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ORIGINAL ARTICLE

Pathological and High Resolution CT Findings in Churg-Strauss Syndrome

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Key words: vasculitis; asthma; Churg-Strauss syndrome; granulomatosis; hypereosinophilia

Objective To investigate the Churg-Strauss syndrome (CSS) associated lung involvement, concentrating on clinical characteristics, pathological findings of lung involvements, response to treatment, and prognosis.

Methods We retrospectively analyzed the characters of the clinical manifestations, thin-section CT and pathological findings of CSS. The study involved 16 patients. Clinical data were obtained by chart review. All patients underwent transbronchial lung biopsy (TBLB). Six of them underwent surgical lung biopsy as well.

Results The patients included 7 men and 9 women, aged from 14 to 61 years (median, 47.5 years). Extrathoracic organs involved included nervous system (7/16) and skin (5/16). Respiratory symptoms included cough (12/16), exertional dyspnea (11/16), hemoptysis (4/16), and chest pain (3/16). CT findings included bilateral ground-glass opacities (12/16), bilateral patchy opacities (12/16), and centrilobular nodules (6/16). The pathological findings of TBLB demonstrated increased eosinophils (3/16), vasculitis (3/16), and interstitial pneumonia (16/16). The pathological findings of surgical lung biopsy of 6 cases showed necrotizing vasculitis in 4 cases, capillaries in 5, eosinophilic pneumonia in 3, granulomas in 2, and airway abnormalities in 3. All patients improved in symptoms after therapy during the study period (range, 3 to 51 months; median, 15 months).

Conclusions Asthma may be present in CSS patient when there is bronchial involvement. Ground-glass opacities and consolidation seen on high-resolution CT reflect the presence of eosinophilic pneumonia, vasculitis, and pulmonary alveolar hemorrhage. TBLB has significant limitations for the diagnosis of CSS. Early diagnosis and therapy can result in satisfactory prognosis.

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CHURG-STRAUSS syndrome (CSS) is characterized by bronchial asthma, eosinophilia, and systemic necrotizing vasculitis with or without granulomas. Clinical diagnosis of CSS is not simple, and there have been a variety of definitions in the literature. Several classifications have been used including the original Churg and Strauss definition,¹ the Chapel Hill Consensus Conference definition,² the Lanham's criteria,³ and American College of Rheumatology's definition.⁴ All of these classification systems and definitions have limitations, especially in patients with mild or limited disease.⁵ Cases have also been reported that overall features are suggestive of CSS but lack of typical features of the syndrome such as asthma, even in the absence of prior treatment.⁶ CSS spectra of histologic changes include the combination of tissue infiltration by eosinophils, necrotizing vasculitis, and extravascular granulomas. However, experience with increasing numbers of cases indicates that this definition is too narrow and few pathologists are aware of these issues, and CSS appears to be under-diagnosed by pathologists.^{1,7-9} These diagnostic difficulties highlight the need to better understand the characteristics of CSS in order to avoid being simply dependent on clinical manifestations or histologic changes for the purpose of diagnosis. This study was designed to review the clinicopathological features of 16 patients with CSS associated lung involvement, concentrating on clinical characteristics, pathological findings of lung involvements, response to treatment, and prognosis.

PATIENTS AND METHODS

Selection of cases

A computer-aided search was conducted to retrospectively identify all adults seen at our hospital from May 2005 to May 2009 with CSS and lung involvement. There were a total of 28 patients diagnosed as having CSS during the 4-year period. Sixteen of these CSS patients had lung biopsies performed, and they formed the final study group. All 16 patients underwent transbronchial lung biopsy (TBLB). Six of 16 patients underwent surgical lung biopsy as well. Open lung biopsy was performed in 1 patient and biopsy *via* video-assistant thorascopic surgery (VATS) was performed in 5 patients. Their clinical features, radiological pictures, and pathological findings were reviewed and analyzed.

This study was approved by the Peking Union Medical College Foundation Institutional Review Board. Patients who did not authorize the use of their medical records for research were excluded from this study.

Definitions

CSS was diagnosed on the basis of the classification criteria of the American College of Rheumatology.⁴ Briefly, 4 of the following 6 findings were required: (1) a history of asthma, (2) eosinophilia > 10%, (3) mononeuropathy or polyneuropathy, (4) nonfixed pulmonary infiltrates, (5) paranasal sinus abnormality, and (6) biopsy evidence of extravascular eosinophil infiltration.

