

Churg-Strauss Syndrome with Cutaneous and Neurological Manifestations Preceding Asthma

Tamihiro Kawakami, Yoshinao Soma, Eri Hosaka and Masako Mizoguchi

Department of Dermatology, St Marianna University School of Medicine, 2-16-1 Sugao, Miyamae-ku, Kawasaki, Kanagawa 216-8511, Japan. E-mail:

tami@marianna-u.ac.jp

Accepted 18 April, 2005.

Sir,

Allergic granulomatosis and angiitis (Churg-Strauss syndrome – CSS) is a relatively uncommon systemic disease with characteristic clinical and pathologic features. The syndrome is characterized by systemic vasculitis, extravascular granuloma and hypereosinophilia, occurring almost exclusively in patients with asthma or an allergic history. The American College of Rheumatology (ACR) has proposed six classification criteria, with four being necessary for CSS to be diagnosed. The six criteria are asthma, eosinophilia (>10%), paranasal sinusitis, pulmonary infiltrate, histological proof of vasculitis and mononeuritis multiplex (1). However, the ACR criteria are not designed to serve as diagnostic criteria for individual patients, and are thought to function poorly in this capacity (2–5). Although extremely rare, there have been some reported cases of non-asthmatic patients who present with other symptoms of CSS (6–10). We report a patient with CSS with various characteristic skin lesions and paraesthesias as initial findings preceding asthmatic symptoms. These findings may lead to an early diagnosis of CSS and prevent irreversible tissue damage with treatment.

CASE REPORT

A 42-year-old man was referred in September 2003 with a 1-week history of painful purpuric and papular skin lesions of the lower limbs and soles. He had no history of asthma or allergic rhinitis. His medical history and family medical history were not significant. Two weeks after onset, purpuric skin lesions developed and an erythematous rash resembling erythema multiforme appeared, progressively involving the patient's inner thighs, trunk, upper extremities, face and head (Fig. 1). Additionally, he began to experience paraesthesias in conjunction with his cutaneous lesions (mainly on the extremities) and unintentional weight loss and fever were recorded. Laboratory tests revealed a leukocyte level of 9000/ μl (normal 4000–9000/ μl), eosinophils at 1746/ μl (19.4%; 0–8%) and raised IgE 2700 IU/ml (<170 IU/ml). Serum eosinophil cationic protein (ECP) level was 147 $\mu\text{g/l}$ (<15.7 $\mu\text{g/l}$). No significant laboratory abnormalities were found, including rheumatoid factor, antinuclear antibodies, total haemolytic complement, anti-neutrophil cytoplasmic antibodies (ANCA), hepatitis A and B serological tests, cryoglobulins, cryofibrinogen, serum protein electrophoresis, serum immunoglobulins and echocardiogram. Chest and abdominal X-ray, ultrasound examination and computerized tomography did not show any abnormalities. Stool examinations for ova and parasites were negative. Myelogram and bone marrow biopsy showed only a mild medullary hypereosinophilia without any morphological or neoplastic changes.

Microscopic examination of skin biopsy specimens obtained from the purpura on the left lower extremity and the abdominal

erythema revealed a dermal perivascularly with neutrophils, red blood cells and numerous eosinophils, consistent with leukocytoclastic vasculitis and extravascular granuloma (Fig. 2). There was a predominance of eosinophils infiltrating the dermis around the nerve fibre.

The patient was given 30 mg prednisone daily, which led to an improvement in his symptoms. His condition stabilized and the peripheral eosinophilia and IgE levels normalized. The corticosteroids were tapered without any recurrence of the skin lesions. Two months after start of treatment, the patient received 15 mg prednisone daily, and his clinical and laboratory findings were normalized. The corticosteroids were then slowly tapered off. The patient was re-admitted to the hospital in April 2004 with light dyspnoea and firm palpable and haemorrhagic purpuric eruptions on the extremities with paraesthesias. He reported some asthma-like symptoms that coincided with the onset of the rash. Laboratory studies revealed an elevated white blood cell count of 9000/ μl and eosinophilia of 13.0%. The IgE level was elevated to 2000 IU/ml. Serological tests were negative for perinuclear and cytoplasmic pattern ANCA. An end-expiratory wheeze was noted on chest auscultation. Pulmonary function

