Case Report

Mycophenolate mofetil in cyclosporin-associated thrombotic microangiopathy

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Introduction

Thrombotic microangiopathy is a syndrome in which thrombocytopenia and microangiopathic haemolytic anaemia occur together with acute renal failure and a characteristic renal vascular pathology [1]. Its prevalence in renal transplant recipients is estimated to be 4% [2]. Both experimental and clinical data suggest a direct role for cyclosporin A (CsA) in the pathogenesis of post-transplant thrombotic microangiopathy. Renal endothelial cell injury mediated through the inhibition of PGI2 is believed to be the pathogenetic mechanism of CsA-induced thrombotic microangiopathy [3,4]. Despite different therapeutic strategies, the prognosis of CsA-associated thrombotic microangiopathy remains poor. CsA withdrawal is the cornerstone of treatment. However, CsA withdrawal exposes the patient to a major risk of acute rejection. Although some authors have suggested that CsA reintroduction is possible, this attitude remains controversial because of the possible relapse of a life-threatening disease [5]. Some authors have reported successful conversion from CsA to Tacrolimus [6] but Tacrolimus has also been associated with thrombotic microangiopathy [7]. We describe a favourable course of CsA-associated thrombotic microangiopathy in three renal transplant recipients after CsA withdrawal and concomitant switch from azathioprine (AZA) to mycophenolate mofetil (MMF).

Case

Table 1 summarizes the three case reports.

Discussion

Allograft biopsies confirmed the diagnosis of thrombotic microangiopathy in cases 2 and 3. In case 1, biopsy was not performed but the laboratory parameters were typical of thrombotic microangiopathy. They all had thrombocytopenia and schizocytes with other signs indicative of haemolysis. Moreover, the stability of SCr argue against vascular rejection. We attributed the thrombotic microangiopathy to CsA because no patient had a past history of pre-transplant thrombotic microangiopathy, allograft biopsies did not demonstrate any signs of acute rejection and all the patients improved without rejection therapy after CsA withdrawal. No infection previously associated with thrombotic microangiopathy could be detected in any of the patients.

In these cases, we decided to avoid the use of both CsA and Tacrolimus and to replace AZA by MMF. Large studies have demonstrated that MMF is superior to AZA as a post-transplant immunosuppressant [8]. MMF may have a CsA-sparring effect allowing CsA withdrawal without acute rejection in post-transplant thrombotic microangiopathy. None of the three patients have experienced acute rejection 8, 11 and 17 months after transplantation, respectively. Although not controlled, this report suggests that an immunosuppressive regimen with steroids and MMF could be effective when both CsA and Tacrolimus are contra-indicated. Interestingly, Van Gelder et al. recently described a similar case report [9]. Because CsA-induced thrombotic microangiopathy is a rare condition, individual anecdotes are the only information we have on managing this problem.

It should be noted that it was a first transplantation for the three patients and that none of them had panel reactive antibody. Moreover, all of them had received immunosuppressive induction with polyclonal antilymphocyte globulins. Our conclusion might be not true for other patient categories.

It is conceivable that MMF might have a favourable direct effect on the course of thrombotic microangiopa-
By inhibiting the proliferation of vascular smooth muscle cells [10], MMF may have a beneficial effect on TMA-induced myointimal proliferation. In addition, because neutrophil adhesion to endothelial cells contributes to endothelial damage in thrombotic microangiopathy, MMF, which interferes with the glycosylation of adhesion molecules [10], may interact with this pathway and limit vascular damage.

To conclude, CsA-associated thrombotic microangiopathy is a serious complication in renal transplantation. Prompt CsA withdrawal with concomittant switch from AZA to MMF seems to be a safe and effective therapeutic option.

References


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