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A Case of Churg-Strauss Syndrome with Polyneuropathy That Incompletely Improved by Corticosteroid Administration

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Abstract This paper reports a rare case of Churg-Strauss syndrome (CSS), in a sixty-five- year old female with a 10-year history of bronchial asthma complicated with eosinophilia, pneumonia and later polyneuropathy of sensory and motor disturbances in the extremities. After administration of prednisolone, the eosinophilia and pneumonia promptly ameliorated, however, improvement of the polyneuropathy was delayed with incomplete recovery. The pathological findings in the specimen of the biopsied sural nerve revealed thickening of the vessel walls infiltrated with inflammatory cells, compatible with vasculitis, and these results suggested the ischemic effect on the nerve fibers as the pathogenesis of polyneuropathy in CSS.

Introduction

Churg-Strauss syndrome (CSS) is a disorder characterized by hypereosinophilia and systemic vasculitis of small arteries and veins occurring in individuals with asthma and allergic rhinitis.[1-3] Originally reported histological findings characterized by necrotizing vasculitis, tissue infiltration by eosinophils and extravascular granuloma, are observed in the heart, liver, spleen, lungs, skin and sural nerves.[1] However, these three histological findings do not frequently coexist, and are only found in a minority of cases or in the autopsied cases.[2] For the traditional format classification for clinical diagnosis, 6 criteria were selected: asthma, eosinophilia, mononeuropathy (including multiplex) or polyneuropathy, non-fixed pulmonary infiltration, paranasal sinus abnormality, and biopsy specimen containing a blood vessel with extravascular eosinophils, and the presence of 4 or more of the 6 items is required.[3] For the treatment of CSS including neurological manifestation, administration of corticosteroid and/or other immunosuppressive agents yielded improvement or stabilization[4),5)] This paper reports a case of CSS with asthma, eosinophilia, pneumonia, polyneuropathy and biopsy-proved angitis, in which eosinophilia and pneumonia promptly

Table 1. Laboratory data on admission

CBC		Chemistry,Serology	
RBC	492x10⁴/μl	CRP	19.7mg / dl
Hb	10.5g / dl	Total protein	6.1g / dl
Ht	34%	Total bilirubin	0.7mg / dl
WBC	20200 / μl	GOT	22IU / l
Neutro	47%	GPT	28IU / l
Baso	1%	LDH	437IU / l
Eosino	44%	BUN	15mg / dl
Lympho	4%	Cr	0.6mg / dl
Mono	4%	IgG	1450mg / dl
Plt	10.2x10⁴/μl	IgA	327mg / dl
		IgM	68mg / dl
		IgE	2420IU / ml
		C - ANCA	(−)
		P - ANCA	(−)

Nerves		SCV	MCV
Median	R	Not evoked	43.8m / sec,144 μV
	L	Not evoked	44.0m / sec,708 μV
Ulnar	R	Not evoked	45.9m / sec,16.1 μV
	L	Not evoked	53.9m / sec,319 μV
Posterior tibial	R	N.D.	Not evoked
	L		Not evoked
Sural	R	Not evoked	N.D.
	L	Not evoked	
Peroneal	R	N.D.	Not evoked
	L		Not evoked

Table 2. Nerve conduction study on admission
SCV: sensory conduction velocity, MCV: motor conduction velocity
R: right, L: left, N.D.: not determined

ameliorated but the improvement of neurological manifestation of polyneuropathy was delayed with incomplete response to corticosteroid administration. Sural nerve biopsy supported the previous reports that ischemic damage to the nerve fibers by complicated angitis was the pathogenesis of polyneuropathy in CSS[6)−10)].

Case Report

A sixty-five-year old female who had suffered from bronchial asthma for 10 years, complained of general dullness, cough, sputum, and numbness, hypoesthesia and weakness of the upper and lower extremities of polyneuropathy type since 2 weeks ago and was admitted to the hospital in the middle of September 2000 . Moist rales were audible in both lungs, and a chest X-ray revealed pneumonia in the left lung and pleural fluid in the right thorax. Echocardiography did not reveal evidence of endomyocardiopathy. Laboratory data on admission are shown in Table 1. CBC revealed leukocytosis with eosinophilia. A diagnosis of CSS was made. The clinical course is shown in Fig. 1. Administration of prednisolone, 40mg/day, was started at the end of September, and the eosinophilia disappeared promptly after 5 days and the pneumonia

also improved. Nerve conduction study (Table 2) revealed that in the arms, sensory conduction velocity (SCV) was not evoked in the median or ulnar nerves, and although motor conduction velocity (MCV) was evoked in those nerves,the amplitudes were markedly reduced suggesting axonal damages. In the legs, MCV and SCV of posterior tibial, sural and peroneal nerves were not totally evoked. These results showed that the sensory disturbance was mainly in the upper extremities, while sensory and motor disturbances were observed in the lower extremities. A sural nerve biopsy was performed ; nerves fibers appeared intact by hematoxylin-eosin staining, and perineural infiltration of lymphocytes and eosinophils, and thickening of the vessel walls infiltrated with eosinophils and lymphocytes, compatible with angitis, were observed (Fig. 2). Vasculitis-like purpura appeared on the arms in October. These neurological disturbances did not improve promptly and completely with the administration of corticosteroid, and the patient was discharged in March 2001. The neurological complaints improved gradually except for numbness of hands and feet as of July 2001.

