

Case Report

Purpuric skin rash on extremities: Churg-Strauss syndrome

四肢的紫癍皮疹：變應性肉芽腫性血管炎

CK Kwan 關志強, WY Lam 林永賢, WYM Tang 鄧旭明

A 21-year-old lady presented with right foot pain and numbness and a subsequent asthmatic attack with multiple purpuric rashes over the extremities. Blood tests showed peripheral blood eosinophilia. The constellation of clinical features and skin biopsy result were consistent with the diagnosis of Churg-Strauss syndrome.

一名二十一歲女士，初呈右腳痛及麻痺，隨後哮喘病發作及在四肢出現紫紅色皮疹，其血液報告發現嗜酸性細胞增多，臨床表現及皮膚活組織檢查符合變應性肉芽腫性血管炎的診斷。

Keywords: Asthmatic attack, Churg-Strauss syndrome, eosinophilia

關鍵詞：哮喘病，變應性肉芽腫性血管炎，嗜酸性細胞增多

Introduction

Churg-Strauss syndrome is a multisystem disorder that may involve the respiratory system, heart, liver, spleen, kidney and intestine. The prominent features include asthma, rhinitis,

hypereosinophilia and vasculitis. The epidemiology remains undefined. There is no gender predominance and no racial difference. It is not common in Hong Kong. We report a young Chinese lady suffering from Churg-Strauss syndrome who presented with multiple purpuric skin rashes with blisters on the extremities.

Social Hygiene Service, Department of Health, Hong Kong

CK Kwan, MBBS(HK), MRCP(UK)
WYM Tang, FHKCP, FHKAM(Medicine)

Department of Pathology, Tuen Mun Hospital, Hong Kong

WY Lam, FRCPath, FHKAM(Pathology)

Correspondence to: Dr. CK Kwan

Yaumatei Dermatology Clinic, 12/F Yaumatei Specialist Clinic (New Extension), 143 Battery Street, Yaumatei, Kowloon, Hong Kong

Case report

A 21-year-old Chinese lady presented to the orthopaedic unit with right foot pain progressing to right foot numbness and difficulty in walking. She had a history of allergic rhinitis and mild intermittent asthma since childhood. During hospitalisation, she had a severe asthmatic attack requiring intubation, mechanical ventilation and intensive care. No precipitating

factor for her asthmatic attack could be identified. She was not a smoker. Although she had history of allergy to celecoxib, no culprit drug was taken before the attack. Examination of her chest found wheezing and reduced air-entry. Right foot drop was noted. Moreover, multiple purpuric skin rashes associated with blisters were found on her extremities, especially the hands and feet (Figures 1 & 2). The rash was not associated with sun-exposure. Complete blood picture revealed an elevated white blood cell count to $16.7 \times 10^9/L$ (normal range: $3.9-10.7 \times 10^9/L$) with eosinophil dominance. The eosinophil count was $6.6 \times 10^9/L$ (normal range: $<0.45 \times 10^9/L$), making up 39.4% ($<6\%$) of total white cell count. A skin biopsy from the medial aspect of left foot was performed (Figures 3 &

4). There was a mild to moderately hyperplastic epidermis with intraepidermal vesicles and adjacent cell ballooning and spongiosis. The dermis showed superficial and deep dermal perivascular and interstitial infiltrate of lymphocytes and many eosinophils. There were focal changes of vasculitis with endothelial cell swelling, fibrinoid deposits in the vessel wall, extravasation of red blood cells and focal leucocytoclasia. The skin biopsy showed vasculitis with eosinophilia and spongiotic vesiculation. In summary, this young lady was



Figure 1. Purpuric lesions on the palm.



Figure 2. Purpuric lesions on the foot with blistering.

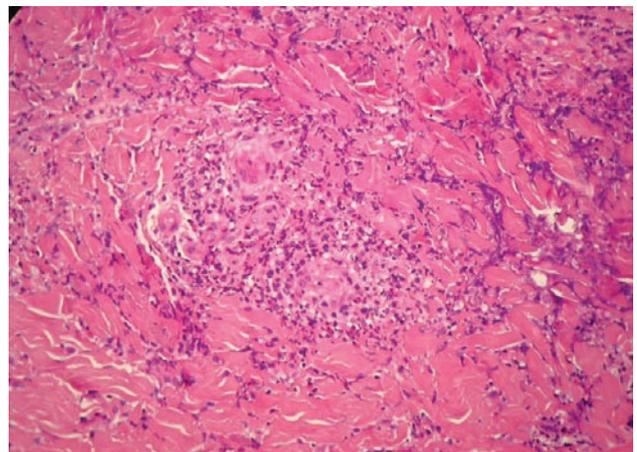


Figure 3. Skin biopsy showing necrotising vasculitis in Churg-Strauss syndrome. (H&E, Original magnification x 100)

