Treatment of Late Class II Antibody-Mediated Rejection Status Postkidney Transplantation: Two Case Reports

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Abstract

Keywords

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We are describing the successful treatment of two cases of late Class II antibody mediated rejection status postkidney transplantation. The first patient was treated with a combination of plasmapheresis, intravenous immunoglobulin (IVIG), and stenting of the transplanted renal artery. The second was treated with IVIG and pulse steroids.

Antibody mediated rejection (AMR) occurs in ~5 to 8% of kidney transplantations¹ and accounts for 20 to 30% of cases of acute rejection.² Currently no proven treatments for AMR exist. There are a few reports that describe the use of plasmapheresis, intravenous immunoglobulin (IVIG),³ thymoglobulin,⁴ rituximab,⁵ proteasome inhibitors,⁶ or pulse steroids in acute AMR, in varying combinations and degrees of efficacy. In addition, there are case reports of splenectomy followed by plasmapheresis and IVIG as rescue therapy for acute AMR 1 week posttransplantation.⁷ Most of these reports have focused on acute Class I human leukocyte antigen (HLA) type AMR, which occurs immediately to up to 6 months posttransplantation. Class I HLA is associated with better prognosis as opposed to Class II HLA, which is characterized as a late form of rejection, presenting at after 6 months posttransplantation.⁸

Reports on the management of late Class II AMR are rare in the literature. Here we describe the successful treatment of two Class II AMR cases. The diagnosis was based on the presence of allograft dysfunction, the serological demonstration of donor-specific antibodies (DSAs), and histological confirmation of alloantibody-induced tissue dysfunction. The first patient was successfully treated with plasmaphere-

sis, IVIG, and angioplasty and stenting of the transplanted renal artery. The second patient was successfully treated with IVIG and pulse steroids.

Case Reports

Case 1

GM is a 52-year-old man who underwent kidney transplantation for end-stage renal disease secondary to hypertension and type 2 diabetes mellitus. His wife, who had tested positive for DQ-7 class II HLA mismatches, provided the living donor kidney. GM underwent plasmapheresis (one plasma volume and 5% albumin as a replacement fluid) before the transplantation. He tolerated the transplantation procedure well without complication and had immediate graft function. He returned to the hospital 7 months posttransplantation with right lower quadrant abdominal pain at the site of the transplanted kidney and dysuria. His creatinine level was 3.3 mg/dL from a baseline of 2.3 mg/dL, with a blood urea nitrogen level of 42 mg/dL. A kidney biopsy was not performed at this time due to the patient's concurrent coagulopathy. Based on his known DQ-7 mismatches he underwent three IVIG treatments and two

Figure 1 Angioplasty of transplanted renal artery.

sessions of plasmapheresis. For each 10% IVIG (20 g/200 mL, Gammagard Liquid [Baxter]), he was premedicated with 100 mg intravenous (IV) methylprednisolone and 50 mg IV diphenhydramine. The patient underwent two sessions of plasmapheresis before and during the IVIG treatments. The patient tolerated the treatments well.

During concurrent ultrasound of the transplanted kidney the patient was found to have a 30 mm Hg pressure gradient in the transplanted renal artery. A decision was made to place a 5-mm expandable balloon endovascular stent in the transplanted renal artery. Placement was successful and confirmed by angiography. The renal artery stenosis was felt to have been caused by his AMR. HLA class II antibodies have been shown to have antiendothelial components causing intimal hyperplasia and inflammation leading to a form of posttransplant-accelerated arteriosclerosis.⁹ GM was discharged with a normalized creatinine level. Follow-up renal Doppler, 1 month after discharge demonstrated a patent transplanted renal artery and vein with no evidence of renal artery stenosis (→Fig. 1).

Case 2

MR is a 47-year-old woman who underwent kidney transplantation secondary Focal to Segmental Glomerulosclerosis. The living donor kidney was provided by her friend who was positive for the HLA class II DSA mismatch DR-17. The patient had immediate graft function posttransplantation. After 4 years posttransplantation, she presented with acute rise in the creatinine level, up to 2.9 mg/dL from a baseline of 1.5 mg/dL. It was revealed that she had stopped her steroid regimen for personal reasons. A biopsy was performed which revealed interstitial fibrosis, tubular injury, and an inflammatory infiltrate of mononuclear. Immunofluorescence microscopy showed C4d positive cells in peritubular and glomerular capillaries. The diagnosis of AMR type II was made. The patient was given two treatments of IVIG, 28.6 g (0.5 g/kg) with 250 mg Solu-Medrol (methylprednisolone). She tolerated the treatments well and her creatinine returned to baseline. She was discharged from the hospital without further incident (→Fig. 2A, B).

Discussion

Class II HLA is a late form of rejection presenting at more than 6 months posttransplantation. This diagnosis is based clinically on the presence of allograft dysfunction and the serological demonstration of DSAs. This rejection is characterized histologically by the presence of interstitial fibrosis, tubular atrophy, and/or arterial intimal fibrosis on light microscopy. The positive immune staining of C4d cells at peritubular capillaries, as well as the presence of circumferential

Figure 2 Histological slides of transplanted renal biopsy—showing peritubular capillary congestion, interstitial inflammation, and leukocyte infiltration.

basement membrane as seen with electron microscopy confirms the diagnosis of Class II AMR.¹⁰

Late Class II AMR is a rare form of transplant rejection typically associated with a poor prognosis. There is scant evidence regarding the best treatment for this presentation; most of the literature is based on case reports and single-center experiences. We have illustrated the successful diagnosis and treatment of late Class II AMR, and hope that this data will further enhance the understanding of this complicated disease process.

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