows; *subpleural sparing*) typical of non-specific interstitial pneumonia with foci of organizing pneumonia resulting in areas of consolidation at HRCT.

with or without associated smooth inter- and intralobular lines resulting in a *crazy paving* pattern associated with signs of fibrosis from the pre-existing interstitial pneumonia (distortion of pulmonary architecture, traction bronchiectasis, reticulation and honeycombing) (Figure 6)<sup>(15,16)</sup>. Areas of focal or bilateral dependent consolidation may be present. The main differential diagnosis for ground-glass attenuation at

HRCT in patients with collagen vascular disease and fibrotic interstitial pneumonia includes opportunistic infections (particularly by *Pneumocystis*) and drug-induced lung disease (Figure 7)<sup>(1-3)</sup>. Consolidation may be due to organizing pneumonia or an infectious process (by bacteria, mycobacteria or fungi).

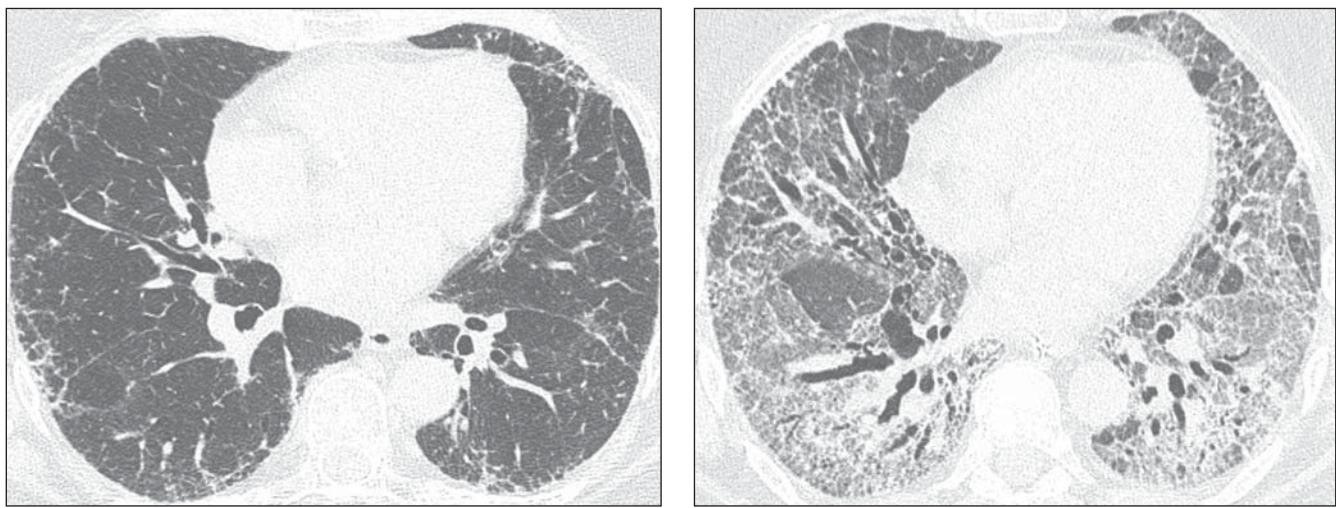
It is important to note that, in smoking patients with collagen vascular disease,

smoking-related interstitial pneumonias such as respiratory bronchiolitis with interstitial pulmonary disease and desquamative interstitial pneumonia may also be found<sup>(2,9)</sup>.

