Sirolimus tolerability in a kidney transplant recipient with acute intermittent porphyria

Sir,

Acute intermittent porphyria (AIP) is transmitted as autosomal dominant disorder with incomplete penetrance. It results from a deficiency of the porphobilinogen deaminase enzyme of haeme biosynthesis. Clinical manifestations of acute attacks include abdominal pain, hypertension and neuro-psychiatric dysfunction, and are often triggered by exposure to exogenous precipitating factors, such as drugs [1]. In porphryic patients, drug treatment should be prescribed only after reference to a drug list that considers safe and unsafe medications. For a long time, only steroids and azathioprine were considered to be safe in porphryic patients undergoing organ transplantation. Recently mycophenolate mofetil and calcineurin inhibitors (cyclosporin and tacrolimus) were reported to be safe in one kidney transplant recipient with AIP [2]. However, nephrotoxicity represents the principal side-effect of calcineurin inhibitors [3].

Sirolimus is a new potent immunosuppressant, which does not share the nephrotoxicity of calcineurin inhibitors and could facilitate recovery from delayed graft function [3,4]. We report for the first time the use of sirolimus in a kidney transplant recipient with AIP.

Case. A 49-year-old man suffering from AIP, diagnosed since 1981, had experienced more than 30 acute attacks, the last in June 2001. He had chronic renal failure due to chronic interstitial nephritis, diagnosed in June 1995 and had been on haemodialysis treatment since August 2000. A renal transplantation was then performed in September 2001. He received a marginal cadaver kidney graft from a 63-year-old donor who had died of cardiac arrest without successful recovery after cardiopulmonary resuscitation leading to brainstem death. Cold ischaemia time was 38 h.

In the absence of information about the tolerability of sirolimus in AIP, and, given the hoped benefit of avoiding contribution of calcineurin inhibitor nephrotoxicity in delaying function recovery of this sub-optimal graft, a calcineurin inhibitor-free immunosuppressive regimen was considered. Thus, sirolimus was administered concomitantly with steroids, mycophenolate mofetil and rabbit antithymocytic globulin; at the same time, attention was given to early detection of any sign of a possible acute attack of porphyria that could be precipitated by the administration of sirolimus.

Graft function improved; serum creatinine decreased from 755 μmol/l on the pre-operative day to 103 μmol/l by the 15th post-operative day. The patient did not develop any clinical sign of acute attack of porphyria and was discharged from the hospital on 17th post-operative day. Regular follow-up until the 6th month post-transplantation confirmed sirolimus tolerability in addition to excellent graft function; serum creatinine was 98 μmol/l.

Comment. This is the first reported kidney transplant recipient with documented AIP to tolerate sirolimus safely.

Clemenceau University Hospital
Caen
France
Email: elhaggan-w@chucaen.fr

Wael El Haggan
Thierry Lobbedez
Jean-Philippe Ryckelynck
Bruno Hurault de Ligny

3 Hong JC, Kahan BD. A calcineurin antagonist-free induction strategy for immunosuppression in cadaveric kidney transplant recipients at risk for delayed graft function. Transplantation 2001; 71: 1320–1328