BK and JC polyomavirus infection in a patient with chronic lymphocytic leukaemia and renal failure

Sir,

We read with interest the paper of Boudville et al. [1] who described a patient with chronic lymphocytic leukaemia (CLL), progressive renal failure, and polyomavirus particles in the tubular cells at the renal biopsy. In the pathogenesis of renal failure, the authors considered not only the role of interstitial lymphocyte infiltration but also the possible role of polyomavirus and concluded their paper by stating that this is a pathogen worth searching for in patients with CLL.

Herein we describe a patient with CLL, renal failure, ‘decoy cells’ in the urine suggestive of polyomavirus infection, and positive BK virus DNA in blood and urine, and a positive JC virus DNA in urine.

Case. A 56-year-old man with CLL diagnosed in 1990 was hospitalized on March 2, 2001 in our ward for renal failure (which was first noted on February 14, 2001) when his serum creatinine was 4.1 mg/dl, whereas it had been normal (1.3 mg/dl) 1 month before.

The patient had been treated for his CLL from June 1991 through to October 2000 with various therapeutic regimens, which included chlorambucil and prednisone (globally 30 cycles), cyclophosphamide, vincristine, prednisone, and epirubicin (four cycles), fludarabin (four cycles), fludarabin and cyclophosphamide (seven cycles), and anti-CD20 antibody, always with little or no effect on CLL.

On admission, physical examination showed hepatosplenomegaly, without signs of any central nervous system disease. Serum creatinine was 8.8 mg/dl, with serum calcium of 8.4 mg/dl, phosphate of 7.3 mg/dl, and uric acid of 7.4 mg/dl. The white blood count was 30000/ml, 26400 of which were lymphocytes. Haemoglobin was 77 g/l, and platelet count 50000/ml. A small monoclonal component was present in both serum and urine, which was not further defined. Urinalysis revealed a proteinuria of 0.42 g/24 h (urine output 1700 ml/24 h) without haemoglobin, leukocyte esterase, or nitrites. Urine microscopy, performed on a centrifuged sample examined by a phase-contrast microscope, showed between 1 and 5 epithelial cells/high-power field at 400×. Most of these cells appeared to be of tubular origin, and were characterized by marked nuclear changes such as size increase, ground-glass appearance, chromatin...
clumping and clearing, and coarse inclusion bodies (Figure 1). These cells, which were confirmed at a second examination performed 7 days later, were identical to ‘decoy cells’ as described in immunosuppressed kidney transplant recipients with BK polyomavirus reactivation [2,3]. Blood and urine samples were analysed for the presence of polyomavirus DNA by a previously described PCR technique [4]. In addition, PCR products were analysed by sequencing using an automatic sequencer (ABI PRISM 377XL, Applied Byosystem, Foster City, CA) in order to differentiate JC virus DNA and BK virus DNA. BK virus DNA was found in both blood and urine, whereas JC virus DNA was found in the urine specimen only. All other laboratory tests including C3 and C4 serum levels and C-reactive protein in the urine specimen only. All other laboratory tests were normal.

Abdomen ultrasound showed a hepto-splenomegaly, and a diffuse and severe adenopathy, with markedly enlarged lymphnodes at the hepatic hylus, the celiac tripode, the inferior vena cava, and at both sides of the bladder. The kidneys were of a normal size and normal parenchyma, with a mild pelvicalyceal dilatation in the right kidney. This prompted a cystoscopy and a bilateral retrograde pyelography, which however did not show any abnormalities. These cells, which were confirmed at a second examination performed 7 days later, were identical to ‘decoy cells’ as described in immunosuppressed kidney transplant recipients with BK polyomavirus reactivation [2,3]. Blood and urine samples were analysed for the presence of polyomavirus DNA by a previously described PCR technique [4]. In addition, PCR products were analysed by sequencing using an automatic sequencer (ABI PRISM 377XL, Applied Byosystem, Foster City, CA) in order to differentiate JC virus DNA and BK virus DNA. BK virus DNA was found in both blood and urine, whereas JC virus DNA was found in the urine specimen only. All other laboratory tests including C3 and C4 serum levels and C-reactive protein in the urine specimen only. All other laboratory tests were normal.

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Comment. This case reinforces the hypothesis of Boudville et al. [1] that polyomavirus infection is worth looking for in patients with CLL. This in our patient may have been favoured by the heavy immunosuppressive therapy.

In addition, our case shows that both BK and JC virus can co-exist in the same patient with CLL. Even though the co-existence of the two viruses has already been demonstrated both in renal transplant patients [5] and in non-immunosuppressed subjects [6], to our knowledge this has not been shown in patients with CLL. In fact, so far only a few patients with CLL and JC infection have been described, all of whom had JC in the brain and PML [7–9].

Finally, this case suggests that BK polyomavirus infection may have played a role in the pathogenesis of renal failure. In fact, the urine sediment contained many ‘decoy cells’, which are considered a specific marker of urinary tract infection by BK virus [2,10]. In addition, BK virus DNA was found in the blood, which greatly increases the probability of viral nephropathy [11]. Thus, we think we can reasonably hypothesize that our patient suffered from a tubulo-interstitial disease due to BK virus, similar to that described in immunosuppressed renal transplant recipients [10]. However, we are all aware that for the lack of renal biopsy we cannot exclude other causes of renal failure such as, for instance, lymphocytic infiltration.

The role of JC virus in causing the renal disease in our patient is unclear. However, if on one hand tubular lesions similar to those caused by BK virus have been reported in patients infected by JC virus [12,13], the absence of JC DNA in the blood makes its pathogenetic role unlikely.

**Fig. 1.** Urinary tubular cells with an enlarged nucleus (left) and others with coarse chromatin clumping (arrows) (phase-contrast microscopy, original magnification 400×).
