Renal Thrombotic Microangiopathy Associated with Anticardiolipin Antibodies in Hepatitis C-Positive Renal Allograft Recipients

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Abstract. Hepatitis C virus (HCV) infection has been associated with de novo or recurrent membranoproliferative glomerulonephritis and acute transplant glomerulopathy in transplanted kidneys. Recently, anticardiolipin antibodies (ACA) have been linked with chronic HCV infection. A few reports have suggested an association between ACA and renal allograft thrombosis. This study examines the clinical and pathologic features of HCV-positive renal allograft recipients at our institution. From 1990 to 1996, 379 kidney transplants were performed. We identified 18 recipients (4.8%) with HCV-positive serology pretransplant. Determination of IgG and IgM ACA was performed by enzyme-linked immunosorbent assay, using pretransplant sera. Among the 18 patients, five patients presented with biopsy-proven de novo renal thrombotic microangiopathy (RTMA), occurring 5 to 120 d (median, 14 d) after transplant. No differences in pretransplant characteristics were observed between patients with (n = 5) or without (n = 13) RTMA. All five patients had a positive ACA test (either IgG or IgM titer > 2 SD above normal), compared with only one of 13 patients without RTMA. The mean value for IgG ACA was significantly higher in the RTMA patients than in patients without RTMA (22.9 ± 14.1 versus 6.9 ± 4.9 IgG phospholipid units, P = 0.02); however, there were no significant differences in IgM ACA titers. Rheumatoid factor and complement C4 levels were normal in pretransplant sera of patients with RTMA. Patients with RTMA had their cyclosporine withdrawn (four of five) or the dose was decreased (one of five), and one of five underwent plasmapheresis. Four of five patients died within 5 yr after transplant, compared with no deaths in the other 13 patients. Finally, as a control group, seven HCV-negative renal allograft recipients who presented with RTMA/hemolytic uremic syndrome during the same time period were found to have normal ACA values (IgG or IgM). RTMA associated with ACA in HCV-positive renal allograft recipients may represent a new clinical entity. The occurrence of this syndrome may have deleterious consequences for patient and graft survival.
association of RTMA and ACA in a subset of HCV-positive renal allograft recipients.

Materials and Methods

Between May 1990 and December 1996, 379 kidney transplants were performed at the Massachusetts General Hospital. Among these, we identified 18 recipients (4.8%) who had HCV-positive serology at the time of transplantation. Clinical information, posttransplantation course, laboratory values, and histopathologic studies were reviewed for all of the patients. The immunosuppressive protocol consisted of cyclosporine (Sandimmune, initiated at 6 mg/kg orally twice a day, and then tapered depending on the serum levels and renal function), prednisone, and azathioprine. None of these 18 patients received induction therapy with OKT3 or antithymocyte globulin. One patient (patient 2) received anti-intercellular adhesion molecule-1 antibody as induction therapy as part of a study protocol and was not on cyclosporine at the time of first biopsy (see below). The clinical course, outcome, and pathology of seven renal allograft recipients who had undergone transplantation within the same time period, who were HCV-negative and developed hemolytic uremic syndrome (HUS) after transplantation, were also reviewed.

Virologic Studies

The presence of antibodies to HCV was determined initially (from May 1990 to February 1992) by first-generation enzyme-linked immunosorbent assay (ELISA; Abbott Laboratories, Abbott Park, IL) and then by second-generation ELISA (Ortho Diagnostic Systems, Raritan, NJ) from March 1992 onward. Recipient and donor cytomegalovirus status was tested by serology.

Renal Allograft Pathology

Renal tissue was obtained by percutaneous renal biopsy at the time of renal dysfunction. Samples were processed to perform light microscopy (stains for hematoxylin-eosin, periodic acid-Schiff), direct immunofluorescence (IgG, IgM, IgA, albumin, fibrin/fibrinogen), and electron microscopy evaluation using standard procedures. In addition, special immunoperoxidase studies were done to identify platelets. The avidin-biotin-peroxidase complex technique was used in 2-μm frozen cryostat sections, using a monoclonal antibody to CD62 p-selectin (Becton-Dickinson, Mountain View, CA) (21). Staining was achieved using 3-amino-9-ethylcarbazole (Aldrich Chemical Co., Milwaukee, WI), a chromogen for horseradish peroxidase.

