Case Reports

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Nonasthmatic Churg–Strauss syndrome superimposed on chronic pyelonephritis: a case report

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Abstract

Churg–Strauss syndrome (CSS) is a granulomatous small-vessel vasculitis. Asthma is seen in the majority of patients with CSS, but atypical nonasthmatic forms of CSS are also being recognized. We herein describe a 67-year-old woman with a history of chronic pyelonephritis and drug allergy reactions who was admitted to our hospital because of worsening renal function preceded by fever, purpura, sinusitis, and a positive urine culture that confirmed a urinary infection. She was initially treated with pipemidic acid for 7 days, followed by clarithromycin for sinusitis. Laboratory tests on admission showed an absolute eosinophil count of 1750 cells/μL and serum creatinine concentration of 4.72 mg/dL. Urine and blood cultures showed no growth. Kidney biopsy revealed crescent formations with diffuse interstitial fibrosis and foci of eosinophil infiltration. An atypical form of CSS was diagnosed based on tissue eosinophilia, peripheral eosinophilia, and sinusitis. Intravenous methylprednisolone and cyclophosphamide pulse therapy together with hemodialysis treatment improved the patient's clinical condition but did not resolve the kidney damage. The onset of an atypical form of CSS in our patient manifested as symptoms and signs mimicking those of chronic pyelonephritis and drug allergy reactions. The patient's chronic kidney disease finally progressed to dialysis dependence.

Keywords

Churg–Strauss syndrome, rapidly progressive glomerulonephritis, chronic pyelonephritis, chest computed tomography, kidney biopsy, case report

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Introduction

Churg–Strauss syndrome (CSS) is a granulomatous small-vessel vasculitis also known as eosinophilic granulomatosis with polyangiitis of unknown cause.[1] The most commonly involved organ is the lung, but CSS can affect any organ system, including the kidneys. In 1990, the American College of Rheumatology proposed six criteria for diagnosis of CSS: asthma, paranasal sinusitis, eosinophilia (>10% in peripheral blood), pulmonary infiltrates, histological proof of extravascular eosinophil infiltration, and mononeuritis multiplex or polyneuropathy.[2] The presence of four of these criteria indicates a CSS diagnosis with high probability. Asthma is seen in almost 98% of patients with CSS (classic form), but nonasthmatic CSS (a limited form of CSS) is being recognized and reported.[3,4] We herein present a case of pauci-immune crescentic glomerulonephritis in a patient with nonasthmatic CSS superimposed on chronic pyelonephritis. The reporting of this case conforms to the CARE guidelines.[5] All patient details were deidentified; therefore, written informed consent from the patient was not required for publication of this case report and accompanying images. However, consent was obtained for treatment.

Case report

A 67-year-old woman with a history of chronic kidney disease due to recurrent urinary infections was admitted to the nephrology department of our institution because of worsening renal function preceded by fever, urticaria, and sinusitis. At a regular control visit 3 months earlier, her serum creatinine level had been 1.42 mg/dL. Her medical history included several episodes of urticaria provoked by certain antibiotics and a few episodes of unknown origin; the current admission, however, she denied use of novel drugs that could have provoked urticaria. At the same time, a urine culture confirmed a urinary infection caused by *Escherichia coli*. The general practitioner prescribed pipemidic acid for treatment of the urinary tract infection and levocetirizine for treatment of the urticaria. Despite this therapy, she experienced persistent urticaria and a fever of up to 38°C. Her clinical picture was complicated by development of frontal sinusitis. Clarithromycin was administered. She remained febrile in spite of this antibiotic treatment, but her urticaria disappeared. Because of her serum creatinine level of 4.58 mg/dL in the control laboratory tests, she was sent to a nephrologist. Physical examination on admission revealed pale skin with slight lower extremity edema. Her blood pressure was 180/100 mmHg, pulse rate was 92 beats/minute (regular sinus rhythm), and body temperature was 38.5°C. Other physical findings were unremarkable. A laboratory examination revealed the following findings: hemoglobin, 7.9 g/dL; white blood cell count, $10.3 \times 10^3/\mu L$ with 16.6% eosinophils (absolute eosinophil count: 1750 cells/μL); erythrocyte sedimentation rate, >150 mm in the first hour; C-reactive protein, 107.6 mg/dL; serum creatinine, 4.72 mg/dL; and glomerular filtration rate estimated by the Modification of Diet in Renal Disease equation, 9.8 mL/minute/1.73 m^2. Urinalysis showed proteinuria (1.06 g/day), hematuria (12–15 erythrocytes per high-power field), and leukocyturia (10–12 leukocytes per high-power field) with no casts. Sputum, urine, and blood cultures showed no growth. Nasal and throat swabs indicated normal flora.