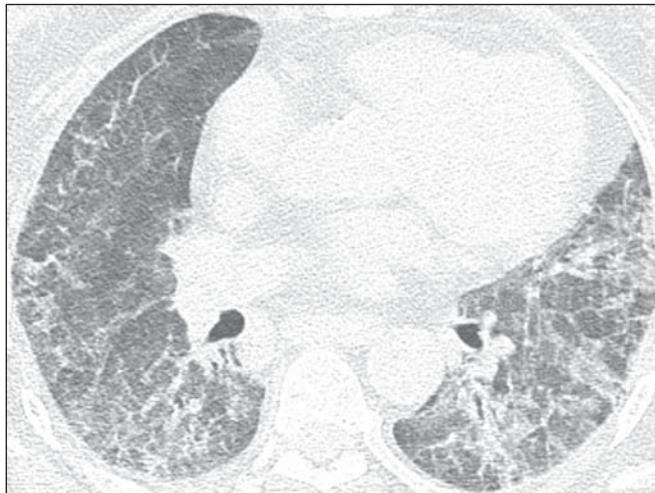
## 2. Pulmonary vascular disease

Pulmonary vasculopathy in collagen vascular diseases generally manifests as pulmonary hypertension, diffuse pulmonary hemorrhage (capillaritis) or small and medium vessel vasculitis<sup>(2,8)</sup>. Pulmonary venoocclusive disease and pulmonary capillary hemangiomatosis, although rare, have been described in some patients with collagen vascular disease such as scleroderma and systemic lupus erythematosus<sup>(8,17)</sup>.

Pulmonary hypertension in collagen vascular disease may result from a range of different pathophysiological mechanisms including loss of pulmonary capillary network as a result of fibrotic interstitial disease; intrinsic pulmonary arteriopathy with vascular remodelling and pulmonary arterial hypertension; left ventricular diastolic dysfunction with pulmonary venous hypertension; and chronic thromboembolic disease associated with hypercoagulability and antiphospholipides (patients with systemic lupus erythematosus)<sup>(8,18)</sup>. It may occur as an isolated finding (Figure 8) or occurring in association with fibrotic inter-

**A****B**

**Figure 6.** Acute exacerbation of usual interstitial pneumonia in a patient with rheumatoid arthritis. HRCT image (**A**) demonstrates typical findings of usual interstitial pneumonia characterized by peripheral reticulation, pulmonary architectural distortion and minimal subpleural honeycombing, without the presence of ground-glass opacities. HRCT image (**B**) acquired two months later, when the patient presented with respiratory failure in the absence of precipitating factors, such as respiratory infection, cardiac decompensation or use of medication, demonstrates extensive areas of ground-glass attenuation and inter- and intralobular septa thickening ("crazy paving" pattern), and tortuous and irregular bronchi. These abnormalities correspond to findings of acute idiopathic pulmonary injury (diffuse alveolar damage) in a patient with pulmonary fibrosis and collagen vascular disease.



**Figure 7.** Drug-induced lung disease secondary to the use of metotrexate in a patient with rheumatoid arthritis and no previous parenchymal abnormalities. HRCT image demonstrates diffuse bilateral ground-glass opacities and minimal reticulation.



**Figure 8.** Pulmonary hypertension in a patient with mixed connective tissue disease. HRCT image photographed at soft tissue windows shows increased caliber of the pulmonary artery trunk. Lung window images (not shown) demonstrated no parenchymal abnormalities.

stitial pneumonia. The incidence of pulmonary hypertension in collagen vascular diseases is variable, depending on the type of collagen vascular disease, on the concomitant presence of interstitial disease and on the diagnostic method utilized<sup>(8,18)</sup>. Pulmonary hypertension is most common in scleroderma (approximately 25% of patients), systemic lupus erythematosus (5–10%) and mixed connective tissue disease<sup>(8,18)</sup>.

Increase in the diameter of the main pulmonary artery trunk (> 2.9 cm) (Figure 8),

main, lobar and segmental pulmonary arteries represent typical findings of pulmonary hypertension at HRCT<sup>(3)</sup>. Artery wall calcification may be identified in patients with severe and longstanding hypertension, as well as thrombi, especially in patients with systemic lupus erythematosus and antiphospholipid antibodies. A mosaic perfusion pattern may be present. Rarely, centrilobular nodules and diffuse or patchy ground-glass opacities are identified at HRCT (Figure 9). These abnormalities may

be multifactorial and result from the pulmonary hypertension itself (proliferation of small muscular arteries, chronic passive congestion which may lead to engorgement of the capillary bed, deposition of cholesterol granulomas, focal areas of hemorrhage) or may be associated with the presence of pulmonary capillary hemangiomatosis (Figure 9) (exaggerated multifocal capillary proliferation within the alveolar walls). The concomitant presence of interlobular septal thickening in patients with

pulmonary hypertension can be secondary to right cardiac failure or, less frequently, pulmonary venoocclusive disease.

