Thoracic Manifestation of Churg-Strauss Syndrome*

Radiologic and Clinical Findings

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Study objectives: To describe the radiologic and clinical findings of Churg-Strauss syndrome (CSS) and its thoracic manifestations.

Design: We used retrospective analysis to review and characterize the radiographic, thin-section CT, and clinical findings of CSS.

Patients: The study involved nine patients with CSS. The patients included four men and five women, whose ages ranged from 18 to 60 years (median, 35 years). Thin-section CT scans and chest radiographs were retrospectively analyzed by three radiologists in consensus. Clinical data were obtained by chart review. Histologic samples were available in eight patients.

Results: All patients had a history of asthma averaging 28 months (range, 4 to 72 months) prior to the initial symptom of vasculitis and marked peripheral blood eosinophilia (mean peak count, 8,726/μL; range, 3,000 to 32,000/μL; mean differential count, 41%; range, 19 to 67%). All patients had systemic vasculitis involving the lung and two to four extrapulmonary organs, most commonly the nervous system (n = 8) and skin (n = 7). Chest radiographs showed bilateral nonsegmental consolidation (n = 5), reticulonodular opacities (n = 3), bronchial wall thickening (n = 3), and multiple nodules (n = 1). The most common thin-section CT findings included bilateral ground-glass opacity (n = 9); airspace consolidation (n = 5), predominantly subpleural and surrounded by the ground-glass opacity; centrifibular nodules mostly within the ground-glass opacity (n = 8); bronchial wall thickening (n = 7); and increased vessel caliber (n = 5). Other findings were hyperinflation (n = 4), larger nodules (n = 4), interlobular septal thickening (n = 2), hilar or mediastinal lymph node enlargement (n = 4), pleural effusion (n = 2), and pericardial effusion (n = 2).

Conclusions: In CSS, thoracic organs are invariably involved with additional diverse manifestations. The possibility of CSS should be raised in patients with a history of asthma and hypereosinophilia who present with thin-section CT findings of bilateral subpleural consolidation with lobular distribution, centrifibular nodules (especially within the ground-glass opacity) or multiple nodules, especially in association with bronchial wall thickening.

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Abbreviation: CSS = Churg-Strauss syndrome

Originally described in 1951 as an allergic angitis and granulomatosis, Churg-Strauss syndrome (CSS) is a very rare systemic disease with clinical and pathologic features that overlap with those of polyarteritis nodosa and Wegener’s granulomatosis.1–5 The syndrome is characterized by systemic vasculitis, extravascular granulomas, and eosinophilia, and occurs almost exclusively in patients with asthma or a history of allergy.1,6,7 Although recognized as a multisystem disorder, the predominant sites of involvement are the lungs, skin, and nervous system.6,7 As pulmonary involvement is seen in virtually all the patients with CSS, Lie‡4,8 considered CSS to be a valid addition to the five varieties of pulmonary angitis and granulomatosis that were previously defined by Liebow9: classic and limited forms of Wegener’s granulomatosis,10 lymphomatoid granulomatosis, necrotizing sarcoid granulomatosis, and bronchocentric granulomatosis. Although these con-
ditions differ widely in their causes and pathogenesis, the radiologic features can be similar and the histologic appearance difficult to distinguish. Clinically, there are three distinct phases: (1) a prodromal phase that may persist for many years, consisting of asthma, often preceded by allergic rhinitis; (2) a second phase of marked peripheral blood eosinophilia and eosinophilic tissue infiltrates resembling Löeffler’s syndrome, or chronic eosinophilic pneumonia, which may recur over a period of years; and (3) a third, life-threatening vasculitic phase. Although CSS can be readily diagnosed on clinical grounds, histologic confirmation should always be sought by biopsy of involved skin, nerve, and/or lung. Corticosteroid therapy has dramatically improved the prognosis of this disease, and long-term remission is a realistic expectation. It is important, therefore, to separate CSS from other necrotizing vasculitides because Wegener’s granulomatosis and, to a lesser extent, polyarteritis nodosa often require treatment with cytotoxic agents, whereas corticosteroids alone are effective in CSS.

