Case Report

Severe renal failure and polyneuritis induced by foscarnet

Eric Chatelain¹, Colette Deminière², Jean Yves Lacut³ and Luc Potaux¹

Departments of ¹Nephrology, Dialysis and Transplantation, ²Anatomopathology, ³Infectious Diseases, Hôpital Pellegrin Tripode, Bordeaux, France

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Introduction

Foscarnet nephrotoxicity usually consists in early reversible renal tubular injury, in immunocompromised patients. Neurotoxicity of this drug is uncommon. We report the case of an immunocompetent 41-year-old woman without underlying disease, who was treated with foscarnet for severe herpes kerato-uveitis and had serious adverse effects.

Case

In September 1995 an immunocompetent 41-year-old woman with an unremarkable medical history was treated with acyclovir (16 mg/kg/day) for 11 months for severe herpes kerato-uveitis. Herpes recurred in August 1996 and to prevent blindness, intravenous foscarnet was administered after verification of renal function (serum creatinine 80 µmol/l) and prehydration, at an initial dose of 200 mg/kg/day, which was decreased to 100 mg/kg/day (total cumulative dose 1.5 kg).

In January 1997 the patient had polyneuritis with sensory impairment of all four extremities and absence of tendon jerks. Neurological symptomatology increased during foscarnet infusions. Electromyography demonstrated symmetrical sensory neuropathy and neuromuscular biopsy revealed myelin breakdown and axonal degeneration. Electron microscopy showed clear round inclusions with peripheral condensations in Schwann cells and histiocytes of peripheral nerves. Clonazepam improved the neurological symptoms. An electromyogram performed 6 months later showed that the polyneuritis continued to progress.

In April 1997, despite adequate hydration, renal failure occurred (serum creatinine 210 µmol/l), with proteinuria (2 g/day) and haematuria (30 000 red cells/min). Although foscarnet was withdrawn at that time, haemodialysis was required 1 month later. Blood tests excluded an immune disorder. Renal ultrasonography images were suggestive of nephrocalcinosis and biopsy revealed crystals (refringent on polarized microscopy) within glomerular capillaries on frozen cuttings, onset of fibrosis, mixed inflammatory infiltrate and epithelial crescents. Polarized infrared microscopy identified the crystals as precipitates of foscarnet (Figure 1). Electron microscopy localized crystals in the cytoplasm of epithelial cells (Figure 2). Forty-five days after haemodialysis was started, renal function had not recovered and a second biopsy was performed, showing extensive renal sclerosis. Immune complexes were not detected on renal biopsies.

In June, recurrent fever appeared and endocarditis was diagnosed by transoesophageal echocardiography. Staphylococcus epidermidis was isolated from the endoprosthesis that had been used for foscarnet infusions. Four months intravenous treatment with fosfomycin (6 g/week) and teicoplanin (0.7 g/week) was successful.

In March 1998, renal function improved: glomerular filtration reached 15 ml/min and dialysis was withdrawn.

Fig. 1. Periodic acid–Schiff coloration × 130. Crystals within the glomerular capillaries, crushing the mesangium and the other capillaries. Onset of fibroepithelial proliferation. Moderate tubulointerstitial inflammatory infiltrate.

Correspondence and offprint requests to: E. Chatelain, Department of Nephrology, Dialysis and Transplantation, Hôpital Pellegrin Tripode, Place Amélie-Raba-León, F-33076 Bordeaux, France.

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Discussion

Reports of glomerular crystals of foscarnet are rare [1,2]. A case of foscarnet-induced glomerulonephritis with crystalline deposits and peripheral neuropathy, assumed to be AIDS related, with partial recovery of renal function, has been reported [2]. Foscarnet nephrotoxicity, predominantly affecting immunocompromised patients, usually consists of early reversible renal tubular injury [3,4]. Prehydration with 2.5 l/day of isotonic saline during foscarnet therapy greatly reduces the risk of acute tubular necrosis [3].

The case of our patient was quite different. Adequate prehydration was employed, the onset of renal failure was delayed, the nephropathy was glomerular and renal function recovery was mild. The evidence indicating foscarnet therapy as the cause of renal failure include: (i) normal renal function before administration of foscarnet and its deterioration during the treatment, (ii) absence of associated nephrotoxic drug or underlying disease, and (iii) presence of intraglomerular foscarnet crystals. Sequential renal biopsies suggested a two-step mechanism. Apparently, foscarnet crystals first injured the glomerular endothelium, then a probably self-sustaining inflammatory reaction culminated in extensive glomerular fibrosis. Crystals in epithelial cells may have induced the crescentic proliferation.

Neurotoxicity ascribed to foscarnet is uncommon, although headache, seizures, and hand cramping have been described [5]. To our knowledge, polyneuritis has never been reported. The neurotoxicity of foscarnet is probably different from that of antiretroviral agents. Foscarnet inhibits viral DNA polymerases and reverse transcriptase, while most antiretrovirals are nucleoside analogues. Normal neurological status before therapy, absence of underlying disease or concurrent treatment, appearance of symptoms during treatment, the high cumulative dose, and the unusual histological aspect support the hypothesis that foscarnet caused this polyneuritis. Foscarnet may have altered peripheral-nerve metabolism, leading to the observed myelin destruction, axonal degeneration and vacuole formation in Schwann cells and histiocytes.

References


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