Sarcoidosis in the renal allograft of a recipient whose primary disease was autosomal dominant polycystic kidney disease

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Abstract

We report a 55-year-old man with a renal allograft that developed sarcoidosis. His autosomal dominant polycystic kidney disease (ADPKD) progressed to end-stage stage renal disease when he was 52 years old, and he underwent living-donor kidney transplantation at the age of 53 years. His proteinuria worsened at 19 months post-transplantation, and his renal function began to decline at 29 months post-transplantation. A renal allograft biopsy performed at 31 months post-transplantation revealed non-caseating granulomatous interstitial nephritis. The patient was treated with prednisolone (0.5 mg/kg/day), with gradual reduction in the dose. His proteinuria improved and renal function did not deteriorate any further. To the best of our knowledge, this is the first case of sarcoidosis in a renal allograft recipient whose primary renal disease was ADPKD.

Keywords Sarcoidosis · Kidney transplantation · Autosomal dominant polycystic kidney disease

Introduction

Sarcoidosis is a non-caseating granulomatous disease of unknown etiology involving multiple organs. Patients whose primary renal disease was sarcoidosis or unknown have been reported as developing sarcoidosis in their renal allograft [1–8]. To the best of our knowledge, there have not been any reports of sarcoidosis that has developed in the renal allograft of a recipient whose primary renal disease was not sarcoidosis.

Herein we report a patient whose primary renal disease was autosomal dominant polycystic kidney disease, who developed sarcoidosis in his renal allograft.

Case report

The patient was a 55-year-old man who was diagnosed with pulmonary sarcoidosis at the age of 20. He was observed for several years at a hospital, but then stopped coming in for monitoring. At the age of 52 years, he visited a hospital

because of dyspnea, and had already developed end-stage renal disease. He was diagnosed with autosomal dominant polycystic kidney disease (ADPKD) because almost all of the parenchyma in both his kidneys had been replaced by cysts (Fig. 1), and he had a family history of ADPKD. A renal biopsy was not performed. He visited our hospital to receive a kidney transplant at the age of 53 years. The pre-operative physical examination only revealed mild edema. Computed tomography of the chest revealed enlarged mediastinal and bilateral hilar lymph nodes (Fig. 2), but there were no active lesions in the lungs, and lesions due to sarcoidosis were not seen in other organs before kidney transplantation. By computed tomography, the total kidney volume was estimated to be 1907 cm³. No findings suggestive of sarcoidosis that involved the heart or uveas were observed. Laboratory testing demonstrated the following: blood urea nitrogen 85 mg/dL (normal range 8–20 mg/dL), creatinine 9.32 mg/dL (normal range 0.63–1.03 mg/dL), total protein 7.9 g/dL (normal range 6.9–9.4 g/dL), albumin 4.2 g/dL (normal range 3.9–5.1 g/dL), sodium 142 mmol/L (normal range 136–148 mmol/L), potassium 3.6 mmol/L (normal range 3.6–5.0 mmol/L), chloride 103 mmol/L (normal range 96–108 mmol/L), calcium 10.0 mg/dL (normal range 8.8–10.1 mg/dL), phosphate 7.9 mg/dL (normal range 2.4–4.6 mg/dL), hemoglobin 11.4 g/dL (normal range 13.5–17.6 g/dL), angiotensin converting enzyme 23.0 U/L

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Fig. 1 Both kidneys, in which almost all the parenchyma had been replaced by cysts (abdominal computed tomography)

Fig. 2 Enlarged mediastinal and bilateral hilar lymph nodes (chest computed tomography)

(normal range 8.3–21.4 U/L). The patient's urine calcium excretion was 0.08 g/day (normal range <0.4 g/day).

He underwent a pre-emptive living-donor kidney transplantation. His native kidney was not removed because there was sufficient space for the renal allograft. The donor was his wife, and because her blood group was ABO incompatible with his, he received desensitization therapy with rituximab. The patient received immunosuppressive therapy consisting of basiliximab for induction and triple therapy consisting of tacrolimus, mycophenolate mofetil (MMF), and methylprednisolone. After transplantation, his serum level of creatinine

was 1.1–1.3 mg/dL, and dipstick analysis for urinary protein was negative to 1+. At 17 months post-transplantation, dipstick analysis for urinary protein had increased to 2+, but the serum level of creatinine had not increased. At 19 months post-transplantation, methylprednisolone was replaced by everolimus because of new-onset diabetes. At 29 months post-transplantation, the patient's serum level of creatinine began to increase, and a biopsy of the renal allograft was performed 2 months later. The biopsy revealed focal interstitial inflammatory infiltrates, with non-caseating granulomas consisting of epithelioid cells, mononuclear cells, and a few eosinophils (Fig. 3); and nonspecific changes in the glomeruli. Medications that could cause granulomatous interstitial nephritis, such as antimicrobials, analgesics, or other drugs, had not been administered; and there were no concomitant inflammatory, rheumatologic, or infectious diseases, except for sarcoidosis. We diagnosed the findings in the renal allograft as sarcoidosis. No extra-renal lesions

