CASE REPORT

ANCA - Positive Churg Strauss Syndrome with Necrotizing Crescentic glomerulonephritis

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ABSTRACT

Churg Strauss Syndrome (CSS) is an ANCA associated small vessel vasculitis with eosinophilic infiltration. Renal involvement is frequent, although usually mild. We report a case of CSS with renal failure. Renal biopsy revealed necrotizing crescentic glomerulonephritis, eosinophilic arteritis and diffuse eosinophilic infiltration. Patient was successfully treated with combination of corticosteroids and cyclophosphamide. (*J Med Sci* 2009;12(1):21-23)

Key words: Churg Strauss syndrome, renal failure, necrotizing crescentic glomerulonephritis.

Introduction

CSS was described in 1951, as a granulomatous variant of polyarteritis nodosa with eosinophilic tissue infiltration.¹ It frequently presents with atopy in the form of allergic rhinitis, bronchial asthma and hyper-eosinophilia.² Renal involvement has been frequently described but is mild in majority of cases. Several patients with advanced renal failure have also been described.^{1, 3-8} We present a case of CSS with advanced renal failure and necrotizing crescentic glomerulonephritis.

Case report

A 60-year old man suffering from hypertension for last 2 years presented with rhinitis, cough and breathlessness for last 9 months and was treated for late onset

bronchial asthma. He received bronchodilators, prednisolone and enalapril, without significant relief of respiratory symptoms. He was referred to nephrology unit with symptoms of edema, decrease in urine output, intermittent fever and arthralgias of one month duration. On examination patient had bilateral pedal edema, hypertension (Blood pressure of 140/100 mmHg) and bilateral diffuse rhonci on chest auscultation. Laboratory examination disclosed hemoglobin of 13 gms/dl, total leucocyte count of 27.81 cells/mm³ with marked eosinophilia (35%). Serum biochemistry revealed BUN of 64 mg/dl, creatinine of 5.97 mg/dl, LDH 672 IU/l, total proteins 8.4 gm/dl and albumin 4.1 gm /dl. The chest x-ray showed infiltrates in right base and left lower zone and the CT scan of chest showed area of consolidation in left lateral basal segment and minimal pleural effusion left side. The urine examination showed 1+ proteinuria, micro-hematuria and 24 hour protein excretion of 1.2 grams. A positive C-reactive proteins (10.2 mg/dl), rheumatoid factor (110 iu/ml) and p-ANCA (11.42 Units/ml with specificity against myeloperoxidase) were confirmed. His other investigations included normal C-ANCA (1.01 Units/ml), negative ANA, anti DS DNA, cry-globulin and normal complement levels.

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Renal biopsy confirmed the diagnosis of Churg Strauss Syndrome(Figure). Fifteen glomeruli were obtained that showed hyper cellularity of tufts with focal necrotic changes and infiltration by eosinophils. Six glomeruli showed fibro-cellular crescents. Two medium

Figure showing Churg-Strauss syndrome renal biopsy which was showing glomerulus revealing epithelial cell proliferation resulting in the crescent formation and eosinophilic infiltration. (H&E X400).

sized vessels showed features of vasculitis with predominantly eosinophilic infiltration. Tubules showed focal dilatation and interstitium showed diffuse infiltration by eosinophils with few lymphocytes and neutrophils. Immunofluorescence showed sparse IgG positivity in two glomeruli only. Patient was treated with combination of prednisolone 60mg per day and continuous oral cyclophosphamide 100mg per day.

After one month of treatment patient showed significant improvement in respiratory symptoms with improvement in FEV 1 from 35% to 55%. His kidney functions improved, serum creatinine stabilized at 2.5 mg/dl, hematuria and proteinuria resolved and the eosinophil count dropped down to 1.5%.

Discussion

The primary systemic vasculitic disorders are a group of inflammatory disorders of unknown etiology.⁹ Diverse forms of vasculitis were classified in the Chapel Hill international consensus conference.¹⁰ Wegener granulomatosis, microscopic polyangiitis and Churg Strauss syndrome are described as small vessel vasculitides and are acknowledged to be commonly associated with antineutrophil cytoplasm antibodies (ANCA).¹¹

The accurate diagnosis of CSS remains problematic. Churg and Strauss described in 1951 three pathologic features associated with the disease; an eosinophilic tissue infiltration, granuloma formation, and necrotizing vasculitis involving small and medium sized vessels.¹

Majority of patients described by them were studied by postmortem examination. These pathological findings yield a low sensitivity for diagnosis of CSS. Alternative diagnostic criteria were proposed by Lanham and more recently by American Rheumatology Association (ARA). Lanham *et al*³ Proposed following three criteria for diagnosis of Churg Strauss syndrome: (1) Asthma (2) peak peripheral blood eosinophil count $>1.5 \times 10^6/\text{cc}$ (3) systemic vasculitis involving two or more extra-pulmonary organs.