Radiographically, the pulmonary abnormalities are variable, with fleeting infiltrates occurring most frequently. As there have been only anecdotal reports on CT findings of CSS in the literature, we present the clinical, radiographic, and thin-section CT findings of nine patients with the
histologic diagnosis of CSS collected from six institutes during a 12-year period to better characterize the radiologic findings of this rare disease entity. We also review the pertinent literature.

**Materials and Methods**

From January 1986 through November 1997, nine patients with CSS were seen at six institutes. The patients included five women and four men, ranging in age from 18 to 60 years (median, 35 years). Diagnosis of CSS was established using the criteria presented by Lanham et al in subjects who met the clinical criteria for asthma or a history of allergy, peak peripheral blood eosinophil counts $>1.5 \times 10^9/L$ (1500/μL), and systemic vasculitis involving two or more extrapulmonary organs. In eight cases, tissue obtained from the skin ($n=5$), lung ($n=2$), nerve ($n=2$), muscle ($n=2$), pericardium ($n=1$), pleura ($n=1$), lymph node ($n=1$) and kidney ($n=1$) were examined histologically. In four patients, representative histologic specimens were available from two or more sites.

The clinical findings were obtained by means of chart review and included allergic history (asthma, allergic rhinitis, or other allergic tendency); symptoms and signs of vasculitic skin rash or mononeuritis multiplex; laboratory findings including peak eosinophil count in peripheral blood; the organs involved in vasculitis; treatment; and outcome.

In all patients, both chest radiographs and thin-section CT scans of the lung were obtained. The CT scanning was performed with scanners from different manufacturers. CT scans were obtained with 1.5- to 2-mm collimation at 10-mm intervals from apices to lung bases. The scanning parameters were 140 peak kilovolt, 170 mA, and 2 s exposure. The scans were reconstructed with a high–spatial frequency algorithm. Both mediastinal (width 450; level 35) and lung window (width 1,500; level −700) images were obtained. All scans were obtained in inspiration with the patient in supine position. Contrast medium was not administered.

The radiographs and thin-section CT scans were reviewed by three radiologists (Y.H.C., J.-G.I., B.K.H.), and decisions were reached by consensus. Images demonstrating abnormalities at presentation and during follow-up were reviewed. The radiographic findings were evaluated for the presence and location of parenchymal abnormalities, such as patchy consolidation, reticulonodular opacities, nodules, bronchial wall thickening, septal lines, presence of mediastinal widening, hilar enlargement, pleural effusion, and cardiomegaly. The CT scans were analyzed specifically for the presence, pattern, and distribution of pulmonary abnormalities, as well as the presence of bronchial wall thickening, cardiomegaly, pleural effusion, and hilar or mediastinal lymph node enlargement.

**Results**

**Clinical Features**

Clinical features are summarized in Table 1. All patients had a history of asthma, and six patients had allergic rhinitis. The peak eosinophil count in peripheral blood ranged from 3,200 to 32,100/μL (mean, 8,726/μL) with the differential eosinophil count ranging from 19 to 67% (mean, 41%) of WBCs (Table 1). IgE levels were elevated in the vasculitis phase in all six cases in which IgE data were available.
Most common clinical findings at initial onset of vasculitis were respiratory symptoms (56%), painful paresthesia (44%), and erythematous nodular skin lesions (44%). Involvement of a single system dominated the clinical picture in seven patients: pulmonary disease was the major feature in four, mononeuritis multiplex in two, and cutaneous lesions in one case. Thoracic involvement with CSS was present in all patients at initial presentation or at some point during the course of the disease, with the involvement of lung (n = 9), pleura (n = 2), and pericardium (n = 2; Table 2). Extrathoracic organs most commonly involved were the nervous system (n = 8) and skin (n = 7; Table 1).

Figure 3. Patient 4, an 18-year-old man with pericardial involvement. Top, A: radiograph shows patchy consolidation at right lower lung, bilateral hilar lymph node enlargement, reticulonodular opacities, and increased cardiac size compared with his prior study (not shown). Middle, B: thin-section CT scan at lung bases shows multifocal ill-defined areas of ground-glass opacity associated with numerous nodular lesions in subpleural region. Note interlobular septal thickening (arrow), increased vascular diameters, and bronchial wall thickening. Bottom, C: mediastinal setting of CT scan at subcarinal level shows enlargement of subcarinal and both hilar lymph nodes and bilateral pleural effusions.

