Henoch–Schönlein purpura nephritis associated with methicillin-resistant Staphylococcus aureus infection

Sir,

Environmental agents reported to be associated with the pathogenesis of Henoch–Schönlein purpura nephritis (HSPN) include viral antigens, bacterial antigens, drugs. A high incidence of upper respiratory tract infections preceding HSPN was also reported [1,2]. On the other hand, patients with HSPN did not have an increased frequency of positive cultures for haemolytic streptococci in a carefully controlled study [3]. HSPN associated with other bacterial antigen has been reported, however, we have been unable to find a report of HSPN after staphylococcal infection. The present paper describes a case of HSPN, with rapidly progressive glomerulonephritis, associated with methicillin-resistant Staphylococcus aureus (MRSA) infection.

A 60-year-old Japanese man, who had a subphrenic abscess after an operation for acute appendicitis, developed proteinuria and haematuria. He also complained of arthralgia, and areas of purpura were seen over his extremities. Urinary protein excretion was 5–7 g/day, occult blood in urine was detected, and creatinine clearance was about 50 ml/min. The levels of serum CRP, IgA and immune complexes were highly elevated. Bacteriological analysis showed coagulase type II MRSA producing staphylococcal enterotoxin A and C. Analysis of peripheral lymphocyte subsets using 3-colour flow cytometry showed increased the ratios of some variable parts of β-chain (Vβ) of T cell receptor (TCR) positive T-cells (Figure 1). Histopathological findings demonstrated focal mesangial and endocapillary proliferative glomerulonephritis with crescent formation and tubulointerstitial nephritis. On immunofluorescence examination, IgA, IgG and C3 were intensely positive in both the mesangium and peripheral capillary wall. Leukocytoclastic vasculitis was also observed on skin biopsy. We promptly administered antibiotic therapy consisting of vancomycin. However, the patient had persistent complaints of purpura and arthralgia, levels of CRP was not normalized, MRSA remained detectable, proteinuria did not decrease, and kidney function rapidly worsened. After 4 weeks, the serum creatinine level was 7.1 mg/dl, and the patient needed dialysis therapy. About 4 weeks after the initiation of haemodialysis, purpura and arthralgia disappeared, the CRP level normalized, MRSA was no longer detected.

Fig. 1. PBMC were isolated from the patient’s peripheral blood by density centrifugation at the on-set of HSPN. PBMC were stained with phycoerythrin, biotin or FITC-labelled monoclonal antibodies and stained cells were analyzed by three-colour staining with a fluorescence-activated cell sorter. FITC-conjugated anti-T cell receptor Vβ antibodies (x-axis) and phycoerythrin-conjugated anti-CD3 antibody (y-axis) fluorescence profiles plotted on a logarithmic scale. This analysis shows increased the ratios of Vβ 5.2+5.3-, Vβ8 family-, and Vβ12.1-positive cells.

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detectable, and the ratios of enhanced TCR V\(\beta\)-positive cells were decreased. However, the patient could not discontinue haemodialysis therapy.

Staphylococcal enterotoxins have been called 'superantigens' because of their efficient activation of T lymphocytes and because of the stimuliarity of the mechanism of T-cell stimulation to antigen recognition [4]. The interaction sites on the major histocompatibility complex molecule and on the TCR V\(\beta\) T-cell surface have been reported to play a role in the pathogenesis of numerous human diseases, including toxic shock syndrome [5], with an increase in specific TCR V\(\beta\) T-cells. On the other hand, it has recently been reported that clonal expansion of T cells occurs in peripheral blood mononuclear cells (PBMC) in local lesions of rheumatoid arthritis [6,7], Sjögren's syndrome [8] and Kawasaki disease [9] as a result of variable-diversity-joining gene combinations or complementarity-determining region 3 according to TCR analysis. In the present case, HSPN developed after the MRSA infection and an increase in specific TCR V\(\beta\)+ cells was elevated after the onset of HSPN and reduced during vancomycin treatment. This suggested that superantigens and/or conventional antigens might be involved in the pathogenesis of HSPN.

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**Treatment of progressive renal failure in idiopathic membranous nephropathy with azathioprine and prednisolone**

Sür,

We agree with the conclusion of Brown et al. [1] that azathioprine and prednisolone treatment is of benefit in patients with idiopathic membranous nephropathy and significant renal impairment. We write to draw attention to our own findings [2] in, admittedly, a smaller number of patients with this condition, in whom serum creatinine concentration had risen by 90 \(\mu\)mol/l or more to reach a concentration of 300 \(\mu\)mol/l or more over a 12-month period of observation and in whom proteinuria of nephrotic proportions was present. Treatment with azathioprine and prednisolone was associated with a significant reduction in serum creatinine concentration at 1 year with a decline in proteinuria. A small number of patients fulfilling the above criteria who were not so treated suffered progressive deterioration in renal function.

We agree with Brown et al. that such improvement is not normally to be expected in this situation and is likely to have been a consequence of treatment, although formal proof of benefit must await data from a prospective controlled trial.

We agree that side-effects of prednisolone and azathioprine may well be less severe than with regimens employing cyclophosphamide or chlorambucil and, as they and we point out, prednisolone and azathioprine treatment has the additional advantage of being familiar to nephrologists.

**Mesangial hyperplasia in a patient with renovascular hypertension and proteinuria**

Sür,

We have read with interest the report of Bhowmik et al. [1] describing renal-artery stenosis and focal segmental glomerulosclerosis in the contralateral kidney. In recent years similar cases have been reported [2–5]. Recently a 17-year-old female patient with hypertension 170/120 mmHg (while under antihypertensive treatment) and 2.5 g/24 h proteinuria was admitted to our Nephrology Clinic. The patient’s history was unremarkable. She seemed to have been well until 2 weeks prior to admission, when she suddenly complained of headaches, dizziness, and palpitations. Her physician detected hypertension (240/130 mmHg) and subnephrotic proteinuria. Administration of methyldopa, propranolol, and diuretics did not result in normalization of the blood pressure.