Case Report

# Membranoproliferative glomerulonephritis due to Hepatitis C in renal allograft

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## ABSTRACT

Membranoproliferative glomerulonephritis type 1 is an etiologically divergent disorder. Hepatitis C with or without cryoglobulinemia is considered one of the principal causes of de novo and post transplant membranoproliferative glomerulonephritis type 1. A 49-year-old male who underwent renal allograft for end stage renal disease developed proteinuria and positive hepatitis C serology during the post-transplant period. This was associated with moderate hepatic dysfunction, which necessitated both liver and renal biopsies. Features of both chronic active hepatitis and membranoproliferative glomerulonephritis type 1 were seen as a result of histological examination of both liver and renal biopsies. Ultra structural studies showing mesangial and membranous deposits which are characteristic of membranoproliferative glomerulonephritis have been observed. The case is reported with a review of pertinent medical literature.

**Keywords:** Membranoproliferative glomerulonephritis, Hepatitis C, renal allograft.

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Membranoproliferative glomerulonephritis (MPGN) type 1 may relentlessly progress to end stage renal disease demanding a transplant in a number of patients.[1] Membranoproliferative glomerulonephritis is of diverse etiology and persistent antigenemia is considered to be an important pathogenetic mechanism.[2] In addition to the idiopathic variant, there are several disorders associated with similar glomerular morphology. These include systemic auto-immune disorders, neoplasms, chronic liver diseases, infections principally hepatitis C and cryoglobulinemia. It is also well documented that allograft glomerulopathy morphologically resembles type 1 MPGN.[1]

**Case Report.** A 49-year-old Bahraini male underwent renal transplantation for an end stage renal disease following MPGN type 1 in February 1996. The donor who was the patient's brother was human leukocyte antigen (HLA) matched. The kidney remained in excellent function under continued immunosuppression regimen that included prednisolone, immuran and cyclosporin. However the patient developed steroid induced diabetes mellitus that was effectively controlled by insulin. In 1998 he developed abnormal liver functions with elevated hepatic enzymes. Serology revealed Hepatitis C infection with positive hepatitis C virus (HCV) core ribonucleic acid (RNA). A liver biopsy in September 1998 confirmed chronic active hepatitis with portoseptal inflammation and focal bridging fibrosis that was histologically grade 3 and stage 3. The patient received Ribavirin over the next 12 months, however, he subsequently developed progressive anemia with a fall of his hemoglobin to 7gm/dl and ribavirin was stopped. He started to have ankle edema and deterioration in renal function in September 1999. The serum creatinine was 159.1

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μm/L with urinary protein of 8gm in 24 hours. The transplant biopsy showed features of type 1 MPGN **(Figure 1).** Ultrastructural studies carried out on the renal biopsy revealed extensive effacement of epithelial foot process with electron dense deposits in the sub endothelial and mesangial areas **(Figure 2).** The mesangial matrix has been observed in the subepithelial location corresponding to the 'tram track' capillary loops on light microscopy. A year later in August 2000, a transplant biopsy was carried out as the patient continued to have renal dysfunction. The morphological features remained the same and the diagnosis of MPGN was made again. The patient received interferon on a weekly dose and following his 2nd injection, the patient developed signs of upper respiratory infection, low-grade fever and shortness of breath. This was associated with a rapid decline in the renal function necessitating hemodialysis. The patient was advised to have a regraft and is currently awaiting a donor with continuous hemodialysis.

**Discussion.** Membranoproliferative glomerulonephritis can arise as a de novo disease in native kidney, or affect the grafted kidney during the post transplant period.[3,4] It is often difficult to establish the etiopathogenesis of MPGN in transplant kidney if the patient had end stage renal disease due to MPGN. It is also well documented that liver disease due to HCV is one of the causes leading to morbidity and mortality in renal transplants.[5] Proteinuria with liver dysfunction often indicates Hepatitis C induced hepatic and renal disorders in the post transplant period.[6] Membranoproliferative glomerulonephritis due to hepatitis C with or without cryoglobulinemia is a well known morphological entity and careful serological studies are always indicated before labeling MPGN as idiopathic.[4]

