Case Report

Recurrence of sarcoidosis in renal allograft during pregnancy

Štefan Kukura¹, Ondřej Viklický¹, Jiří Lácha¹, Luděk Voska², Eva Honsova² and Vladimír Teplan¹

¹Department of Nephrology and ²Department of Pathology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic

Keywords: granulomatous disease; pregnancy; recurrence; renal transplantation; sarcoidosis

Introduction

Sarcoidosis is a multisystem disorder of unknown aetiology characterized by the accumulation of lymphocytes, mononuclear phagocytes, and non-caseating granulomas in involved tissues. Renal involvement leading to renal function deterioration in sarcoidosis is rare: it is observed in <10% of patients. In the relevant literature, there have been only a few cases of sarcoidosis recurrence in renal allograft recipients published. We present here the first case of sarcoidosis recurrence in renal allograft during pregnancy.

Case

A 27-year-old woman was diagnosed with sarcoidosis at age 14 by lacrimal and parotid gland biopsy. Initial therapy did not include steroids as no pulmonary or other organ involvement was documented. However, hypertension and renal insufficiency (serum creatinine [sCr] 300 mmol/l) were present 4 years later. Renal biopsy revealed sarcoid interstitial granulomatous nephritis with granulomatous arteritis. The patient was treated with steroids for 3 years, at which time re-biopsy revealed no granulomas but interstitial nephritis and nephrosclerosis. During the next 3 years renal function progressively deteriorated and haemodialysis was initiated. At age 22, the patient underwent cadaveric kidney transplantation with excellent kidney graft function (sCr 70–90 mmol/l, creatinine clearance [CCr] 1.32 ml/s) and negative urinalysis. Immunosuppression consisted of CsA (trough level 119 ng/ml, with target trough levels 100–200 ng/ml for the period of 12 months post-transplant upward) and azathioprine (100 mg/day).

Because of a progressive increase in body weight (body mass index 31), steroids were tapered and 2 years after transplantation an allograft biopsy was performed before steroid withdrawal. Mild chronic allograft nephropathy was found (Figure 1A). Allograft function was excellent (sCr 83 mmol/l, CCr 1.37 ml/s), urinalysis was negative, calciuria was normal and serum calcium levels were normal (2.38 mmol/l). Immunosuppression consisted of CsA (trough level 119 ng/ml, with target trough levels 100–200 ng/ml for the period of 12 months post-transplant upward) and azathioprine (100 mg/day).

Almost 3 years after transplantation, the patient became pregnant. At week 29 of pregnancy, renal function deteriorated (sCr 266 mmol/l, CCr 0.42 ml/s), CsA trough level was 53 ng/ml and urinalysis showed mild proteinuria (0.8 g/day); no hypercalciuria and no cells were present. The serum activity of angiotensin-converting enzyme (ACE) was not evaluated. Because of suspected acute rejection, a renal allograft biopsy was performed. The biopsy revealed numerous non-caseating granulomas bound to the arteries, intimal arteritis in one artery, mild interstitial mononuclear inflammation and tubulitis (Figure 1B). The graft function improved (sCr 180 mmol/l, CCr 0.77 ml/s, proteinuria 0.7 g/day) when pulse methylprednisolone therapy (total dose of 2 g) and tapered steroids were used (prednisone 30 mg → 15 mg daily). The course of pregnancy was uneventful and delivery was performed, as requested by the patient, via Caesarean section in the ninth month of pregnancy. The newborn’s weight was 2800 g and no hereditary diseases were obvious.

To evaluate the graft morphology before conversion from azathioprine to mycophenolate mofetil (intimal arteritis in biopsy during pregnancy), a renal allograft biopsy was performed 6 months after delivery (4 years post-transplant). The renal graft function was stable (sCr 170 mmol/l, CCr 0.55 ml/s, proteinuria 1.12 g/day and no cells in urinalysis). Biopsy showed mild chronic allograft nephropathy and sporadic granulomas (Figure 1C). To date, kidney graft function has
remained stable with sCr 156 μmol/l, CCr 0.7 ml/s and persisting mild proteinuria of 0.6 g/day at 5 years post-transplant.

Discussion

Sarcoidosis is a multisystem disorder of unknown aetiology characterized by the accumulation of lymphocytes, mononuclear phagocytes and non-caseating granulomas in involved tissues [1]. Renal involvement in sarcoidosis is observed in <10% of patients. Clinically significant renal glomerular, tubular, or arterial involvement is rare. Overproduction of 1,25-dihydroxyvitamin D is fairly common. It may result in increased intestinal absorption of calcium, enhanced bone resorption leading to hypercalcaemia with or without hypercalciuria which may ultimately result in nephrocalcinosis [2]. While in our case there was no hypercalcaemia and hypercalciuria, sarcoid interstitial granulomatous nephritis combined with granulomatous arteritis were noted in the original native kidney biopsy. Despite the disappearance of non-caseating granulomas in the follow-up biopsy of the native kidney after steroid treatment, renal function deteriorated probably due to interstitial fibrosis and nephrosclerosis [3].

Organ transplantation is an accepted treatment for patients with end-stage organ failure and it has been proven that transplantation can also be carried out safely in patients with sarcoidosis. Survival and complication rates are similar to those of patients undergoing transplantation for other indications than Renal Failure due to Sarcoidosis. In lung transplantation, recurrence of pulmonary sarcoidosis has been estimated to be 47% [4]. There was a report of multisystemic sarcoidosis reactivation in a patient with immunosuppression discontinued after kidney graft function had failed; the patient returned to dialysis [5]. There have been cases of sarcoidosis recurrence in a renal allograft that caused graft dysfunction and did respond to steroid therapy [6,7]. Graft loss due to disease recurrence has not yet been reported.

As regards sarcoidosis treatment, oral corticosteroids are indicated as first-line therapy [8]. The better outcome of pregnancy after kidney transplantation seems to be associated with the lower prednisone dosage, but probably reflects the fact that the patients selected to receive the low-dose regimen had had a longer and less complicated post-transplantation course [9,10]. In our case, obesity was the reason for steroid discontinuation. We did not expect recurrence of sarcoidosis as the cause of renal graft dysfunction. The high-dose steroid treatment was indicated due to biopsy-proven sarcoidosis recurrence and intimal arteritis. Granulomatous arteritis might be a part of the morphology of sarcoidosis; however, endothelial changes were similar to those observed in intimal arteritis of rejection origin [11,12]. In our case, steroid treatment has led to improvement of the graft function and morphological findings.
This case demonstrates that steroid withdrawal after kidney transplantation may lead to sarcoidosis recurrence. Interestingly, we report the first case of sarcoidosis recurrence in renal allograft during pregnancy.

Conflict of interest statement. None declared.

References


Received for publication: 13.8.03
Accepted in revised form: 5.2.04