

Atypical clinical presentation of Churg-Strauss syndrome with rapidly progressive glomerulonephritis

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KEY WORDS

Churg-Strauss syndrome, hypereosinophilia, rapidly progressive glomerulonephritis

ABSTRACT

The case of a 48-year-old man presented in this paper illustrates an atypical clinical course of Churg-Strauss syndrome with rapidly progressive glomerulonephritis with no signs of bronchial asthma.

INTRODUCTION Churg-Strauss syndrome (CSS) is an allergic, granulomatous, medium- and small-vessel vasculitis with symptoms of bronchial asthma and peripheral eosinophilia. The etiology of CSS remains unknown, although its incidence is slightly higher among atopic subjects. In 1990, the American College of Rheumatology published 6 criteria for the differentiation of CSS from other forms of primary systemic vasculitis, and the presence of 4 of them indicates a definite diagnosis with high probability. These criteria include¹:

- 1 bronchial asthma
- 2 paranasal sinus abnormality
- 3 pulmonary infiltrates, nonfixed
- 4 mono- or polyneuropathy
- 5 peripheral blood eosinophilia
- 6 tissue infiltration by eosinophils.

Lanham et al. described 3 characteristic stages in clinical evolution of CSS. The first phase (prodromal) involves allergic sinusitis and bronchial asthma; the second phase (after several years) involves peripheral blood eosinophilia (>10% of the cells in the white blood cell smear) and eosinophilic tissue infiltrations; the third phase (systemic vasculitis) begins with general symptoms such as asthenia, fever, and weight loss. Necrotising vasculitis and extravascular granulomas develop in the lungs, heart, peripheral nervous system, kidneys, lymph nodes, muscles, and skin.²

Respiratory symptoms are dominant, with bronchial asthma occurring in 98% of cases. On average, the kidneys are affected in about 30% of cases and the changes are usually mild. Advanced renal lesions occur in less than 10% of cases.³ The presence of perinuclear antineutrophil cytoplasmic antibodies (p-ANCA) in serum is observed in 60% to 70% of CSS patients.⁴

We present the case of CSS with rapidly progressive glomerulonephritis with no severe airway obstruction.

CASE REPORT A 48-year-old man was referred to our clinic in May 2008 due to progressive renal failure. His medical history revealed chronic sinusitis of over 10-year duration, surgery for recurrent nasal polyposis, but he did not report bronchospastic symptoms or paroxysmal dyspnea. In April 2008, the patient was diagnosed in a local hospital due to fever and progressive weight loss persisting for 3 months prior to hospitalization. Subsequently, he was referred to the Department of Infectious Diseases and Allergology, Military Medicine Institute, Warsaw, Poland.

Additional laboratory tests performed at the department revealed elevated inflammatory markers: erythrocyte sedimentation rate (ESR) (70 mm/h), C-reactive protein (16.4 mg/dl); urinalysis showed isosthenuria (specific gravity: 1010), hematuria (the view field was loosely covered with red blood

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Received: October 17, 2009.

Revision accepted:

November 20, 2009.

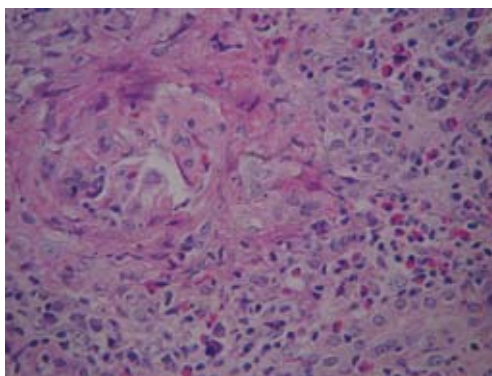
Conflict of interest: none declared.