Data analysis

Clinical data and diagnostic results were extracted from the medical records and included demographic data, clinical presentation, physical findings, laboratory results, and radiographic findings. Presenting signs and symptoms were recorded from the first encounter at our hospital that led to a diagnosis of CSS. Spirometry and carbon monoxide diffusion capacity (DLco) measurement were performed in our pulmonary function laboratory, and pulmonary function values were expressed as percentage of predicted normal values (%pred). All expressed values were $\bar{x} \pm s$ unless stated otherwise. CT scans of the lungs were reviewed by a chest radiologist with specific interest in interstitial lung disease. Lung biopsy slides were reviewed by two pulmonary pathologists. Values for the bronchoalveolar lavage cell profile were expressed as percentage of total bronchoalveolar lavage cells.

RESULTS

The diagnostic features of the 16 CSS patients are summarized in Table 1.

Clinical features

The median age of our 16 patients at the time of lung biopsy was 47.5 years (range, 14 to 61 years), and 9 were women. Four patients had a smoking history. Clinical features at initial presentation are summarized in Table 2. The duration of respiratory symptoms ranged from 1 to 60 months (median, 10 months) prior to lung biopsy. Thirteen of 16 patients had a history of asthma, and 4 patients had allergic rhinitis. Extrathoracic organs most commonly involved were the nervous system in 7 cases and skin in 5 cases. Most common respiratory symptoms were cough (12/16), exertional dyspnea (11/16), hemoptysis (4/16), and chest pain (3/16). The peak eosinophil count in peripheral blood ranged from 300 to 13 400/mL (mean, 3374/mL) with the differential eosinophil count ranging from 4.6% to 52.2% (mean, 23.0%) of white blood cells.

Table 1. CSS in 16 patients fulfilling feature of the American College of Rheumatology diagnostic criteria

Case no.	Sex/Age	American College of Rheumatology diagnostic criteria of CSS					
		Asthma	PNS abnormality	Eo>10%	Neuropathy	Pulmonary abnormality	Biopsy
1	F/51	Yes	No	Yes (12.7%)	No	Yes	VATS/TBLB
2	M/55	No	Yes	Yes (11.2%)	No	Yes	VATS/TBLB
3	M/60	Yes	No	Yes (20.0%)	Yes	Yes	VATS/TBLB
4	F/54	Yes	Yes	Yes (13.4%)	No	Yes	VATS/TBLB
5	F/14	Yes	Yes	No (7.0%)	Yes	Yes	VATS/TBLB
6	M/62	No	No	No (4.6%)	No	Yes	VATS/TBLB
7	F/44	Yes	Yes	Yes (43.8%)	Yes	Yes	TBLB
8	F/53	Yes	Yes	Yes (19.6%)	No	Yes	TBLB
9	F/17	Yes	Yes	Yes (52.2%)	Yes	Yes	TBLB
10	M/37	Yes	Yes	Yes (37.3%)	Yes	Yes	TBLB/skin biopsy
11	F/30	Yes	Yes	Yes (20.7%)	Yes	Yes	TBLB/skin biopsy
12	M/54	Yes	Yes	Yes (45.4%)	Yes	Yes	TBLB/skin biopsy
13	M/25	No	No	Yes (47.6%)	Yes	Yes	TBLB/GI biopsy
14	F/61	Yes	Yes	No (6.9%)	Yes	Yes	TBLB
15	M/30	Yes	No	Yes (14.7%)	Yes	Yes	TBLB
16	F/18	Yes	No	Yes (16.3%)	Yes	Yes	TBLB

CSS: Churg-Strauss syndrome; M: male; F: female; PNS: paranasal sinus; Eo: peripheral blood eosinophil; VATS: biopsy *via* video-assistant thorascopic surgery; TBLB: transbronchial lung biopsy; GI: gastrointestinal.

Table 2. Presenting symptoms and laboratory results of the 16 CSS patients[§]

Item	Result
Symptoms	
Cough	12/16
Dyspnea	11/16
Fever	7/16
Skin rash	7/16
Laboratory test	
EOS percentage (%)	23.3±16.1
EOS count (×10 ⁹ /L)	3.37±3.55
ESR (mm/h)	38.5±28.8
ANA (+)	5/16
ANCA (+)	1/16
Urine red blood cells (+)	0/16
PaO ₂ (mm Hg)	66.1±24.8
Pulmonary function	
VC (%pred)	87.3±12.3
FEV1/FVC	78.1±11.5
FEV1 (%pred)	91.2±10.8
RV/TLC	87.9±14.2
DLco	54.6±15.6
BALF	
Total cells (×10 ⁷)	17.1± 3.5
Macrophages percentage (%)	34.1±21.1
Lymphocytes percentage (%)	33.5±23.2
Eosinophils percentage (%)	26.3±23.4
Neutrophils percentage (%)	5.61±7.85
Hemosiderin laden macrophages	3/16
CD4/CD8	0.9±0.2

§: Plus-minus values are means±SD.

