Pulmonary manifestations of systemic lupus erythematosus

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Pulmonary involvement is more common in systemic lupus erythematosus (SLE) than in any other connective tissue disease, and more than half of patients with SLE suffer from respiratory dysfunction during the course of their illness. Although sepsis and renal disease are the most common causes of death in SLE, lung disease is the predominant manifestation and is an indicator of overall prognosis. Respiratory disease may be due to direct involvement of the lung or as a secondary consequence of the effect of the disease on other organ systems.

Index words: Lung, diseases

Lupus erythematosus

Thoracic involvement is more common in systemic lupus erythematosus (SLE) than in any other connective tissue diseases (1, 2), and more than half of all patients with the disease suffer from respiratory dysfunction during the course of their illness. Although sepsis and renal disease are the most common causes of death in SLE, lung disease is the predominant manifestation and is an indicator of overall prognosis. Respiratory disease may be due to direct involvement of the lung or as a secondary consequence of the effect of SLE on other organ systems. This pictorial essay will review the radiographic and CT findings of various pulmonary manifestations of SLE, including secondary pulmonary manifestations.

Primary Involvement of the Respiratory System

Acute lupus pneumonitis

Acute lupus pneumonitis is an abrupt febrile pneumonic process mostly without infectious etiology, and antibiotics usually fail to favorably alter its course. A favorable response to corticosteroid, with normalization of the clinical and radiological manifestations, can be helpful in establishing its diagnosis. The histopathologic findings are not diagnostic or pathognomonic (1, 2), but include alveolar wall damage and necrosis, inflammatory infiltrates, hemorrhage, edema, and hyaline membrane. The radiologic findings consist of patchy unilateral or bilateral areas of ground glass opacity or air space consolidation, involving mainly lung bases (2) [Figs. 1, 2], features which may be indistinguishable from those of a pneumonic process caused by bacterial and nonbacterial opportunistic infection, or of thromboembolic disease. Because infection is common, particularly in patients undergoing corticosteroid or immunosuppressive therapy, differentiation between these causes is critical (2).

Pulmonary hemorrhage

Pulmonary hemorrhage in SLE, the pathogenesis of which is unknown, varies from a mild, subclinical, chronic form to acute, massive, life-threatening bleeding. Some of its cardinal features, such as hemoptysis and hypoxemia, may be lacking even where hemorrhage is severe. In patients with hemoptysis, two find-
Fig. 1. Acute lupus pneumonitis in a 46-year-old woman with SLE. She was presented with abrupt onset of dyspnea and fever, but laboratory data showed no evidence suggestive of infectious origin.

A. Frontal chest radiograph shows ill-defined hazy opacities in both lower lungs.
B. Thin-section CT at the level of basal lung shows areas of nodular consolidation and ground-glass attenuation in both lower lobes. After steroid pulse therapy for 2 weeks, most lung lesions resolved (not shown).

Fig. 2. Acute lupus pneumonitis in a 21-year-old woman with SLE.

A. Frontal chest radiograph shows focal air-space consolidation in the left upper lung.
B. CT scan at the level of the aortic arch shows air-space consolidation and multiple, ill-defined nodular opacities. Laboratory studies, including biopsy of the lung, did not reveal any infectious organism at this time.
C. Thin-section CT at the level similar to B, obtained after steroid medication for 1 month, shows improvement of the consolidation but newly developed lung cysts or airway dilatation (arrows).
ings may suggest significant pulmonary hemorrhage: a marked drop in hematocrit over a period of 12 to 36 hours, and an otherwise unexplained increase in the diffusive capacity of carbon monoxide, or DLCO [2]. Chest radiography depicts areas of ill-defined, patchy, acinar opacity that are usually bilateral and located in the lower lung zones (Fig. 3). With the cessation of hemoptysis, the findings of radiography improve rapidly and often normalize within 2-4 days [2]. CT demonstrates ground-glass opacity and, sometimes, frank consolidation. A nodular pattern with no zonal predominance or bronchocentricity may be also seen, especially during complete or partial clinical remission [3].

**Bronchiolitis obliterans organizing pneumonia**

Bronchiolitis obliterans organizing pneumonia (BOOP) is a pathologic entity characterized by the formation of plugs of fibrous tissue in bronchioles and alveolar ducts. Most cases are idiopathic, but a BOOP-like reaction has been described in association with several connective tissue diseases. Radiologically, BOOP is characterized by peripheral and basilar ground-glass opacities or consolidations, and may be associated with pleural and/or pericardial effusions.

A woman with SLE presented with abrupt onset of fever, dyspnea, and anemia. Frontal chest radiograph shows air space consolidation in parahilar and lower lung field bilaterally. The patient revealed increased diffusing capacity for carbon monoxide, or DLCO, and hemosiderin-laden macrophages in bronchoalveolar lavage, confirming the diagnosis.

