G42 Use of Expert Consultation in the Evaluation of Tissue Donors With a Postmortem Diagnosis of "Hepatitis" to Determine Eligibility For Transplantation

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The goals of this presentation are 1) to emphasize the importance of attempting to specifically determine and report infectious vs. noninfectious etiologies of hepatitis in cadaveric donors of tissue for allotransplantation, 2) to emphasize that correlation of morphology with viral serologic testing results is integral to establishing the initial diagnosis of viral hepatitis, and 3) to assess the utility of expert consultation in making this determination.

Introduction and Hypothesis: Chronic hepatitis is a clinicalpathologic syndrome which may result from a number of causes including viral infections, autoimmune or metabolic diseases, drugs (medications), or other unknown etiology (cryptogenic). Chronic hepatitis is defined clinically as inflammatory liver disease continuing for at least 6 months. However, patients with chronic hepatitis may have asymptomatic clinical phases, for example in hepatitis C and autoimmune hepatitis. Patients with viral hepatitis, especially infections due to hepatitis C virus (HCV) or to hepatitis B virus (HBV) with or without hepatitis D virus (HDV) superinfection, are at significantly increased risk for developing hepatic cirrhosis and hepatocellular carcinoma. Chronic hepatitis due to viral infection is a clear contraindication for blood donation and is likewise a contraindication for allogeneic organ and tissue donation. The Federal Drug Administration (FDA) and American Association of Tissue Banks (AATB) standards require tissue donors to be screened by medical / social history for risk factors for viral hepatitis and to have negative laboratory tests for hepatitis B surface antigen (HBsAg), Hepatitis B core antibody (antiHBc), hepatitis C virus antibody (anti-HCV), and human immunodeficiency virus, types 1 and 2 (anti-HIV-1/2). Cadaveric donation of tissue (e.g. bone, skin, fascia, tendons, heart valves, and corneas) may also be preceded or followed by postmortem examination of the donor, including liver biopsy. Since chronic hepatitis is a clinical-pathologic syndrome resulting from both infectious and non-infectious causes, it was hypothesized that many potential tissue donors with a postmortem diagnosis of "hepatitis" without reference to etiology made initially at autopsy, but with otherwise acceptable AATB donor criteria, would have minimal liver inflammation resulting from non-specific or non-infectious causes and would therefore be acceptable donors.

Methods: Seven potential cadaveric donors ranging in age from 16 to 72 years were referred to a regional tissue bank by either hospital (n=4) or medical examiner's office (n=3) staff. The causes of death included cardiac events (n=3; 1 acute myocardial infarction, 1 hypertensive cardiovascular disease, and 1 hemopericardium with cardiac tamponade), vascular rupture (n=2; 1 abdominal aortic aneurysm and 1porta hepatis), and head trauma (n=2; 1 gunshot and 1 blunt injury). Based on initial screening criteria, including a detailed medical / social history obtained from next-of-kin and an external physical examination, the donors were approved as being suitable for tissue donation. After informed consent was obtained from next-of-kin, donor tissues including skin, saphenous and femoral veins, heart (for valves), ilia, fascia lata, long bones and achilles tendons of the lower extremities were procured under aseptic conditions within 24 hours of asystole. In all cases, a postmortem examination was performed either before or after the tissue procurement by a pathologist from the referring institution. Infectious disease testing was performed on anteor postmortem plasma or serum samples meeting acceptable plasma dilution criteria with FDA-approved cadaveric test systems for HBsAg, anti-HBc, anti-HCV, anti-HIV-1/2, HIV p24 Ag, and HIV DNA by PCR. These seven donors, each with an autopsy diagnosis of "hepatitis" without reference to specific etiology, were re-evaluated after procurement of tissues. These cases, with complete clinical and laboratory findings including routine histological sections of liver from autopsy and results of infectious disease tests, were subsequently referred to independent expert gastrointestinal / liver pathologist consultants for a formal second opinion regarding the possible diagnosis of viral / infectious hepatitis. Tissues of donors with clinical and histological findings determined by the expert to be insignificant, non-specific or non-infectious were processed to a variety of grafts at an AATB-certified processing facility and released for transplantation. Clinical follow-up was obtained.

Results: For all seven potential donors, screening criteria from the medical / social history, including risk factors for infectious hepatitis, and the physical examination were acceptable on re-evaluation. In each case, all infectious disease laboratory test results for viral hepatitis markers were also acceptable. In addition to other findings, each autopsy report from the referring institution listed "hepatitis" as a significant postmortem finding. As these reports did not specify either an infectious or non-infectious etiology of hepatitis, histological sections of liver from autopsy were obtained in order to assess the suitability of grafts derived from each donor for transplantation. Preliminary review in all cases showed only minimal to mild, patchy inflammation limited to portal areas. The histological sections, along with clinical and laboratory results, were forwarded to independent expert gastrointestinal / hepatic pathologist consultants for a formal opinion of the possibility of hepatitis of infectious cause. In all seven cases, in the opinion of the expert,

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the findings were either a) unremarkable hepatic parenchyma (n=2), b) non-specific portal triaditis (n=4), or c) non-diagnostic of chronic hepatitis of viral etiology (n=1). Based upon these opinions, the donors were approved as suitable for transplantation and tissues from the seven donors were processed into a total of 254 surgical allografts, potentially benefiting an equivalent number of recipient patients. At the time of this writing (12.5 to 47.5-month follow-up from date of procurement), no cases of infectious hepatitis have been reported in the graft recipients.

Conclusion: Chronic hepatitis of viral etiology is a contraindication for cadaveric tissue donation. In contrast, hepatic inflammation due to non-infectious etiologies may not be prohibitive for donation. Thus, at postmortem examination of decedents who have donated tissues for transplantation, efforts should be made to accurately diagnose hepatitis and, if possible, to further determine the specific etiology (infectious or non-infectious) of hepatic inflammation. Correlation of morphology with viral laboratory testing is often integral to establishing the diagnosis. Typical histological findings of hepatitis of varying etiologies will be discussed. Microscopic findings of only mild, patchy portal triaditis should be interpreted as "hepatitis" with caution when viral serologic tests are negative or in the absence of such tests. The use of consultation by expert gastrointestinal/hepatic pathologists may assist hospital autopsy pathologists, forensic pathologists and/or tissue bank medical directors in making this determination and may result in an increase in the supply of acceptable tissue for transplantation to many patients needing surgical allografts.

Hepatitis, Tissue, Allograft

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