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LETTER TO THE EDITOR

Prevalence of anti-HLA antibodies after liver transplantation

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The pathogenic role of anti-human leukocyte antigen (HLA) antibodies (AHA) after kidney transplantation is well established. Prospective studies have shown that donor-specific antibodies (DSA) can be detected before a decline in graft function or graft loss [1–3]. However, the potential clinical significance of AHA or DSA after liver transplantation (LT) remains unclear, although a recent study by Castillo-Rama *et al.* has shown that the presence of AHA and DSA before LT can play a significant role in decreasing graft survival [4,5]. We therefore determined the prevalence of AHA after LT. Between January 2007 and November 2007, all LT recipients who underwent transplantation at least 6 months before and were followed up regularly at our clinic ($n = 95$) were screened for AHA. All post-transplantation analyses were performed with the screening anti-HLA tests using Multiplex technology and, if positive, determination of specificity was performed using the Single Antigen test (Labscreen Mixed and Labscreen Single Antigen, One Lambda, Canoga Park, CA, USA).

A liver biopsy had previously been performed in 55 of the 95 patients based on clinical grounds. No protocol biopsies were performed. Immunosuppression was calcineurin inhibitor-based in 90 patients, sirolimus-based in four patients and one patient had no anti-rejection therapy (operationally tolerant). There were 65 males and 30 females. The causes of liver disease were: alcoholic cirrhosis ($n = 31$), hepatitis C ($n = 19$), hepatitis B ($n = 10$), metabolic and congenital ($n = 10$), autoimmune hepatitis ($n = 8$), cryptogenic cirrhosis ($n = 6$), carcinoma ($n = 5$), primary biliary cirrhosis ($n = 3$), primary sclerosing cholangitis ($n = 1$), Echinococcosis ($n = 1$) and retransplant ($n = 1$).

The mean time from LT to study was 85 months (range 6–248 months). Overall, AHA were found in 23 (24.2%) of patients. Five had anti-class I alone, 14 anti-class II alone, and 4 had both anti-class I and II. Only 4 of the 95 patients (4.2%) had DSA (one anti-class I and 3 anti-class II).

Of note, patients with autoimmune hepatitis ($n = 8$) were not more likely to have AHA (1/8) or DSA (0/8) when compared with the other patients. Similarly, there were no significant differences in the prevalence of AHA or DSA between males and females, and we did not find a trend to a higher prevalence of AHA in long-term (i.e. >85 months post-LT) recipients.

Twenty-one of 95 patients (22.1%) had a history of past or current biopsy-proven or radiological biliary complications (e.g. ischemic type biliary lesions or biliary anastomosis stricture, chronic rejection), but the prevalence of biliary complications was not different in patients with or without AHA. However, among the four patients with DSA, 3/4 had biliary complications (two with biopsy-proven chronic rejection, in association with biliary strictures, and one retransplanted patient with ischemic cholangitis following late hepatic artery thrombosis with class I DSA directed against the second donor), vs. 1/19 (5.3%) patients with AHA but no DSA ($P = 0.009$), vs. 16/72 (22.2%) patients without AHA ($P = 0.046$). Among the four patients with post-transplant DSA, we could determine that these were *de novo* DSA in two cases (both with biliary complications), whereas pretransplant sera were not available for testing in the other two patients. Immunosuppression was not different in patients with or without DSA.

We found an AHA prevalence after LT of 24%; however, only those patients with DSA had an increased prevalence of biliary complications. Future larger prospective studies should precisely analyze the time course of DSA development to determine if the association between DSA and biliary complications is causative and of clinical significance. This association, if confirmed, should be further analyzed.

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References

1. Cardarelli F, Pascual M, Tolkoff-Rubin N, *et al.* Prevalence and significance of anti-HLA and donor-specific antibodies long-term after renal transplantation. *Transpl Int* 2005; **18**: 532.
2. Campos EF, Tedesco-Silva H, Machado PG, *et al.* Post-transplant anti-HLA class II antibodies as risk factor for late kidney allograft failure. *Am J Transplant* 2006; **6**: 2316.
3. Terasaki PI, Ozawa M, Castro R. Four-year follow-up of a prospective trial of HLA and MICA antibodies on kidney graft survival. *Am J Transplant* 2007; **7**: 408.
4. McKenna RM, Takemoto SK, Terasaki PI. Anti-HLA antibodies after solid organ transplantation. *Transplantation* 2000; **69**: 319.
5. Castillo-Rama M, Castro MJ, Bernardo I, *et al.* Preformed antibodies detected by cytotoxic assay or multibead array decrease liver allograft survival: role of human leukocyte antigen compatibility. *Liver Transpl* 2008; **14**: 554.