**Fig. 3.** Pulmonary hemorrhage in a 33-year-old woman with SLE.

She was presented with abrupt onset of fever, dyspnea, and anemia. Frontal chest radiograph shows air space consolidation in parahilar and lower lung field bilaterally. The patient revealed increased diffusing capacity for carbon monoxide, or DLCO, and hemosiderin-laden macrophages in bronchoalveolar lavage, confirming the diagnosis.

**Fig. 4.** Bronchiolitis obliterans organizing pneumonia in a 24-year-old woman with SLE and lupus cardiac disease.

A. Frontal chest radiograph shows cardiomegaly, bilateral pleural effusion, and peripheral patchy increased opacities, predominantly in the right lung. Also note a chest tube [arrowheads] in the left pleural space which was inserted to drain pleural effusion. BOOP was confirmed by gun biopsy. Frontal chest radiograph became normalized after steroid pulse therapy for one month [not shown].

B, C. Thin-section CT scans at levels of the aortic arch (B) and basal lungs (C) at the same time as A show nodules [arrow] and consolidations predominantly in the peripheral lung. Interlobular septal thickening and dilated pulmonary veins [arrowhead] indicate pulmonary congestion associated with lupus cardiac disease.
tissue diseases including SLE. The prognosis is generally excellent. Bronchiolitis obliterans organizing pneumonia typically manifests with scattered, bilateral ground-glass attenuation or air space consolidation. All lung zones are equally affected (1, 2). Distinct subpleural and/or peribronchial distribution may be seen in 50-60% of cases (Fig. 4), and discrete centrilobular nodules may be associated.

**Constrictive bronchiolitis (obliterative bronchiolitis)**

At lung function testing, constrictive bronchiolitis is characterized by airflow obstruction due to submucosal and peribronchiolar inflammation and fibrosis, which primarily involves respiratory bronchioles, and the absence of diffuse parenchymal inflammation. Chest radiography usually reveals no parenchymal abnormality. The most obvious thin-section CT findings are focal, often sharply defined, areas of decreased lung attenuation associated with vessels of decreased caliber in the absence of parenchymal consolidation; bronchiectasis, mainly at a subsegmental level, may also be noted (Figs. 5, 6). In addition, expiratory CT shows focal areas of air trapping consistent with small airway obstruction. In rare cases, areas of opacity, either centrilobular branching or ill-defined centrilobular, may be a predominant finding (Fig. 5).

**Chronic interstitial pneumonitis and fibrosis**

The prevalence of clinically significant interstitial lung disease in SLE has been reported in as few as 1-6% of patients. However, with the use of thin-section CT, the detection rate of early, SLE-associated, interstitial disease is increasing (1, 4). Although the disease which complicate SLE resemble those of idiopathic pulmonary fibrosis, including both usual and nonspecific interstitial pneumonitis, both pathologically and radiologically, its course is usually less severe from clinical and functional points of view. The radiographic findings include bibasilar areas of irregular linear opacity, ground-glass attenuation, and loss of lung volume (Fig. 7). The typical CT appearance includes interlobular and intralobular interstitial thickening, areas of ground-glass attenuation, and
traction bronchiectasis with predominantly subpleural and basal involvement (1, 4) (Fig. 7). End-stage disease is accompanied by honeycombing, traction bronchiectasis, and architectural distortion, as in the case of usual interstitial pneumonitis (Fig. 7). Mild enlargement of the mediastinal lymph nodes is common.

**Pulmonary vascular disease**

Pulmonary vascular involvement in SLE may include the capillary, arterial, and venous systems. Venous involvement, however, is radiographically distinct from pulmonary hypertension caused by arterial involvement.

**Pulmonary arterial hypertension**

In approximately 10% of SLE patients, clinically evident pulmonary arterial hypertension is present (2, 3). The potential mechanisms of the condition include interstitial pneumonitis, small pulmonary arterial vasculitis, thrombosis in situ or pulmonary thromboembolism, and primary pulmonary hypertension (2). Vascular abnormalities typically affect small muscular arteries (2). During the early phase, chest radiographic findings may be normal, but advanced radiographic findings include...

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**Fig. 6.** Constrictive bronchiolitis in a 21-year-old woman with SLE who showed severely obstructive pattern on pulmonary function test.

A. Inspiratory thin-section CT at the level of basal lungs shows focal, relatively well defined normal areas of increased attenuation (arrows) interspersed with radiolucent areas indicative of air trapping. Also, note bronchial dilatation.

B. Expiratory thin-section CT at the same level as A show marked air trapping.

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**Fig. 7.** Chronic interstitial lung disease in a 22-year-old woman with SLE.

A. Frontal chest radiograph shows ill-defined reticular opacity in the left lower lung.

B. Thin-section CT at the level of basal lungs shows interlobular and intralobular septal thickening and patchy ground-glass attenuation.
enlargement of the right ventricle, and prominent main pulmonary artery with distal attenuation of the arteries (3) [Fig. 8]. Ventilation/perfusion scanning or pulmonary angiography can help exclude pulmonary embolism.

