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Original contribution

Polyoma virus nephropathy with simian virus 40 antigen–containing tubular basement membrane immune complex deposition

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Summary Polyoma nephropathy is an increasingly prevalent complication in kidney transplant recipients. We identified tubular basement membrane immune complexes in allograft recipients with polyoma nephropathy. To evaluate this lesion, biopsies demonstrating polyoma infection over a 2-year period were assessed for the presence, localization, and composition of tubular basement membrane immune complexes including simian virus 40 (SV40) antigen and for histologic classification according to Drachenberg. Charts were reviewed for clinical information. Thirteen of 26 biopsies from 11 of 20 patients demonstrated tubular basement membrane immune complexes, all of which contained C3, immunoglobulin G, and SV40 antigen. Deposits were in all nephron segments associated with tubular cell viral infection and tubulointerstitial inflammation; no SV40 antigen was in glomeruli. The Drachenberg histologic classification tended to be more advanced in biopsies with tubular basement membrane immune complexes, but not significantly so. There were no differences in patients with and without immune complexes with respect to age, sex, time after engraftment, and plasma viral load. Tubular basement membrane immune complexes were present in 5 of 6 patients who lost renal function and in 5 of 12 with currently functioning grafts ($P < .1$). Polyoma-associated tubular basement membrane immune complexes seem to be a local phenomenon, likely related to viral antigen shedding. The clinical significance is uncertain but may portend a worse prognosis.

1. Introduction

Polyoma virus nephropathy is an increasingly significant complication in renal transplantation, occurring in 2% to 10% of renal allograft recipients with up to 60% of these grafts lost [1,2]. Although asymptomatic polyoma virus reactivation in renal allografts is a well-documented occurrence, clinically apparent nephropathy occurs with direct infection of tubular epithelial cells with associated tubulointerstitial nephritis [3-5]. Tubular basement membrane (TBM) immune complex (IC) deposition is uncommon in renal allografts, usually occurring in the setting of lupus nephritis or other systemic immune-mediated processes. This is not known to be a factor in polyoma virus nephropathy. We and others recently have identified TBM IC deposits in patients with polyoma virus infection in renal transplant biopsies [6,7]. This study was undertaken to assess the incidence and possible significance of these IC deposits.

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2. Materials and methods

The study comprises renal allograft biopsies obtained over a 2-year period that demonstrated polyoma virus infection identified using morphology and immunoperoxidase with anti–simian virus 40 (SV40) antibody. Only those with adequate material for light, immunofluorescence, and electron microscopy were included. Biopsies were evaluated in the usual manner by light and electron microscopies. In addition, each biopsy was evaluated for the histologic pattern of polyoma virus nephropathy, evaluating viral cytopathic changes, tubular atrophy, interstitial fibrosis, and inflammation as described by Drachenberg [8]. For purposes of quantitation and comparison, the Drachenberg patterns were given numerical values such that pattern A = 0, B1 = 1, B2 = 2, B3 = 3, and C = 4. Electron microscopy was performed specifically in cortical and/or medullary areas of tubulointerstitial inflammation, which were available for all biopsies with and for all but 2 biopsies without TBM deposits by immunofluorescence, with between 40 and 85 tubular profiles per case examined. Areas with tubular cell viral inclusions and uninflamed renal parenchyma also were examined ultrastructurally when available.

All biopsies in this study, including controls, were subjected to routine immunofluorescence performed with antibodies to human immunoglobulin (Ig) G, IgM, IgA, C3, C1q, albumin, fibrinogen, κ light chain, and λ light chain by direct immunofluorescence and with antibody to C4d by indirect immunofluorescence. Biopsies additionally were assessed with anti-SV40 antibody using an indirect