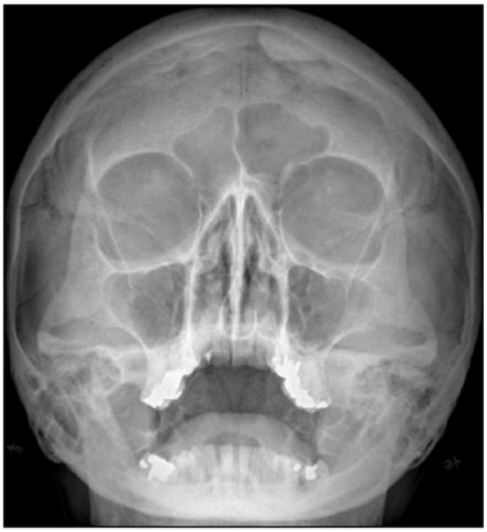

Figure 1. Sinus X-ray examination showed bilateral acute frontal sinusitis.

Examination by an otolaryngologist showed bilateral acute frontal sinusitis, which was confirmed by X-ray (Figure 1). The chest X-ray was unremarkable. Ultrasound revealed normally sized kidneys (around 110 mm) with hyperechogenic parenchyma. Echocardiography was not performed. Ciprofloxacin was started immediately upon admission, but the patient's inflammatory indices remained elevated. In addition, acute diarrhea (*Clostridium difficile*-negative) developed and was suspected to have been caused by the antibiotic therapy. An enzyme-linked immunoassay detected myeloperoxidase antineutrophil cytoplasmic antibodies (MPO-ANCA) at 62 IU/mL (reference, <20 IU), whereas the antinuclear antibody titer was 1:160 and components of C3 and C4 were normal. Anti-double-stranded DNA and anti-glomerular basement membrane antibodies were not detected. Hepatitis B surface antigen and serological tests for hepatitis C and HIV were negative. We performed a kidney biopsy to determine the etiology of the aggravated kidney function. The analysis showed 10 glomeruli: 2 were globally sclerotic and the others had cellular and fibrocellular crescent formations. Diffuse interstitial fibrosis and tubular atrophy with lymphocytic–monocytic infiltration and foci of eosinophil infiltration were present, but without granuloma formation (Figure 2). Immunofluorescent micrography revealed only slight positivity for IgM and C3 deposits. The diagnosis of pauci-immune crescentic glomerulonephritis was confirmed. The presence of tissue eosinophilia in association with peripheral eosinophilia and sinusitis led us to suspect CSS. After obtaining the patient's consent for treatment, intravenous pulse therapy of methylprednisolone (500 mg/day, three doses, followed by oral prednisolone at 1 mg/kg/day) and cyclophosphamide (750 mg/infusion for first dose; this was repeated in 2 weeks and then every 4 weeks thereafter) was administered. Despite the patient's rapidly progressive course, plasma exchange was not performed because of her advanced kidney failure on admission, histopathological findings of diffuse interstitial fibrosis and tubular atrophy, and prolonged diarrhea. Her clinical condition improved markedly after two series of cyclophosphamide, but her kidney function further deteriorated and hemodialysis treatment was initiated.

Immunosuppressive therapy improved the patient's clinical condition and normalized her eosinophil count, but the patient remained hemodialysis-dependent. An additional computed tomography scan of the lungs showed a few scattered nodules in the pulmonary parenchyma (Figure 3). After 24 months of follow-up, the patient remained stable with no other organ involvement.