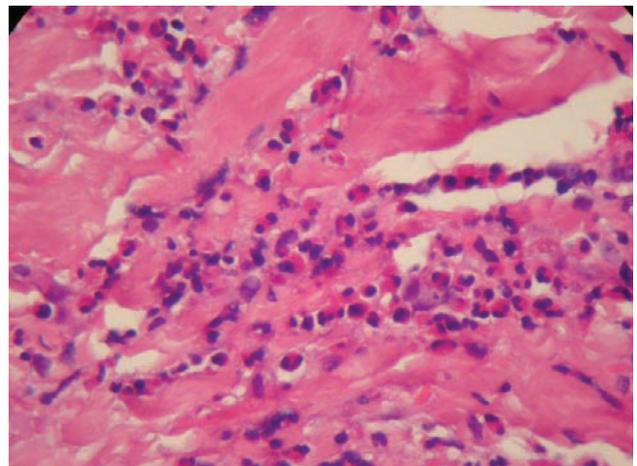


Figure 4. Skin biopsy showing tissue infiltration of eosinophils. (H&E, Original magnification x 400)

suffering from severe asthma, peripheral blood hypereosinophilia, mononeuritis multiplex with right foot drop and small vessel vasculitis with eosinophilia. These features point to the diagnosis of Churg-Strauss syndrome. The patient showed marked improvement after treatment with systemic prednisolone.

Discussion

Churg-Strauss syndrome, also known as allergic granulomatosis angiitis, is a multi-organ disorder involving the respiratory system, heart, kidneys, gastrointestinal tract and skin. It is characterised by asthma, allergic rhinitis, hypereosinophilia and vasculitis occurring in different phases. It was first reported by two pathologists Churg and Strauss in 1951. They reported 13 cases of severe asthmatic patients with striking clinical features including fever, hypereosinophilia, extravascular granulomatosis and necrotising vasculitis.¹ However, the diagnosis is difficult to make, because individual presentations can occur in isolation and each presentation may last for many years before the appearance of another presentation. For instance, asthma may occur for many years before the development of hypereosinophilia and even vasculitis. There is no gender and race predominance. The exact aetiology remains unknown. The mean age of onset is around middle age, as opposed to bronchial asthma, which is common in childhood. Cutaneous lesions are present in 55% of patients. The most common skin lesions are palpable purpura, followed by subcutaneous nodules that occur typically on the extensor surfaces of the extremities and on the scalp. Less often, urticaria, livedo reticularis, papulonecrotic lesions can also occur in Churg-Strauss syndrome.² One study revealed that Churg-Strauss syndrome was strongly related to HLA-DRB4, particularly in those associated with vasculitic manifestations such as purpuric rash, pulmonary haemorrhage, mononeuritis multiplex and glomerulonephritis.³

Briefly, Churg-Strauss syndrome can be divided into three phases – prodromal, eosinophilic and vasculitic phases. The prodromal phase often occurs in second and third decades of life and is characterised by atopic diseases such as asthma and allergic rhinitis. The prodromal phase may last for more than ten years before entering the eosinophilic and vasculitic phases. The eosinophilic phase is dominated by hypereosinophilia. There is not only peripheral eosinophilia but also eosinophilic infiltration involving internal organs especially gastrointestinal tract and lungs. The vasculitic phase may present with non-specific symptoms such as fever, weight loss and malaise. The systemic vasculitis involving the medium and small vessels may be life threatening. It is often associated with vascular and extravascular granulomatosis.⁴

Asthma is the cardinal feature of Churg-Strauss syndrome. Almost all patients have asthma that often precedes the vasculitic phase by eight to ten years like our patient, and even up to thirty years.⁴ The asthma is often chronic and severe to the extent that long term corticosteroid therapy is required. When the vasculitic phase sets in, the severity of asthma will increase.

Skin manifestations are common in the vasculitic phase. Approximately two-thirds of patients may have skin manifestations, which include palpable purpura on legs and feet, cutaneous or subcutaneous nodules, macular or papular erythematous rash and sometimes haemorrhagic lesions ranging from petechiae to extensive ecchymoses.⁵

Neurological involvement is also commonly found in Churg-Strauss syndrome. Peripheral neuropathy like mononeuritis multiplex is the commonest and may occur in 50-78% of patients.⁶ The patients may have cranial nerve II, III, VII, VIII palsy, cerebral haemorrhage or infarction secondary to cerebral vessel vasculitis and hypertension.