EOS: eosinophil; ESR: erythrocyte sedimentation rate; ANA: antinuclear antibody; ANCA: antineutrophil cytoplasmic antibody; PaO₂: arterial partial pressure of oxygen; VC: vital capacity; FEV1: forced expiratory volume in the first second; FVC: forced vital capacity; RV: residual volume; TLC: total lung capacity; DLco: carbon monoxide diffusion capacity; BALF: bronchoalveolar lavage fluid.

CT findings

CT scans showed bilateral patchy opacities in 12/16 patients (Fig. 1C) with predominantly subpleural and lobular distribution and a lobular sparing pattern in 4/16 cases (Table 3). Six out of 16 patients had lower lung zone predilection of their infiltrates (Table 3). Ground-glass opacities (GGO) were found in 12 patients (Figs. 1A, 2A) with predominantly patchy and subpleural distribution (Fig. 2A). Numerous nodules were present in 6 patients (Fig. 3A).

Histopathologic findings

The pathologic findings of surgical lung biopsy are summarized in Table 4.

The vascular abnormalities included small vessel vasculitis and infiltration of eosinophils. Necrotizing vasculitis was observed in 4 specimens from 6 patients, characterized by intimal and medial infiltration by chronic inflammatory cells containing numerous eosinophils (Fig. 3D). In 2 cases, the vasculitis only consisted of infiltration of the vascular wall by inflammatory cells without any obvious tissue necrosis. The affected capillaries and small venules were seen in 5/6 cases. Interstitial erythrocytes and/or hemosiderin and fibrinoid necrosis of capillary walls were found in these patients (Fig. 2D). HE staining analysis in 2 of these cases of pulmonary capillaritis demonstrated extensive intra-alveolar hemorrhage. In these cases, erythrocytes and fibrin filled alveolar spaces (Fig. 2E), whereas in chronic case, hemosiderin deposition was seen within alveolar macrophages and in the interstitium.

Eosinophilic pneumonia was found in 3/6 cases, manifested by the accumulation of large numbers of eosinophils

(>70%) and macrophages within alveolar spaces accompanied by alveolar septal expansion (Fig. 2D). Tissue eosinophilia was found in 3/6 cases, manifested by a chronic inflammatory cell infiltration containing numerous eosinophils (Fig. 1E, F). Granulomas were present in 2 patients (Fig. 3E).

Airway abnormalities were found in 3 cases including muscle hypertrophy and eosinophilic and lymphocytic infiltration of the airway walls (Fig. 1G).

Transbronchial biopsies (Table 4) demonstrated increased eosinophils in 3 cases, vasculitis in 3 cases, and interstitial pneumonia in 16 cases. No granulomas were found in TBLB specimens.

The diagnostic yield of specimens obtained by surgical lung biopsy and by transbronchial biopsy was reviewed. The correlation between TBLB and surgical lung biopsies was very poor (Table 4).