In cases with no demonstrable hepatic manifestations, Hepatitis C induced renal disease is to be suspected in cases when post transplant proteinuria occurs.[7,8] Brunkhorst et al[7] in a study of over 1000 renal transplant recipients, detected proteinuria of more than 1gm/24hours, in 23% of 140 anti HCV positive cases. Similarly a study was conducted by Hestin et al[8] consisting of 322 consecutive renal transplant recipients with anti HCV at the time of graft. This was associated with an estimated risk of 5.36 developing proteinuria. These studies fortunately did not however, record significant deviation in graft survival rates between anti HCV positive and negative recipients. The glomerular lesions in 26 out of 44 transplant proteinuric patients revealed transplant glomerulopathy and none of the proteinuric anti HCV patients had MPGN.[8]

Cockfield and Prieksaitis[9] noted frequent occurrence of hepatitis C in both de novo and transplant glomerulopathy cases, as compared to the negative cases. The data supports HCV infection and proteinuria as directly associated in renal transplant recipients.[10] Membranoproliferative glomerulonephritis type 1 can affect the grafted kidney similar to native kidneys. Nearly 53% of renal graft exhibiting MPGN type 1 pathology in renal grafts are known to develop proteinuria and progressive renal failure needing dialysis as in the present case.[11] Significant morbidity and mortality has been found in renal transplant patients with liver disease. Liver failure as a principle cause of death has been recorded in 8% to 28% of long term survivors following renal transplantation.

Refinement of tests for the detection of HCV such as cloning and characterization of the virus have allowed us to detect it in over 48% of transplant recipients. Nearly 86% with seropositivity developed complaints of liver disease with histologically proven chronic active hepatitis and hepatitis C RNA positivity confirmed the etiologic correlation.[12] It is difficult to assess at this stage the source of infection.

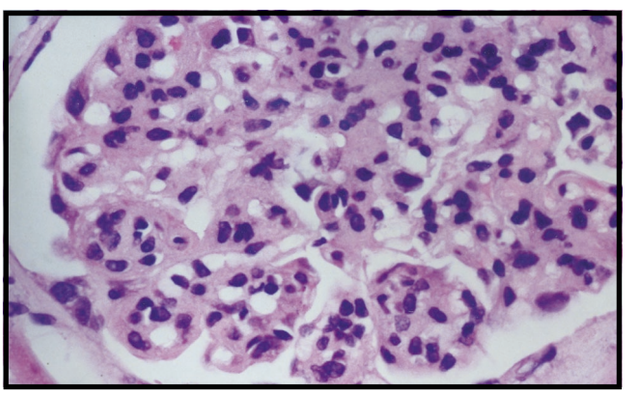

**Figure 1 -** Increase in mesangial cellularity with basement membrane thickening and extension of mesangial matrix into peripheral capillary loops. Periodic Acid Schiff 200X.

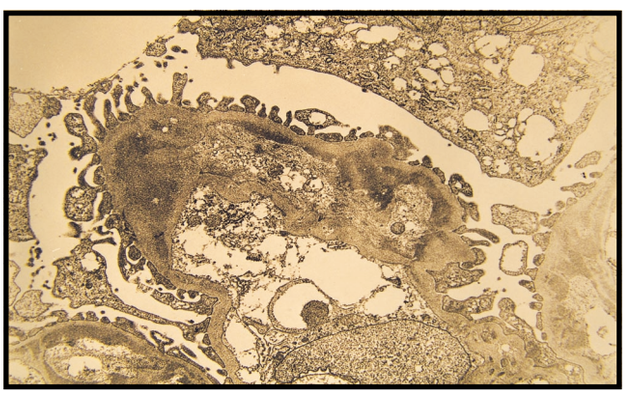

**Figure 2 -** Ultrastructural features of partial effacement of foot process with subendothelial electron dense deposits. Uranyl acetate 3000X.

As the donor has been screened for hepatitis C virus prior to transplantation it is unlikely that neither the liver disease nor the renal pathology are attributable to activation/recurrence of MPGN in this case. It is therefore probable that the patient has developed the hepatic and renal sequelae due to Hepatitis C infection which was acquired following the graft.

It is virtually impossible by light microscopy to distinguish between type 1 MPGN (denovo or recurrent) from chronic transplant glomerulopathy, which reveal identical morphologic abnormalities. Andersdottir et al[1] reported immunohistochemical and ultra structural features delineating the 2 disorders. In patients of chronic transplant glomerulopathy there is an electron lucent zone of finely flocculent material in the sub endothelial space, whereas sub endothelial electron dense deposits characterize Type one MPGN.[1,10]

In conclusion, MPGN has been recorded in the renal graft of a 49-year-old patient who developed hepatitis C related hepatic disease in the post transplant period. Both the hepatic and renal diseases are considered to be due to Hepatitis C virus.

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