The main HRCT manifestations of diffuse pulmonary hemorrhage (capillaritis) in collagen vascular disease consist in diffuse ground-glass opacities (Figure 10), "crazy paving" pattern, patchy consolidation, and centrilobular nodules, or lobular areas of ground-glass opacities<sup>(3)</sup>. The main differential HRCT diagnosis includes: pulmonary infections, especially pneumonia by *Pneumocystis*, diffuse alveolar damage (Figure 6) and drug-induced lung disease (Figure 7)<sup>(4)</sup>.

### 3. Pulmonary nodules or masses

The differential diagnosis of pulmonary nodules or masses in patients with collagen vascular disease is broad and includes op-

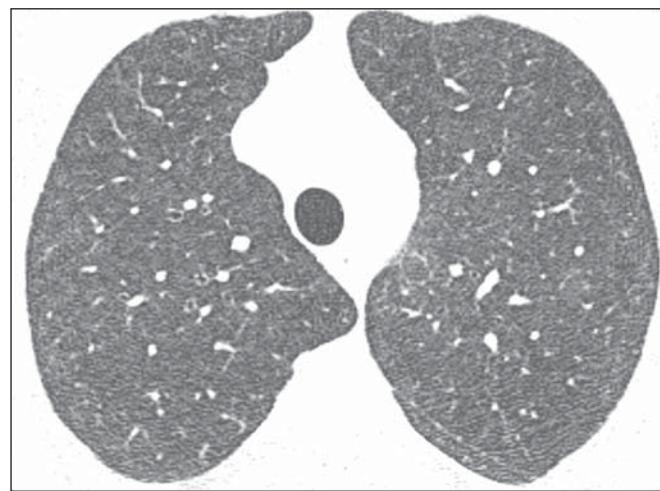
portunistic infectious processes (*Nocardia*, *Cryptococcus*, *Aspergillus*, *Histoplasma*, atypical mycobacteria), neoplasms (carcinoma, lymphoma), metabolic process (amyloidosis), and immunological process (rheumatoid nodules)<sup>(19)</sup>. The main causes of pulmonary nodules and masses found at HRCT of patients with collagen vascular disease are summarized as follows:

**a) Rheumatoid nodules** – Rare, but may be found in patients with rheumatoid arthritis, subcutaneous nodules and positive rheumatoid factor<sup>(1,20)</sup>. Sizes range between 0.5 cm and 7 cm in diameter, and may be single or multiple. These nodules rarely develop in the pleura or pericardium. Rheumatoid nodules may cavitate (up to 50%), causing hemoptysis or pneumothorax, or become infected<sup>(19-21)</sup>. Spontaneous resolution may occur. Calcification is

rare<sup>(19)</sup>. An unusual association between rheumatoid nodules and pneumoconiosis (particularly in coal-mining workers) in patients with rheumatoid disease is called Caplan's syndrome<sup>(19)</sup>.

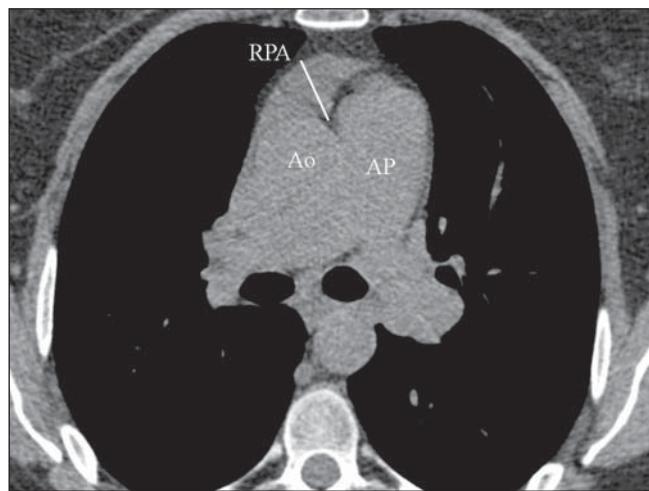
**b) Pulmonary lymphoma** – Most frequently occurring in patients with Sjögren's syndrome, it also can be found in patients with rheumatoid arthritis<sup>(19,22)</sup>. At HRCT, pulmonary lymphomas may present as nodules (generally with > 1.0 cm in diameter), consolidation or, rarely, ground-glass opacities<sup>(12,22)</sup>.