Figure 4. Patient 2, a 50-year-old man with vasculitic kidney and liver involvement. Top, A: thin-section CT at subcarinal level shows diffuse ill-defined distribution of ground-glass opacity associated with centrilobular nodules. Bronchial wall is diffusely thickened. Note hyperinflation of lingula. Vessels are prominent with irregular satellite margin (arrows). Bottom, B: left renal angiography showed multiple variable-sized aneurysmal dilata-

ions of medium and small-sized renal arteries.
Tissue biopsy was positive in eight patients. Necrotizing vasculitis was observed in 12 specimens from eight patients, mainly from the skin, with associated eosinophilic infiltration in 8 specimens. Granulomas were present in two patients, from one lung and one pleura specimen. Reactive hyperplasia with eosinophil infiltration was found in 10 specimens from six patients. Eosinophilic infiltration was found in 10 specimens from six patients.

A rapid initial response to treatment with prednisolone or prednisone (20 to 60 mg/d) was observed in all except one case. Azathioprine and cyclophosphamide were introduced in three cases when incomplete remission or relapse followed early reduction in the steroid dose. CSS was not fatal in any patients.

Radiologic Findings

The most common radiographic findings were bilateral multifocal consolidation: patchy nonsegmental consolidation (Fig 1, top, A) in five patients and multiple nodules in one patient. Four out of six had the lower lung zone predilection (Fig 2, top, A). Diffuse reticulonodular opacities and bronchial wall thickening were each observed in three patients. Patient 2, who showed patchy right lower lung consolidation, also showed diffuse reticulonodular opacities, bronchial wall thickening, increased cardiac size compared with previous film, bilateral hilar lymph node enlargement, and small bilateral pleural effusions (Fig 3, top, A). Open thoracotomy and biopsy of the right lower lobe revealed findings of eosinophilic pneumonia and asthmatic bronchitis with eosinophil infiltration and vasculitis in pleura and pericardium. In patient 4, diffuse ill-defined multifocal distribution of the ground-glass opacity was associated with the reticulonodular opacities and bronchial wall thickening (Fig 4, top, A). He had associated multiple aneurysms involving medium-sized arteries of both kidneys and the liver (Fig 4, bottom, B). Patient 5 showed diffuse reticular opacities, septal lines, and bronchial wall thickening (Fig 5). This patient also had left hilar enlargement. Patient 9 showed multiple variable-sized nodules in both lung zones. The upper and lower lungs were evenly affected. She had mediastinal lymph node enlargement. Thoracoscopic biopsy of the nodular lesion of the lung revealed a granulomatous lesion and necrotizing vasculitis with eosinophil infiltration.

Thin-section CT scans showed bilateral patchy ground-glass opacity in all patients (Table 3). It had predominantly patchy (8/9, 89%) and subpleural

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<td>Upper</td>
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<td>GGO (n = 9, 100%)</td>
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<td>Consolidation (n = 5, 56%)</td>
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<td>Centrilobular nodules within GGO (n = 8, 89%)</td>
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<td>Larger nodules (n = 4, 44%)</td>
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<td>Hyperinflation (n = 4, 44%)</td>
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<td>Interlobular septal thickening (n = 2, 22%)</td>
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*Numbers are the frequency of the pattern present, either alone or as part of a mixed pattern; GGO = ground-glass opacity.
Distribution was observed in four patients. Findings of interlobular septal thickening were present in two patients. Consolidation was found in five patients with predominantly subpleural and lobular distribution and a lobular sparing pattern in 80% (Fig 2, bottom, B). Three out of five patients showed ground-glass opacity that surrounded the consolidation; ie, the halo sign (Fig 1, bottom, B). In patient 6, consolidation was also distributed along the bronchovascular bundles (Fig 1, bottom, B). Numerous centrilobular nodules with a diameter of < 5 mm were present in eight patients. We found that the nodules were more prominently distributed within the lesion of ground-glass opacity. Hyperinflation with lobar or lobular distribution was observed in four patients. Findings of interlobular septal thickening were present in two patients (Fig 3, middle, B). Bronchial wall thickening was present in seven patients. Increased vascular caliber was present in five patients, with peripheral arteriole involvement in three patients. Other thoracic manifestations are summarized in Table 2.