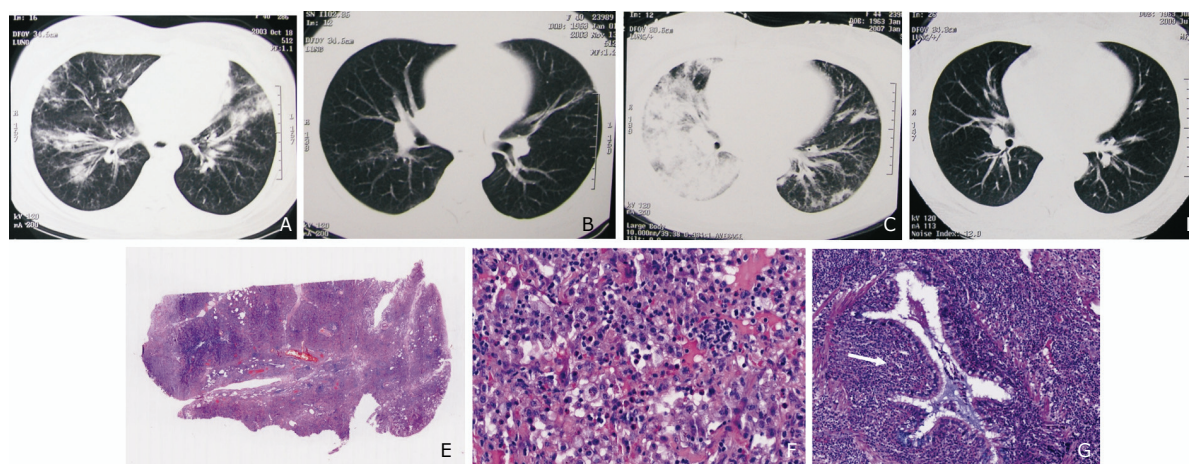


Figure 1. A. A 44-year-old female had a history of asthma for 4 years, CT scan showing multifocal ill-defined areas of ground-glass opacity in both middle and lower lung fields. Note increased vascular diameters and bronchial wall thickening.
B. After 1 month of prednisone therapy ground-glass opacities have resolved.
C. When prednisone was tapered and stopped for 7 months, CT scan showing focal areas of consolidation in the right middle and lower lobes. Also note small areas of ground-glass attenuation in the left lower lung.
D. After the therapy with prednisone and cyclophosphamide for 12 months, areas of consolidation and ground-glass attenuation have resolved.
E. Surgical lung biopsy showing idiopathic interstitial pneumonia (IIP) that is characterized by the accumulation of large numbers of chronic inflammatory cells within alveolar spaces. HE staining $\times 5$
F. High-magnification photomicrograph demonstrating alveolar spaces were filled with large numbers of macrophages, lymphocytes, and scattered eosinophils accompanied by alveolar septal expansion. HE staining $\times 200$
G. Small bronchiole with muscle hypertrophy, submucosal and submembranous inflammatory infiltrate (arrow). Replacement of ciliated columnar epithelium by goblet cell. HE staining $\times 100$

Table 3. Distribution of lung parenchymal abnormalities at CT in 16 patients with CSS

Case no.	CT findings			
	Consolidation	GGO	Bronchial wall thickening	Nodules
1	RML, RLL	No	Yes	No
2	RUL, LUL	No	No	No
3	No	No	Yes	RLL
4	No	Yes	Yes	RUL
5	No	Yes	Yes	RML
6	RML, RLL, LUL	Yes	No	No
7	RUL, RML, RLL, LUL	Yes	Yes	RUL
8	RML, RLL, LLL	Yes	Yes	No
9	No	Yes	Yes	No
10	RML, RLL, LLL	Yes	Yes	RUL
11	RLL, LLL	Yes	Yes	RUL, LUL
12	LUL	No	Yes	No
13	RLL, LLL	Yes	No	No
14	RML, LUL, LLL	Yes	No	No
15	LUL	Yes	No	No
16	RML, RLL	Yes	Yes	No

GGO: ground-glass opacity; RML: right middle lobe; RLL: right lower lobe; RUL: right upper lobe; LUL: left upper lobe; LLL: left lower lobe.

Correlation of high-resolution CT and pathological findings

In the 6 surgical lung biopsy cases, consolidation on high-resolution CT was found in 3 cases, and pathological findings were eosinophil infiltration and vasculitis. Thoracoscopic biopsy of the nodular lesions revealed granulomatous inflammation and necrotizing vasculitis with eosinophilic infiltration. Bilateral patchy ground-glass opacities coincided with capillaritis and diffuse alveolar hemorrhage.

Treatment and follow-up

At the initiation of treatment, all patients received a course of oral prednisone, starting at $0.5\text{--}1.0\text{ mg}\cdot\text{kg}^{-1}\cdot\text{d}^{-1}$ for 1 month which was then tapered every 3 weeks to $5.0\text{--}7.5\text{ mg}\cdot\text{d}^{-1}$. The total length of treatment was 12 to 18 months. A rapid initial response to treatment with prednisone was observed in all cases (Figs. 1B, 2B).

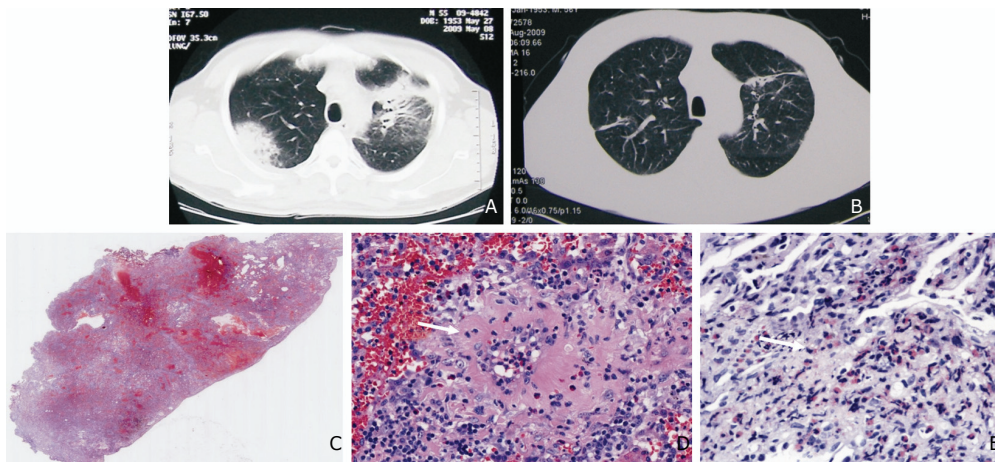


Figure 2. A 55-year-old man presented with cough and dyspnea.