**c) Amyloidosis** – The parenchymal nodular presentation of amyloidosis may occur in patients with Sjögren's syndrome and lymphocytic interstitial pneumonia<sup>(22,23)</sup>. The nodules may be single or multiple, may have foci of calcification and localization in the pulmonary parenchyma

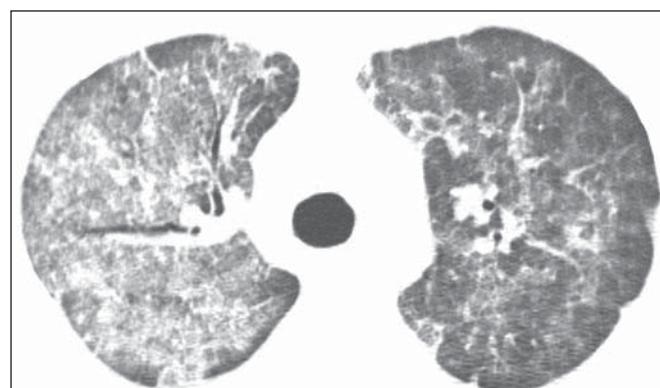


A

**Figure 9.** Pulmonary capillary hemangiomatosis in a patient with progressive systemic sclerosis and severe pulmonary hypertension. HRCT image (A) demonstrates diffuse ground-glass opacities and centrilobular nodules mimicking hypersensitivity pneumonitis. Image photographed at soft tissue windows (B) demonstrates increase in the caliber of the pulmonary artery (AP) trunk and presence of fluid in the anterior pericardial recess (RPA) with more than 10 mm in thickness a finding shows to correlate with poor prognosis. Ao, ascending aorta.



B



**Figure 10.** Diffuse pulmonary hemorrhage in a patient with systemic lupus erythematosus. HRCT image demonstrates diffuse ground-glass opacities predominating in the right lung and nodular opacities.

or within pulmonary cysts. The diffuse presentation of pulmonary amyloidosis is rare, but may be found in patients with rheumatoid arthritis and Sjögren's syndrome<sup>(12,19,22,24)</sup>. At HRCT, diffuse pulmonary amyloidosis is characterized by diffuse micronodules and interlobular septal thickening.

**d) Pulmonary carcinoma** – Some studies have shown an increased incidence of pulmonary carcinoma in patients with collagen disease and concomitant fibrotic interstitial vascular disease<sup>(1,19)</sup>, however, this relationship is not well established<sup>(25,26)</sup>.

The incidence of neoplasms (including lung cancer) in patients with scleroderma is estimated to range from 3.6% to 10.7%<sup>(27)</sup>. Recently, a study has observed that the incidence of lung cancer in patients with scleroderma is not related to the concomitant presence of pulmonary fibrosis, scleroderma subtype, or to the immunological status of the patient; on the other hand, smoking patients with scleroderma have a seven times higher risk for developing lung cancer than non-smoking patients<sup>(28)</sup>. At HRCT, pulmonary carcinoma may manifest as a spiculated nodule or pulmonary mass (Figure 11). The main differential diagnosis includes rheumatoid nodule (in rheumatoid arthritis), infectious processes (especially fungi), focal amyloidosis and pulmonary lymphoma (particularly in patients with Sjögren's syndrome) and localized organizing pneumonia (BOOP) (Figure 12).

#### 4. Diffuse pulmonary consolidation

In patients with systemic lupus erythematosus, diffuse consolidation may result from lupus pneumonitis or diffuse pulmonary hemorrhage (Figure 10)<sup>(1,19)</sup>. Drug-induced lung disease and infection should always be considered in the differential

diagnosis. The presence of predominant consolidation in dependent pulmonary regions, particularly in association with centrilobular nodules, may correspond to aspiration pneumonia, a quite common finding in patients with scleroderma and dermatopolymyositis caused by esophageal dysmotility<sup>(19,29)</sup>.

#### 5. Airway

##### a) Large airways – bronchiectasis

Bronchiectasis occurs most commonly in rheumatoid arthritis (up to 30%), and also may be found in Sjögren's syndrome and systemic lupus erythematosus<sup>(1,3,19)</sup>. At HRCT, it is more common in the lower lobes, and of cylindrical type (Figure 13)<sup>(7)</sup>. The cause for bronchiectasis in patients with collagen vascular disease is multifactorial; it may be due to repeated infections (particularly in rheumatoid arthritis), involvement of the small airways or airway dryness (Sjögren's syndrome)<sup>(1-3,7)</sup>.