Serum Samples

All patients had pretransplant serum stored within 3 mo before transplantation. All of the samples were used to determine the presence of IgG and IgM ACA titers by ELISA (Quanta Lite™ ACA IgG/IgM, INOVA Diagnostics, San Diego, CA). Positive ACA levels (either IgG or IgM) were defined as greater than 2 SD above the mean derived from the results of healthy blood donors (n = 31). Complement C3 and C4 levels and rheumatoid factor levels were also mea-

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RTMA (n = 5)</th>
<th>No RTMA (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>45.8 ± 7.1</td>
<td>42 ± 10.3</td>
</tr>
<tr>
<td>Race (% Caucasian)</td>
<td>100</td>
<td>92</td>
</tr>
<tr>
<td>Gender (% male)</td>
<td>60</td>
<td>62</td>
</tr>
<tr>
<td>Donor (cadaver/living)</td>
<td>5/0</td>
<td>10/3</td>
</tr>
<tr>
<td>Retransplantation</td>
<td>2/5</td>
<td>5/13</td>
</tr>
<tr>
<td>PRA peak (%)</td>
<td>62.8 ± 50.5</td>
<td>46.9 ± 44.5</td>
</tr>
<tr>
<td>PRA at transplant (%)</td>
<td>56.2 ± 50.2</td>
<td>39.4 ± 40.5</td>
</tr>
<tr>
<td>No. of HLA mismatches</td>
<td>2.4 ± 1.8</td>
<td>3.9 ± 1.8</td>
</tr>
</tbody>
</table>

* No significant differences were observed between the two groups. RTMA, renal thrombotic microangiopathy; PRA, panel-reactive antibody.

Table 2. Clinical features of HCV-positive patients with RTMA

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age in Years/Gender</th>
<th>RTMA (time from Tx to Bx)</th>
<th>Dose of CyA at the Time of RTMA (mg/kg per d)</th>
<th>Prior OKT3/ATG or Other Ab</th>
<th>Other Thromboembolic Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50/M</td>
<td>14 days</td>
<td>5.5</td>
<td></td>
<td>Ischemic necrotic bowel</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Necrotic renal allograft with</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>thrombus in the renal artery</td>
</tr>
<tr>
<td>2b</td>
<td>54/F</td>
<td>Bx1: 9 days</td>
<td>0</td>
<td>Anti-ICAM</td>
<td>Acute myocardial infarction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bx2: 50 days</td>
<td></td>
<td>MP, OKT3</td>
<td>posttransplant at 12 wk (recurrent vascular access thrombosis pretransplant)</td>
</tr>
<tr>
<td>3</td>
<td>45/F</td>
<td>5 days</td>
<td>6</td>
<td>OKT3</td>
<td>Pulmonary embolism</td>
</tr>
<tr>
<td>4</td>
<td>45/M</td>
<td>21 days</td>
<td>8.5</td>
<td></td>
<td>posttransplant at 16 wk (recurrent vascular access thrombosis pretransplant)</td>
</tr>
<tr>
<td>5</td>
<td>35/M</td>
<td>120 days</td>
<td>4.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Tx, transplant; Bx, biopsy; CyA, cyclosporine; MP, methylprednisolone; Ab, antibody; Anti-ICAM, anti-intercellular adhesion molecule-1 antibody.

b Patient 2 had two biopsies showing RTMA.
survived in all of the stored sera. Rheumatoid factor was measured as a surrogate for serum cryoglobulins.

**Statistical Analyses**

All results are expressed as mean ± SD. Comparisons between groups were done using the Mann–Whitney U test, unpaired t test, and Fischer exact test. Two-sided P values <0.05 were considered significant.