Pol Arch Med Wewn. 2009;

119 (12): 830-833

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FIGURE Masson's trichrome staining: a glomerulus with a cellular crescent, segmental necrosis of a vascular loop and interstitial eosinophil infiltrate



cells), leukocyturia, proteinuria (1.8 g/day), and eosinophilia (50%) in the peripheral blood smear. Serological tests excluded parasitic diseases (toxocariasis, trichinosis, hydatidosis), viral diseases (cytomegaly, hepatitis B and C, HIV), and bacterial diseases (borreliosis). Additional laboratory diagnostic tests revealed elevated immunoglobulin (Ig) E levels (844 IU/ml, normal range 10–135 IU/ml), blood protein electrophoresis indicative of polyclonal hypergammaglobulinemia. Bone marrow needle aspiration biopsy yielded smears rich in cells, mainly mature eosinophils (37.3%). Endoscopic examinations of the gastrointestinal tract showed chronic gastrocolitis. Diagnostic tests also included computed tomography (CT) scan of the sinuses showing polypoid hypertrophy of the turbinates, with signs characteristic of chronic sinusitis; high-resolution CT of the chest showing no abnormalities; and spirometry that revealed mild airway obstruction. Due to the signs of nephrosonephritis in urinalysis and a progressive decrease in glomerular filtration rate (GFR) (estimated GFR [eGFR] 41–31 ml/min/1.73 m²) during a 10-day monitoring, the patient was referred to a nephrologist. Based on the clinical presentation of the disease, Churg-Strauss syndrome was suspected and testing for anti-dsDNA, antinuclear antibodies, p-ANCA, classic ANCA, anti-glomerular basement membrane (anti-GBM) antibodies was recommended. An indirect immunofluorescence test detected serum anti-GBM antibodies. The patient was transferred to our department to undergo further diagnostic evaluation of progressive renal failure. On admission, he was in a poor general condition, with muscle weakness and fever up to 39°C. Abnormalities in additional tests included elevated ESR (76 mm/1 h), hemoglobin (8.6 g/dl), eosinophilia (43%) in peripheral blood smear, urinary sediment erythrocyturia (the view field was loosely covered with red blood cells), proteinuria (250 mg/dl). The levels of complement C3 and C4 components were within the normal range. The immunofluorescence was confirmed by an enzyme-linked immunosorbent assay (ELISA) that showed p-ANCA of 274 U/ml (norm <7 U/ml) with no anti-GBM antibodies, which finally confirmed the previously suspected systemic vasculitis. A continuous decrease in eGFR to 22 ml/min/1.73 m² led to a decision to perform an urgent diagnostic renal biopsy.

The renal biopsy specimen (**FIGURE**) revealed the following: out of 14 renal glomeruli present in the sample, 8 showed cellular crescents, glomerular extracapillary proliferation, collapse and segmental sclerosis of vascular loops, diffuse interstitial inflammatory infiltration consisting of mononuclear cells and numerous eosinophils, focal renal tubular atrophy. The immunofluorescence test did not reveal the presence of IgG, IgM, IgA, C3, C1q, nor λ or κ light chain deposits. The patient was diagnosed with pauci-immune crescentic glomerulonephritis secondary to ANCA-associated small-vessel vasculitis (**FIGURE**). The final diagnosis of Churg-Strauss syndrome with rapidly progressive glomerulonephritis was made based on the clinical and morphologic presentation. The patient was scheduled for immunosuppressive treatment and plasmaphereses. A total of 7 plasma exchange procedures were conducted, with a subsequent initiation of immunosuppression involving oral prednisone (60 mg) and pulse cyclophosphamide (1 g). The patient's general condition improved, fever resolved, renal function stabilized at GFR of 27 ml/min/1.73 m². A follow-up ELISA-based assay showed the p-ANCA level of 21.9 U/ml.

A total of 7 cyclophosphamide pulses were administered in monthly cycles. Except for 1 zoster episode, no significant adverse events were observed. Resolution of erythrocyturia and leukocyturia was achieved, as well as an improvement in renal function with eGFR of 41 ml/min/1.73 m². Currently, that is 17 months after the diagnosis, the patient is followed on an outpatient basis and takes prednisone 5 mg once daily. The levels of p-ANCA measured during the follow-up were normal.

