

Trauma and reconstruction

De novo minimal change disease in the renal allograft

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A B S T R A C T

De Novo minimal change disease in the renal allograft is an infrequently reported cause of glomerulopathy. The paucity of reported cases in the medical literature and strict clinical-pathological criteria for diagnosis has made this entity an infrequently encountered disease process. We describe a case of MCD sixteen months post-transplant that has initially responded well to corticosteroid therapy.

Introduction

There are three main categories when describing glomerular causes of nephrotic-range proteinuria in the renal allograft patient beyond the immediate post-transplantation period: Transplant glomerulopathy, recurrent glomerular disease, and *de novo* glomerulopathy. Transplant glomerulopathy is most commonly encountered and is characterized by a membranoproliferative pattern without immune complex deposition.¹

The renal allograft disease registry documented the incidence of recurrent and *de novo* disease in the renal allograft to be 3.4% with a mean follow up of 5.4 years. A Canadian review reported a 10.5% incidence of glomerular disease in renal transplant patients without a history of biopsy proven GN over 15 years follow up. The discrepancy between recurrent and *de novo* disease is in part because only 10–15% of kidney recipients have had biopsies of their native kidneys. Most cases of *de novo* glomerulopathy are due to membranous nephropathy.²

The etiology of MCD is associated with drugs (NSAIDs, ampicillin, rifampicin, cephalosporins, lithium, bisphosphonates), hematologic malignancies, infections (syphilis, tuberculosis, mycoplasma, HCV), and a history of allergies have been described in up to 30% of cases with MCD. The pathogenesis of MCD is unclear and is thought to be related to T/B cell dysfunction, glomerular permeability factor (cardiotrophin-like cytokine-1 or urokinase-plasminogen receptor), and IL-13.³

First-line therapy for MCD is a low-sodium diet, diuretics (ACE or ARB), and prednisone. *De novo* MCD also has a favorable prognosis with a sustained remission of nephrotic syndrome with good graft outcomes in most cases.³

Our patient is a combined heart-kidney transplant that developed clinical & pathological features consistent with *de novo* MCD 16 months after transplant.

Case report

A 67 year-old Caucasian male status-post combination cadaveric cardiac/renal transplant sixteen months prior for heart failure reduced ejection fraction secondary to non-ischemic dilated cardiomyopathy and ESRD secondary to diabetes & hypertension presents with profuse lower extremity edema and frothy, bubbly urine of one week duration. Patient received induction immunosuppression with solumedrol and thymoglobulin and maintenance immunosuppression with low dose prednisone, mycophenolate, and tacrolimus. Patient required hemodialysis for three years until transplant. Serum creatinine during dialysis was approximately 2.4 and post transplant his baseline is approximately 1.5.

Patient's past medical history is remarkable for COPD, OSA, HLD, anxiety/depression, cataracts, colostomy secondary to recurrent diverticulitis, bilateral internal jugular occlusion status-post bilateral recanalization and venoplasty, adrenal insufficiency, and hypothyroidism.

Urinalysis on presentation demonstrated +3 proteinuria that was quantified with a spot Protein-Creatinine ratio of 2342. Previous Pr-Cr ratios were approximately 100. Serum creatinine was near his baseline. Patient was hypertensive with a blood pressure of 160/100 with a baseline of 130/80. Patient's weight was relatively stable at 263 pounds. On physical exam patient had +3 bilateral pitting edema with no other pertinent positives to report. Before the biopsy results the patient's repeat Protein-Creatinine ratio increased to 4466 with no underlying AKI.

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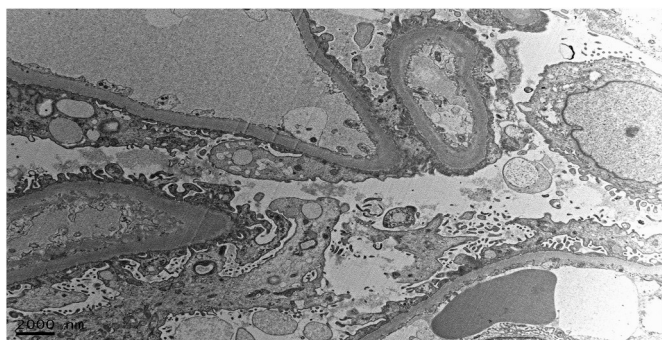


Fig. 1. Electron microscopy of renal biopsy.