**Results**

**Patient Characteristics and Clinical Course**

We reviewed 18 renal allograft recipients who had HCV-positive serology at the time of transplantation. There were 11 male and seven female patients with a mean age at the time of transplantation of 43.1 ± 9.5 yr. Seventeen patients were Caucasian and one was African-American. Fifteen patients had received cadaveric allografts and three patients received allografts from living related donors. All donors were HCV antibody-negative. All patients were hepatitis B surface antigen-negative and HIV-negative. Among the 18 patients, five patients demonstrated histopathologic evidence of de novo renal thrombotic microangiopathy early in the posttransplant period (RTMA group). The time between transplantation and the histopathologic diagnosis of RTMA ranged from 5 to 120 d (median, 14 d). Thirteen patients did not develop RTMA (No RTMA group). Table 1 summarizes the patient characteristics at the time of transplantation. No significant differences were observed between the two groups. The clinical features of the five patients with RTMA are shown in Table 2. The primary renal diagnoses were chronic immune-complex glomerulonephritis of unknown etiology (patient 1), hypertensive nephrosclerosis (patients 2 and 3), focal and segmental glomerulosclerosis (patient 4), and chronic pyelonephritis with secondary focal and segmental glomerulosclerosis (patient 5). Two patients also had renovascular disease (patients 2 and 3). Among the other 13 patients, the diagnoses were reflux nephropathy (n = 2), HUS (n = 2), Alport’s syndrome (n = 2), membrano-

![Figure 1. Patient 1 renal biopsy. (A) The glomerular capillary loops contain granular material consisting largely of platelet aggregates. Periodic acid-Schiff stain, ×400. (B) The material in the glomerular capillaries stain with an antibody to CD62p (p-selectin), a marker of platelets (arrows). Immunoperoxidase stain, ×100.](image1.png)

![Figure 2. Patient 2 renal biopsy. The arteriole (arrow) shows marked swelling of the endothelium, proliferation, and a few apoptotic bodies. The glomerulus shows partial collapse and loss of capillary lumina by swollen endothelium. Hematoxylin and eosin, ×250.](image2.png)
proliferative glomerulonephritis type 1 (n = 1), medullary cystic disease (n = 1), membranous nephropathy (n = 1), chronic glomerulonephritis of unknown etiology (n = 1), diabetic nephropathy (n = 1), hypertensive nephrosclerosis (n = 1), and interstitial nephritis secondary to sarcoidosis (n = 1). None of these patients had received antiviral treatment for HCV infection. The clinical presentation of RTMA was a rise in serum creatinine (patients 1, 4, and 5) or delayed graft function (patients 2 and 3) leading to allograft biopsy. Systemic manifestations of HUS were present in only one patient (patient 1). Of note, in patient 2, cyclosporine was started on day 12 but at a low dose (2.5 mg/kg) due to the presence of delayed graft function. The number of patients with acute cellular rejection within 6 mo was two out of five (40%) and six out of 13 (46%) in the RTMA and No RTMA groups, respectively (NS). Disseminated cytomegalovirus infection and positive cytomegalovirus antigenemia occurred in patients 2 and 3, respectively. None of the other three patients with RTMA had evidence of cytomegalovirus infection or disease.

Renal Pathology and Immunohistochemistry
Each renal biopsy contained at least 10 glomeruli (range, 10 to 20 glomeruli). The morphologic features in the five patients with RTMA were as follows. By light microscopy, all patients demonstrated acute vascular lesions consisting of swollen arterial endothelium and narrowed capillary lumen in the glomeruli. Focally occlusive platelet thrombi in glomeruli extending into afferent arterioles were present in patient 1 (Figure 1A). Arterioles showed intimal thickening, basophilic degeneration, and thrombi. As an example, patient 2 showed marked swelling of endothelium, proliferation, and a few apoptotic bodies (Figure 2). Tubular injury was present in three patients. In one patient, glomerular capillary lumina were filled with mononuclear cells.

Immunofluorescence revealed IgM, C3, and fibrin in arteriolar walls of three patients. IgM and/or IgG, C3, and fibrin were present in glomeruli in four patients. By immunoperoxidase, positive staining for platelets with anti-CD62 p-selectin monoclonal antibody (Figure 1B) was found in three out of four patients, ranging from 1+ to 4+. In one patient, immunoperoxidase was not performed because of lack of glomeruli in the remaining tissue available for study. Electron microscopy of three patients studied showed similar features: glomerular endothelial swelling, loss of fenestration, focal loss of endothelium, and accumulation of platelets and compacted red blood cells in the lumina (Figure 3). In addition, monocytes and lymphocytes were also noted in two patients.

