bcl-2, Epstein-Barr Virus–Latent Membrane Protein, EBNA-1, and EBNA-2 Staining in Posttransplantation Lymphoproliferative Disorders

To the Editor:

We read with great interest the report by Murray et al. We have analyzed 31 posttransplantation lymphoproliferative disorders (PTLDs; 18 renal and 13 heart/heart-lung cases) for bcl-2, Epstein-Barr virus–latent membrane protein (EBV-LMP), EBNA-1, and EBNA-2. We used the same antibodies as Murray et al.

All cases were EBV-LMP-positive. In more than 90% of cases, 80% of the neoplastic population showed strong LMP expression, ie, cytoplasmic and membrane staining, with dot-like Golgi accentuation in many cases. bcl-2 was uniformly strongly expressed in all cells seen in the various histologic types of PTLD. The bcl-2 and EBV-LMP staining pattern paralleled each other, and dot-like cytoplasmic accentuation was noted with bcl-2 as well.

Seventeen of the 31 cases were EBNA-1- and EBNA-2-positive. Only 2 cases showed discordant EBNA staining, ie, 1 case was EBNA-1-positive but EBNA-2-negative and another case displayed the reverse staining pattern. Positive staining was seen in the entire cellular spectrum encountered in PTLD: small lymphoid cells, immunoblasts, and Reed-Sternberg-like cells. Strikingly, variation in staining intensity was noted within each case and between cases. This heterogeneity was also noted by Oudejans et al. They concluded that PTLD exhibited a heterogenous pattern of EBV gene expression within individual cases.

The apparent downregulation of EBNA-1 expression has important implications, because EBNA-1 is thought to be necessary for maintaining the EBV genome in an episomal form and to be consistently expressed in all EBV infections. EBNA-1 and -2 are not consistently expressed in all EBV-associated conditions using immunohistochemistry. This may be due to lack of sensitivity of the antibodies, which cannot detect small amounts of protein that may be expressed. Alternatively, this negative reaction may be a true reflection of the EBNA status. This can be verified with the use of other monoclonal antibodies when they become available.

Our studies agree with and confirm the findings of Murray et al. There is a strong and consistent association between EBV-LMP and bcl-2 in the setting of PTLD, unlike in the setting of Hodgkin’s disease. We showed a heterogenous pattern of EBNA-1 and EBNA-2 staining within and between cases of PTLD. We conclude that EBV latent gene expression in PTLD may be variable, but a lymphoblastoid cell line pattern (unrestricted pattern of expression) is the commonest.

Runjan Chetty
Department of Anatomical Pathology
University of Natal Medical School
Durban, South Africa
Simon Biddolph
Kevin Gatter
University Department of Cellular Science
Oxford, UK

REFERENCES

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R Chetty, S Biddolph and K Gatter