

## CHURG-STRAUSS SYNDROME: A CASE REPORT

Asja Stipić-Marković<sup>1</sup>, Jagoda Stipić<sup>2</sup>, Marija Crnčević-Urek<sup>1</sup> and Vesna Crnek-Kunstelj<sup>3</sup>

<sup>1</sup>Department of Clinical Immunology and Pulmonology, Sveti Duh General Hospital;  
<sup>2</sup>Department of Neurology, Zagreb University Hospital Center; and <sup>3</sup>Department of Biology,  
School of Medicine, University of Zagreb, Zagreb, Croatia

**SUMMARY** – Churg-Strauss syndrome (CSS) is a necrotizing small vessel vasculitis characterized by the presence of asthma, hypereosinophilia and sinusitis. Other common manifestations are pulmonary infiltrates, skin, gastrointestinal and cardiovascular involvement. Although not a criterion for the diagnosis of CSS, the presence of antineutrophil cytoplasmic autoantibodies (ANCA) is now established as being associated with CSS. In this report, a 31-year-old male with a history of difficult-to-control asthma is presented. It was associated with peripheral and bronchoalveolar eosinophilia, sinusitis, and high level of ANCA (perinuclear labeling pattern). Clinical manifestations observed at the time of relapses were palpable purpura, erythema nodosum, arthralgia, musculoskeletal complications, and episcleritis. In spite of vasculitis remission, low doses of steroids to control asthma were necessary for 10 years. The aim of this case report is to point to the possibility of CSS in patients with severe persistent asthma and atypical allergic diathesis.

**Key words:** *Churg-Strauss syndrome; Churg-Strauss syndrome, diagnosis; Treatment – Outcome; Case report*

### Introduction

Churg-Strauss syndrome (CSS) is a systemic vasculitis characterized by the presence of asthma, hypereosinophilia, and necrotizing vasculitis with extravascular eosinophil granulomas. Three phases have been described in the natural history of the disease (rhinitis, asthma, vasculitis), although they do not always occur successively. Initial reports described CSS as a condition that is usually highly responsive to corticosteroids<sup>1</sup>. The American College of Rheumatology has proposed 6 cri-

teria for CSS classification, 4 being necessary for CSS to be diagnosed with 85% sensitivity and 99.7% specificity: asthma, eosinophilia >10%, paranasal sinusitis, pulmonary infiltrate, histologic proof of vasculitis, and mononeuritis multiplex<sup>2</sup>.

However, it is well accepted that the lesions described by Churg and Strauss based on histologic examinations and postmortem studies not commonly seen on biopsies<sup>3</sup> are not specific, and their absence should not serve as a basis to reject the diagnosis of CSS. Although not a criterion of the diagnosis, the presence of antineutrophil cytoplasmic autoantibodies (ANCA) is now established as being associated with it<sup>3</sup>. A sizable proportion of patients with CSS require not only steroids but also more aggressive treatment<sup>4-6</sup>. Many centers use treatment protocols devised for Wegener granulomatosis, i.e. daily oral or intravenous pulse cyclophosphamide<sup>3-5</sup>. The value of cyclophosphamide is limited by its high toxicity, particu-

Correspondence to: *Marija Crnčević-Urek, M.D.*, Department of Immunology and Pulmonology, Sveti Duh General Hospital, Sveti Duh 64, HR-10000 Zagreb, Croatia

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larly by its detrimental effects on host defense against infections, its myelotoxic effects, and oncogenic potential<sup>6-7</sup>. Treatments other than corticosteroids and cyclophosphamide are definitely needed.

CSS has to be distinguished from asthma, eosinophilic pneumonia, and peripheral blood eosinophilia related to other diseases. These include allergy to molds (particularly *Aspergillus fumigatus*), allergy to drugs (antibiotics such as minocycline used to treat acne) and parasitic infection.