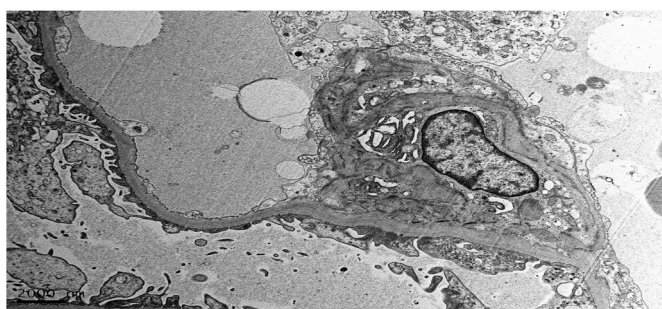


Fig. 2. Electron microscopy of renal biopsy.

Pathological evaluation

Thirteen glomeruli specimen were recovered, five of which were used for light microscopy with PAS staining. The glomeruli were focally enlarged with patent capillaries and delicate walls with mildly reactive podocytes. Albumin showed 1–2+ normal pseudolinear staining of the glomerular and tubular basement membranes. The podocytes are reactive and display diffuse (yet incomplete; approximately 60%) attenuation of the foot processes as seen in Figs. 1 and 2. All sections were negative for acute/chronic cellular or humoral rejection. The final pathologic diagnosis was diffuse podocyte foot process effacement compatible with podocytopathy. Of note, patient recently had a cardiac allograft biopsy of which no rejection was demonstrated.

Discussion

Although a limited number of glomeruli were available for pathological evaluation, the clinical presentation combined with no history of nephrotic disease as well as the light microscopic, immunofluorescent, and ultrastructural findings make MCD the most likely diagnosis.

Markowitz et al. and Truong & colleagues reported a combined number of fourteen total *de novo* MCD cases. The time course from transplant to biopsy ranged from 4 days to 30 months with a mean of approximately 7 months and mode of 4 months. Our patient's renal function has been stable and this may be considered a good prognostic sign. Adults with MCD are more likely to presents with acute renal failure that requires longer periods of steroid treatment and has been reported to occur in as many as 20% of adults with MCD.⁴

An interesting correlate with this patient's presentation is his history of adrenal insufficiency. The patient has been on chronic low dose prednisone therapy since his transplants. November 6th and December 4th, 2017 he was given 50mg IVP of hydrocortisone in preparation for cataract surgery that day. December 8th the patient presented to clinic with the aforementioned symptoms. Leisti & Koskimies described glucocorticoid-induced adrenocortical suppression from MCD treatment that was associated with early relapse. 201 cases were described of which 102 episodes displayed adrenocortical suppression stratified as moderate or severe based on a two-hour ACTH suppression test.⁵ Those with severe suppression relapsed quickly with the longest remission time being six months. Moderate suppression was also associated with early relapse but generally after one year. Although this study was in pediatric patients it may be applicable to our patient.⁵

There is also the possibility that viral infections can induce activation of innate and/or adaptive immunity that have been implicated as the source of dysfunctional T cells. The patient was admitted on October 25th, 2017 for shortness of breath. Patient had a negative right heart cath, negative V:Q scan, CXR, and a negative infectious disease workup with multiple viral agents. Infectious disease considered the symptoms due to a viral URI and otitis media considering the patient was neutropenic (WBC of 3.7).

These two events, either isolated or in combination, may be the eliciting factors for the patient's disease process. More recently the patient's Pr-Cr ratio has increased to 3330 from 2750. This is still a dramatic improvement from 4466 three weeks prior. This ratio was determined using spot measurements rather than 24-h urine collection and may be considered equivocal at this time. The last two reported Pr-Cr ratio were 2100 and 1500 indicating an excellent response to glucocorticoid therapy (Fig. 3).

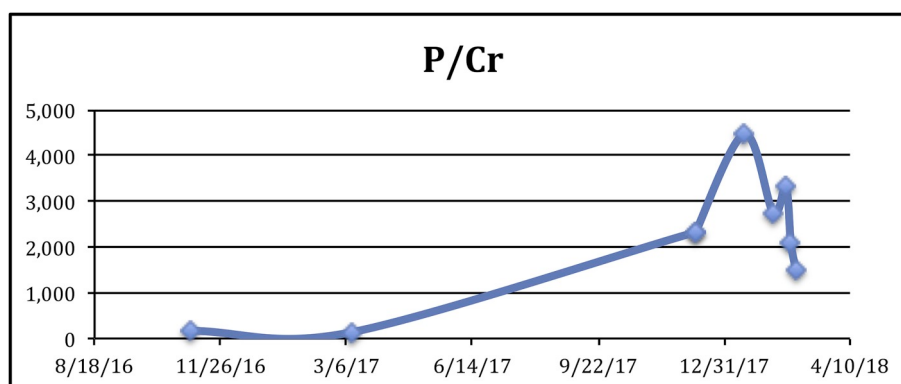


Fig. 3. Protein to creatinine ratio versus time.

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