**Discussion**

**Clinical Features**

According to Churg and Strauss, the diagnosis is made on the basis of three major histologic criteria: necrotizing vasculitis, tissue infiltration by eosinophils, and extravascular granulomas. Because these three histologic components often do not coexist temporally or spatially, and this histologic picture is not pathognomonic of CSS, Lanham et al proposed a new clinical definition based on extensive literature review. We adopted their clinical criteria, consisting of asthma, peak peripheral blood eosinophil counts of > 1.5 × 10^9/L (1,500/µL), and systemic vasculitis involving two or more extrapulmonary organs. In 1990, the American College of Rheumatology developed traditional format classification, and the diagnosis of CSS can be made with four or more of the six criteria: asthma; eosinophilia > 10% on differential WBC count; mononeuropathy or polyneuropathy; transient and fleeting pulmonary infiltrates on radiography; paranasal sinus abnormality; and biopsy containing a blood vessel with extravascular eosinophils.

The etiology of CSS is still unknown, but an allergic or immune pathogenesis for the disease was suggested by the presence of asthma, eosinophilia, and elevated levels of serum IgE in some cases. Asthma is the central feature of CSS, but is unusual in Wegener’s granulomatosis and polyarteritis nodosa. Relatively late age of onset (mean, 32 years) distinguishes the asthma of CSS from asthma in the general population. Asthma preceded the development of systemic vasculitis by up to 6 years in this series and 30 years in literature review. Chronic respiratory infection associated with bronchiectasis may antedate the vasculitic illness by many years. As in our series, allergic rhinitis and pansinusitis may represent the initial phase of the syndrome.

Although peripheral blood eosinophilia is a hallmark of CSS, patients with eosinophilic tissue infiltration in the absence of peripheral blood eosinophilia have been reported. While asthma is often accompanied by eosinophilia that seldom exceeds 0.8 × 10^9/L, the eosinophilia is generally of a much higher order in CSS: all the patients in our series had peak counts of > 3 × 10^9/L. The significance of the eosinophilia of CSS is unknown. Eosinophils may play a protective role by their capacity for phagocytosis or be directly responsible for tissue damage. Chronic eosinophilic pneumonia is commonly associated with asthma and tissue eosinophilia, but it does not show granulomatous arteritis and is not associated with extrapulmonary lesions. Hypereosinophilic syndrome is characterized by eosinophilia of > 1.5 × 10^9/L persisting for > 6 months.

Thoracic manifestations with transient pulmonary infiltrates are a central feature of CSS and antedated the systemic vasculitis in 40% of cases. Less common intrathoracic manifestations include pleural effusions (29%) containing a large number of eosinophils or pericardial effusion. Hilar lymphadenopathy with other pulmonary infiltrates is infrequent and thought to represent reactive hyperplasia. The heart is a primary target organ in CSS. Cardiac disease accounts for 48% of deaths attributed to CSS, including acute pericarditis, constrictive pericarditis, cardiac failure, and myocardial infarction. Delayed treatment can lead to myocardial infarction and intractable cardiac failure. In our series, two patients showed pericardial effusion.

Extrathoracic manifestations of CSS include diverse GI involvement of both eosinophilic gastroenteritis and polyarteritis nodosa. Submucosal infiltrates of eosinophils can produce obstructive nodular masses, and mucosal involvement may result in diarrhea and bleeding. Skin rash is one of the most common features of the vasculitic phase of CSS, reflecting involvement of smaller vessels. In contrast to the respiratory tract and GI manifestations of CSS, involvement of skin is generally restricted to the vasculitic component of the syndrome. One or more of the following skin lesions were seen in 70% of all cases: purpura, macular or papular erythematous rash, urticaria, and subcutaneous nodules. Neuropathy with the typical lesion of mononeuritis multiplex was found in 75%. Cranial nerve palsies are infrequent, but we had one case with facial nerve palsy. Renal involvement is infrequent; the charac-
teristic lesion is a focal segmental glomerulonephritis. The generally benign nature of the renal disease in CSS distinguishes it from the other necrotizing vasculitides. Myalgia and joint pain occurred because of vasculitic involvement of muscles and joints.

