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LETTERS TO EDITOR

ABO ANTIBODIES

I read with great interest the article by Hanto, Brunt, Goso, and Cole on the accelerated acute rejection of an A_2 renal allograft in an O recipient (*Transplantation* 1993; 56: 1580). I am in complete agreement with the authors' findings and am frankly surprised that this event does not occur more frequently in A_2 to O grafts. The presence of high titers of anti-A are quite common in group O individuals due to constant antigenic challenge from the environment and from A-like substances found in common bacterial vaccines.

However, since I was an ardent student of the ABO blood group system before becoming involved in HLA, it troubles me to see someone refer to an anti-A_2 antibody. Antibodies of such a specificity do not exist. In fact, the ABO blood group system has within it two distinct types of anti-A. An anti-A_1, which reacts only with group A_1 cells, and another antibody usually referred to as anti-A_{common}, which reacts with all group A red cells and tissues. The anti-A_{common} antibodies are the ones the authors describe.

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REJECTION AND HEPATITIS IN LIVER TRANSPLANTS

Roberts et al. (*1*) recently described the successful treatment of a liver allograft recipient with azathioprine and prednisone after failed courses of CsA, FK506, and RS61443. The ostensible diagnosis in their patient was rejection. However, the alternative possibility should be considered that the postoperative graft dysfunction was caused by hepatitis. Their patient underwent liver transplantation for cirrhosis secondary to hepatitis C and two small foci of hepatocellular carcinoma. This group has previously reported that recurrence of HCV hepatitis after liver transplantation may mimic the vanishing bile duct syndrome of rejection (*2*).

We also have recent data that support an association between these 2 conditions. In a study of 738 adults treated with cyclosporine from 5/1/87 to 7/31/89, 618 recipients (85%) who survived beyond the first 3 postoperative months served as a study population that now has a mean follow-up of 1200±490 (SD) days. Chronic rejection, manifested by the vanishing bile duct syndrome was diagnosed in 118 (19%) of these patients after a mean 530±400 posttransplantation days. Sixty-three (53%) of the 118 patients had recurrent or de novo hepatitis at a mean of 415±379 posttransplant days that was classified "non-A, non-B" in 46 (69%) of the 63 cases. In contrast, only 75 (15%) of the 500 patients without the vanishing bile duct syndrome ever had the diagnosis of hepatitis. As in the case reported by Roberts et al. (*1*), the histopathologic findings in patients with the dual diagnosis overlapping chronic hepatitis and chronic rejection were portal inflammation with bile duct damage involving a variable percentage of the ducts present and bile duct loss in <50% of the triads.

During the first clinical trials of FK506 for cases of refractory rejection (1989–1990), many liver recipients were sent to us from all parts of the United States for rescue from "acute" or "chronic" rejection. More than a third arrived with errors in diagnosis. These included unrecognized technical accidents such as arterial thrombosis or bile duct obstruction, lymphoproliferative disorders, and hepatitis due to CMV, HBV, or HCV. The first therapeutic adjustment in such cases was almost always reduction of immunosuppression. The report by Roberts et al. (*1*) would appear to be another such example in which the primary diagnosis turned out to have been recurrent hepatitis in a patient who was being systematically overimmunosuppressed. Recovery occurred when this error was corrected.

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REFERENCES

1. Roberts JP, Lake JR, Hebert M, Nikolai B, Ascher NL, Ferrell LD. Reversal of chronic rejection after treatment failure with FK506 and RS 61443. Transplantation 1993; 56: 1021.
2. Ferrell LD, Wright TL, Roberts J, Ascher N, Lake J. Hepatitis C viral infection in liver transplant recipients. Hepatology 1992; 16: 865.

EBER-1 GENE EXPRESSION IN POSTTRANSPLANT LYMPHOPROLIFERATIVE DISEASE

In their recent article on Epstein-Barr virus–associated lymphoproliferative disorders (*Transplantation* 1993; 56: 1394), Sokal et al. have quoted work at the University of Pittsburgh to suggest that immunosuppression should be lowered as soon as EBER-1 RNA is detected in liver transplant recipients. It is necessary to clarify that EBER-1 gene expression in itself is only a marker for the presence of latent Epstein-Barr virus infection. Small numbers of EBER-1–positive cells can be seen in tissues of healthy seropositive individuals (*1*). It is only a high viral load reflected by a sequential increase in the number of EBER-1–positive cells that should serve as a warning sign for the development of posttransplant lymphoproliferative disease. The actual function of EBER-1 RNA is not known with certainty, but there is no firm evidence yet that it is per se important in the pathogenesis of PTLD. Gene deletion experiments have shown that the EBER genes are not a prerequisite for B lymphocyte transformation in vivo (*2*). However, it is possible that EBER molecules could modulate the antiviral effects of interferons, and thereby create a milieu more favorable for survival of the virus in vivo (*3*, *4*).

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REFERENCES

1. Randhawa P, Jaffe R, Demetris A, et al. Expression of Epstein-Barr virus coded small RNA (by the EBER-1 gene in liver specimens from transplant recipients with post transplantation lymphoproliferative disease. N Engl J Med 1992; 327: 1750.
2. Swaminathan S, Tomkins B, Kieff E. Recombinant Epstein-Barr Virus with EBER genes deleted transforms lymphocytes and replicates in vitro. Proc Natl Acad Sci USA 1991; 88: 1546.
3. Clarke PA, Sharp NA, Arnad JR, Clemens M. Epstein Barr virus gene expression in interferon treated cells: implications for the regulation of protein synthesis and the antiviral state. Biochim Biophys ACTA 1990; 1050: 167.
4. Clarke PA, Schwemmie M, Schickinger J, Hilse K, Clemens MJ. Binding of Epstein-Barr virus small RNA EBER-1 to the double-stranded RNA activated protein kinase DAI. Nucleic Acids Res 1990; 19: 243.