Transplant Glomerulopathy in the Absence of Donor Specific Antibodies

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BACKGROUND

Banff 05 eliminated chronic allograft nephropathy and divided anti-allograft lesions into antibody-mediated rejection (AMR) (acute and chronic) and T-cell-mediated rejection (CMR) (acute and chronic). Transplant glomerulopathy (TG) became a criterion for the diagnosis of chronic AMR, along with peritubular capillary (PTC) basement membrane multilayering and positive C4d staining. This nosology is consistent with the increasing presumption that TG is largely a manifestation of AMR. We report here our experience with TG in patients screened for donor specific antibodies (DSAs).

METHODS

The 50 cases were retrieved from the Surgical Pathology database of Thomas Jefferson University Hospital. All biopsies were obtained for cause and examined by both light and electron microscopy (**Figure 1**). C4d staining was by immunofluorescence microscopy until 12/2008 and thereafter by immunohistochemistry. DSAa were detected by Luminex Lab Screen.

RESULTS

The mean age of the 50 patients was 50.5 years (**Table 1**). Eleven patients were retransplants. The mean donor age was 39.3 years (31 deceased and 17 living). DSAs were absent in 24 of the 50 patients and detected in 26. 23 patients were completely negative and 1 patient had a weak antibody titer of 1600 MFI. The mean time to biopsy in those with DSAs was 62 months and 74 months in those without. The mean creatinine (mg/dL) at biopsy in the DSA group was 3.0 + 1.2 (SD) and 2.8 + 1.4 in the negative group. The mean proteinuria at biopsy in the same groups was 1.7 g + 1.6 and 3.6 + 3.9, respectively. None of the DSA-negative patients experienced acute CMR, whereas 10 patients with DSAs did. Two of the 26 DSA-positive patients had acute AMR, whereas none of the 24 DSA-negative patients did. None of the DSA-negative patients had C4d staining of PTC, whereas 7 of the DSA-positive patients did. Fifteen of the DSA-negative and 21 of the positive patients showed PTC basement membrane multilayering (**Figure 2**).

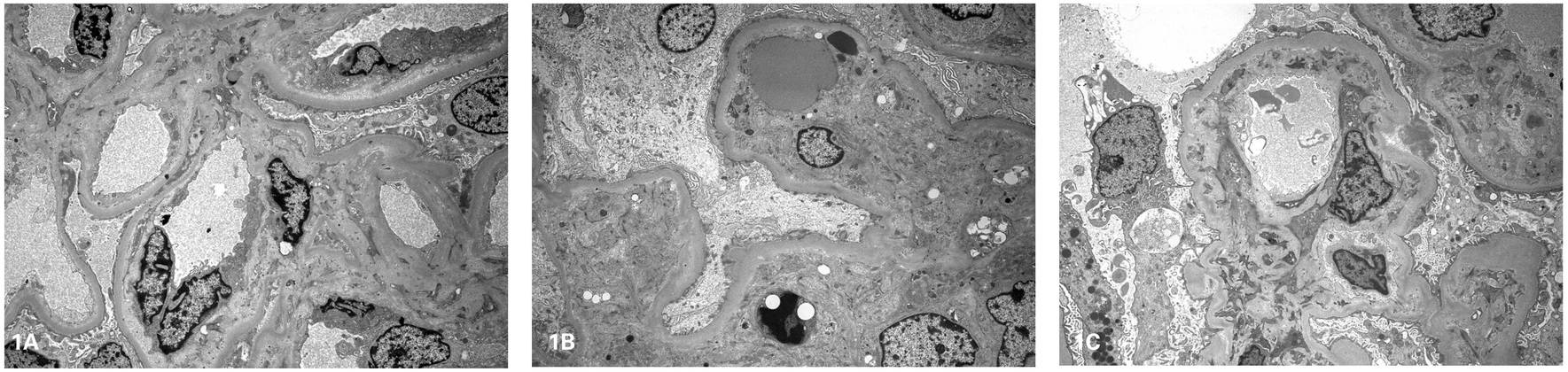

Figure 1A-C: Electron micrographs of 3 patients with transplant glomerulopathy.

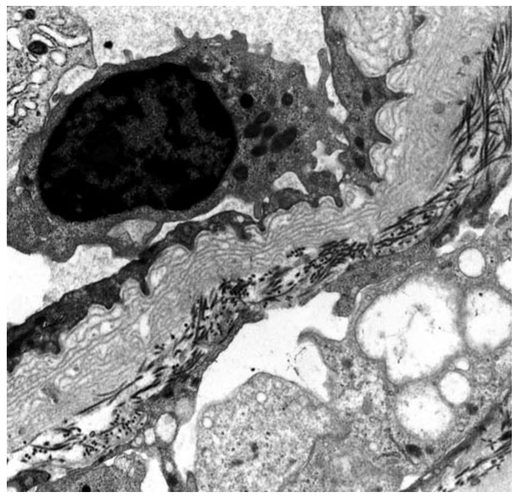

Figure 2: Prominent multilayering of the basement membrane of a peritubular capillary.

Table 1: DSA Data Analysis

	DSA +	DSA -
Number of patients	26	24
Males	12	9
Females	14	15
ACR	9/26	1/24
AHR	2/26	0/24
Chronic T cell rejection	25/26	24/24
Chronic Humoral rejection	2/26	0/24
Borderline rejection	5/26	2/24
C4d Glomeruli	9/26	9/24
C4d cappilaries	7/26	0/24
PTCBMML	21/26	15/24
Mean time to biopsy (months)	62 ± 48	74.2 ± 60.5
Mean Cr @ time of biopsy (mg/dL)	3.0 ± 1.24	2.86 ± 1.42
Mean proteinuria @ of biopsy (gm)	1.7 ± 1.6	3.6 ± 3.9
Graft loss	5/18	2/14
Recent Cr (mg/dL)	2.8 ± 1.24	2.9 ± 1.2
Recent Proteinuria (mg)	1.6 ± 1.3	2.3 ± 3.2

CONCLUSIONS

Half of our 50 patients with TG documented by EM had no DSAs or positive C4d staining in PTCs. Almost 70% of the patients evidenced PTC basement membrane multilayering. These patients were all diagnosed with chronic active CMR independently of the presence of TG. Cellular rejection mechanisms are likely the cause of the TG in this group. Patients with TG and DSAs are at greater risk for episodes of acute AMR and CMR. C4d staining of PTCs was evident in less than 40% and in the glomeruli in less than half. Interestingly, 25 of the 26 DSA+ patients were independently diagnosed with chronic active CMR.