Discussion

This case report has described a patient who developed MPO-ANCA-associated

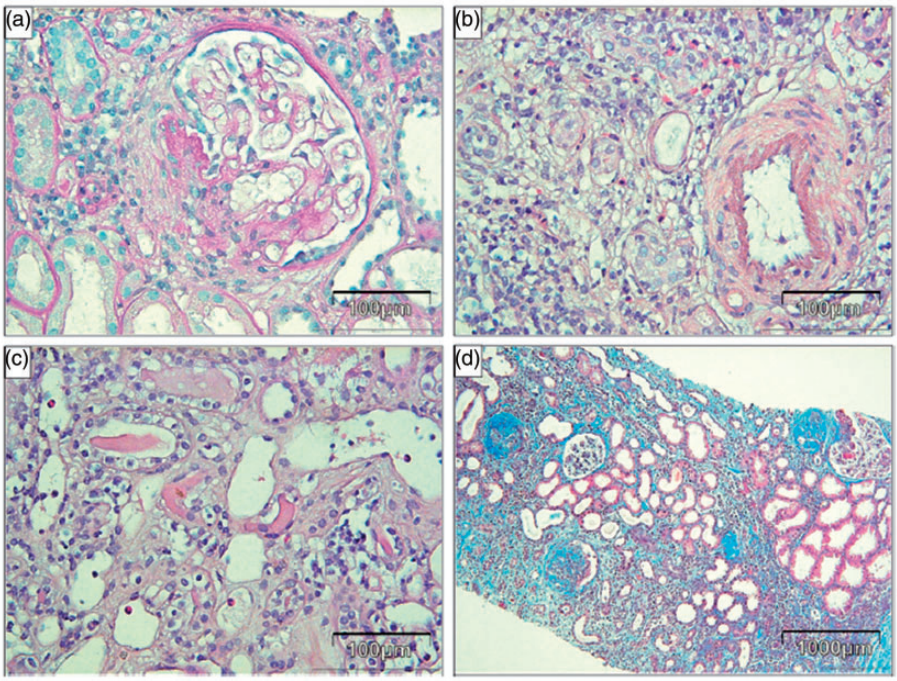

Figure 2. Light microscopy findings of kidney biopsy specimen. (a) Glomerulus with fibrocellular crescent formation, fibrinoid necrosis of the glomerular basement membrane visible in the lower left part of the glomerulus, and stratification of Bowman's capsule (periodic acid–Schiff, ×400). (b) Focus of eosinophils within a lymphocytic–monocytic infiltration in the kidney interstitium, adjacent to a blood vessel (hematoxylin–eosin, ×400). (c) Presence of eosinophils within tubular lumen (hematoxylin–eosin, ×400). (d) Diffuse interstitial fibrosis with tubular atrophy and sclerotic glomeruli (Masson's trichrome staining, ×200).

vasculitis with rapidly progressive glomerulonephritis superimposed on chronic pyelonephritis. The initial disease presentation involving fever, skin rash, rapid and acute renal impairment, and peripheral eosinophilia suggested tubulointerstitial nephritis caused by drugs; however, this diagnosis was ruled out because the skin rash and fever had appeared without previous novel drug use.

The finding of ANCA positivity suggested vasculitis, although infection could have triggered the occurrence of MPO-ANCA. Many authors have reported ANCA-associated vasculitis following bacterial pneumonia, wound infection, and pyelonephritis.[6–8] Although CSS is an ANCA-associated systemic vasculitis, ANCA may not always be present, and ANCA is not a diagnostic criterion for CSS. Only about 40% of patients with CSS are ANCA-positive, and most show a perinuclear pattern and with the presence of anti-MPO antibodies.[9] In one study, 75.0% of patients with CSS who showed glomerular involvement were ANCA-positive in contrast to 25.7% of patients without nephropathy.[9]

The final diagnosis of an atypical form of CSS in our patient was established by kidney biopsy (eosinophil infiltration in the tubulonterstitium), clinical findings (paranasal sinusitis), and laboratory data (eosinophilia). Pulmonary infiltrates, which are transient, were confirmed later by computed tomography. Several similar

