Dear Sir,

The differential diagnosis between renal allograft rejection and chronic cyclosporin (CS) nephrotoxicity presents serious difficulties for the histopathologist [1]. Vimentin expression in the cytoplasm of proximal tubule cells from drug-induced toxic nephropathies suggests that this intermediate filament could be used as a marker of both active cell regeneration and irreversible chronic tubular injury [2]. Chronic tubular injury has also been associated to changes in the expression of other antigens such as the epithelial membrane antigen (EMA), which is normally expressed by the distal tubule and collecting duct [3], and the CD15 antigen (Leu M1) on the proximal tubule brush border [4].

We have studied the expression of vimentin, EMA and CD15 in 48 renal allograft biopsies from patients subject to 2 different immunosuppressive protocols: prednisone plus low-dose CS (n = 31), and prednisone plus azathioprine (AZA; n = 17). Controls (n = 10) were obtained from otherwise normal kidneys removed after traumatic rupture. In the group treated with CS, a histopathological diagnosis of glomerulointerstitial allograft rejection was reached in 18 cases, while 5 of them showed chronic vasculointerstitial rejection, 4 acute interstitial rejection, 2 acute vascular rejection, 1 chronic transplant glomerulopathy and 1 recidivant focal and segmental hyalinosis. Among those patients treated with AZA, the most common histological diagnosis was chronic vasculointerstitial rejection (5 cases), followed by acute vascular rejection (4 cases), acute interstitial rejection (4 cases) and acute glomerulointerstitial rejection (4 cases). All biopsies were evaluated in a semiquantitative manner (0 = absent; 1 = mild; 2 = severe) for the presence of CS-associated changes including striped interstitial fibrosis, tubular calcifications, megamitochondria and hyaline droplets in the proximal tubules, peritubular capillary congestion, vascular myointimal fibrosis and hyaline arteriopathy. Ultrastructural confirmation of megamitochondria and hyaline droplets was performed in 50% of cases. The expression of vimentin, EMA and CD15 by the tubular cells was analyzed by avidin-biotin immunoperoxidase in paraffin-embedded tissue sections. The number of immunostained tubular profiles per 10 high-power (400 ×) microscopic fields was assessed.
Striped interstitial fibrosis and tubular megamitochondria and hyaline droplets were the changes significantly more common among the CS-treated patients than among those treated with AZA (59.25 vs. 38.46%, p < 0.05, for the presence of striped interstitial fibrosis, and 51.72 vs. 23.07%, p < 0.05, for the presence of megamitochondria and hyaline droplets; \( \chi^2 \) test). On the other hand, myointimal fibrosis and hyaline arteriopathy were more common in the group treated with AZA than in those patients treated with CS (76.92 vs. 51.72%; p < 0.05), which correlates with higher incidence of vascular rejection in the AZA-treated group.

Tubular atrophy was analyzed similarly by counting the number of profiles with thickening and/or splitting of the basement membrane and hyaline or granular casts. Both CS- and AZA-treated patients showed higher levels of expression of all 3 antigens (vimentin, EMA and CD15) than the controls (fig. 1a). CS-treated kidneys showed a significantly higher number of immunostained profiles than the AZA-treated ones, while atrophic tubules were more abundant in the AZA-treated group. Within the CS-
toxicity, are needed in order to confirm the diagnostic and therapeutic benefits of this type of analysis.

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