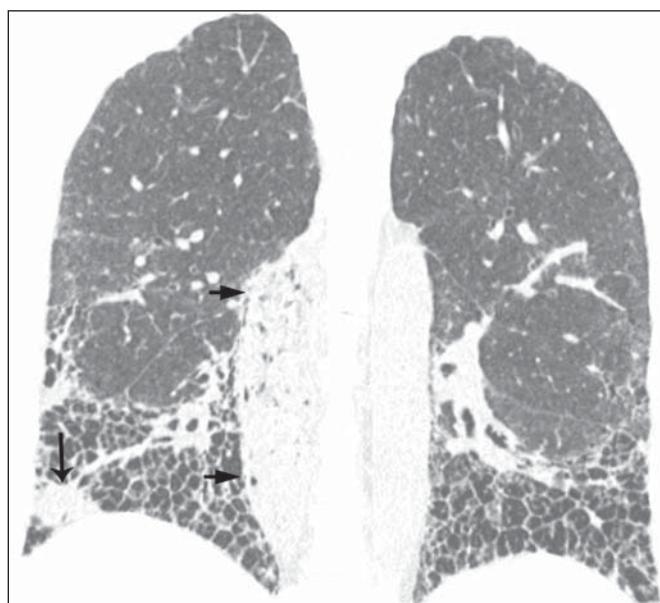
##### b) Small airways-- bronchiolitis

– *Bronchiolitis obliterans (constrictive bronchiolitis)* occurs most commonly in women with rheumatoid arthritis and less frequently in patients with Sjögren's syndrome<sup>(1-3)</sup>. Main HRCT findings include

areas of decreased attenuation and vascularity, with or without redistribution of the blood flow towards non-involved regions, resulting in mosaic perfusion pattern (Figure 13)<sup>(3,7)</sup>. Expiratory HRCT demonstrates air trapping. Dilated bronchi (bronchiectasis) (Figure 13) and thickened bronchial walls also can be found<sup>(3,7)</sup>. It is important to note that bronchiolitis obliterans may also result from penicillamine therapy in patients with rheumatoid arthritis<sup>(19)</sup>. Pulmonary hypertension also may result in mosaic perfusion (attenuation) at HRCT; however, at expiratory HRCT, air trapping is not usually found and, differently from bronchiolitis obliterans, an increase in the pulmonary artery caliber is observed.

– *Follicular bronchiolitis* represents bronchiocentric lymphoid hyperplasia most frequently found in rheumatoid arthritis, Sjögren's syndrome and scleroderma<sup>(1-3,30)</sup>. The HRCT may be normal or show centrilobular and peribronchovascular nodules<sup>(31)</sup>. The main differential diagnosis at HRCT includes infectious process and aspiration (most frequently found in dependent pulmonary regions).

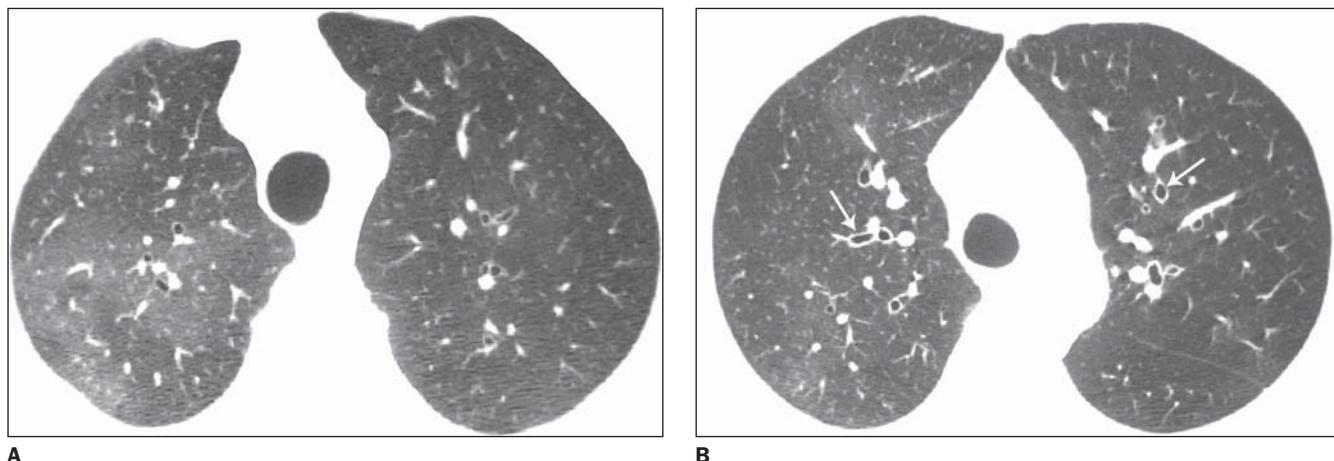
– *Exudative bronchiolitis (cellular)*, generally of infectious nature, characterized at HRCT as centrilobular nodules or



