performing a transbronchial biopsy or a transthoracic needle aspiration under CT guidance when a lesion is accessible.

Conflict of interest statement. None declared.

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Rituximab: effective treatment for severe steroid-dependent minimal change nephrotic syndrome?

Sir,

Minimal change disease (MCNS) accounts for 70–90% of the cases of idiopathic nephrotic syndrome in children.

Most patients respond to steroid therapy. However, the relapse rate is high and ~50% of patients are steroid-dependent or frequent-relapers [1]. These patients are often treated with other immunosuppressive agents, such as cyclophosphamide or ciclosporin (CsA). Ultimately ~75% of these patients will develop a long-lasting remission. However, 25% of patients will experience a relapsing course of the disease and many of them need immunosuppressive maintenance therapy [2]. New therapeutic strategies are desirable. We report the results of treatment with rituximab, a monoclonal anti CD-20 antibody, in a 20-year-old Caucasian female with steroid-dependent MCNS.

The patient presented at the age of 2 years with an idiopathic nephrotic syndrome. Treatment with high-dose prednisone resulted in a remission of proteinuria, but the nephrotic syndrome recurred immediately after tapering of the prednisone dose. Frequent relapses necessitated repeated courses of prednisone therapy over the following two years. A renal biopsy was performed at the age of 4 years and showed MCNS. Treatment with ciclophosphamide was started and resulted in a remission which lasted for 18 months. Despite prednisone maintenance therapy, multiple relapses occurred over the next 4 years. Therefore treatment with ciclosporin (CsA) was started. At the age of 11 years, relapses necessitated a higher dose of steroids. The clinical course was complicated by a herpes zoster infection and osteoporosis. The treatment regimen was changed in an attempt to decrease the amount of prednisone. At the age of 18, the nephrotic syndrome was under control with the use of low-dose prednisone (5 mg every other day) in combination with mycophenolate mofetil (MMF 1000 mg bid) and tacrolimus (target through level 5–10 mg/l). Over the next year, the patient again developed relapses, necessitating higher doses of prednisone. In time, the steroid-dependency...
increased and finally she responded only to very high-dose prednisone (60 mg qd), with an immediate relapse during tapering (Figure 1). Ultimately she remained nephrotic while using prednisone (20 mg qd), MMF (1000 mg bid) and tacrolimus (15 mg bid to attain a target trough level of 8-12 mg/l). Laboratory values while on triple therapy were: serum albumin 12 g/l, serum creatinine 67 μmol/l and proteinuria averaged 10 g/day. This situation lasted for more than 12 months and became unacceptable. Therefore we decided to treat our patient with rituximab. She was given two doses of 1000 mg i.v. with a 2-week interval. MMF was stopped. Within 2 weeks there was a remarkable decrease in proteinuria (2–3 g/day) as well as an increase of serum albumin (21 g/l). Tacrolimus and prednisone were tapered (Figure 1).

Currently, 4 months after treatment with rituximab, the patient has attained a partial remission (proteinuria 0.9 g/day, serum albumin 34 g/l, serum creatinine 47 μmol/l) and only uses prednisone in a dose of 7.5 mg/day, without any signs of relapse.

Discussion

Treatment with rituximab resulted in a dramatic improvement of the nephrotic syndrome in our patient with a severe steroid-dependent MCNS. She had remained nephrotic while on combined treatment with tacrolimus, MMF and 20 mg prednisone. We feel that it is highly unlikely that the remission could have occurred by chance, in view of the documented long history of steroid-dependency.

We are aware of one other recent case report of the successful use of rituximab in idiopathic MCNS. François et al. [3] reported the intentional use of rituximab in a 23-year-old patient with a relapsing MCNS. This patient had failed to respond to many other immunosuppressive agents, including the IL2-receptor-antagonist basiliximab. Rituximab (weekly dosis of 375 mg/m2/C2 4 weeks) resulted in the development of a complete remission, allowing a discontinuation of all immunosuppressive drugs including prednisone.

Controlled and long-term studies must evaluate the risk-benefit profile of rituximab for patients with MCNS who need maintenance immunosuppressive therapy. Treatment with rituximab results in a complete and long-lasting depletion of mature B-cells. Theoretically, this may lead to more severe infectious complications. However, in phase II and III studies performed in patients with active rheumatoid arthritis who were treated with rituximab, infection rates did not significantly differ between the patients treated with addition of rituximab and the control groups that were treated with immunosuppressive drugs alone [4]. On the other hand, the U.S. Food and Drug Administration (FDA) has recently issued a warning on the use of rituximab, after the death of two patients with SLE who were treated with rituximab [5]. The cause of death was progressive multifocal leukoencephalopathy (PML), that was caused by reactivated JC virus.