DISCUSSION Diagnosis of systemic vasculitis is particularly challenging because of the variety of clinical manifestations and stages in the course of the disease. In the present case, general symptoms including progressive muscle weakness, fever, weight loss, and a characteristic 3-stage course led to a suspicion of CSS, after excluding infectious and proliferative disorders. No history of bronchial asthma as one of the main CSS criteria constituted a diagnostic challenge.

So far, there have been 8 cases of CSS without bronchial asthma described worldwide. Kawakami et al. reported the case of a 42-year-old man who presented with diffuse skin lesions diagnosed as maculopapular rash and muscle weakness. He had no history of bronchial asthma or chronic rhinitis. Additional tests revealed eosinophilia (19.4% of leukocytes) and significantly elevated IgE levels, up to 2700 IU/ml. Imaging examinations were inconclusive. Due to persistent skin lesions, a skin biopsy was performed, revealing extravascular granulomas and eosinophilic infiltration typical of CSS.⁵ Sharma et al. described the case of a 35-year-old woman with CSS without evidence of bronchial asthma or eosinophilia, but mainly with clinical manifestations of

polyneuropathy, skin lesions in the form of a macular rash, and positive p-ANCA. Chest CT revealed bilateral, spotty infiltrates in the lung tissue. Lung biopsy showed leukocytoclastic vasculitis with extravascular eosinophilic infiltrates.⁶

Renal involvement occurs in approximately 30% of CSS cases and is usually mild, with advanced renal damage occurring in up to 10% of cases. The case described by Yamashita et al. is similar to that presented here. They reported a 61-year-old man with signs of rapidly progressive glomerulonephritis without evidence of bronchial asthma. Clinical presentation included peripheral neuropathy and peripheral blood eosinophilia (58.2% of leukocytes). Chest imaging showed transient pulmonary infiltrates. Renal biopsy confirmed the diagnosis of pauci-immune crescentic glomerulonephritis.⁷

The pauci-immune crescentic glomerulonephritis in our patient required a differential diagnosis including medium- and small-vessel vasculitis other than CSS. Serological ELISA used to determine p-ANCA proved an invaluable diagnostic tool, because it helped to finally confirm suspected systemic vasculitis.

Among different infectious nephropathies, the high percentage of eosinophils is rarely present and is limited to such diseases as drug-induced tubulointerstitial nephritis, tubulointerstitial nephritis as a cause of CSS syndrome, and renal involvement in inflammatory pseudotumor. Nevertheless, the final diagnosis depends on the microscopic evaluation.

Glucocorticosteroids are the mainstay of treatment in patients with CSS. Oral glucocorticosteroids alone are recommended in mild CSS; however, advanced organ lesions require a combined treatment with immunosuppressive agents (methylprednisolone i.v., cyclophosphamide i.v., therapeutic plasma exchange).⁸

The use of pulse methylprednisolone, cyclophosphamide, and therapeutic plasma exchange in our patient helped to improve renal function and reduce immunological symptoms.

Conclusions The case of an atypical Churg-Strauss syndrome, i.e., with no history of bronchial asthma but with clinical evidence of rapidly progressive glomerulonephritis, including manifestations of nephrosonephritis, anemia, and rapid decrease in GFR, indicates a significant diagnostic value of p-ANCA determination by ELISA as well as renal biopsy.

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OPIS PRZYPADKU

Gwałtownie postępujące kłębuszkowe zapalenie nerek w przebiegu zespołu Churga i Strauss o nietypowym obrazie klinicznym

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SŁOWA KLUCZOWE

gwałtownie
postępujące
kłębuszkowe
zapalenie nerek,
hypereozynofilia,
zespół Churga
i Strauss

STRESZCZENIE

Na podstawie przypadku 48-letniego chorego przedstawiono nietypowy przebieg kliniczny zespołu Churga i Strauss z gwałtownie postępującym kłębuszkowym zapaleniem nerek bez objawów astmy oskrzelowej.

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Praca wpłynęła: 17.10.2009.
Przyjęta do druku: 20.11.2009.
Nie zgłoszono sprzeczności
interesów.

Pol Arch Med Wewn. 2009;
119 (12): 830-833
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