Laboratory Data
The laboratory values at the time of RTMA varied among the patients (Table 3). Moderate thrombocytopenia and elevation of serum lactate dehydrogenase were noted in three and four patients, respectively. Anemia (hematocrit <30%) was present in three patients, however, there was no significant fall in hematocrit from baseline values. Schistocytes in peripheral blood smear were present in patients 1 and 3; their presence was not assessed in the other patients. Of significance were the elevated concentrations of ACA (more than 2 SD of normal) in all of the patients with RTMA (100%), compared with only one of the 13 other patients (7.7%) (P = 0.007). Four of the five patients in the RTMA group were positive for IgG ACA, and one for IgM ACA (Figures 4 and 5). The mean value for IgG was significantly higher in the RTMA group (22.9 ± 14.1 versus 6.9 ± 4.9 IgG phospholipid units, P = 0.02), however, there were no significant differences in IgM ACA (5.3 ± 5.6 versus 5.4 ± 1.7 IgM phospholipid units, P = 0.3). One patient in the No RTMA group had a positive IgG ACA. Of interest, the renal biopsy of this patient on posttransplant day 9 demonstrated partial cortical infarction, suggesting that a thrombotic event had occurred in the days before biopsy. Subsequently, this patient did well and now has excellent allograft function with a follow-up of 1 yr.

To determine whether the occurrence of RTMA was associated with the presence of cryoglobulins in the recipients, we measured rheumatoid factor, C3, and C4 in the pretransplant sera of these five patients. Rheumatoid factors were negative,

Figure 3. Electron micrograph from patient 3. A glomerular capillary is occluded by compacted erythrocytes (curved arrow) and has lost most of its endothelium. A platelet aggregate is present in an adjacent capillary (straight arrow). ×1250.
and C4 values were normal in all five patients. The level of C3 was significantly low only in one patient.

**Therapy and Outcome**

The mean follow-up was 29 ± 29.4 mo and 29.9 ± 27.3 mo in the RTMA and No RTMA groups, respectively. The therapy and outcome data of these patients are given in Table 4. In patients with RTMA, cyclosporine was withdrawn (four of five) or the dose was decreased (one of five). Patient 1 also received plasmapheresis. In one patient (patient 5), cyclosporine was restarted 5 d later. The prognosis was significantly worse in patients with RTMA. There were two deaths within 1 yr, and four deaths within 5 yr after transplant (80% death rate), compared with no deaths in the other 13 patients. The surviving patient (patient 5) is doing well after 5 yr with stable renal function (creatinine 1.8 mg/dl). The causes of death in the four patients were sepsis in the setting of pneumonia (n = 2), HUS with multiorgan failure (n = 1), and acute myocardial infarction with disseminated cytomegalovirus infection and aspergillosis (n = 1). Eleven patients in the No RTMA group are doing well with a mean creatinine of 1.4 ± 0.3 mg/dl. Two patients lost their allografts after 6 mo and 6 yr, respectively, due to chronic rejection with transplant glomerulopathy.

**Determination of ACA in HCV-Negative Renal Allograft Recipients with HUS Posttransplant**

To determine whether all posttransplant RTMA/HUS were associated with ACA and/or HCV infection, we next screened

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**Table 3. Laboratory values at the time of diagnosis of RTMA**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Creatinine (mg/dl)</th>
<th>Platelet Count (×1000/μl)</th>
<th>Hematocrit (%)</th>
<th>LDH a (U/L)</th>
<th>Bilirubin Direct/Total (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.8 to 7</td>
<td>80 to 130</td>
<td>31.9</td>
<td>2122</td>
<td>2.1/3.3</td>
</tr>
<tr>
<td>2</td>
<td>Bx 1: 7 to 8</td>
<td>250 to 300</td>
<td>24.5</td>
<td>366</td>
<td>0.3/0.7</td>
</tr>
<tr>
<td></td>
<td>Bx 2: 3 to 4</td>
<td>60 to 135</td>
<td>34</td>
<td>493</td>
<td>0.5/1.2</td>
</tr>
<tr>
<td>3</td>
<td>9.8</td>
<td>300 to 350</td>
<td>24</td>
<td>460</td>
<td>0.1/0.3</td>
</tr>
<tr>
<td>4</td>
<td>2.5</td>
<td>170 to 185</td>
<td>29</td>
<td>NA</td>
<td>1.7/3.0</td>
</tr>
<tr>
<td>5</td>
<td>2.4</td>
<td>130 to 160</td>
<td>36</td>
<td>249</td>
<td>0.3/1.1</td>
</tr>
</tbody>
</table>