## Case Report

A 31-year-old man developed rhinitis, sinusitis and asthma in 1990. He started taking depot steroid therapy prescribed by his general practitioner. In 1991, tests which showed strong bronchial hyperreactivity, very prominent bronchoalveolar eosinophilia, and positive skin test to a number of allergens (*Ambrosia elatior*, feathers, tree pollen, flour) were done. A few months later, serious worsening of asthma occurred and the patient had to be hospitalized. In the discharge letter, it was stated that a 'higher dosage of steroids' had to be used.

In May 1992, the patient was hospitalized at Sveti Duh General Hospital, Department of Clinical Immunology and Pulmonology. On admission, he was in a stable asthmatic condition with normal pulmonary function tests. Therefore, for the first few days, he was treated only with salbutamol as needed. He had received his last depot steroid shot 7 days prior to hospitalization. On the sixth day of hospitalization, severe bronchial obstruction developed, with a fall in FEV1 by 55% and VC by 25% compared to the values measured on admission. PEF had fallen to 200 l/min (the best personal value was 610 l/min). Treatment with methylprednisolone at a dose of 40 mg i.v. and theophylline i.v. was introduced for asthma exacerbation. The dose of steroids was reduced to 20 mg orally after three days and inhaled beclomethasone 600 µg daily added on. As the dosage of systemic steroid was further reducing, the patient's condition worsened two weeks later, and methylprednisolone was increased to 20 mg orally daily.

Laboratory findings showed a very high level of total IgE (>1000 kU/L) and positive skin test to some allergens but negative specific IgE by RAST (*Dermatophagoides pteronyssinus*, milk, cat, dog, *Ambrosia elatior*). Tuberculin test was hyperreactive (18×18 mm). Absolute peripheral blood eosinophil count of  $1.27 \times 10^9/l$  and sputum eosino-

philia of 80% were detected. ANCA were positive in dilution up to 1:1024. CSS was considered, based on the clinical features and laboratory findings, and additional tests were performed to assess the possible affection of other organ systems (peripheral nerves, skin, nose, kidneys). The results showed that the disease was limited to the respiratory system only. Methylprednisolone 20 mg orally together with topical steroids (1000 µg/day) led to remission of the disease, with a very good eosinopenic response (absolute eosinophil count dropped from  $1.27 \times 10^9$  to  $0.28 \times 10^9$ ). The patient was discharged from the hospital in a stable asthma condition. After 4 months of disease improvement and stable asthma condition, tapering of oral steroids and maintaining of only inhaled ones were tried. However, the patient's condition seriously worsened 10 days later; circulating eosinophil count increased to  $1.2 \times 10^9$ , eosinophil percentage in sputum to 37%, and pulmonary function tests deteriorated seriously. Treatment with methylprednisolone at a dose of 40 mg intravenously started. The dosage of 20 mg orally daily continued after a week, along with salbutamol and topical steroids. All laboratory findings and clinical parameters normalized, and the patient was discharged on 1200 µg inhaled beclomethasone and 16 mg oral methylprednisolone daily. In January 1993, ANCA were still positive, but in dilution of 1:16, circulating eosinophils were normal ( $0.04 \times 10^9$  and  $0.2 \times 10^9$ ), but pulmonary eosinophilia was considerable (percentage of eosinophils in sputum was 80%). Two months later, the proportion of eosinophils in sputum was reduced to 12%, eosinophils completely disappeared from nasal swab, and ANCA titer became negative. In May 1993, bronchoalveolar eosinophilia disappeared as well, and pulmonary function tests were completely normal.

During 1994, the patient did not present for control check-up. In the meantime, he continued taking 16 mg of methylprednisolone orally daily and excluded the inhaled ones. At the beginning of 1995, the patient exhibited clear signs of iatrogenic Cushing syndrome. Serum cortisol levels were below normal, densitometry showed moderate spinal osteopenia. In order to taper systemic steroids, the patient was hospitalized. Immediately after the corticosteroid dosage was reduced (with continued inhaled steroid treatment), the patient developed morning asthma attacks. On day 7, marked deterioration with serious obstruction of ventilation occurred (decrease of FEV1 from 70% to 31%). Upon the introduction of methylprednisolone, 24 mg daily, pulmonary function improved (FEV1 66%). Bronchoalveolar eosinophilia flared

up again (percentage of eosinophils in sputum was 72%), eosinophils increased from  $0.04 \times 10^9$  to  $0.65 \times 10^9$ . Serum ANCA titer was negative.