Radiologic Findings

The radiologic appearance of CSS is variable, with 27 to 93% showing any abnormalities on chest radiographs in the literature. In a large series of 154 cases reported by Lanham et al, nonsegmental airspace disease was reported to be present in 72% and transient Löfgren’s pneumonia in 40%. In our series, we found abnormalities on chest radiographs in all cases; patchy multifocal peripheral consolidation (67%) was the most common finding. Although the infiltrates in the prodromal and the vasculitic phase of the disease may be similar radiologically, the histologic picture in the former is usually that of extensive eosinophilic infiltration of alveoli and interstitium, whereas in the latter, necrotizing vasculitis and granulomas are seen. However, in the lung, extravascular granulomas may be infrequent, and the presence of vasculitis is essential for diagnosis. Multiple nodular lesions with rare cavitation or diffuse interstitial pattern were also reported.

On thin-section CT, the parenchymal abnormal findings of CSS could be classified into three patterns in our series. The first pattern is subpleural consolidation with lobular distribution. The consolidation proved to be mainly hemorrhagic necrosis. The peripheral location and lobular distribution of the consolidation implies that the lesion is due to vasculitis involving small and medium-sized arteries. The second pattern is centrilobular perivascular consolidation. In one patient in whom adequate tissue was available, the halo sign corresponded to interstitial infiltration of eosinophils and giant cells that surrounded a central core of hemorrhagic necrosis and granuloma.

Bronchial wall thickening, with or without bronchial dilatation, and hyperinflation are likely to be related to asthma, which is an essential component of CSS. Bronchial wall thickening and bronchial dilatation are common CT findings in asthmatic patients. Bronchial wall thickening is thought to be the only finding that could differentiate CSS from other pulmonary infiltrates with eosinophilia.

Interlobular septal thickening may reflect the interstitial pulmonary edema attributed to the cardiac and pericardial involvement of CSS, with associated findings of pericardial effusion and increased caliber of vessels. As there was no associated sign of cardiac involvement in one patient, cellular infiltration and accumulation of water could be the cause of the septal thickening.

Differentiation of CSS from chronic eosinophilic pneumonia is necessary in patients with hypereosinophilia and pulmonary abnormality. CT findings of chronic eosinophilic pneumonia are characterized by the presence of homogeneous peripheral airspace consolidation that responds promptly to corticosteroid therapy, whereas in CSS, peripheral consolidation has a tendency toward lobular distribution and frequent association of centrilobular nodules within the ground-glass opacity.

Radiologic differentiation of CSS from other pulmonary angiitis and granulomatosis groups might be possible in some cases. Solitary or multiple parenchymal nodules with frequent cavitation or associated consolidation are the most common findings in Wegener’s granulomatosis, lymphomatoid granulomatosis, and necrotizing sarcoid granulomatosis; in CSS, on the other hand, the most common finding is peripheral consolidation, and multiple nodules are rather infrequent. In bronchocentric granulomatosis, the most common finding is consolidation, atelectasis, or less confluent pneumatic infiltration involving less than a lobe (73%), reflecting bronchocentricity of the lesion. Although the radiologic patterns will suggest the diagnosis of CSS, the specific diagnosis must rely on clinical, immunologic, and pathologic evidence.

In our study, the overall prevalence of abnormal findings on CT was 100%, a rate somewhat higher than the 88% reported in a previous study using CT. The difference may be attributed to the difference in the inclusion criteria for CSS. In addition, CT is superior to radiographs for detecting minor abnormalities such as bronchial wall thicken-
ing or small lymph node enlargement. This study has limitations to characterize the clinical and CT findings of CSS thoroughly, including only a small number of cases. As lung biopsy was performed in only two cases, we could not correlate each CT finding with pathologic findings.

In summary, CSS invariably involves the thorax, and thoracic manifestations are multiple and varied. Pulmonary parenchymal involvement is the most typical expression, and cardiac involvement is not uncommon. Radiographically, it usually appears as bilateral nonsegmental consolidation or reticulonodular opacities. The most common thin-section CT findings include subpleural consolidation with lobular distribution, centrilobular nodules, bronchial wall thickening, and increased vessel caliber. Less common findings include hyperinflation, mediastinal or hilar lymphadenopathy, and pleural or pericardial effusion. Although not specific, thin-section CT findings including bronchial wall thickening in a patient with hypereosinophilia and history of asthma should raise the possibility of CSS, and the diagnosis could be more confident when the patient has an associated skin lesion or mononeuritis multiplex.

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