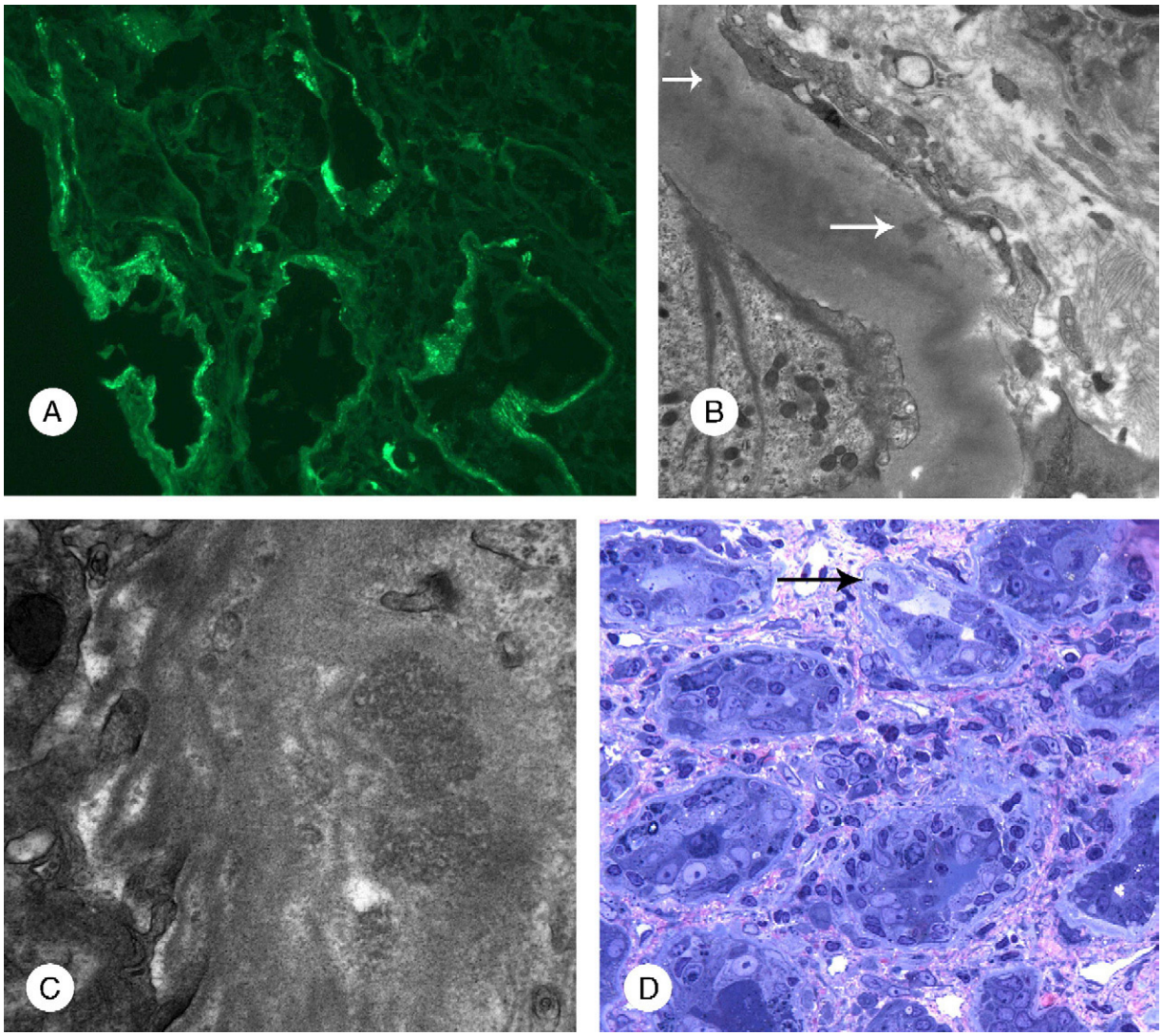

Fig. 1 Tubules with basement membrane IC deposits. A, Granular staining of TBM ICs for IgG (original ×80). B, C, and D, Biopsy with renal cortical tubules containing basement membrane deposits. B, Electron-dense deposits in TBMs (arrows) (original ×10 000). C, The deposits have a medium to coarsely granular appearance, occasionally occurring with an annular substructure with an electron-dense periphery and more lucent center (original ×19 000). D, Light microscopy demonstrating tubulointerstitial inflammation and acute tubular cell injury (arrow) (methylene blue ×80).