

### IgA glomerulonephritis associated with Churg-Strauss syndrome

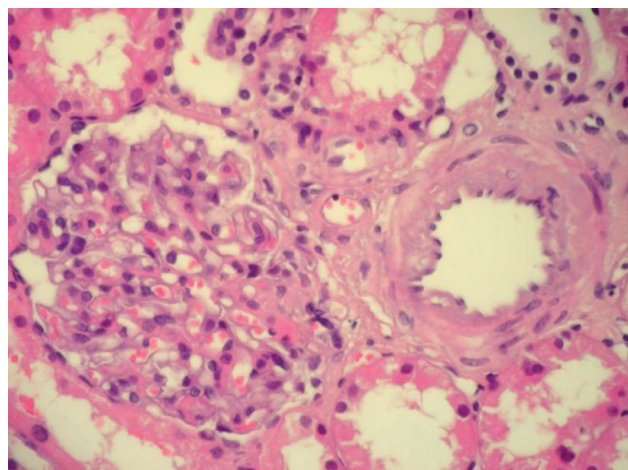
Sirs,

We describe a case of a patient with Churg-Strauss syndrome (CSS) which, after many years of follow-up, is presenting urinary abnormalities associated with histological findings of IgA glomerulonephritis. Concomitant CSS and IgA nephropathy have rarely been reported. This uncommon association may be coincidental, but might also represent a possible overlap syndrome. In April 1992, a 33-year-old woman, with a 3-year history of asthma and paranasal sinus pain, showed fever and dyspnea in concomitance with asymmetric dysesthesia-hyperalgesia involving the legs and infiltrated purpuric lesions in the lower extremities. Chest radiographs showed bilateral and patchy pulmonary infiltrates. Flexible bronchoscopy with bronchoalveolar lavage (BAL) and transbronchial biopsy excluded neoplastic or infectious lesions: eosinophils accounted for more than 25% of the cells in the BAL fluid. Laboratory data showed elevated inflammatory markers, eosinophilia ( $5,600/\text{mm}^3$ ) and normal renal function. Serum complement, protein and immunoglobulin levels were also normal. Autoantibodies, and in particular ANCA, were absent. Biopsy skin specimen showed accumulation of eosinophils in extravascular sites. These features were consistent with CSS and were successfully treated with oral prednisone ( $1\text{mg}/\text{kg}/\text{die}$ ). Over the next years the patient was treated with low dose of oral corticosteroids ( $5\text{--}12.5\text{mg}/\text{die}$ ) to control the relapsing asthmatic attacks and the purpuric lesions.

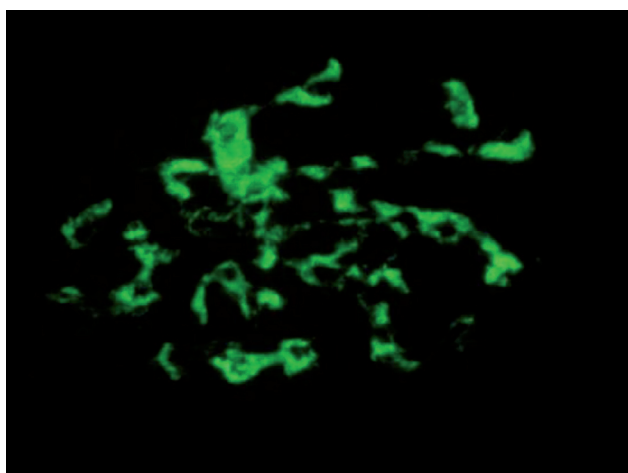
In June 2008, urinary abnormalities (microscopic dysmorphic haematuria, proteinuria and cellular casts) appeared in the absence of urinary infection, with a lightly reduced renal function. On physical examination, the patient showed only infiltrated purpuric lesions in the lower extremities. The laboratory investigation demonstrated a leukocyte count of  $10,020/\text{mm}^3$  with  $41\text{ eosinophils}/\text{mm}^3$ . Inflammatory markers, autoantibodies, immunoglobulins, and serum complement were normal. Renal biopsy showed a picture of diffuse proliferative mesangial glomerulonephritis associated with mesangial deposits of IgA (Fig. 1). Steroid pulses ( $500\text{mg iv}$ ) were given for 3 consecutive days, followed by a dose of  $25\text{mg}$  given orally on alternate days for 6 months. In January 2009, laboratory tests showed normal renal function and the absence of proteinuria.

In CSS, renal involvement is less severe and less prominent than in other ANCA-associated vasculitides. The main histological picture is a focal and segmental form of pauci-immune necrotising crescentic glomerulonephritis, while arteritis, interstit-

**Fig. 1A.** Light microscopy of a glomerulus with moderate, segmental, mesangial hypercellularity and mild increases in mesangial matrix (H&E;  $\times 200$ ).



**Fig. 1B.** IF (20x): immuno-fluorescence findings: diffuse mesangial granular IgA deposits.



ial eosinophil-rich infiltrates and focal mesangial proliferative glomerulonephritis without immune deposits (1-3) are rarely found. Usually, renal involvement is already present at the time of diagnosis. The majority of patients with renal involvement, and particularly those with necrotising glomerulonephritis, are ANCA(MPO) positive and frequently have necrotising small-vessel vasculitis.

IgA nephropathy may be associated with systemic vasculitides, such as cryoglobulinemia, Henoch-Schönlein purpura (4), polyarteritis nodosa (5). On the contrary, the occurrence of IgA nephropathy in patients with ANCA-associated vasculitides is rare. To our knowledge, association of CSS and IgA nephropathy has been previously reported only by Richer *et al.* (6). They described a patient with ANCA-negative CSS of 10 years duration characterised by asthma, nasal polyps and frequent episodes of sinusitis. After an episode of septicaemia, he experienced a sudden deterioration of renal function associated with mesangial IgA deposits. Richer *et al.* also reported a p-ANCA(MPO)-positive patient with microscopic polyangiitis characterised by systemic vasculitis and renal insufficiency associated with arteriolar hyaline degeneration and mesangial deposits of IgA

(6). Andrassy *et al.* reported the occurrence of IgA glomerulonephritis in 3 patients with WG during remission of the disease (7). Several cases of patients suffering from IgA nephropathy associated with ANCA-positivity without vasculitis have also been reported suggesting that high titres of p-ANCA (anti-MPO) may confer a worse prognosis in patients with IgA nephropathy (8, 9).

The occurrence of IgA nephropathy in our patient may be accidental as this nephropathy is the commonest primary glomerulonephritis. However, a pathogenic link between IgA nephropathy and CSS, possibly through non-ANCA related mechanisms, cannot be excluded. Both our patient and the patient described by Richer *et al.* were ANCA-negative and developed nephropathy many years after the disease onset and when the vasculitic disease showed low activity. One possible mechanism might be that recurrent infections of respiratory tract, which are frequent in patients with CSS, may induce a local immune response and possibly a stimulation of secretory IgA with production of immune complexes that, in turn, may cause local tissue damage such as IgA nephropathy. This hypothesis could be supported by the case described by O'Donovan *et al.* in which in a CSS

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patient a peripheral neuropathy was found to be associated with IgA and C3 deposits (10). Additional reports are required to further confirm this hypothesis and to establish relationships between CSS and the occurrence of IgA nephropathy.

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