Chapter 3.1. Liver Donor Organ Evaluation
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Protocols for histologic evaluation of potential donor livers for steatosis and other pathology vary by center. This assessment may be performed by frozen section at the time of organ evaluation, “back-table” or postreperfusion “time-zero” biopsies, or routine biopsy of potential living donors during evaluation for organ donation. Mild mononuclear portal inflammatory cell infiltrates (Figure 3.1.1), bile ductular proliferation (Figure 3.1.2), and cholestasis (Figure 3.1.3) are nonspecific findings and do not preclude successful transplantation.

Hepatic steatosis is assessed as the percentage of the biopsy involved by macrovesicular or “large-droplet” steatosis. In macrovesicular steatosis, one or a few large fat droplets displace the nucleus to the edge of the hepatocyte (Figure 3.1.4). Frozen section may be used to assess potential graft organs for steatosis because steatosis cannot be reliably assessed by gross

**Figure 3.1.1.** Mild portal inflammation. Donor organs may exhibit mild portal inflammation with or without bile ductular proliferation. These changes are common and are not a contraindication to transplantation.

**Figure 3.1.2.** Bile duct proliferation. This donor liver biopsy demonstrates several bile duct profiles (arrows) with only one hepatic arteriole. This finding is not a contraindication to using this liver for transplantation.

**Figure 3.1.3.** Cholestasis. Mild hepatocellular and/or canalicular cholestasis may be seen in a cadaveric donor liver. These changes may be related to circumstances around the donor’s demise and are not a contraindication to transplantation.
Figure 3.1.4. Macrovesicular steatosis. In macrovesicular steatosis, one or a few round fat droplets displace the hepatocyte nucleus to the edge of the cell.

Figure 3.1.5. Mild macrovesicular steatosis (<30%; frozen section). Cadaveric livers with mild steatosis are widely considered suitable for transplantation.

Figure 3.1.6. Moderate macrovesicular steatosis (30%–60%). Although this liver contains greater than mild steatosis, it may be considered acceptable for use in selected settings.

Figure 3.1.7. Severe macrovesicular steatosis (>60%). This graft was found to be severely steatotic (80% steatosis overall) on routine time-zero biopsy; no frozen section was performed prior to implantation. Although in this case the organ functioned well and the recipient experienced a normal posttransplant recovery, severely steatotic livers would not be used in most settings if detected prior to implantation.

Figure 3.1.8. Small droplet steatosis. This previously frozen biopsy demonstrates scattered small fat droplets (arrows) that neither fill the cell nor displace the nucleus. These droplets resolve after implantation of the liver and do not impact graft function.

evaluation, and moderate or severe steatosis has been associated with increased risk of poor or delayed graft function in some series. There is no uniformly acceptable amount of steatosis, and reported graft and patient outcomes for steatotic livers vary widely. Grafts with less than 30% steatosis are usually considered suitable for transplantation (Figure 3.1.5), whereas those with greater than 30% (Figure 3.1.6) or even greater than 60% (Figure 3.1.7) are less desirable but have been used successfully in some circumstances. Special stains for fat (oil red O) may be used in steatosis assessment but are not required. “Small-droplet”
steatosis refers to a single or few small lipid droplets that do not displace the nucleus (Figure 3.1.8). This finding alone does not adversely impact graft function. Pure microvesicular steatosis is a rare finding that manifests as multiple tiny lipid droplets that surround the nucleus and impart a foamy or vesicular appearance to the hepatocyte cytoplasm (Figure 3.1.9). Pure microvesicular steatosis likely represents an agonal or ischemic change that does not impact graft function.

Extended-criteria grafts do not meet standard donation criteria due to factors that increase the risk of early graft failure or predispose to inferior graft or patient survival. Examples include steatotic livers, livers harvested after cardiac death, and organs from hepatitis-C–positive donors (Figure 3.1.10) or donors of advanced age. These organs are offered to patients who will not, or likely will not, receive a standard criteria graft due to advanced donor age, tumor burden, or low graft availability. Frozen sections may be performed to assess these organs for advanced scarring, vascular pathology, or other abnormalities. While precise staging of fibrosis requires a trichrome stain, advanced scarring is generally apparent and can be visualized more easily with use of polarized light. A host of other unusual and unexpected findings, including alpha-1 antitrypsin deficiency, amyloidosis, histoplasmosis, and varying degrees of iron overload (Figure 3.1.11 and 3.1.12), have also been reported in living and cadaveric donor livers. While a few cases of “recurrent” iron overload have been reported with use of hemochromatotic donor livers, in other reports organs with iron and other pathologies such as alpha-1 antitrypsin deficiency have been used successfully.
References
Preservation injury, also termed ischemia–reperfusion injury or simply reperfusion injury, is commonly seen in early posttransplant biopsies, is typically mild, and usually resolves within 1 to 2 weeks. These changes are attributed to ischemic and inflammatory injury incurred during donor demise or graft harvesting, preservation, and reperfusion. These changes may be worse in the setting of preexisting donor disease. Biopsy during the early posttransplant period may be performed to evaluate a poorly functioning graft or per protocol. The major role of the surgical pathologist in this setting is to avoid misdiagnosis of the changes as a form of rejection or other posttransplant complication.

Preservation injury may be manifest as a spectrum of changes ranging from mild hepatocyte swelling with Kupffer cell hyperplasia and scattered apoptotic hepatocytes (Figures 3.2.1 and 3.2.2) to areas of necrosis and hemorrhage (Figure 3.2.3).}

Figure 3.2.1. Preservation injury. This allograft biopsy taken 4 days after transplantation demonstrates diffuse hepatocyte swelling with scattered apoptotic hepatocytes (arrows) and Kupffer cell hyperplasia. These changes are most prominent in the centrilobular region.

Figure 3.2.2. Preservation injury. This day 2 posttransplantation liver biopsy demonstrates mild lobular injury manifest as increased lobular cellularity with hepatocyte swelling, cholestasis, mild lobular inflammation, and Kupffer cell hyperplasia. These changes are most prominent in the centrilobular region (arrow indicates central vein).

Figure 3.2.3. Preservation injury: necrosis and hemorrhage. This liver biopsy taken 2 days after transplantation demonstrates areas of confluent hepatocyte necrosis and hemorrhage.
congestion, hemorrhage, and even confluent hepatocyte necrosis (Figure 3.2.3). Cholestasis is common (Figure 3.2.4), and mitotic figures are commonly seen (Figure 3.2.5). The changes are often most prominent in the centrilobular areas. The portal tracts may exhibit mild inflammation, bile ductular proliferation, and even evidence of mild bile duct injury (Figure 3.2.6). These changes can be distinguished from acute cellular rejection (ACR) based on the nature of the inflammatory cell infiltrates and absence of endotheliitis.

The portal infiltrates seen in rejection are more dense with enlarged, activated—appearing lymphocytes and often also contain eosinophils. The inflammatory cells also tend to be centered on the vein and bile duct in ACR. Neutrophils may be a prominent part of the portal infiltrate in preservation injury, often associated with a periportal ductular reaction (Figure 3.2.7). These findings are distinguished from acute ascending cholangitis by the absence of intraluminal neutrophil collections and portal edema. Antibody-mediated rejection may be difficult to distinguish from preservation injury. Fibrinoid necrosis, complement C4d positivity, and correlation and detection of donor-specific antibodies would support a diagnosis of antibody-mediated rejection.
References