In conclusion, our case suggests that rituximab offers great promise for the treatment of patients with severe steroid-dependent MCNS. Cohort studies and clinical trials in well-defined patient groups are needed to document the efficacy and safety.

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Acute nephritis induced by human parvovirus B 19 infection

Sir,
The relationship of human parvovirus B 19 (HPB 19) with renal disease is rare, with only two studies describing glomerulonephritis in patients with erythema infectosum and sickle cell disease (SCD) [1]. We describe a case of acute nephritis associated with HPB 19, which, to the best of our knowledge, is the first case reported without associated SCD.

A 54-year-old Caucasian woman was admitted to a medical ward with a 3-week history of generalized malaise, arthralgia and a widespread macular rash. She was in frequent contact with her grandson, who had been recently diagnosed with erythema infectosum (fifth disease). She had a past history of Raynaud’s disease, migraine, sinusitis and breast carcinoma, previously treated with surgery and radiotherapy. Her only long-term medication was tamoxifen. There was no family history of autoimmune or renal disease. Although she was discharged, the patient failed to improve, and was subsequently re-admitted to our renal unit with haematuria and proteinuria.

On examination, she was apyrexial, tachycardic and hypertensive, with a blood pressure of 163/90 mmHg. There was a widespread macular rash with a mottled appearance, consistent with erythema infectosum. Although previously normal, the patient’s serum creatinine was elevated to 195 mmol/l. There was a normochromic normocytic anaemia with haemoglobin of 9.5 g/dl. Serum ANCA, anti-GBM and ANA titres were negative, with a weakly positive dsDNA antibody. Complement C3 and C4 levels were reduced at 0.34 g/l (normal range: 0.70–1.70 g/l) and 0.10 g/l (normal range: 0.18–0.58 g/l) respectively. Other investigations showed rheumatoid factor increased at 43 IU/ml (normal range <20 IU/ml) and creatinine clearance reduced to 15 ml/min (normal range: 60–140 ml/min) with a proteinuria of 0.97 g/24 h (normal range: <0.15 g/24 h). The C-reactive protein was elevated at 30 mg/l (normal range: <5 mg/l) with an ESR of 26 mm/h (normal range: <20 mm/h).

Renal ultrasonography, immunoglobulins, paraproteinaemia and cryoglobulins were normal. Subsequently, polymerase chain reaction (PCR) for HPB 19 was positive, confirming current infection.

Her condition improved with symptomatic treatment. The laboratory abnormalities, including urinary protein, microscopic haematuria and rash improved within a few days; renal functions and complement levels returned to the normal range and her dsDNA became negative.

A link between renal disease and human parvovirus was first implied by Markenson et al. [2], who described two siblings with SCD and hypoplastic crises, who developed nephrotic syndrome. Similarly, Wierenga et al. [1] described seven patients with homozygous SCD who showed proliferative segmental glomerulonephritis with proteinuria and nephritic syndrome after aplastic crisis induced by HPB 19.

There have recently been several reports indicating that HPB 19 infection may elicit symptoms and laboratory findings resembling those of systemic lupus erythematosus, such as polyarthritis, positive antinuclear antibodies and hypocomplementaemia [3]. However, these reports have not demonstrated renal abnormalities as a complication of the disease. Although HPB 19 infection has been reported to be associated with vasculitis including Henoch–Schönlein purpura [4] and necrotizing vasculitis resembling polyarteritis nodosa [5], there has been no previous accounts of involvement of the renal vasculature.

Our patient with confirmed erythema infectiosum suffered an acute nephritis manifesting as acute renal failure with an active urinary sediment. The temporal relationship between the two conditions strongly suggests causality. Nephritis with HPB 19 infection has not been previously reported in patients without SCD. As the patient’s condition improved spontaneously, renal biopsy to confirm a glomerulonephritis was not justified.

In conclusion, infection with HPB 19 should be considered as a possible cause of acute nephritis in adults. This usually occurs in patients with SCD but can also occur in its absence.

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Six cases of successful cinacalcet cessation in haemodialysis patients treated for secondary hyperparathyroidism

Sir,
Cinacalcet acts as an allosteric activator of calcium-sensing receptor (CaR) and diminishes Parathyroid hormone (PTH) secretion [1]. For more than 2 years, it has been successfully used for the treatment of secondary hyperparathyroidism (SHPT) [2], and has been shown to facilitate achievement of the KDOQI-recommended targets for PTH, calcium, phosphorus and Ca × P product [3], with a sustained effect lasting for ≥2–3 years [4]. This expensive treatment is thought to be...