*Normal laboratory values: creatinine = 0.6 to 1.5 mg/dl; total bilirubin = 0 to 1.0 mg/dl; direct bilirubin = 0 to 0.4 mg/dl; LDH = 110 to 210 U/L. LDH, lactate dehydrogenase; NA, not available. Other abbreviations as in Tables 1 and 2.*
pretransplant sera for the presence of ACA in a series of patients (n = 7) who presented with biopsy-proven RTMA/HUS during the same time period, and who were HCV-negative. The time between transplantation and the histopathologic diagnosis of RTMA/HUS ranged from 9 d to 7 yr (median, 6 mo) in this group of patients. In this group, all of the ACA values (IgG or IgM) were negative (not shown). The mean IgG ACA level was 4.3 ± 4.1 GPL units, and the mean IgM ACA level was 3.5 ± 3.0 MPL units. The underlying renal diseases in these patients were HUS (n = 2), membranoproliferative glomerulonephritis type 1 (n = 1), focal and segmental glomerulosclerosis (n = 1), lupus nephritis (n = 1), diabetic nephropathy (n = 1), and juvenile rheumatoid arthritis with secondary amyloidosis (n = 1). The two patients with HUS had recurrence of HUS in the allograft, one at 45 d and the other at 15 mo posttransplantation.

**Discussion**

We describe five HCV-positive renal allograft recipients who developed biopsy-proven *de novo* RTMA after renal transplantation. ACA were detected in pretransplant sera of these patients. The time between transplantation and the diagnosis of RTMA was relatively short, ranging between 5 and 120 d (median, 14 d). In addition to RTMA, three patients also presented with other thrombotic complications, including infarction of the renal allograft and bowel, acute myocardial infarction, and pulmonary embolism. Of note, two of the five patients had a history of recurrent vascular access thrombosis before transplantation. Four patients died within 5 yr after transplantation, one from HUS and three in the setting of sepsis or disseminated infection.

In the past, the occurrence of *de novo* RTMA/HUS after renal transplantation was linked to the use of cyclosporine or tacrolimus (23,24), suggesting that these agents may directly damage the vascular endothelium and possibly also induce platelet aggregation (23–26). Despite the widespread use of cyclosporine, however, RTMA/HUS occurs rarely after renal transplantation, *i.e.*, in approximately less than 5% of recipients (24,26,27). Therefore, it is likely that other factors play an important role as well. Whether the presence of ACA in the sera of renal transplant recipients predisposes to the occurrence of RTMA/HUS is unknown. Indeed, ACA or lupus anticoagulants have been shown to be present in a subset of chronic hemodialysis patients (6 to 22%), and their presence was associated with recurrent vascular access thrombosis (28,29). Furthermore, ACA are frequently found in patients with HCV infection (11), which is prevalent worldwide among chronic hemodialysis patients (30). Thus, circulating ACA are likely to be present in a subset of patients before transplant.

Our series suggests that ACA may be implicated in the pathogenesis of RTMA/HUS in a subset of HCV-positive renal transplant recipients. ACA were positive in these five patients, compared with only one of 13 other HCV-positive recipients.

**Table 4. Therapy and outcome**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Therapy</th>
<th>Outcome (time of death or most recent follow-up)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Plasmapheresis, CyA discontinued</td>
<td>Died (21 d): HUS associated with fulminant hepatic and renal failure with necrotic bowel and renal allograft</td>
</tr>
<tr>
<td>2</td>
<td>Bx 1: No change in therapy, Bx 2: CyA discontinued</td>
<td>Died (3 mo): acute myocardial infarction + coagulopathy + disseminated CMV infection and aspergillosis</td>
</tr>
<tr>
<td>3</td>
<td>CyA discontinued</td>
<td>Died (21 mo): renal allograft failure + pneumonia with sepsis</td>
</tr>
<tr>
<td>4</td>
<td>CyA reduced from 8.5 to 7 mg/kg, and MP pulses</td>
<td>Died (5 yr): pneumonia with sepsis</td>
</tr>
<tr>
<td>5</td>
<td>CyA discontinued for 4 d, then restarted; MP pulses + OKT3 for associated ACR</td>
<td>Doing well (5 yr): creatinine 1.8 mg/dl, CyA dose 2.5 mg/kg</td>
</tr>
</tbody>
</table>

