Modern Pathology (2004) 17, 1303

www.modernpathology.org

Response

Modern Pathology (2004) **17,** 1303. doi:10.1038/modpathol.3800233

In reply: The questions posed by Dr Meehan are important as they relate to a better understanding of the complex relations between herpesvirus infections and episodes of acute rejections.

We did not observe significant differences in the clinical and histological parameters in acute rejection episodes arising before, during, or after viral infections. Only one patient had a primary cytomegalovirus infection and so he was not exposed to the virus before the rejection (in this case the rejection followed the infection); all the other patients experienced reactivations. It is tempting to speculate that asymptomatic reactivations may have occurred. In agreement with this hypothesis, IL-10, which is supposed to mediate the effect of the viruses on B-cell proliferation and differentiation in plasma cells, was found in the plasma of renal transplanted patients with asymptomatic cytomegalovirus infections and liver transplanted patients with circulating EBV with or without symptoms.[1,2] We observed the deposition of C4d in rejections occurring during or after the infection, but not in those occurring before the infections. Thus, it could be easier to detect an antibody-mediated injury if the infection precedes the rejection. However, probably due to the low number of patients, this difference was not significant.

A reduction of the immunosuppressive therapy may have favored the occurrence of subsequent rejections; however, although the data concerning the treatment of the viral infections are not available, we believe that this is unlikely. In our department, immunosuppressive therapy is not reduced unless the disease is severe and the symptoms do not improve with the therapy; this, as mentioned in the paper, was observed in only one patient. To conclude, we would like to mention a recent study showing that anticytomegalovirus antibodies, present in patients with atherosclerosis, and crossreacting with a human heat-shock protein, are able to induce the apoptosis of endothelial cells[3] as further support of the concept that cytomegalovirus is an immunogenic stimulus and could play a role in the pathogenesis of chronic graft failure.

Marialuisa Valente[1] and Francesca Aiello[2]
[1]Universita Degli Studi Di Padova, Institute of Pathological Anatomy, Via A. Gabelli, 61, 35121 Padova, Italy and [2]Università Degli Studi Di Chieti, Department of Oncology and Neuroscience, Via dei Vestini 66100, Chieti, Italy

References

1 Nordoy I, Muller F, Nordal KP, *et al.* The role of the tumor necrosis factor system and interleukin-10 during cytomegalovirus infection in renal transplanted patients. J Infect Dis 2000;181:51–57.
2 Martinez OM, Villanueva JC, Lawrence-Miyasaki L, *et al.* Viral and immunologic aspects of Epstein–Barr infection in pediatric liver transplant recipients. Transplantation 1995;59:519–524.
3 Bason C, Corrocher R, Lunardi C, *et al.* Interaction of antibodies against cytomegalovirus with heat shock protein 60 in pathogenesis of atherosclerosis. Lancet 2003;362:1971–1977.