nefrología
Revista de la Sociedad Española de Nefrología
www.revistanefrologia.com

Case report

Recurrence of ANCA-associated vasculitis in a patient with kidney trasplant☆

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ARTICLE INFO

Article history:
Received 2 February 2015
Accepted 31 August 2015
Available online 23 April 2016

Keywords:
Anti-neutrophil cytoplasmic antibodies-associated vasculitis
Kidney transplantation
Relapse

ABSTRACT

Renal disease secondary to vasculitis associated with anti-neutrophil cytoplasmic antibodies (ANCA) can lead to chronic renal disease requiring renal replacement therapy. In these patients, kidney transplantation offers excellent long-term rates of allograft and patient survival; consequently, they can be trasplanted when the clinical disease activity has remitted. However, the risk of disease relapses in the renal allograft remains, although at lower rates due to modern immunosuppressive regimes. We describe the case of a male patient with extracapillary glomerulonephritis type III C-ANCA (+) who developed a recurrence in the renal allograft 8 years after transplantation. Intensive immunosupression with plasmapheresis controlled the disease.

Recidiva de vasculitis asociada a anticuerpos anticitoplasma de neutrófilos en un paciente con trasplante renal

Palabras clave:
Vasculitis asociada a anticuerpos anticitoplasma de neutrófilos
Trasplante renal
Recidiva

RESUMEN

La afectación renal de las vasculitis asociadas a anticuerpos anticitoplasma de neutrófilos (ANCA) puede conducir a enfermedad renal crónica con necesidad de tratamiento renal sustitutivo. En estos enfermos el trasplante renal ofrece excelentes tasas de supervivencia del injerto y del receptor a largo plazo, por lo que pueden ser trasplantados cuando la enfermedad está en remisión. Sin embargo, la amenaza de recidivas de la enfermedad en el

☆ Please cite this article as: García Cosmes P, Fraile Gómez P, Lewczuk K, Rodríguez González M, Ruiz Ferreras E, Tabernero Fernández G. Recidiva de vasculitis asociada a anticuerpos anticitoplasma de neutrófilos en un paciente con trasplante renal. Nefrología. 2016;36:176–180.

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injerto se mantiene, aunque, con las modernas pautas de inmunosupresión, su incidencia es menor. Presentamos el caso de un varón diagnosticado de glomerulonefritis extracapilar tipo III C-ANCA (+) que desarrolló una recidiva de la enfermedad en el injerto renal 8 años después de ser trasplantado. La intensificación de la inmunosupresión con plasmaféresis consiguió controlar la enfermedad.

Introduction

Currently, extracapillary glomerulonephritis type III with the demonstration of cytoplasmic antibodies (ANCA) is part of one of the three variants of ANCA-associated vasculitis (AAV) but affecting the kidneys only. The other two would be granulomatosis with polyangiitis (Wegener's granulomatosis) and microscopic polyangiitis.[1] These vasculitis are the most frequent cause of rapidly progressive glomerulonephritis. With early diagnosis and the application of therapy, based mainly on steroids and cyclophosphamide, the survival of patients and preservation of renal function is improved. However, more than 20% of these patients, develop end-stage renal disease, requiring renal replacement therapy.[2–4]

In these patients, renal transplantation is an alternative that provides excellent results, still there are issues that have to be resolved.[4–6] First, due to the possibility of recurrence of the disease in the graft,[6–11] it is not clear when would be the most appropriate time to include patients on the transplant waiting list. Second, there is no clear agreement on the treatment of recurrences.[12]

We report the case of a patient with Type III extracapillary glomerulonephritis associated with anti-proteinase 3 ANCA (C-ANCA) who, after 8 years of cadaver kidney graft transplant, had a recurrence of the disease in the graft. Concerning the case, a brief review of the subject has been included.

Clinical case

A 60-year-old male diagnosed in another hospital in 2000 of C-ANCA associated Type III extracapillary glomerulonephritis. He was treated with 5 intravenous bolus of 6-methylprednisolone followed by oral corticosteroids in decreasing doses associated to oral cyclophosphamide (unable to obtain information about exact dosing). At one point, cyclophosphamide was discontinued due to myelotoxicity.

In 2002 the patient was included in a regular haemodialysis program.

In September 2006, he received a cadaver kidney graft in another transplant center. The patient was receiving tacrolimus monotherapy, although we cannot rule out having received some other combination of immunosuppressant therapy. Serum creatinine levels ranged from 1.5 to 1.7 mg/dl.

In December 2013, during the implantation of a percutaneous aortic valve in our hospital, a pre and post-intervention clinical evaluation was carried out in our department. At that time his clinical condition was satisfactory, with serum creatinine level of 1.5 mg/dl and proteinuria 0.3 g/day, with a normal urinary sediment.

In October 2014, due to onset of respiratory symptoms with fever and impaired renal function, the patient requested to be transferred to our hospital for clinical follow-up. He had absence of microbiological and radiologic infections; he improved after empirical treatment with levofloxacin. However in a few days, renal function deteriorated reaching serum creatinine levels of 4 mg/dl with proteinuria of 6.8 g/day accompanied by haematuria. Determination of C-ANCA was 74.2 IU/ml (normal range: 0–5 IU ml) and P-ANCA 8.4 IU/ml (normal range: 0–6 IU/ml). The other autoimmunity parameters (ANA, anti-GBM antibodies, complement, cryoglobulins, etc.) were negative. HIV, HCV, HBV serology, and CMV and BK viremia were also negative.

A renal graft biopsy was performed and the most relevant findings were (Fig. 1): 3 out of the 19 evaluable glomeruli had global glomerular sclerosis, and 12 glomeruli had cellular crescents. Some of them had Bowman's capsule disruption causing pseudo-granulomatous inflammatory reaction of mononuclear cells. Two glomeruli had injuries consistent with fibrinoid necrosis. We found tubular necrosis in 15%, tubular atrophy 20% and some casts, plus interstitial infiltration in 25% with some eosinophils and foci of recent interstitial hemorrhage and arteriolar hyalinosis, with some images of wall mucoid degeneration without transmural infiltrate. Immunofluorescence study was negative. Immunohistochemistry for C4d was negative.

Given the evidence of a recurrence of the underlying disease, the patient received 3 intravenous bolus of 500 mg of 6-methylprednisolone (the patient was diabetic) on consecutive days, followed by oral prednisone at a dose of 0.5 mg/kg/day in descending dosing. Likewise, 8 sessions of plasmapheresis were applied, and we started treatment with mycophenolate mofetil (1 g/12 h, orally) associated with tacrolimus.

Twelve days after admission, the patient was discharged with a serum creatinine level of 2.9 mg/dl. In an outpatient check-up a month later, creatinine level was of 2.3 mg/dl with proteinuria of 3.6 g/day.

Discussion

Treatment of AAV is based mainly on the association of cyclophosphamide and corticosteroids; this therapy has shown clear efficacy in improving patient survival and preservation of renal function. However, more than 20% of patients develop end stage renal disease requiring renal replacement