**Figure 11.** Pulmonary carcinoma in a patient with progressive systemic sclerosis and pulmonary fibrosis. Coronal HRCT image demonstrates a tortuous and dilated esophagus (arrowheads), spiculated nodule (arrow) in the periphery of the right lung base and signs of advanced-stage pulmonary fibrosis, characterized by honeycombing, reticulation and traction bronchiectasis mainly in the lung bases.



**Figure 12.** Organizing pneumonia mimicking neoplasm or infectious process in a patient with Sjögren's syndrome. HRCT image demonstrates pulmonary nodules with halo sign in the left upper lobe and focal bilateral ground-glass opacities. CT-guided biopsy demonstrated typical findings of organizing pneumonia. Post-corticosteroid-therapy follow-up (not shown) demonstrated complete resolution of the findings.

**A**

**Figure 13.** Airway abnormalities in a patient with rheumatoid arthritis. HRCT images (**A, B**) demonstrate dilated bronchi (arrows on **B**) and signs of small airway involvement (bronchiolitis obliterans) characterized by areas of decreased attenuation and vascularity with blood flow redistribution to non-involved regions resulting in a pattern of mosaic perfusion (attenuation).

branching nodular opacities (tree-in-bud pattern) with bilateral and asymmetrical distribution<sup>(3)</sup>.

#### 6. Other intrathoracic manifestations of collagen vascular diseases

Collagen vascular diseases may also be associated with other intrathoracic abnormalities summarized as follows:

##### a) Lymphonodomegaly

Enlargement of mediastinal lymph nodes is frequently found in patients with collagen vascular disease; it is most commonly associated with the presence of interstitial lung disease, and is found in approximately 70% of patients with scleroderma<sup>(19,32)</sup>. Usually, lymph nodes measure up to 1.5 cm in short axis diameter, and only one or two nodal stations are involved. Enlarged hilar and mediastinal lymph nodes may, however, be found in any patient with collagen vascular disease, including in the absence of interstitial disease, from varied causes such as: sarcoidosis, infection, lymphoma, metastasis, inflammatory response to the presence of reflux or aspiration pneumonia<sup>(19,32)</sup>.

##### b) Abnormalities of the pleura and pericardium

Pleural involvement (effusion or thickening) is quite frequent particularly in systemic lupus erythematosus and rheumatoid arthritis<sup>(1,19,33)</sup>. The presence of concomitant pericardial effusion is common. More

than half of patients with systemic lupus erythematosus, as the disease progresses, develop pleural effusion, generally bilateral and with a serous or serosanguinous appearance<sup>(33)</sup>. Pleural effusion, as well as pericardial effusion, may also be a result from the use of procainamide and hydralazine in patients with systemic lupus erythematosus<sup>(19)</sup>. In rheumatoid arthritis, pleural thickening is found in 70% of patients and pleural effusion in approximately 5% of patients<sup>(19)</sup>.

In many patients (up to 50%), pericardial abnormalities (pericardial effusion, pericardial adherence and fibrotic or fibrinous pericarditis) are asymptomatic<sup>(34)</sup>. Pericardial effusion, frequently in association with pleural effusion, is one of the most common intrathoracic manifestations of systemic lupus erythematosus. Generally, pericardial effusion has a good prognosis. However, it is important to note that the presence of pericardial effusion associated with pulmonary hypertension (defined by means of echocardiography) in patients with collagen vascular disease, particularly in cases where fluid is detected in the anterior pericardial recess, measuring > 10 mm (Figure 9B), is associated with a poor prognosis<sup>(34,35)</sup>.