- A. CT scan obtained at the level of aortic arch shows multifocal patchy ground-glass opacity around the patchy consolidation.
- B. After 3 months treatment, CT scan shows resolution of ground-glass opacity and persistence of minimal linear abnormalities.
- C. Surgical lung biopsy specimen showing diffuse acute alveolar hemorrhage. HE staining $\times 5$
- D. High-magnification photomicrograph demonstrating necrotizing vasculitis involving alveolar wall capillary. Capillary wall is thickened with eosinophil infiltration and necrosis (arrow). HE staining $\times 200$
- E. High-magnification photomicrograph demonstrates eosinophilic pneumonia characterized by numerous eosinophils infiltration admixed with fibrin in alveolar spaces (arrow). HE staining $\times 200$

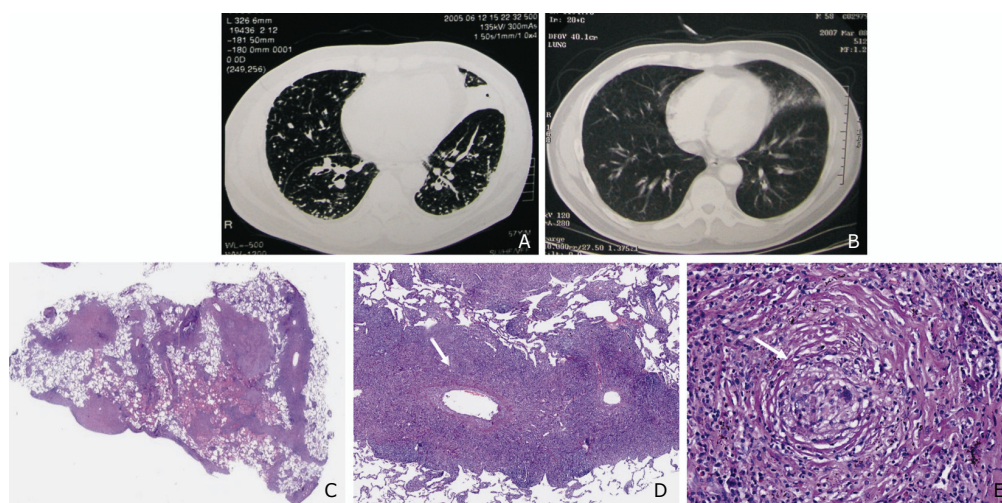


Figure 3. A 60-year-old man presented with recurred cough for 4 years.

- A. CT at the level of lung bases showing numerous nodular lesions in the subpleural region. Bronchial wall is diffusely thickened. Note atelectasis in lingula.
- B. After the therapy with prednisone and cyclophosphamide, nodular lesions have resolved. Atelectasis of lingula is resolved.
- C. Surgical lung biopsy of the nodular lesion of the lung revealing a granulomatous lesion and necrotizing vasculitis with eosinophils infiltration. HE staining $\times 5$
- D. Vasculitis: transmurial inflammatory infiltrate consisting of mixed histiocytes, lymphocytes, and numerous eosinophils (arrow). HE staining $\times 100$
- E. High-magnification photomicrograph showing granulomatous lesion with large numbers of macrophages, lymphocytes, and scattered eosinophils (arrow). HE staining $\times 200$

Table 4. Comparison of pathological findings of surgical lung biopsy and TBLB

Biopsy method	<i>n</i>	Chronic asthmatic inflammation	Eosinophilic pneumonia	Granulomatous inflammation	Vasculitis	Capillaritis	Interstitial pneumonia
VATS	6	4	3	3	6	5	6
TBLB	16	0	3	0	3	2	16

Thirteen patients also received cyclophosphamide (CTX) therapy. In 5 cases, oral CTX was administered at a dose of 100 mg·d⁻¹ for 12 months when relapse occurred after reduction of steroid dose to 15 mg·d⁻¹ (Fig. 1C). In the remaining 8 patients (7 patients with neurological involvement and 1 case with gastrointestinal involvement), CTX was administered at the beginning with steroid therapy at the dose of 0.2 g administered intravenously every other day for 3 months followed by a dose of 100 mg·d⁻¹ given orally for 9 months (Fig. 3A).

When CTX was given, blood cell counts were done about 7 days after starting treatment and then checked every week for 1 month, every 2 weeks for 1 month, and every 4 weeks for 10 months. If the white blood cell count fell below 3.5×10⁹/L, CTX was temporarily stopped. Side-effects such as myelosuppression, opportunistic infections or hemorrhagic cystitis did not develop in any of the patients after CTX therapy.