In 1997, cataract developed on both eyes and the patient underwent an operation. Atrophic skin changes appeared on both legs and striae disseminated. Erythema nodosum appeared on the legs, and palpable purpura on the chest and back. A short course of cyclophosphamide was introduced.

After remission of the signs of vasculitis, we tried to reduce the systemic corticosteroid dosage several times until 1999, but every attempt resulted in serious deterioration of ventilation function.

In March 1999, a decision was made to initiate treatment with montelukast, a leukotriene receptor antagonist, at a dose of 10 mg daily in the evening. The goal of the treatment was to maintain stable asthma condition while tapering the dose of systemic steroids. After four months of treatment, the patient reported reduced methylprednisolone dosage to 12 mg daily (previously, minimum dosage was 16 mg daily). He was taking salbutamol as needed only. Immunological, functional and routine laboratory parameters were normal. Peripheral blood and bronchoalveolar eosinophilia were absent. The signs of iatrogenic Cushing syndrome were still present, but there were no signs of systemic vasculitis activity.

## Discussion

CSS is distinguished from other systemic vasculitides by the presence of asthma. Involvement of the myocardium, peripheral nerves, gastrointestinal tract, and skin is common. Perinuclear ANCA, present in most patients, should be considered as a major diagnostic criterion but have not proven useful for follow-up purposes<sup>8</sup>. Glucocorticoids have largely improved patient outcome in this disorder, and continue to be the basis of treatment. When control of the inflammatory disease has been achieved, an alternate-day regimen should be preferred whenever possible in order to reduce adverse events<sup>9</sup>. The physician should always be vigilant to detect infection, the manifestation of which may be clinically indistinguishable from that of vasculitis. Antileukotriene drugs are new therapeutic agents that have recently been introduced for the treatment of asthma<sup>10</sup>. Several cases of eosinophilic conditions including CSS have been reported to be associated with zafirlukast, a cystenyl leukotriene antagonist<sup>11</sup>.

We present a 31-year-old man with difficult-to-control asthma and rhinosinusitis, which were the prodromal phase of CSS. After clinical recovery from vasculitis, systemic steroids in a dose of 16-20 mg daily were required for 10 years to control asthma. In order to diminish the severe signs of Cushing syndrome, repeated attempts to reduce the dose of oral steroid were made. The attempts always resulted in severe asthma exacerbation and decision was made to initiate the treatment with montelukast for tapering the dose of corticosteroids<sup>12,13</sup>. After approximately four months, the patient could reduce methylprednisolone to 12 mg daily, without the need of dosage increase on any of the days.

According to clinical and laboratory findings, the patient had CSS. Inhalation steroids could not control his asthma. The leukotriene receptor antagonist enabled reduction of the dose of systemic steroids and control of asthma symptoms<sup>14</sup>. At the same time, it did not induce relapse of the underlying autoimmune disease.