##### c) Diaphragmatic dysfunction

This is an uncommon condition, but may be found in patients with systemic lupus erythematosus and, occasionally, in patients with dermatopolymyositis<sup>(1,3)</sup>, re-

sulting in dyspnea, restrictive pattern of pulmonary function in the absence of pulmonary abnormalities and diaphragmatic elevation with adjacent basal atelectasis.

##### d) Esophageal dysmotility

This is a common condition in patients with scleroderma and dermatopolymyositis<sup>(19)</sup>. Asymptomatic esophageal dilatation may be identified in 40% to 80% of patients with scleroderma (Figure 4)<sup>(29)</sup>. At HRCT, the coronal diameter of the esophageal lumen in patients with scleroderma ranges between 1.2 cm and 4.0 cm (mean 2.3 cm)<sup>(29)</sup>. Esophageal dysmotility may lead to aspiration pneumonia.

#### CONCLUSION

Intrathoracic manifestations of collagen vascular diseases are common and are clinically important. The main pulmonary manifestations include diffuse interstitial pneumonia and pulmonary hypertension which, as a whole, represent the main causes of morbidity and mortality in these patients. The pattern and frequency of parenchymal, vascular, pericardial, pleural and airway involvement, as well as diaphragmatic and esophageal abnormalities depend on the specific type of collagen vascular disease. Awareness of the several patterns of involvement found at HRCT, as well as their clinical/radiological correlation is essential. Intrathoracic manifestations of collagen vascular diseases may be

multicompartimental, be due to the underlying disease or be secondary to treatment and thus include drug reaction and opportunistic infection.