**Pulmonary veno-occlusive disease**

Pulmonary veno-occlusive disease is a rare form of pulmonary hypertension characterized pathologically by repeated pulmonary venous thrombosis, and clinically by pulmonary arterial hypertension and edema. The disorder has been reported in association with a variety of autoimmune diseases. Radiographically, pulmonary veno-occlusive disease shows signs of pulmonary arterial hypertension very similar to those associated with primary pulmonary arterial hypertension or thromboembolic disease, but includes an important additional sign of pulmonary edema. The most common CT findings include smooth interlobular thickening and areas of ground-glass attenuation consistent with interstitial pulmonary edema, enlarged central pulmonary arteries,
and pulmonary veins of normal caliber (Fig. 9). A mosa-
ic pattern of lung attenuation, as well as pleural effu-
sion, is frequently present.

**Secondary Involvement of the Respiratory System**

Severe multi-organ diseases often confound the clini-
cal status of patients with SLE, treatment for such dis-
ease, and its attendant complications. Renal failure, cen-
tral nervous system involvement, or cardiac involve-
ment may lead to pulmonary edema (Fig. 10). In addi-
tion, pericardial effusion, neuromuscular disease, and
diaphragmatic dysfunction can affect the respiratory
system, resulting in passive atelectasis, for example, and
oxygen therapy or cytotoxic chemotherapy may cause
pulmonary toxicity. Infection, however, is the most im-
portant cause of indirect involvement of the lungs in
SLE [2].

**Pulmonary infection other than tuberculosis in SLE**

Pulmonary infection is a major cause of morbidity and
mortality in SLE, with either common bacterial agents
or more unusual opportunistic organisms causing pul-
monary infections. Opportunistic infections in SLE pa-

tients include aspergillosis, cryptococcosis, pneumocys-
tis carinii (Fig. 11), cytomegalovirus, and nocardia.

Though the exact impact of early diagnosis of oppor-
tunistic infection is difficult to predict, clearly some
such infections, including Pneumocystis carinii, Can-
dida albicans, and Nocardia, may be treatable.

Uncommon clinical and radiographic abnormalities
may, however, accompany common bacterial infec-
tions. The risk of infection in the absence of immuno-
suppression is small, though an aggressive diagnostic
approach to exclude infection in any patient with SLE pre-

centing with new pulmonary infiltrates is warranted,
particularly if immunosuppressive therapy is ongoing.

**Fig. 10.** Pulmonary edema in a 34-year-old woman with SLE.

Thin-section CT at the level of the diaphragm shows typical
features of pulmonary edema, including dilated pulmonary
vessels [arrow], smooth thickening of the interlobular septa
[arrowheads], and areas of ground-glass attenuation.

**Fig. 11.** Pneumocystis carinii pneumonia in a 33-year-old woman with SLE who had been taking pulse therapy with corticosteroid
and cyclosporin for a month.

A, B. Thin-section CT scans at levels of the aortic arch (A) and basal lungs (B) show mosaic pattern of ground-glass opacities admixed with intra- and interlobular septal thickening, namely crazy-paving appearance. Also note clear sparing of isolated secondary lobules [arrows]. Left lung shows fibrosis and marked volume contraction secondary to longstanding tuberculosis. The organism was isolated from bronchoalveolar lavage fluid.
Pulmonary Tuberculosis in SLE

Pulmonary tuberculosis in patients with SLE may manifest differently than in immunocompetent patients, and because of the abnormal functioning of alveolar macrophages and exposure to corticosteroid and cytotoxic drugs, the incidence in the former may be higher (5). Delayed diagnosis may contribute to a higher incidence of miliary, far-advanced, and extrapulmonary tuberculosis. In patients with SLE who are taking steroids, the radiologic findings can be similar to those seen in secondary tuberculosis, such as areas of apical nodular opacity (Fig. 12), or in primary tuberculosis, such as large air-space consolidation, lymphadenitis, pleural effusion, or miliary tuberculosis (Fig. 13) (5). Thin-section CT findings of miliary tuberculosis resemble those described in that previous report: miliary nodules associated with interlobular septal thickening, intralobular reticulation, ground-glass attenuation, and pleural effusion (Fig. 13).

Conclusion

Because pulmonary disease is the predominant manifestation of the illness and a primary indicator of overall prognosis, an understanding of the various radiographic and CT findings of pulmonary involvement in SLE per-

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**Fig. 12.** Pulmonary tuberculosis in a 26-year-old man who had been taking steroid medication for SLE for one year.
A. Magnified frontal chest radiograph shows poorly-defined nodular and linear opacities in both upper lungs.
B. Magnified thin-section CT showing the right lung apex reveals centriflobular nodular and branching opacities (arrowheads) in the right upper lobe.

**Fig. 13.** Miliary tuberculosis in a 58-year-old woman who had been taking steroid therapy for SLE for 6 months.
A. Plain chest radiograph obtained at admission shows innumerable tiny nodular shadows in the entire lung.
B. Thin-section CT at the level of the carina shows miliary nodules of random distribution and areas of ground-glass attenuation.
mits appropriate patient management.

References