*ACR, acute cellular rejection; HUS, hemolytic uremic syndrome; CMV, cytomegalovirus. Other abbreviations as in Table 2.*
without RTMA. Indeed ACA, particularly of the IgG isotype, have been strongly associated with the development of both arterial and venous thrombosis (17,31,32), as well as RTMA in primary antiphospholipid antibody syndrome, in lupus patients, or during pregnancy (14–16). The precise underlying mechanisms linking ACA to RTMA remain to be determined. They could include antiendothelial or antiplatelet activity of some ACA (17,33). The possible role of HCV, in association with ACA, also remains to be clarified since it has been suggested that HCV per se may possess procoagulant properties (34). In addition, we have recently observed “idiopathic HUS” in the native kidneys of two patients with chronic HCV infection and high titers of ACA. The first patient presented with “idiopathic HUS,” and the second patient was a liver transplant recipient with recurrence of HCV infection in the allograft (our unpublished observations). Finally, it should be emphasized that some posttransplant RTMA/HUS are not associated with the presence of ACA. In our experience, seven HCV-negative patients were identified who developed RTMA/HUS after renal transplantation without demonstrably elevated ACA levels in their sera.

The demonstration of RTMA reported here represents a previously unreported acute renal syndrome occurring in HCV-positive renal allograft recipients. In native kidneys, the association of HCV infection with cryoglobulinemic membranoproliferative glomerulonephritis is now well established (1,3,4,35). In transplant kidneys, de novo or recurrent membranoproliferative glomerulonephritis has also been recently reported (3,6–8). Interestingly, when membranoproliferative glomerulonephritis occurs after renal transplantation, cryoglobulin detection and characterization can be very difficult, possibly due to the immunosuppressive therapy that may reduce the cryoglobulin levels and/or alter the antigen-antibody ratio (6,8). Notably, in the reported series, none of the patients with cryoglobulinemic glomerulonephritis had extrarenal manifestations of cryoglobulinemia (6–8). Another complication of renal transplantation, “acute transplant glomerulopathy” or “acute allograft glomerulopathy,” is believed to represent an unusual variant of acute cellular rejection, possibly associated with cytomegalovirus infection (36,37). Recently, acute transplant glomerulopathy has been associated with HCV infection, both in HCV-positive recipients and in HCV-negative recipients who received kidneys from HCV-positive donors (9,10). In their series, Cosio et al. found a high prevalence of acute transplant glomerulopathy (approximately 50%) in HCV-positive patients, and these authors proposed that acute transplant glomerulopathy may be due to a direct effect of the virus on endothelial cells, and not due to cryoglobulins, because rheumatoid factors were negative and C3 levels were normal before transplantation (10). Similarly, in our study, rheumatoid factors were negative and C4 levels were normal in all five patients with RTMA, suggesting that significant levels of circulating cryoglobulins were not present before transplantation. It remains to be determined whether some patients with acute transplant glomerulopathy and HCV infection (10) also present with histologic features consistent with RTMA/HUS, and/or ACA in their serum.

Overall, it appears that the renal transplant recipient infected with HCV may be prone to a spectrum of acute renal manifestations, including de novo or recurrent membranoproliferative glomerulonephritis, acute transplant glomerulopathy, and/or RTMA/HUS. It is interesting to note that HCV infection has been associated with the development of several autoantibodies, some of which have the potential to be pathogenic, e.g., cryoglobulins with rheumatoid factor activity, and recently ACA (3,4,11,34). Whether the presence of cryoglobulins or ACA determines the type of renal manifestation remains to be studied. Finally, more work is needed to determine whether renal allograft recipients infected with HCV will benefit from antiviral strategies to prevent some of these renal manifestations.

Acknowledgments

This work was supported in part by the Helen and George Burr Endowed Research and Educational Fund in Support of Transplantation. Dr. Baid was supported by a Fellowship Training Award from the International Society of Nephrology (Amsterdam, The Netherlands). Dr. Chung was supported by National Institutes of Health Grant K08DK02209.

References


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