## REFERENCES

1. Devaraj A, Wells AU, Hansell DM. Computed tomographic imaging in connective tissue diseases. *Semin Respir Crit Care Med.* 2007;28:389–97.
2. Woodhead F, Wells AU, Desai SR. Pulmonary complications of connective tissue diseases. *Clin Chest Med.* 2008;29:149–64, vii.
3. Tanaka N, Newell JD, Brown KK, et al. Collagen vascular disease-related lung disease: high-resolution computed tomography findings based on the pathologic classification. *J Comput Assist Tomogr.* 2004;28:351–60.
4. Tansey D, Wells AU, Colby TV, et al. Variations in histological patterns of interstitial pneumonia between connective tissue disorders and their relationship to prognosis. *Histopathology.* 2004;44:585–96.
5. Primack SL, Müller NL. Radiologic manifestations of the systemic autoimmune diseases. *Clin Chest Med.* 1998;19:573–86, vii.
6. Lamblin C, Bergoin C, Saelens T, et al. Interstitial lung diseases in collagen vascular diseases. *Eur Respir J Suppl.* 2001;32:69S–80.
7. Tanaka N, Kim JS, Newell JD, et al. Rheumatoid arthritis-related lung diseases: CT findings. *Radiology.* 2004;232:81–91.
8. Hooper MM. Pulmonary hypertension in collagen vascular disease. *Eur Respir J.* 2002;19:571–6.
9. Lynch DA, Travis WD, Muller NL, et al. Idiopathic interstitial pneumonias: CT features. *Radiology.* 2005;236:10–21.
10. Won Huh J, Soon Kim D, Keun Lee C, et al. Two distinct clinical types of interstitial lung disease associated with polymyositis-dermatomyositis. *Respir Med.* 2007;101:1761–9.
11. Desai SR, Veeraraghavan S, Hansell DM, et al. CT features of lung disease in patients with systemic sclerosis: comparison with idiopathic pulmonary fibrosis and nonspecific interstitial pneumonia. *Radiology.* 2004;232:560–7.
12. Parambil JG, Myers JL, Lindell RM, et al. Interstitial lung disease in primary Sjögren syndrome. *Chest.* 2006;130:1489–95.
13. Park JH, Kim DS, Park IN, et al. Prognosis of fibrotic interstitial pneumonia: idiopathic versus collagen vascular disease-related subtypes. *Am J Respir Crit Care Med.* 2007;175:705–11.
14. Sato T, Fujita J, Yamadori I, et al. Non-specific interstitial pneumonia; as the first clinical presentation of various collagen vascular disorders. *Rheumatol Int.* 2006;26:551–5.
15. Silva CI, Müller NL, Fujimoto K, et al. Acute exacerbation of chronic interstitial pneumonia: high-resolution computed tomography and pathologic findings. *J Thorac Imaging.* 2007;22:221–9.
16. Horoupiian N, English J, Müller NL. Accelerated deterioration of usual interstitial pneumonia with acute development of honeycomb cysts in rheumatoid arthritis. *J Thorac Imaging.* 2004;19:127–30.
17. Kishida Y, Kanai Y, Kuramochi S, et al. Pulmonary venoocclusive disease in a patient with systemic lupus erythematosus. *J Rheumatol.* 1993;20:2161–2.
18. Handa T, Nagai S, Miki S, et al. Incidence of pulmonary hypertension and its clinical relevance in patients with interstitial pneumonias: comparison between idiopathic and collagen vascular disease associated interstitial pneumonias. *Intern Med.* 2007;46:831–7.
19. Rockall AG, Rickards D, Shaw PJ. Imaging of the pulmonary manifestations of systemic disease. *Postgrad Med J.* 2001;77:621–38.
20. Tanoue LT. Pulmonary involvement in collagen vascular disease: a review of the pulmonary manifestations of the Marfan syndrome, ankylosing spondylitis, Sjögren's syndrome, and relapsing polychondritis. *J Thorac Imaging.* 1992;7:62–77.
21. Kobayashi T, Satoh K, Ohkawa M, et al. Multiple rheumatoid nodules with rapid thin-walled cavity formation producing pneumothorax. *J Thorac Imaging.* 2005;20:47–9.
22. Jeong YJ, Lee KS, Chung MP, et al. Amyloidosis and lymphoproliferative disease in Sjögren syndrome: thin-section computed tomography findings and histopathologic comparisons. *J Comput Assist Tomogr.* 2004;28:776–81.
23. Desai SR, Nicholson AG, Stewart S, et al. Benign pulmonary lymphocytic infiltration and amyloidosis: computed tomographic and pathologic features in three cases. *J Thorac Imaging.* 1997;12:215–20.
24. Sumiya M, Ohya N, Shinoura H, et al. Diffuse interstitial pulmonary amyloidosis in rheumatoid arthritis. *J Rheumatol.* 1996;23:933–6.
25. Pearson JE, Silman AJ. Risk of cancer in patients with scleroderma. *Ann Rheum Dis.* 2003;62:697–9.
26. Hill CL, Nguyen AM, Roder D, et al. Risk of cancer in patients with scleroderma: a population based cohort study. *Ann Rheum Dis.* 2003;62:728–31.
27. Wooten M. Systemic sclerosis and malignancy: a review of the literature. *South Med J.* 2008;101:59–62.
28. Pontifex EK, Hill CL, Roberts-Thomson P. Risk factors for lung cancer in patients with scleroderma: a nested case-control study. *Ann Rheum Dis.* 2007;66:551–3.
29. Bhalla M, Silver RM, Shepard JA, et al. Chest CT in patients with scleroderma: prevalence of asymptomatic esophageal dilatation and mediastinal lymphadenopathy. *AJR Am J Roentgenol.* 1993;161:269–72.
30. Hayakawa H, Sato A, Imokawa S, et al. Bronchialar disease in rheumatoid arthritis. *Am J Respir Crit Care Med.* 1996;154:1531–6.
31. Howling SJ, Hansell DM, Wells AU, et al. Follicular bronchiolitis: thin-section CT and histologic findings. *Radiology.* 1999;212:637–42.
32. Wechsler RJ, Steiner RM, Spirl PW, et al. The relationship of thoracic lymphadenopathy to pulmonary interstitial disease in diffuse and limited systemic sclerosis: CT findings. *AJR Am J Roentgenol.* 1996;167:101–4.
33. Kim JS, Lee KS, Koh EM, et al. Thoracic involvement of systemic lupus erythematosus: clinical, pathologic, and radiologic findings. *J Comput Assist Tomogr.* 2000;24:9–18.
34. Fischer A, Misumi S, Curran-Everett D, et al. Pericardial abnormalities predict the presence of echocardiographically defined pulmonary arterial hypertension in systemic sclerosis-related interstitial lung disease. *Chest.* 2007;131:988–92.
35. Baque-Juston MC, Wells AU, Hansell DM. Pericardial thickening or effusion in patients with pulmonary artery hypertension: a CT study. *AJR Am J Roentgenol.* 1999;172:361–4.