American Rheumatology Association (ARA) criteria¹² requires four of following six findings for diagnosis of Churg Strauss syndrome: (1) Asthma (2) eosinophilia $>10\%$, (3) neuropathy (4) non-fixed pulmonary infiltrates (5) Para nasal sinus abnormality (6) extra vascular eosinophils. Churg Strauss syndrome is global in distribution, most commonly reported in 3rd to 5th decade of life with estimated prevalence of 2.4 per million population.² It can present with prodromal and vasculitic phases, although phasic nature may be missing in many patients. During prodromal phase allergic rhinitis occurs in up to 70% of cases and is often the first evidence of disease and may be associated with nasal polyposis, obstruction and recurrent sinusitis.¹⁰ Asthma precedes the development of vasculitis by weeks to years. In vasculitic phase patients develop weight loss, anemia, fever, myalgias, polyarthritides and skin rashes (up to 70%).⁴ Pulmonary involvement presents as progressive dyspnea, alveolar hemorrhage, pleurisy and eosinophil rich pleural effusion.⁵ Cardiac involvement consists of acute pericarditis, pericardial effusion, myocarditis and congestive cardiac failure.⁴⁻⁶ Gastrointestinal involvement results in abdominal pain, ascitis, diarrhea and hematochezia.^{3,4,13} Mononeuritis is a common feature and occasionally cerebral vasculitis may occur.⁵

Renal involvement is usually mild and severe renal failure is uncommon. In different series renal involvement has been shown to occur in 20-80% of cases, majority having proteinuria or microscopic hematuria where as mild to moderate renal failure has been reported in 7-52% and advanced renal failure in 0-4% patients.^{1,3-8}

Renal histology may reveal frank vasculitis, involving arteries of varying sizes, distinguishable from other vasculitides by wide spread infiltration of eosinophils.² The most typical histologic finding is a focal segmental or a diffuse necrotizing glomerulonephritis with an intense eosinophil-rich interstitial infiltrate.² Immunofluorescence microscopy reveals sparse or non-specific staining.

Churg Strauss Syndrome is classified as ANCA associated vasculitis along with Wegener's granulomatosis and Microscopic polyangiitis. ANCA positivity has been reported in one half to two-thirds of patients with Churg Strauss Syndrome. Most studies have reported perinuclear

staining with ANCA specificity to Myeloperoxidase but presence of cytoplasmic staining pattern is not uncommon.²

Prognosis of treated CSS including renal prognosis appears to be good. Long term morbidity after remission of active disease can be due to damage sustained during vasculitic phase or due to immunosuppressive therapy. Asthma, congestive heart failure and peripheral neuropathy remain as frequent long term complications.¹⁰

Churg Strauss syndrome responds rapidly to corticosteroids.⁵ Several patients with serum creatinine up to 2.3 mg/dl on presentation treated with prednisolone alone showed excellent response.¹⁴ In more recent protocols in patients with ANCA associated vasculitis, cyclophosphamide in combination of steroids is the mainstay of induction regimens.² Cyclophosphamide is given either as continuous oral administration at 2 - 3 mg/kg body weight or intravenous pulses of 750 mg to 1gm/m² surface area. Trials by European vasculitis study group (EUVAS) have demonstrated that 3 month course of cyclophosphamide followed by azathioprine is as efficacious as a 12 month cyclophosphamide regimen for patients with ANCA associated vasculitis and moderate renal failure.¹⁵ Daily oral and pulsed cyclophosphamides have been demonstrated to be of equal efficacy with reduced toxicity and cumulative dose in pulsed therapy.¹⁶ Addition of plasmapheresis and pulsed intravenous methylprednisolone have been found to be effective adjuvants in severe renal failure in ANCA associated vasculitis.¹⁷ New drugs found to be effective in resistant cases of ANCA associated vasculitis include anti-TNF- α therapy, CAMPATH-1H, anti-thymocyte globulin and rituximab.²

Our patient had typical clinical features of CSS and diagnosis was confirmed by renal histology showing necrotizing crescentic glomerulonephritis, eosinophilic vasculitis and eosinophilic infiltration of interstitium with P-ANCA positivity. Although renal failure is thought to be rare in Churg Strauss Syndrome, but this case illustrates it can occasionally occur.

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