All 16 patients had follow-up data available over a median duration of 15 months (range, 3 to 51 months). In all patients, symptoms and CT scans improved rapidly within 4 weeks of corticosteroid therapy. No patient died during the study period.

DISCUSSION

Clinical findings

In CSS, asthma is a disease defining feature occurring in almost all patients.¹⁰⁻¹² It precedes the onset of vasculitis in 83% of cases, with a median time of 4 years (interquartile range, 2 to 11.5 years) between onset of asthma and a diagnosis of CSS. In 14% of patients the diagnosis of asthma coincides with that of vasculitis, and in rare cases vasculitis precedes the asthma by over a decade.¹⁰ In our study, only 4/16 cases had a prior history of asthma. In 9/16 cases the diagnosis of CSS coincided with an acute asthmatic attack. There was no history of asthma or asthmatic attack in 3 cases. Surgical lung biopsies were performed in these 3 patients and the pathological findings showed that there were no eosinophils and lymphocytes infiltration in the bronchial walls and no chronic asthmatic inflammation. Although CSS without asthma has been thought to be extremely rare, there are several case reports detailing such occurrence.¹³⁻¹⁸ In Schnabel's study,

one-third of the cases of CSS (2 out of 6) occurred in patients without the symptoms of asthma.¹⁹ Silva and colleagues²⁰ found asthmatic inflammation in surgical lung biopsies in only 2/4 cases. Combined with the previous studies, we propose that asthma is present in CSS patient when there is bronchial inflammation. However, this bronchial involvement, hence the presence of asthma, may not be present in all patients.

Pathological findings

The spectrum of histologic changes described in the lung in CSS includes the combination of tissue infiltration by eosinophils, necrotizing vasculitis, and extravascular granulomas.²¹ In our study, eosinophilic pneumonia could be seen in half of the cases (3/6) in surgical lung biopsy. Sparse eosinophilic infiltration was found in the remaining 3 cases. Among these 3 cases, steroids were given only in 1 case before the lung biopsy, so the administration of corticosteroids cannot be the only reason to make the CSS lesion to appear to have few eosinophils.²² The initial study by Churg and Strauss emphasized that in the acute stage of CSS the predominant cell was the eosinophil which constituted as much as 70%-80% of the exudates. However, the number of eosinophils decreased as the acute inflammation subsided.¹ The composition of the cells in CSS seemed to depend on the phase of the inflammation, whether acute, subacute, or chronic.²³ The syndrome is frequently phasic in nature, with the pathologic findings varying not only with the anatomical site examined but also with the phase of the illness.³

The classic histological hallmarks of the vasculitic phase are an eosinophil rich necrotizing vasculitis involving primarily small arteries, arterioles, venules, and veins and necrotizing granulomas centered on necrotic eosinophils.²² In our study, capillaritis could be seen in 5/6 of surgical lung biopsies (only 1/6 was ANCA positive). The results of lavage fluid showed large numbers of hemosiderin laden macrophages in 3/6 cases and 4/6 cases presented with hemoptysis. These implying the subclinical alveolar hemorrhage is actually quite common in CSS.^{24, 25} Because of this under-recognized form of vasculitis associated with alveolar hemorrhage,^{26, 27} careful examination of lung biopsies for evidence of capillaritis should routinely be carried out in suspected CSS cases.

Although the combination of eosinophilic pneumonia, vasculitis, and granulomatous inflammation is considered diagnostic for CSS, it should be noted that the classic description of the pathologic findings is based almost exclusively on autopsy material in patients with florid disease.¹ In our study, eosinophilic pneumonia could be seen in half of the cases (3/6) in surgical lung biopsies, vasculitis in 6 cases (6/6) and extravascular lung granulomas in 3 of 6 cases. All three histological components coexisted in a given tissue in 50% of biopsy specimens. These observations underscore the need for carefully clinical and pathologic correlation to establish the diagnosis, especially in cases that do not show the full spectrum of histologic changes. In patients with characteristic clinical manifestations, these findings are sufficient to make a confident diagnosis.

Diagnostic values of TBLB

The study reported by Silva showed eosinophilic pneumonia in 3 TBLB specimens; no vasculitis or granulomas were found in the same TBLB specimens.²⁰ Another study from Schnabel showed nonspecific findings in 6 of 6 biopsies.¹⁹ In our study, all 6 patients who underwent surgical lung biopsies also underwent TBLB before surgery. We compared the pathologic findings of TBLB with those of surgical lung biopsies. It was clear that TBLB in our study tended to contain more nonspecific findings. None of the 6 TBLB specimens showed changes considered to be diagnostic. Pulmonary vasculitis was found in none of the TBLB specimens of the 6 patients who had definitive vasculitis demonstrated *via* surgical lung biopsy. Our findings suggest that the small size of the specimens obtained by TBLB is a major impediment to the successful use of TBLB for diagnosing CSS.

