Renal failure in a patient with leukaemic infiltration of the kidney and polyomavirus infection

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Introduction

Leukaemic infiltration of the kidney has been demonstrated on autopsy in 60–90% of patients with chronic lymphocytic leukaemia (CLL) [1,2]. This is rarely associated with renal dysfunction, with only a few cases reported in the literature documenting renal failure secondary to leukaemic infiltration in CLL [3–6]. The polyomaviruses BK and JC are found ubiquitously, with most individuals acquiring the infection in childhood [7]. The disease at this stage is usually subclinical. Polyomavirus infections, thought to be primarily reactivation, have been shown to cause renal dysfunction [8–11]. This has mostly been in the context of immunosuppression, especially with renal and bone-marrow transplantation [8–11].

In this paper we describe the case of a patient with CLL who developed rapidly progressive renal failure. Renal biopsy demonstrated a dense infiltration of leukaemic cells and the presence of polyomavirus infection of the kidney.

Case

We present a 59-year-old man with CLL diagnosed 3 years earlier. The CLL had initially been treated with alkylating agents and fludarabine. Chemotherapy was ceased 12 months prior to presentation with the patient having stable disease. Renal function remained unchanged throughout the course of chemotherapy, as it did during an episode of septicaemia 6 months earlier. This was soon followed by a diagnosis of bronchiectasis, associated with the patient’s known secondary hypoglobulinaemia, and treated with a prolonged course of ciprofloxacin.

Over a period of 6 months there was a progressive deterioration in the patient’s renal function. The renal function went from a baseline creatinine of 90 to 198 μmol/l (50–120 μmol/l) 5 months prior to presentation. Two months later it was 340 μmol/l, 1 month after that it had risen to 441 μmol/l and finally, at the time of presentation to the nephrologist, it was 608 μmol/l.

The only medications were for bronchiectasis and included budesonide 400 mg 2 puffs twice a day, terbutaline 2 puffs twice a day, eproterol 12 mg twice a day, and beclomethasone nasal spray 50 mg twice a day.

On examination the patient’s severely sun-damaged skin was noted. His blood pressure was 130/90 mmHg. He had cervical and axillary lymphadenopathy with moderate hepatomegaly. The rest of the examination was unremarkable.

The full blood picture included a white cell count of 24,100 cells/ml (4000–10,000 cells/ml), of which 22,800 cells/ml (1500–4000 cells/ml) were lymphocytes. The haemoglobin was 84 g/l (130–170 g/l) with a platelet count of 127,000/μl (150,000–400,000 platelets/μl). Serum calcium equalled 2.18 mmol/l (2.25–2.65 mmol/l) with a phosphatase of 1.38 mmol/l (0.8–1.5 mmol/l). C3, C4, antinuclear antibody, cryoglobulins, and antinuclear cytoplasmic antibody were negative. Serum uric acid was mildly elevated at 0.51 mmol/l (0.18–0.48 mmol/l). A minimal amount of serum paraprotein was detected, which was unable to be quantified but was not associated with a Bence Jones protein. Urine microscopy revealed no haematuria and there was no detectable proteinuria. Ultrasound of the kidneys showed a left kidney measuring 148 mm and a right kidney of 124 mm, both with normal echogenicity. There were normal Doppler studies and no calculi or collecting system dilatation were noted.

Renal biopsy was then performed. Histological examination revealed 1 of 6 glomeruli to be sclerosed, with the remaining glomeruli having a mild increase in mesangial matrix and cellularity. There was a diffuse infiltration of the kidney by atypical, small

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lymphocytes (Figure 1). Tubular epithelial cells in 17 tubules, 5–10% of the total, demonstrated nuclear enlargement with chromatin clumping and clearing (Figure 2). On electron microscopy, epithelial cells showed intranuclear and intracytoplasmic inclusions (Figure 3). With higher magnification (Figure 3, inset), the inclusions measured 45 nm, typical of polyomavirus. No inclusions could be demonstrated in non-epithelial cells. There was no necrosis or denudation of the tubules. Twenty per cent of the biopsy contained renal medulla; this showed the dense infiltration of lymphocytes but no viral changes. There was no interstitial fibrosis and no evidence of amyloidosis.

**Discussion**

CLL may cause renal dysfunction in many different ways. They include uric-acid nephropathy, light-chain nephropathy, amyloidosis, hypercalcaemia, urinary obstruction, glomerulonephritis, and cryoglobulinemia. We have demonstrated that none of these conditions was present in our case. We do note, however, the diffuse infiltration of leukaemic cells throughout the renal parenchyma.

Whilst autopsy studies have shown a high rate of leukaemic infiltration of the kidney in patients suffering with CLL, there have only been a few cases reported to have renal dysfunction as a result [3–6]. One case demonstrated moderate tubular atrophy with no associated vascular or glomerular changes [3]. Interstitial fibrosis, tubular atrophy, and ischaemic glomerulosclerosis was shown in a 60-year-old with CLL [4]. Tucker et al. [5] reported a 70-year-old man with CLL who developed renal impairment due to tubulointerstitial nephritis associated with leukaemic infiltration of the kidneys. One of the first reported cases was by Pagniez et al. [6], who described a 73-year-old man with CLL presenting with advanced renal failure thought to be due to leukaemic infiltration, as other causes were excluded, but no biopsy was performed.

Polyomaviruses include BK and JC viruses, though JC virus is thought to be only pathogenic in the brain [7]. Renal dysfunction associated with this infection have been described primarily in renal and bone-marrow transplant recipients [8–11]. The pathological lesion most commonly seen are tubular epithelial cell intranuclear viral inclusions, measuring 40–50 nm in diameter, often in association with tubulointerstitial nephritis [8–10]. Ureteral ulceration and strictures have also been described [11]. BK nephropathy in renal-transplant recipients is always also associated with inclusion-bearing cells in the urine [12,13] and detection of BK-virus DNA by polymerase chain reaction in the serum [14].

Our patient featured a dense interstitial infiltrate of lymphocytes but no significant associated tubular atrophy or fibrosis. There were some mild and probably non-significant changes in the glomeruli. The tubular epithelium had intranuclear and intracytoplasmic inclusions of a typical size and shape for polyomavirus.

The exact cause of the renal failure in this case is not clear. We have excluded the more common causes seen

![Fig. 1. There is separation of renal tubules, predominantly by an infiltrate of atypical lymphoid cells (CLL) (H&E, ×160.)](image1)

![Fig. 2. The tubules’ epithelial cells often show large intranuclear inclusions (H&E, ×250.)](image2)

![Fig. 3. Electron micrograph of a tubular epithelial cell. Arrays of viral particles are seen within the nucleus (×5850). Inset: higher-power view of viral particles which measure 45 nm diameter (×18 000).](image3)
in patients with CLL. This leaves the diffuse infiltration of leukemic cells and the polyomavirus as the only pathologies evident. Tubular necrosis due to polyomavirus replication in epithelial cells was not found in the current case. Based upon previous observations [12,13] tubular necrosis is likely to play an important role in cases of BK nephropathy in renal allograft recipients with graft dysfunction. Thus, in this case renal dysfunction might have been mainly caused by the leukemic infiltrate.

We believe this is the first case report of leukemic infiltration and polyomavirus infection of the kidney resulting in end-stage renal failure in a patient with CLL. The mechanism may have been similar to previous cases. The immunosuppressed state of CLL predisposed to reactivation of the polyomavirus and we believe that it is a pathogen worth searching for in this setting.

References


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