

Liver Transplant Pathology: messages for the non-specialist

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There are about 630 liver transplants per year in the UK, and about 6000 patients alive with a transplanted liver¹. Long term follow-up can be shared with the local hepatology centre; histopathologists outside the transplant centre may therefore receive late post-transplant biopsies.

These biopsies are challenging with a wide differential diagnosis. Because of the importance of comparison with previous biopsies and of good clinico-pathological correlation, it is recommended that post-transplant biopsies are always referred to the pathologist at the transplant centre². However, the local pathologist often provides the initial opinion.

Most indications for liver transplantation in adults can recur in the graft (not so in children where transplant for biliary atresia or metabolic diseases is common). The differential diagnosis in adult liver transplant biopsies includes rejection, recurrent disease, surgical complications (vascular and biliary) and *de novo* liver disease including infection and drug reaction. Liver transplantation pathology is comprehensively reviewed in standard texts and review articles^{3,4}. As in non-transplant biopsies, histological features of the different diagnoses overlap, and more than one condition may be present.

The Banff Working Group has produced a helpful publication on the interpretation of late post transplant biopsies⁵. This focuses on the differential diagnosis of inflammatory changes, based on the distribution, severity, and nature of the inflammation among seven different compartments of the liver biopsy (see table). This approach, from systematic evaluation of individual features, integration into disease patterns, and clinical differential diagnosis is the same as for non-transplant biopsies.

1. https://www.uktransplant.org.uk/ukt/statistics/transplant_activity_report/
2. Tissue pathways for liver biopsies for the investigation of medical disease and for focal lesions
<http://www.rcpath.org/resources/pdf/g064tpliverandfocalmay08final.pdf>
3. Hubscher SG, Portmann BC. Transplantation pathology. In: Burt AD, Portmann BC, Ferrell LD. *MacSween's Pathology of the Liver (5th edition)*. Edinburgh: Churchill Livingstone, 2006:815-879.
4. Jones KD, Ferrell LD. Interpretation of biopsy findings in the transplant liver. *Seminars in diagnostic pathology* 1998;15:306-317
5. Banff Working Group. Liver Biopsy interpretation for causes fo late liver allograft dysfunction. *Hepatology* 2006;44:489-501

Web site for liver CPD: <http://www.virtualpathology.leeds.ac.uk/index.php>

Table: Histopathological features most commonly detected with various causes of late liver allograft dysfunction

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Histopathological features	autoimmune hepatitis	acute rejection	chronic rejection	chronic viral hepatitis B&C	Primary biliary cirrhosis	PSC/biliary stricture
distribution, severity, and composition of portal inflammation	usually diffuse; predominantly mononuclear of varying intensity: often prominent plasma cell component	usually diffuse: variable intensity: mixed 'rejection-type' infiltrate	Patchy: usually minimal or mild lymphoplasmacytic	Patchy: variable intensity: predominantly mononuclear: nodular aggregates	Noticeably patchy and variable intensity: predominantly mononuclear: nodular aggregates and granulomas	Usually patchy to diffuse depending on stage: mild neutrophilic, eosinophilic, or occasionally mononuclear predominant
Presence and type of interface activity	Prominent and defining feature is usually necroinflammatory-type: often plasma cell-rich	Focally present and mild necroinflammatory type	minimal to absent	variable: usually not prominent: necroinflammatory-and ductular-type	important features later in disease development: ductular and necroinflammatory-type with copper deposition	prominent and defining feature: ductular-type with portal and periportal oedema
Bile duct inflammation and damage	variable: if present, involves a minority of bile ducts	present and usually involves a majority of bile ducts	focal ongoing lymphocytic bile duct damage: inflammation wanes with duct loss	variable: if present, involves a minority of bile ducts	granulomatous or focally severe lymphocytic cholangitis is diagnostic in proper setting	periductal lamellar oedema: 'fibrous cholangitis': acute cholangitis: multiple intra-portal ductal profiles
biliary epithelial senescence changes and small bile duct loss	absent or involves only a minority of ducts/portal tracts, but may be focally severe	absent or involves only a minority of ducts	senescence/atrophy/ atypia involve a majority of remaining ducts	absent or involves only a minority of ducts	small bile duct loss associated with ductular reaction	small bile duct loss associated with ductular reaction
perivenular mononuclear inflammation and/or hepatocyte dropout	variable: can involve a majority of perivenular regions, similar to rejection; may be plasma cell-rich	variable, if defining feature should involve a majority of perivenular regions: may also show subendothelial inflammation of vein	usually present but variable	variable but generally mild: if present, involves a minority of perivenular regions	variable, but generally mild: if present, involves a minority of perivenular regions	absent
lobular findings and necroinflammatory activity	variable severity: rosettes may be present and/or prominent	variable: if present, concentrated in perivenular regions	variable: if present, concentrated in perivenular regions	disarray variable: variable severity: necroinflammatory activity	mild disarray: parenchymal granulomas: periportal copper deposition and cholestasis are late features	disarray unusual: neutrophil clusters +/- cholestasis
pattern of fibrosis during progression toward cirrhosis	usually macronodular: posthepatic pattern	rare	uncommon, if present, usually a venocentric pattern, may evolve to biliary pattern over time	usually macronodular, hepatic pattern: may be micronodular	biliary pattern	biliary pattern

to accompany