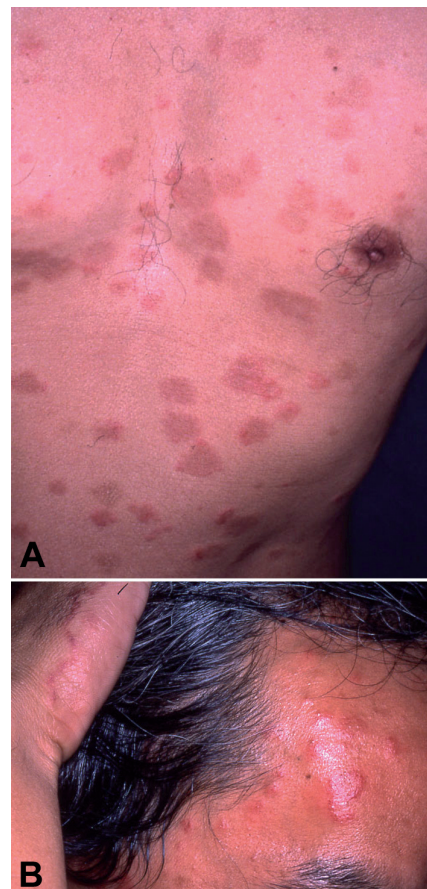


Fig. 1. (A) Sharply margined dull red plaques with centrifugal spreading and central clearing in abdomen. (B) Erythematous and oedematous plaques with ill-defined borders on hand, face and head.

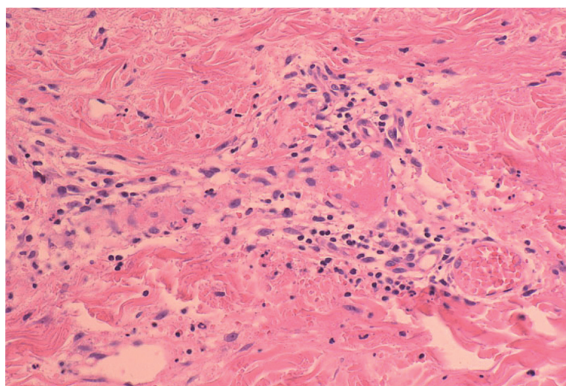


Fig. 2. Fibrinoid necrosis, admixture of neutrophils and lymphocytes in and around blood vessels characteristic of leukocytoclastic vasculitis (H&Ex100).

tests demonstrated mild airflow limitation with improvement after administration of an inhaled bronchodilator. There appeared to be no cardiovascular or abdominal abnormalities upon examination. He was re-treated with 15 mg prednisone daily with an immediate response: resolution of symptoms, blood eosinophilia and serum IgE. A similar recurrence 3 months later showed the same dramatic improvement after start of prednisone.

DISCUSSION

The absence of allergic history in our patient is rather contrary to a diagnosis of CSS. It was not until asthma occurred with increasing skin lesions and paraesthesias that CSS was diagnosed.

CSS responds very well to corticosteroids; however, institution of steroid therapy can induce acute cardiac involvement during the course of this disease (11, 12). The occurrence of CSS in non-asthmatics appears to be extremely rare (6–9). We believe that a diagnosis of CSS should be considered in patients with cutaneous eruptions accompanied by paraesthesias, marked eosinophilia and high IgE levels. CSS should also be considered in the presence of histological leukocytoclastic vasculitis and remarkable eosinophil infiltration around nerve fibres in the dermis.