CT-pathologic comparisons

The high-resolution CT findings in our study are similar to those of previous studies,^{3, 7, 20, 24, 28-32} consolidation histologically corresponded to areas of eosinophilic pneumonia, whereas bronchial wall thickening corresponded to areas of asthmatic bronchitis. Moreover, multiple variable-sized nodules corresponded to areas of necrotizing granulomatous vasculitis with eosinophilic infiltration. In our study, the ground-glass opacities in CT scans histopathologically corresponded to mixed areas of pulmonary hemorrhage related to capillaritis, necrotizing granulomas, and surrounding eosinophilic infiltration. Bilateral thickening of the interlobular septa was not seen in our study but was described in Silva's study corresponding to edematous septa containing numerous eosinophils and mild

fibrosis in surgical lung biopsy specimen.²⁰

Guillevin *et al*³³ recommended that CSS patients without factors indicative of poor prognosis at the time of diagnosis could be successfully treated with prednisone alone and CTX was administered only as the second-line treatment in the cases of persistent disease activity or relapse despite corticosteroid therapy. We suggest that CTX should be administered as the initial treatment because of the high relapse rate observed in patients treated with prednisone alone in our study.

Our study is limited by its retrospective nature. In addition, it includes a small number of patients. Only 6 cases underwent surgical lung biopsy so it does not provide a definite correlation between the high-resolution CT and pathologic findings. However, CSS is rare. The incidence has been estimated to be approximately 1.8 to 3.3 cases per million person-years.^{34, 35}

Based on the results of our study, we conclude that asthma may be present in CSS patient when there is bronchial involvement. Ground-glass opacities and consolidation seen on high-resolution CT reflect the presence of eosinophilic pneumonia vasculitis and pulmonary alveolar hemorrhage. TBLB tends to contain nonspecific findings and has significant limitations for the diagnosis of CSS. Early diagnosis and therapy can result in satisfactory patient outcome.

REFERENCES

1. Guillevin L, Dunogu  B. Definition for eosinophilia in Churg-Strauss syndrome. *Presse Med* 2011;40:224-5.
2. Jennette JC, Falk RJ, Andrassy K, et al. Nomenclature of systemic vasculitides. The proposal of an international consensus conference. *Arthritis Rheum* 1994; 37:187-92.
3. Lanham JG, Elkon KB, Pusey CD, et al. Systemic vasculitis with asthma and eosinophilia: a clinical approach to the Churg-Strauss syndrome. *Medicine* 1984; 63:65-81.
4. Masi AT, Hunder GG, Lie JT, et al. The American College of Rheumatology 1990 criteria for the classification of Churg-Strauss syndrome (allergic granulomatosis and angiitis). *Arthritis Rheum* 1990; 33:1094-100.
5. Churg A, Brallas M, Cronin SR, et al. Formes frustes of Churg-Strauss syndrome. *Chest* 1995; 108:320-3.
6. Reid AJ, Harrison BDW, Watts RA, et al. Churg Strauss syndrome in a district hospital. *Q J Med* 1998; 91:219-29.
7. Buschman DL, Waldron JA Jr, King TE Jr. Churg-Strauss pulmonary vasculitis: high-resolution computed tomography scanning and pathologic findings. *Am Rev Respir Dis* 1990; 142:458-61.
8. Casta er E, Alguersuari A, Gallardo X, et al. When to

