LETTER TO THE EDITOR

Cardiac transplantation without calcineurin inhibitors. Sirolimus as first immunosuppressive line. Based on one case

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Cardiac transplantation is the definitive treatment for eligible patients with end-stage cardiomyopathy. Post-transplant survival rates have improved with the use of new immunosuppression protocols, based on the use of calcineurin inhibitors (CI), cyclosporine A (CsA) or FK506. Cardiac allograft rejection is no longer the limiting factor for early survival, however nephrotoxicity limits their therapeutic benefit. It has been suggested that the nephrotoxic effects of these drugs are mediated via inhibition of phosphatase calcineurin.

Sirolimus (SRL) is a new immunosuppressant and antiproliferative drug which is structurally related to FK506. While it retains a pharmacokinetic and drug interaction profile similar to that of CI, it has no effect on calcineurin and does not alter glomerular filtration rate produced with CI [1].

Information on the use of SRL in cardiac transplantation is limited to a few published cases in which it has been used to control refractory rejection [2] or advanced renal failure associated to CI, showing that its use makes it possible to decrease CI dosage [3].

We present a case in which SRL was used during the early postoperative course of a cardiac transplantation as an alternative to CI because of renal failure, thus avoiding a combined heart–renal transplantation (HRT) in the patient.

A 58-year-old man was referred to our hospital for evaluation of a cardiac transplantation because of hypertensive dilated cardiomyopathy in advanced clinical status [New York Heart Association (NYHA) functional class III–IV] refractory to medical treatment. The pretransplantation study showed moderate chronic renal failure with creatinine plasma levels around 2 mg/dl (creatinine clearance: 35 ml/min). The renal biopsy established the diagnosis of nephroangiosclerosis. The nephrologist did not consider combined HRT indicated, thus an orthotopic cardiac transplantation was performed.

Immunosuppressive induction treatment was performed with daclizumab (1 mg/kg i.v., 5 doses) and steroids (500 mg i.v. intraoperative, 3 i.v. doses of 125 mg in the first 24 h) and the maintenance immunosuppressive treatment was performed with mycophenolate mofetil (2 g/day p.o., target level: 4.5 μg/ml), steroids (0.8 mg/kg/day p.o.) and FK506 (0.075 mg/kg/day p.o., target level: 12–15 ng/ml).

After FK506 was initiated on the fifth day, with plasma levels of 17.5 ng/ml for a dose of 3 mg/day and a baseline creatinine of 2,2 mg/dl the patient developed oligoanuric renal failure, requiring replacement renal therapy and discontinuation of FK506 5 days later, recovering renal parameters progressively (creatinine of 2 mg/dl). Sirolimus was introduced on the 14th day (5 mg/day, target level: 8–12 ng/ml) as first line immunosuppressant agent. During the 6-month follow-up, the patient maintained renal function with creatinine levels similar to baseline (<2 mg/dl) and the cardiac biopsy results were: 0 (at 15 days), 3A (at 1 month), 0 (at 2 months), 0 (at 3 months), 1B (at 5 months), 0 (at 6 months) with SRL plasma levels of 11, 8.9, 22, 24.5, 4.9 and 10.8 ng/ml respectively.

The patient did not present any infectious symptoms and cytomegalovirus antigenemias was negative.

The present case demonstrates that SRL is an effective and safe immunosuppressant agent. This strategy made it possible to avoid a combined HRT.

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