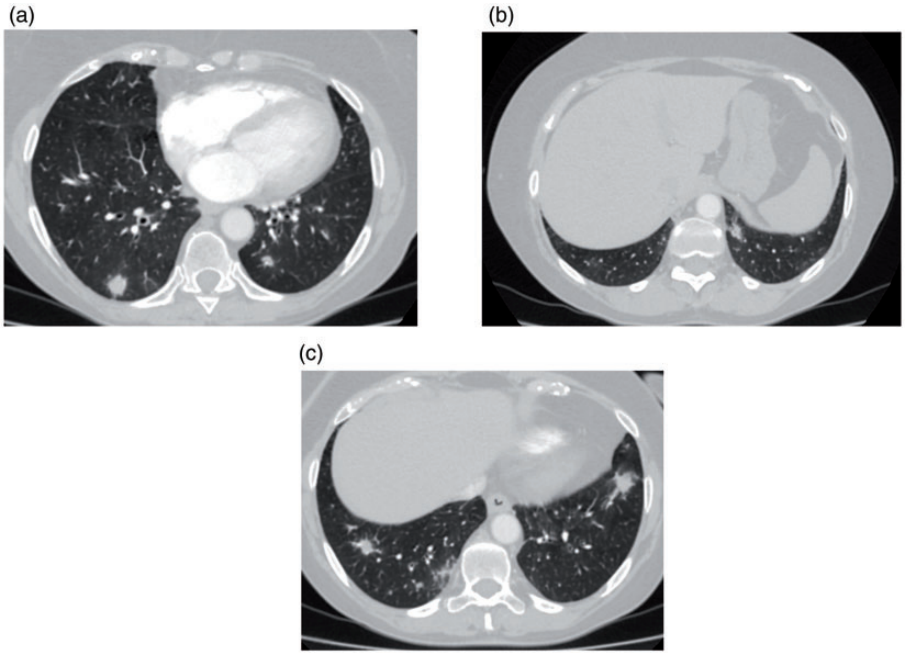

Figure 3. Chest computed tomography scan. (a) One node is present on the right. (b) A small excavated nodule is present on the left. (c) One node is present on each side with an irregular spiculated contour.

cases that lacked complete diagnostic criteria for CSS have been reported, and these cases were diagnosed only by tissue biopsy.[10–13] Clinicians should bear in mind that there are some atypical cases of CSS that do not always meet the diagnostic criteria, and tissue biopsies should be performed if the diagnosis is considered to be difficult.

The main renal histological finding in CSS is pauci-immune focal and segmental necrotizing crescentic glomerulonephritis with crescents that usually involve <50% of the glomeruli; however, other forms of nephropathy have also been detected.[3,4,9,14] Hirohama et al.[15] analyzed published data regarding 31 patients with CSS who presented with rapidly progressive glomerulonephritis or acute kidney injury due to tubulointerstitial nephritis. Extracapillary proliferation in more than 50% of the glomeruli was present in 10 patients, whereas interstitial eosinophil infiltration was seen in 18 patients. Pre- and post-renal function was documented for 28 patients. Partial or complete recovery of kidney function occurred in 24 patients, leading the researchers to conclude that CSS has a good prognosis. The patients with eosinophilic tubulointerstitial nephritis in whom renal function did not recover were diagnosed late, in end-stage renal disease. In a study by Sinico et al.,[9] only 1 of 11 patients with necrotizing crescentic glomerulonephritis reached end-stage renal failure after 5 years of follow-up. Considering the renal outcome, our patient remained hemodialysis-dependent. Because of her delayed referral to a nephrologist, immunosuppressive therapy was started late. In addition, her previous chronic kidney disease in the current exacerbation period did not help in the recovery of kidney function. Other authors have also described CSS

superimposed on other kidney diseases, such as diabetic nephropathy and focal segmental glomerulosclerosis, where the immunosuppressive treatment did not completely resolve the renal damage.[14,16]

By presenting this case report, we intend to point to the possibility of renal involvement by two diseases. Additionally, this case highlights the importance of delineating between two diseases that can mimic each other by similar presentations because early diagnosis and treatment of CSS may prevent the irreversible loss of renal function.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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Author contributions

SR, SK, and AK collected the data and performed the research/study.
MZ and J M-L performed the histopathological analysis.
AK, RN, and VL conceived and designed the study, revised the manuscript, and approved the final version of the manuscript.

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