Discussion

The original description of the pathological features of CSS has been observed only in the autopsied cases.[1] Lanham and his associates reported that the three histologic criteria of CSS were found in only 24% of the autopsied patients with CSS and in only 13% of the tissue biopsies.[2] They emphasized that not all cases of CSS have the major histologic features originally described, the classical histologic components often do not coexist, and their absence is not inconsistent with a diagnosis of CSS.[2] Furthermore, histologic Churg-Strauss granuloma in relation to arteries, arterioles, or venules were found in only 10-20% of CSS cases, and a low occurrence of granulomas may have been partly due to limited pathologic materials from the biopsy sampling.[2] Therefore, allergic granuloma lesion described in CSS is not included among the proposed classification criteria.[3]Lung biopsy for pulmonary lesions was not performed in our case and granuloma was not detected in the clinical course.

There are discussions as to whether CSS is a separate entity versus an overlap syndrome among various other systemic vasculitis conditions.[2),3)] Consequently,

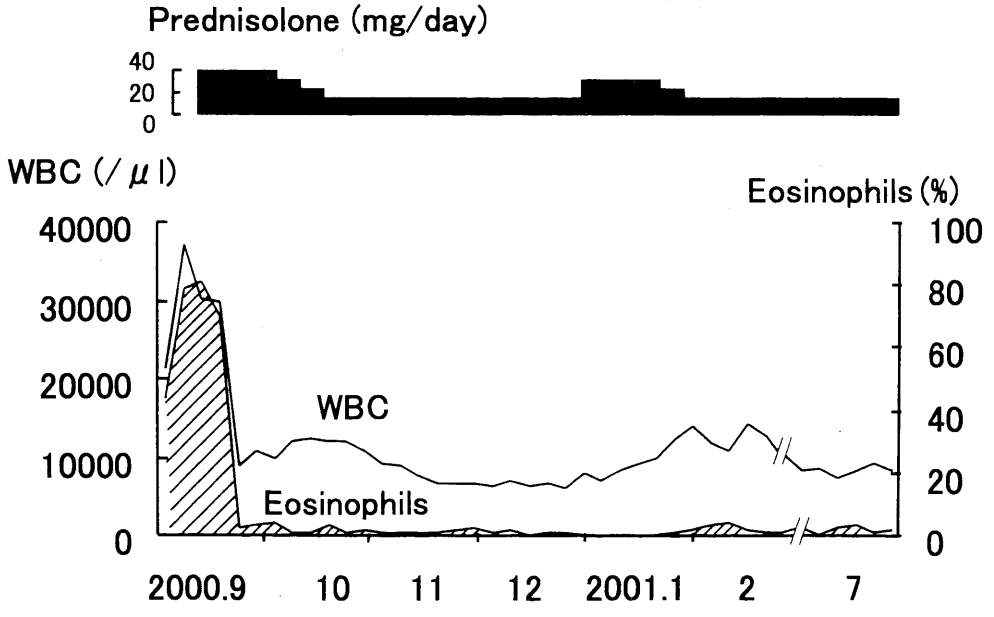

Fig. 1 Clinical course

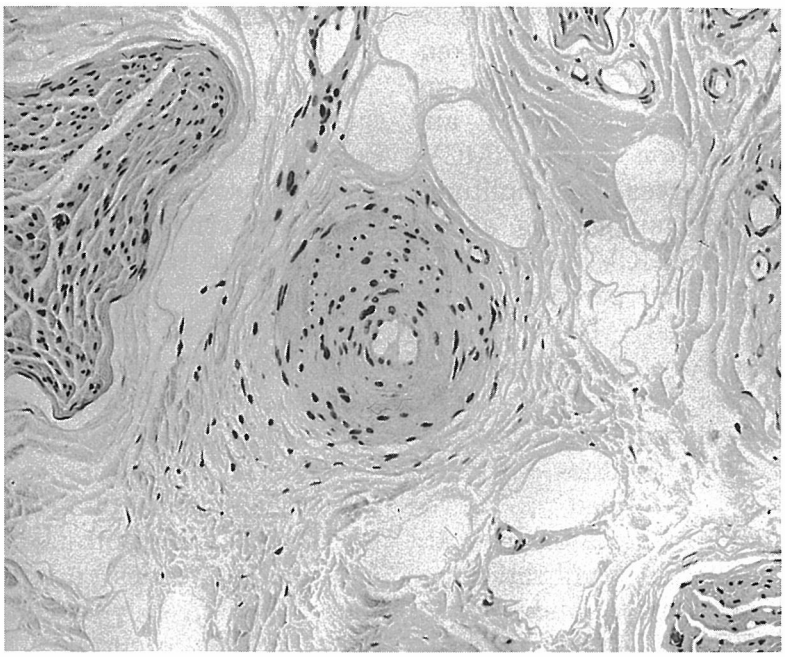

Fig. 2 In the biopsy specimen of sural nerve, the thickening of the vessel walls infiltrated with eosinophils and lymphocytes was observed. Hematoxylin-eosin staining, X400.

CSS was portrayed as a point of overlap among; hypereosinophilic disease (e.g. Loffler's syndrome), systemic vasculitis (e.g. polyarteritis nodosa and hypersensitivity vasculitis), and granulomatous disorders (e.g. Wegener's granulomatosis).[2),3)] The present patient exhibited the 4 characteristic features of asthma, eosinophilia, pneumonia and polyneuropathy associated with vasculitis. These satisfied the criteria for the diagnosis of CSS.[3)]

CSS can be divided on clinical grounds as occurring in three phases: the prodromal phase, consisting of allergic diseases such as asthma and rhinitis, the second phase characterized by peripheral blood eosinophilia with lung and gastroenteric eosinophilic infiltrations, and the third phase consisting of systemic vasculitis in two or more extrapulmonary organs with involvement of the peripheral nervous system.[2)] Our patient followed this clinical course having the preceding asthma, then eosinophilia and pneumonia, and finally peripheral neuropathy.

