Teaching Point
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The patient presenting with proteinuria and a history of brain tumour in childhood: Is there a quietly lurking nephrological nemesis?

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Case report

In August 1995, an 18-year-old youth was initially referred for the evaluation of microscopic haematuria discovered on a routine army pre-recruitment urinalysis. At the age of 8, he had undergone radiotherapy for a brain tumour. Hydrocephalus was managed by the insertion of a ventriculoatrial (VA) shunt. On presentation, physical examination was unremarkable with a body temperature of 37.1°C and blood pressure 122/72 mmHg. At this stage, the only notable laboratory data were a mild leucocytosis (WBC 13 200/mm³), a decreased C₄ level of 11 mg/dl (normal > 16 mg/dl) and urinalysis that showed numerous RBC/HPF with no casts or proteinuria. C₃ level was 130 (normal > 90 mg/dl). Antistreptolysin titre, rheumatoid factor and cryoglobulins were all negative. Repeated blood cultures yielded no growth. Ultrasound showed two kidneys of normal size and echogenicity. In April 1996, proteinuria ranging from 1.4–2.8 g/day developed. C₃ level had decreased to 54 mg/dl, and C₄ to 6 mg/dl. Serum creatinine was unchanged at 1.0 mg/dl while haemoglobin had dropped from 13.4 to 10.8 g/dl. Clinically, the patient felt well, was afebrile with no elevation of blood pressure.

Percutaneous renal biopsy was performed. On light microscopy, accentuated lobular structure of the glomeruli with mesangial cell proliferation and thickening of the glomerular basement membrane (GBM) was shown (Fig. 1). Immunoperoxidase demonstrated intense staining for IgM, IgG and C₃ in a granular pattern along the GBM. Electron microscopy revealed the presence of subendothelial and mesangial electron dense deposits with duplication of the GBM (Fig. 2). A spinal tap yielded a normal, culture negative cerebrospinal fluid (CSF). Blood cultures were persistently sterile. Despite this, presenting a working diagnosis of shunt nephritis, intravenous vancomycin (2 g/day) and oral rifampicin (600 mg/day) were administered for 6 weeks. A neurosurgical consultant refused to accept our recommendation of shunt removal as he was not convinced of the diagnosis. A week after the initiation of antibiotic therapy, C₃ and C₄ levels increased to 205 and 11 mg/dl, respectively. However, a fortnight following the cessation of antibiotics, levels decreased to pretreatment values. A repeat CSF culture was sterile. The above antibiotic regimen was recommended following which, a month later, our neurosurgeons were, finally, persuaded into removing the VA shunt, replacing it with a ventriculoperitoneal (VP) shunt. Culture of the tip of the removed shunt produced a growth of coagulase negative staphylococci, sensitive to both vancomycin and rifampicin. Two weeks after shunt replacement C₃ and C₄ levels were 230 and 37 mg/dl, respectively, and have since remained in the normal range. Currently (1 month post-surgery), microscopic haematuria and proteinuria persist.

Comment

The introduction of shunting procedures for the treatment of hydrocephalus has led to the wide application of this device in clinical practice. Shunt infection has, however, proved to be a troublesome complication. It usually presents with fever, almost a universal occurrence, often with accompanying signs of raised intracranial pressure [1]. In general, either blood or CSF cultures are positive. Whereas, the incidence of shunt infection may range as high as 27% [1], the incidence of glomerulonephritis associated with shunt infection approximates only 3% of cases [2]. This last entity, now known as shunt nephritis, was first described in 1965 by Black et al. [3] who reported two cases of the nephrotic syndrome and macroscopic haematuria associated with Staphylococcus albus bacteraemia after shunt insertion. Since then, more than 80 cases have been reported in the literature. The mean interval between shunt insertion and nephritis is 4.4 years, but, as in our case, much longer intervals of 10 to 14 years have been documented [2].

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Fig. 1. Renal biopsy showing a glomerulus with the typical changes of mesangiproliferative glomerulonephritis; accentuated lobular structure, mesangial cell proliferation and thickening of the GBM (Masson trichrome, magnification ×200).

Fig. 2. Electron microscopy of the same renal biopsy showing interposition of mesangial cells (duplication of the GBM). (magnification × 4000).
Shunt nephritis serves as a model of immune complex mediated glomerulonephritis. Long-standing immunization of the host with bacterial antigen causes antigen–antibody complexes to be formed in antibody excess. These circulating complexes, capable of activating complement, may then lodge in the glomerular capillary loops, leading to the full implementation of the inflammatory response [4].

The clinical and laboratory features of shunt nephritis include fever, hepatosplenomegaly, purpura, anaemia, high erythrocyte sedimentation rate, leucocytosis, hypocomplementaemia and cryoglobulinaemia [2,5]. The commonest renal manifestation is haematuria, usually microscopic, and often accompanied by various degrees of proteinuria (in 25% of cases a full-blown nephrotic syndrome). Renal impairment may be found in nearly 45% of patients. Hypertension is, however, rare (10%). On renal biopsy, type I mesangiocapillary (as seen in our case) or diffuse proliferative glomerulonephritis are, typically, seen [2,5].

Bacterial pathogens causing shunt nephritis are usually low virulent organisms, the commonest isolated being *Staphylococcus epidermidis* (75% of cases) [2,5]. Blood or CSF cultures may, however, be negative (15% of cases) [2]. In fact, as in our patient, *Staphylococcus epidermidis* was only cultured from the shunt after its removal, despite appropriate antibiotic coverage. This serves to point out the difficulty in eradicating shunt infection by antibiotic treatment alone. This fact is borne out by the literature as well as our patient, who was also subject to prolonged antibiotic therapy. In a review by Arze et al. [2], in all but one of 70 patients, shunt removal was necessary in order to control symptoms or halt the progression of renal disease. On close scrutiny of the literature, however, even this apparently lone report of successful non-surgical control of shunt nephritis is questionable, since antibiotic therapy in this particular case was recommenced after initial relapse and continued indefinitely, at least up to the time of publication (a 9-month period) [6].

Although it has been stated that shunt nephritis manifestations are always preceeded by those of shunt infection [2], such is not necessarily the sequence of events. As aptly demonstrated by our patient, shunt nephritis may, in fact, develop in the absence of any clinical signs of shunt infection or the finding of positive blood and/or CSF cultures. This point is worthy of emphasis. Our neurosurgeons were actually very reluctant to accept the diagnosis in our patient. Of note, in keeping with the literature, our patients’ C₃ and C₄ levels proved to be sensitive markers in monitoring the course of the disease and adequacy of therapy [4,7]. The prognosis of shunt nephritis following shunt removal is quite favourable with complete recovery in over 50% of cases. Proteinuria and haematuria usually resolve within a period of 1–6 months [2,7].

**Teaching point**

The presence of haematuria, especially associated with proteinuria, in a patient with a ventriculaoatrial shunt, should be considered as shunt nephritis unless proven otherwise.

**References**