## References

1. LANHAM JG, ELCON KB, PUSSEY CD, HUGHES GR. Systemic vasculitis with asthma and eosinophilia: clinical approach to the Churg Strauss syndrome. *Medicine* 1984; 63:65-81.
2. MASI AT, HUNDER GG, LIE JT, *et al*. The American College of Rheumatology 1990 criteria for classification of Churg-Strauss syndrome (allergic granulomatosis and angiitis). *Arthritis Rheum* 1990;33:1094-100.
3. GUILLEVIN L, VISSER H, NOEL LH, *et al*. Antineutrophil cytoplasm antibodies (ANCA) in systemic polyarteritis nodosa with and without hepatitis B virus infection and Churg Strauss syndrome: 62 patients. *J Rheumatol* 1993;20:1345-49.
4. CLUTTERBOOK EJ, EVANS DJ, PUSSEY CD. Renal involvement in Churg Strauss syndrome. *Nephrol Dial Transplant* 1990;5:161-7.
5. GUILLEVIN L, LHOTE F, COHEN P, JARROUSSE B, LORTHOLARY O, GENEREAU T, *et al*. Corticosteroids plus pulse cyclophosphamide and plasma exchanges *versus* corticosteroids plus cyclophosphamide alone in the treatment in the polyarteritis nodosa and Churg Strauss syndrome patients with factors predicting poor prognosis. A prospective, randomized trial in sixty-two patients. *Arthritis Rheum* 1995;38:1638-45.
6. CHUNG A, BRALLAS M, CRONIN SR, CHUNG J. Formes frustes of Churg Strauss syndrome. *Chest* 1995;108:320-3.
7. FAUCI AS, KATZ P, HAYNES BF, WOLFF SM. Cyclophosphamide therapy of severe necrotizing vasculitis. *N Engl J Med* 1979;301:235-8.
8. GUILLEVIN L, COHEN P, GARYRAUD M, *et al*. Churg-Strauss syndrome. Clinical study and long term follow up of 96 patients. *Medicine* 1999;78:26-37.
9. COTTIN V, CORDIER JF. Churg Strauss syndrome. *Allergy* 1999;54:535-51.
10. P'BYRNE PO, ISREAL E, DRAZEN JM. Antileukotrienes in treatment of asthma. *Ann Intern Med* 1997;127:472-80.

11. WECHSLER ME, GARPESTAD E, FLIER SR, *et al*. Pulmonary infiltrates, eosinophilia, and cardiomyopathy following corticosteroid withdrawal in patients with asthma receiving zafirlukast. *JAMA* 1998;279:455-7.
12. LOFDAHL CG, REISS TF, THEODORE F, *et al*. Randomised, placebo controlled trial of effect of a leukotriene receptor antagonist, montelukast, on tapering inhaled corticosteroids in asthmatic patients. *BMJ* 1999;319:87-90.
13. FRANCO J, ARTES MJ. Pulmonary eosinophilia associated with montelukast. *Thorax* 1999; 54:558-60.
14. TAMAOKI J, KONDO M, SAKAJ N, *et al*. Leukotriene antagonist prevents exacerbation of asthma during reduction of high-dose inhaled corticosteroid. *Am J Respir Crit Care Med* 1997;155:1235-40.

### Sažetak

## CHURG-STRAUSSOV SINDROM: PRIKAZ SLUČAJA

*A. Stipić-Marković, J. Stipić, M. Crnčević-Urek i V. Crnek-Kunstelj*

Churg-Straussov sindrom (CSS) je granulomatozni vaskulitis posredovan antineutrofilnim citoplazmatskim autoantitijelima perinuklearne fluorescencije (P-ANCA). Očituje se kliničkim simptomima ustrajne astme i sinusitisa uz izraženu eozinofiliju, što kod progredirajućih oblika bolesti prethodi migrirajućim plućnim infiltratima uz izvanplućne pojavnosti na perifernim živcima, koži, središnjem živčanom, probavnom i krvožilnom sustavu. Prikazujemo bolesnika s CSS koji se očitovao teškom ustrajnom astmom, perifernom i tkivnom eozinofilijom, sinusitisom i izrazito visokim titrom P-ANCA. Kontrola astme postignuta je tek nakon 10-godišnje steroidne terapije uz mnogobrojne nuspojave. Cilj prikaza je upozoriti na mogućnost CSS kod težih oblika astme i ukazati na mogućnost autoimunih pojavnosti u bolesnika s atopijskom konstitucijom.

*Ključne riječi: Churg-Straussov sindrom; Churg-Straussov sindrom, dijagnostika; Liječenje – Ishod; Prikaz slučaja*