Antineutrophil-cytoplasmic autoantibodies (ANCAs) are useful diagnostic serologic markers for a variety of inflammatory dis eases, especially certain types of small-vessel vasculitis, and may be directly involved in the pathogenesis of diseases. PR3-ANCA (C-ANCAs) are more frequent than MPO-ANCA (P-ANCAs) in patients with Wegener's granulomatosis.[11)] P-ANCAs are more frequent than C-ANCAs in patients with microscopic angitis or CSS.[11)] In CSS, ANCAs have been described in 75% of the cases: C-ANCA in 15% and P-ANCA in 60%[11)]. In our case, both C-ANCA and P-ANCA were negative. The reason for these negative results in our patient is unknown.

Sixty-three to 75% of patients with CSS had neurologic involvement and the most common manifestation was multiple mononeuropathy.[6)–10)] Seventeen patients had multiple mononeuropathy, 7 had distal symmetric polyneuropathy and 1 had an asymmetric polyneuropathy.[9)] The common peroneal nerve was most frequently involved (84%), follwed by the ulnar nerve (55%), internal popliteal nerve (41%) and the radial nerve (29%).[9)] Conduction studies of sensory and motor nerves in the vasculitis patients were consistent with axonal neuropathy.[6),7),10)] Our patient suffered from polyneuropathy involving sensory median and ulnar nerve distur-

banses in the arms, and sensory and motor posterior tibial and peroneal nerve disturbanses in the legs. Nerve conduction study in our patient was compatible with axonal neuropathy, showing reduced amplitpudes. Histological descriptions of the peripheral nerves of CSS are rare and peripheral neuropathy is most likely due to small-vessel vasculitis that results in ischemic damage to the neurons.[6)-10)] The result of sural nerve biopsy in our patient revealed that nerve fibers appeared intact and vasculitis infiltrated by eosinophils and lymphocytes was observed. These findings support the report described above.[6)-10)] However,the exact pathological effect on the affected nerve fibers in our patient is unclear because only hematoxylin-eosin staining was performed in the biopsied specimen, and electronmicrography of toluidine-blue staining embeded in epoxy resin and teased nerve fibers, which provide more precise informations about the nature of the nerve fibers, were not examined. All of the IgE values obtained in CSS patients were elevated as was also in our case, and the possibility has been suggested that hyperallergic mechanisms contribute to this syndrome in the active vasculitis.[2)]The human eosinophil granule contains several cationic proteins: major basic protein (MBP), eosinophil-derived neurotoxin (EDN), etc., and these eosinophil-derived toxins might produce endothelial injury of vascular wall and cause damage to the peripheral nerves.[12,13)]