Cardiac involvement in Churg-Strauss syndrome can occur in up to 60%. It includes acute pericarditis, constrictive pericarditis, heart failure and myocardial infarction. It accounts for almost half of the deaths of patients with Churg-Strauss syndrome.⁷

There is no single diagnostic laboratory test for Churg-Strauss syndrome. Peripheral blood eosinophilia is the most characteristic feature and correlates with the disease activity. Tissue eosinophil infiltration is also found in most biopsy specimens. It can still be found in those who do not have peripheral blood eosinophilia after starting steroid therapy. Around 55-70% of patients have positive anti-neutrophil cytoplasmic antibodies (ANCA).⁸ The majority of these patients are positive for myeloperoxidase (p-ANCA) and few show positivity to c-ANCA. For those with positive ANCA, the frequency of renal involvement, vasculitis, pulmonary haemorrhage and peripheral neuropathy is increased whereas for those with negative ANCA, the incident of cardiac involvement such as pericarditis, cardiomyopathy and pleural effusion is increased.⁹

As there are many different clinical and laboratory presentations for the Churg-Strauss syndrome, the American College of Rheumatology developed a set of diagnostic criteria which include (1) asthma, (2) eosinophilia >10% on differential white blood cell count, (3) mononeuropathy or polyneuropathy, (4) non-fixed pulmonary infiltrates on roentgenography, (5) paranasal sinus abnormality and (6) biopsy containing a blood vessel with extravascular eosinophils. If four of these six criteria are present, the diagnosis of Churg-Strauss syndrome can be reached with a sensitivity of 85% and a specificity of 99.7%.¹⁰ In this case, the diagnosis of Churg-Strauss syndrome is supported by the presence of asthma, eosinophilia >10%, peripheral neuropathy with right foot drop and extravascular eosinophil infiltration of the skin as demonstrated histopathologically.

The mainstay of treatment is high dose systemic corticosteroid (prednisolone 40-60 mg/day). The response is often drastic within weeks with rapid decrease in eosinophil counts, allergic symptoms and severity of vasculitis. The rate of reduction correlates with the improvement in constitutional symptoms as well as cardiac and pulmonary function. The improvement in mononeuropathy multiplex is more gradual and the dose of steroid should only be reduced when progression of nerve damage has been halted.¹¹ Cyclophosphamide is the second line of treatment for patients who fail to respond to corticosteroid or those who have relapse of disease. It can also be combined with corticosteroid in the presence of poor prognostic factors such as impaired renal function, proteinuria (>1 g/day), cardiac and CNS involvement. The 5-year mortality rate is 26% in the presence of one poor prognostic factor and rises to 46% if three or more of these factors are present.¹² More recently, rituximab, a chimeric monoclonal antibody directed against the CD20 surface antigen on B-cell lymphocytes may have some efficacy in Churg-Strauss syndrome. In one study, three patients refractory to conventional treatment have been successfully treated with rituximab.¹³

In summary, Churg-Strauss syndrome is a multisystem disease with prominent features of asthma, eosinophilia and vasculitis. Systemic steroid is the mainstay of treatment. Cyclophosphamide and, recently, rituximab have been used for patients with refractory disease.

References

1. Churg J, Strauss L. Allergic granulomatosis, allergic angiitis and periarteritis nodosa. *Am J Pathol* 1951;27: 277-301.
2. Chung L, Kea B, Fiorentino DF. Cutaneous vasculitis. In: Bologna JL, Jorizzo JL, Rapini RP, editors. *Dermatology*, volume 1, 2nd ed. St. Louis: Mosby Elsevier; 2008, p.361.
3. Vaglio A, Martorana D, Maggiore U, Grasselli C, Zanetti A, Pesci A, et al. HLA-DRB4 as a genetic risk factor for Churg-Strauss syndrome. *Arthritis Rheum* 2007;56:

- 3159-66.
4. Guillevin L, Cohen P, Gayraud M, Lhote F, Jarrousse B, Casassus P. Churg-Strauss syndrome. Clinical study and long-term follow-up of 96 patients. *Medicine (Baltimore)* 1999;78:26-37.
 5. Schwartz RA, Churg J. Churg-Strauss syndrome. *Br J Dermatol* 1992;127:199-204.
 6. Pagnoux C, Guilpain P, Guillevin L. Churg-Strauss syndrome. *Curr Opin Rheumatol* 2007;19:25-32.
 7. Hasley PB, Follansbee WP, Coulehan JL. Cardiac manifestations of Churg-Strauss syndrome: Report of a case and review of the literature. *Am Heart J* 1990; 120:996-9.
 8. James WD, Berger TG, Eiston DM. *Andrews' diseases of the skin: clinical dermatology*, 10th ed. Philadelphia: Saunders Elsevier; 2006, p.840.
 9. Sablé-Fourtassou R, Cohen P, Mahr A, Pagnoux C, Mouthon L, Jayne D, et al. Antineutrophil cytoplasmic antibodies and the Churg-Strauss syndrome. *Ann Intern Med* 2005;143:632-8.
 10. 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 (allergic granulomatosis and angiitis). *Arthritis Rheum* 1990;33:1094-100.
 11. Lanham JG, Elkouf 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.
 12. Guillevin L, Lhote F, Gayraud M, Cohen P, Jarrousse B, Lortholary O, et al. Prognostic factors in polyarteritis nodosa and Churg-Strauss syndrome. A prospective study in 342 patients. *Medicine (Baltimore)* 1996;75: 17-28.
 13. Koukoulaki M, Smith KG, Jayne DR. Rituximab in Churg-Strauss syndrome. *Ann Rheum Dis* 2006;65:557-9.