Little is known about the origin of leukocytoclastic vasculitis in CSS and the reason for the remarkably higher eosinophil levels throughout the dermis. Recently, CSS has been described as 'vasculitides strongly associated with atopic disorder' (13). Activation of Th2 lymphocytes has been implicated in the onset of atopic dermatitis through the production of cytokines, such as IL-4, IL-5 and IL-13, which mediate the accumulation of mast cells, basophils and more importantly, eosinophils. Peen et al. (14) found evidence for eosinophil activation in CSS with deposition of toxic eosinophil granule proteins in affected areas, implicating eosinophils in the pathogenesis. ECPs, one of the major constituents of eosinophil granules, are neurotoxic and

may contribute to direct nerve injury. IL-5 stimulates a massive expansion of eosinophils, which in turn secrete ECP (15). In our patient, the increased serum ECP concentration returned to normal during periods of disease remission. Thus, high ECP levels may play a direct role in the development of paraesthesias. The findings in our patient strongly suggest that this disorder is triggered by an eosinophil and IgE inflammatory response.

REFERENCES

- Masi AT, Hunder GG, Lie JT, Michel BA, Bloch DA, Arend WP, et al. The American College of Rheumatology 1990 criteria for the classification of Churg-Strauss syndrome. *Arthritis Rheum* 1990; 33: 1094–1100.
- Sorensen SF, Slot O, Tvede N, Petersen J. A prospective study of vasculitis patients collected in a five year period: evaluation of the Chapel Hill nomenclature. *Ann Rheum Dis* 2000; 59: 478–482.
- Reid AJ, Harrison BD, Watts RA, Watkin SW, McCann BG, Scott DG. Churg-Strauss syndrome in a district hospital. *Q J Med* 1998; 91: 219–229.
- Hunder GG. The use and misuse of classification and diagnostic criteria for complex diseases. *Ann Intern Med* 1998; 129: 417–418.
- Rao JK, Allen NB, Pincus T. Limitations of the 1990 American College of Rheumatology classification criteria in the diagnosis of vasculitis. *Ann Intern Med* 1998; 129: 345–352.
- Chen KR, Ohata Y, Sakurai M, Nakayama H. Churg-Strauss syndrome: report of a case without preexisting asthma. *J Dermatol* 1992; 19: 40–47.
- Chen KR, Su WP, Pittelkow MR, Leiferman KM. Eosinophilic vasculitis syndrome: recurrent cutaneous eosinophilic necrotizing vasculitis. *Semin Dermatol* 1995; 14: 106–110.
- Lipworth BJ, Slater DN, Corrin B, Kessler ME, Haste AR. Allergic granulomatosis without asthma: a rare 'forme fruste' of the Churg-Strauss syndrome. *Respir Med* 1989; 83: 249–250.
- Jessurun J, Azevedo M, Saldana M. Allergic angitis and granulomatosis (Churg-Strauss syndrome): report of a case with massive thymic involvement in a nonasthmatic patient. *Hum Pathol* 1986; 17: 637–639.
- Davis MD, Daoud MS, McEvoy MT, Su WP. Cutaneous manifestations of Churg-Strauss syndrome: a clinicopathologic correlation. *J Am Acad Dermatol* 1997; 37: 199–203.
- Lanham JG, Elkon KB, Pusey CD, Hughes GR. Systemic vasculitis with asthma and eosinophilia: a clinical approach to the Churg-Strauss syndrome. *Medicine (Baltimore)* 1984; 63: 65–81.
- Noth I, Streck ME, Leff AR. Churg-Strauss syndrome. *Lancet* 2003; 361: 587–594.
- Csernok E, Gross WL. Primary vasculitides and vasculitis confined to skin: clinical features and new pathogenic aspects. *Arch Dermatol Res* 2000; 292: 427–436.
- Peen E, Hahn P, Lauwers G, Williams RC Jr, Gleich G, Kephart GM. Churg-Strauss syndrome: localization of eosinophil major basic protein in damaged tissues. *Arthritis Rheum* 2000; 43: 1897–1900.
- Termeer CC, Simon JC, Schopf E. Low-dose interferon alfa-2b for the treatment of Churg-Strauss syndrome with prominent skin involvement. *Arch Dermatol* 2001; 137: 136–138.