CSS responds well to corticosteroids.[4,5)] Response to steroid treatment is often dramatic, allergic symptoms and eosinophilia improve rapidly, and remission of vasculitis disease occurs in most cases without additional therapeutic agents.[4,5)] Clinical remission of CSS was obtained in 91.5% of patients, and 25.6% relapsed during follow-up.[5)] Five-year survival was 78.9%.[4)] Long-term administration of corticosteroid may be successful for the management of neuropathy, although not all patients with neuropathy respond to corticosteroid.[9)] The use of corticosteroid therapy soon after the onset of asthma, but before development of neurological manifestation may decrease the frequency and severity of neurological diseases.[9)] The follow-up status of neurological manifestation in 18 patients was: improved in 10, stable in 3, worse in 1 and dead in 4 patients during follow-up of a median duration of 3.9 years.[9)] The neurological manifestation in our patient responded incompletely,which suggests that peripheral nerve lesions are mainly axonopathy with frequently irreversible nature.[10)]

A proportion of CSS patients require an immunosuppression agent or treatment as an adjunct to corticosteroid, such as cyclophosphamide and plasma exchange.[14)] Our patient refused to use cyclophosphamide.

References

1) Churg J, Strauss L. Allergic granulomatosis, allergic angitis and periarteritis nodosa. *Am J Path* **27**: 277-300, 1951.
2) Lanham J G, Elkon K B, Pusey C D, Hughes G R. Systemic vasculitis with asthma and eosinophilia: a clinical approach to the Churg-Strauss syndrome. *Medicine* **63**: 65-81, 1984.
3) Masi A, Hunder G G, Lie J T, Michel B A, Bloch D A, Arend W P, Calabrese L H, Edworthy S M, Fauci A S, Leavitt R Y, Lightfoot R W, Mcshane D J, Mills J A, Stevens M B, Wallace S L, Zvaifler N J. The American college of rheumatology 1990 criteria for the classification of Churg-Strauss syndrome (allergic granulomatosis and angitis). *Arthritis Rheum* **33**: 1094-1100, 1990.
4) Guillevin L, Lhote F, Gayraud M, Cohen P, Jarrousse B, Lortholary O, Thibult N, Casassus P. Prognostic factors in polyarteritis nodosa and Churg-Strauss syndrome. A prospective study in 342 patients. *Medicine* **75**: 17-28, 1996.
5) Guillievin L, Cohen P, Gayraud M, Lhote F, Jarrousse B, Csassus P. Churg-Strauss syndrome. Clinical study and long-term follow-up of 96 patients. *Medicine* **78**: 26-37, 1999.

6) Wichman A, Buchthal F, Pezeshkpour G H, Fauci A S. Peripheral neuropathy in hypereosinophilic syndrome. *Neurology* **35**: 1140-1145, 1985.
7) Monaco S, Lucci B, Laperchia N, Tezzon F, Curro-Dossi B, Nardelli E, Giannini C, Rizzuto N. Polyneuropathy in hypereosinophilic syndrome. *Neurology* **38**: 494-496, 1988.
8) Marazzi R, Pareyson D, Boiardi A, Corbo M, Scaioli V, Sghirlanzoni A. Peripheral nerve involvement in Churg-Strauss syndrome. *J Neurol* **239**: 317-321, 1992.
9) Sehgal M, Swanson J W, Deremee R A, Colby T V. Neurologic manifestations of Churg-Strauss syndrome. Mayo *Clin Proc* **70**: 337-341, 1995.
10) Yoshio T. Allergic granulomatous angitis(Churg-Strauss syndrome). Nihon Rinshou(suppl), Series of separatable *clinical entities* **29**, NeurosymptomatologyIV: 290-293, 2000(in Japanese, author's translation).
11) Jennette J C, Falk R J. Antineutrophil cytoplasmic autoantibodies: discovery, specificity, disease associations, and pathogenic potential. Advances in Pathology and Laboratory *Medicine* **8**: 363-378, 1995.
12) Acker A S, Gleich G J. man S J, Loegering D A, Venge P, Olsson I, Harley J B, Fauci A S, Gleich G J. Distinctive cationic proteins of the human eosinophil granule: major basic protein, eosinophil cationic protein, and eosinophil-derived neurotoxin. *J Immunol* **131**: 2977-2982, 1983.
13) Durack D T, Sumi S M, Klebanoff S J. Neurotoxicity of human eosinophils. *Proc Natl Acad Sci USA* **76**: 1443-1447, 1979.
14) Guillevin L, Jarrousse B, Lok C, Lhote F, Jais J P, Du L T H, Bussel A. Long-term follow-up after treatment of polyarteritis nodosa and Churg-Strauss angitis with comparison of steroids, plasma exchange and cyclophosphsmide to steroids and plasma exchange. A prospective randomized trial of 71 patients. *J Rheumatol* **18**: 567-574, 1991.