- suspect pulmonary vasculitis: radiologic and clinical clues. *Radiographics* 2010; 30:33-53.
9. Kallenberg CG. Pathophysiology of ANCA-associated small vessel vasculitis. *Curr Rheumatol Rep* 2010; 12:399-405.
 10. Keogh KA, Specks U. Churg-Strauss syndrome. Clinical presentation, antineutrophil cytoplasmic antibodies, and leukotriene receptor antagonists. *Am J Med* 2003; 115: 284-90.
 11. Guillevin L, Cohen P, Gayraud M, et al. Churg-Strauss syndrome. Clinical study and long-term follow-up of 96 patients. *Medicine* 1999; 78:26-37.
 12. Sablé-Fourtassou R, Cohen P, Mahr A, Pagnoux C, Mouthon L, Jayne D, Blockmans D, Cordier JF, Delaval P, Puechal X, Lauque D, Viallard JF, Zoulim A, Guillevin L; French Vasculitis Study Group. Antineutrophil cytoplasmic antibodies and the Churg-Strauss syndrome. *Ann Intern Med* 2005; 143:632-8.
 13. Sevinc A, Hasanoglu HC, Gokirmak M, et al. Allergic granulomatosis and angiitis in the absence of asthma and blood eosinophilia: a rare presentation of limited Churg-Strauss syndrome. *Rheumatol Int* 2004; 24:301-4.
 14. Malik TQ, Youmbissi TJ, Gacha R, et al. Atypical presentation of Churg-Strauss syndrome: another "forme fruste" of the disease? *Am J Med Sci* 2002; 324:276-8.
 15. Morimatsu Y, Kinoshita M, Koga T, et al. A case of allergic granulomatosis and angiitis without symptoms of asthma. *Nihon Kokyuki Gakkai Zasshi* 2003; 41:655-9.
 16. Jessurun J, Azevedo M, Saldana M. Allergic angiitis and granulomatosis (Churg-Strauss syndrome): report of a case with massive thymic involvement in a nonasthmatic patient. *Hum Pathol* 1986; 17:637-9.
 17. Chen KR, Ohata Y, Sakurai M, et al. Churg-Strauss syndrome: report of a case without preexisting asthma. *J Dermatol* 1992; 19:40-7.
 18. Yamashita Y, Yorioka N, Taniguchi Y, et al. Nonasthmatic case of Churg-Strauss syndrome with rapidly progressive glomerulonephritis. *Intern Med* 1998; 37:561-3.
 19. Schnabel A, Holl-Ulrich K, Dalhoff K, et al. Efficacy of transbronchial biopsy in pulmonary vasculitides. *Eur Respir J* 1997; 10:2738-43.
 20. Silva CI, Müller NL, Fujimoto K, et al. Churg-Strauss syndrome: high resolution CT and pathologic findings. *J Thorac Imaging* 2005; 20:74-80.
 21. Conron M, Beynon HL. Churg-Strauss syndrome. *Am J Clin Pathol* 2000; 114:767-72.
 22. Churg A. Recent advances in the diagnosis of Churg-Strauss syndrome. *Mod Pathol* 2001; 14:1284-93.
 23. Keogh KA, Specks U. Churg-Strauss syndrome. *Semin Respir Crit Care Med* 2006; 27:148-57.
 24. Furuiye M, Yoshimura N, Kobayashi A, et al. Churg-Strauss syndrome *versus* chronic eosinophilic pneumonia on high-resolution computed tomographic findings. *J Comput Assist Tomogr* 2010; 34:19-22.
 25. Sinico RA, Di Toma L, Maggiore U, et al. Prevalence and clinical significance of antineutrophil cytoplasmic antibodies in Churg-Strauss syndrome. *Arthritis Rheum* 2005; 52:2926-35.
 26. Green RJ, Ruoss SJ, Kraft SA, et al. Pulmonary capillaritis and alveolar hemorrhage. *Chest* 1996; 110:1305-16.
 27. Schnabel A, Reuter M, Csernok E, et al. Subclinical alveolar bleeding in pulmonary vasculitides: correlation with indices of disease activity. *Eur Respir J* 1999; 14:118-24.
 28. Clutterbuck EJ, Pusey CD. Severe alveolar haemorrhage in Churg-Strauss syndrome. *Eur J Respir Dis* 1987; 71:158-63.
 29. Lai RS, Lin SL, Lai NS, et al. Churg-Strauss syndrome presenting with pulmonary capillaritis and diffuse alveolar hemorrhage. *Scand J Rheumatol* 1998; 27:230-2.
 30. Worthy SA, Müller NL, Hansell DM, et al. Churg-Strauss syndrome: the spectrum of pulmonary CT findings in 17 patients. *AJR Am J Roentgenol* 1998; 170:297-300.
 31. Choi YH, Im JG, Han BK, et al. Thoracic manifestation of Churg-Strauss syndrome: radiologic and clinical findings. *Chest* 2000; 117:117-24.
 32. Johkoh T, Müller NL, Akira M, et al. Eosinophilic lung diseases: diagnostic accuracy of thin-section CT in 111 patients. *Radiology* 2000; 216:773-80.
 33. Guillevin L, Pagnoux C. When should immunosuppressants be prescribed to treat systemic vasculitides? *Intern Med* 2003; 42:313-7.
 34. Watts RA, Scott DG. Classification and epidemiology of the vasculitides. *Baillieres Clin Rheumatol* 1997; 11:191-217.
 35. Borao-Cengotita-Bengoa M, Corral-Gudino L, Del Pino-Montes J, et al. Long-term follow-up of microscopic polyangiitis, 17-year experience at a single center. *Eur J Intern Med* 2010; 21:542-7.