Fig. 3 Noncaseating granulomatous interstitial nephritis consisting of epithelioid cells, mononuclear cells, and a few eosinophils. **a** Hematoxylin and eosin stain, magnification $\times 100$, **b** hematoxylin and eosin stain, magnification $\times 400$

associated sarcoidosis were observed in the patient, except for the enlarged mediastinal and bilateral hilar lymph nodes that had been seen before transplantation. We subsequently replaced everolimus with prednisolone 30 mg daily (0.5 mg/kg/day) and gradually reduced the dose over 9 months to 5 mg daily. The patient's urinary protein level decreased from 1.0 to 1.5 g/g creatinine to 0.3–0.4 g/g creatinine and his serum creatinine remained stable at 1.5–1.6 mg/dL.

Discussion

In this report, the patient progressed to end-stage renal disease due to ADPKD, underwent kidney transplantation, and subsequently developed sarcoidosis in his renal allograft. Ten cases of sarcoidosis involving a renal allograft have been reported; in seven of these cases, the primary renal disease was sarcoidosis [1, 4–6, 8]. One case of calcium oxalate stones and recurrent urinary tract infections was reported, and the histological analysis of native kidney tissue revealed granulomas [3]; and the etiology of the primary renal disease was unknown in two cases [2, 7]. Although the recurrence rate of sarcoidosis in renal allografts is unclear, it was reported that among the 10 recipients of kidney transplants whose primary renal disease was sarcoidosis, and who were followed for a median period of 52 (range 18–196) months, recurrence of sarcoidosis in their renal allograft was diagnosed in three [4]. No sarcoidosis developed in the renal allografts of eight kidney transplant recipients with sarcoidosis in other organs, whose primary renal disease was not sarcoidosis (polycystic kidney disease in two cases) over a median observation period of 39 (range 24–108) months [4]. To the best of our knowledge, ours is the first case of sarcoidosis in the renal allograft of a patient whose primary renal disease was ADPKD. Although we cannot be sure that sarcoidosis had not developed in the patient's native kidneys, because we did not examine them histopathologically, the main cause of end-stage renal disease of his native kidneys was ADPKD, based on the computed tomography finding that almost all of the parenchyma in both kidneys had been replaced by cysts before kidney transplantation (Fig. 1).

Sarcoidosis is a multisystem granulomatous disorder. Various extrarenal lesions have been reported among the cases of sarcoidosis involving the renal allograft, which included lesions in the lung [1, 4, 5], liver [4], intestine [3], central nervous system [1], lacrimal and parotid glands [6], uvea [5, 7, 8], and multiple joints [5]. In our case, extra-renal sarcoidosis only involved enlarged mediastinal and bilateral hilar lymph nodes. It is indicated that sarcoidosis can develop in the renal allograft even if there are no active lesions due to sarcoidosis in other organs.

Maintenance immunosuppression for the allograft of our patient consisted of tacrolimus (target trough levels 3–5 ng/

mL), everolimus (target trough levels 3 ng/mL), and MMF (500 mg/day) at the time of the diagnosis of sarcoidosis in the allograft. Although the patient's proteinuria was exacerbated before corticosteroids (CS) were replaced by everolimus, his renal function declined after everolimus was initiated. Replacing CS with everolimus might have led to the progression of sarcoidosis. Of the 10 previous cases of sarcoidosis involving a renal allograft, maintenance immunosuppression consisted of a calcineurin inhibitor (CNI), MMF, and CS in 5 cases [1, 3–5], CNI, azathioprine (AZA), and CS in 2 cases [4, 6], CNI and CS in 1 case [7], AZA and CS in 1 case [8], and not reported in 1 case [1]. Almost all the recipients with recurrent sarcoidosis in their renal allograft received maintenance immunosuppressive therapy that included CS. No therapy for preventing recurrent sarcoidosis in a renal allograft has been established.

In a study of 47 patients with renal sarcoidosis, most patients received high-dose prednisone at 1 mg/kg/day, which led to obvious improvement in most cases [9]. All of the 10 renal allograft recipients who developed recurrent sarcoidosis in their allograft were treated with CS at various dosages and over varying treatment periods. Renal function improved in six patients [1, 2, 4, 6–8], renal function first improved but thereafter decreased with loss of the renal graft in one patient [3], renal function was not improved in one patient [4], one patient died of pulmonary embolism [4], and one patient receiving infliximab died of disseminated histoplasmosis [5]. For our patient, treatment with CS at an initial dose of 0.5 mg/kg/day did not lead to improvement in renal function but halted further deterioration, and his proteinuria improved. It is suggested that sarcoidosis involving a renal allograft could be treated with a lower dose of CS than sarcoidosis involving a native kidney, because the allograft recipient is receiving maintenance immunosuppressive drugs in addition to CS.

Compliance with ethical standards

Conflict of interest All the authors have declared no competing interest.

Human and animal rights This article does not contain any studies with human participants performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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