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**Pathology in Patients with Chronic Liver Disease: A Practical Approach to Liver Biopsy Interpretation in Patients with Acute and Chronic Liver Diseases** 361

Audrey Deeken-Draisey, Sambasiva M. Rao, and Guang-Yu Yang

Liver biopsy and histologic examination are the mainstay for diagnosing liver diseases, despite advances in imaging and molecular procedures. Liver biopsy can provide useful information regarding the structural integrity and type and degree of injury, disease activity, response to treatment, progression of disease and degree/staging of fibrosis. Liver biopsies evaluate acute and chronic liver diseases, and mass-forming lesions. The role of the pathologist is to integrate clinical, serologic, and biochemical data with morphologic changes and provide a comprehensive diagnosis. This review focuses on basic principles necessary for proper interpretation of liver biopsy specimens in patients with chronic liver disease.

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Justin R. Boike and Steven L. Flamm

Transjugular intrahepatic portosystemic shunts is an established treatment for portal hypertensive complications. Advancements in technology and technique have led to novel indications, including treatment of chronic portal vein thrombosis and use before abdominal surgery to alleviate portal hypertensive complications. Use of TIPS can facilitate the embolization of large portal-systemic shunts to alleviate refractory hepatic encephalopathy owing to excessive portal shunting. Despite these advances, transjugular intrahepatic portosystemic shunts is an invasive procedure with risk for complications and should be performed at a center with expertise to ensure a successful patient outcome.

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Lauren Myers and Joseph Ahn

Focal nodular hyperplasia and hepatocellular adenoma are benign liver lesions that occur most frequently in women and may be found as incidental findings on imaging. Hepatocellular adenomas may be infrequently associated with malignant progression or risk of rupture and as such, require surveillance or definitive treatments based on their size threshold. It is important clinically to differentiate these lesions, and utilizing imaging modalities such as contrast enhanced ultrasound or magnetic resonance imaging can be helpful in diagnosis. Further molecular subtyping of hepatocellular adenoma lesions may be beneficial to describe risk factors and potential future clinical complications.

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Amanda Cheung and Paul Kwo

Viral hepatitis can cause a wide spectrum of clinical presentations from a benign form with minimal or no symptoms to acute liver failure or death. Hepatitis D coinfection and superinfection have distinct clinical courses, with the latter more likely leading to chronic infection. Management of chronic hepatitis D virus is individualized because of the paucity of

treatment options and significant side effect profile of currently available treatments. Sporadic cases of hepatitis E caused by contaminated meats are becoming increasingly prevalent in immunocompromised hosts. Human herpesviruses are an important cause of disease also in immunocompromised individuals.

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Adam P. Buckholz and Robert S. Brown Jr.

Cholangiocarcinoma is a highly lethal biliary epithelial tumor that is rare in the general population but has increased rates in patients with primary sclerosing cholangitis (PSC). It is heterogenous, and management varies by location. No effective prevention exists, and screening is likely only feasible in PSC. Patients often present in an advanced state with jaundice, weight loss, and cholestatic liver enzymes. Diagnosis requires imaging with magnetic resonance cholangiopancreatography, laboratory testing, and endoscopic retrograde cholangiopancreatography. Potentially curative options include resection and liver transplant with neoadjuvant or adjuvant chemoradiation. Chemotherapy, radiation, and locoregional therapy provide some survival benefit in unresectable disease.

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Kathy M. Nilles and Steven L. Flamm

Thrombocytopenia is common in advanced liver disease, and such patients frequently need invasive procedures. Numerous mechanisms for thrombocytopenia exist, including splenic sequestration and reduction of levels of the platelet growth factor thrombopoietin. Traditionally, platelet transfusions have been used to increase platelet counts before elective procedures, usually to a threshold of greater than or equal to 50,000/ $\mu$ L, but levels vary by provider, procedure, and specific patient. Recently, the thrombopoietin receptor agonists avatrombopag and lusutrombopag were studied and found efficacious for increasing platelet count in the outpatient setting for select patients with advanced liver disease who need a procedure.

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Lamia Y.K. Haque and Joseph K. Lim

Budd-Chiari syndrome (BCS), or hepatic venous outflow obstruction, is a rare cause of liver disease that should not be missed. Variable clinical presentation among patients with BCS necessitates a high index of suspicion to avoid missing this life-threatening diagnosis. BCS is characterized as primary or secondary, depending on etiology of venous obstruction. Most patients with primary BCS have several contributing risk factors leading to a prothrombotic state. A multidisciplinary stepwise approach is integral in treating BCS. Lifelong anticoagulation is recommended. Long-term monitoring of patients for development of cirrhosis, complications of portal hypertension, hepatocellular carcinoma, and progression of underlying diseases is important.

**Alpha1-Antitrypsin Deficiency: A Cause of Chronic Liver Disease**

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Vignan Manne and Kris V. Kowdley

Alpha1-antitrypsin deficiency (A1ATD) is an inherited cause of chronic liver disease. It is inherited in an autosomal codominant pattern with each inherited allele expressed in the formation of the final protein, which is primarily produced in hepatocytes. The disease usually occurs in pediatric and elderly populations. The disease occurs with the accumulation of abnormal protein polymers within hepatocytes that can induce liver injury and fibrosis. It is a commonly under-recognized and underdiagnosed condition. Patients diagnosed with the disease should be regularly monitored for the development of liver disease. Liver transplant is of proven benefit in A1ATD liver disease.

**Microbiome: Emerging Concepts in Patients with Chronic Liver Disease**

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Bradley Reuter and Jasmohan S. Bajaj

The gut microbiome is an exciting new area of research in chronic liver disease. It has shown promise in expanding our understanding of these complicated disease processes and has opened up new treatment modalities. The aim of this review is to increase understanding of the microbiome and explain the collection and analysis process in the context of liver disease. It also looks at our current understanding of the role of the microbiome in the wide spectrum of chronic liver diseases and how it is being used in current therapies and treatments.

**Acute on Chronic Liver Failure: Definition and Implications**

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Ariel Aday and Jacqueline G. O'Leary

Acute on chronic liver failure (ACLF) is an inflammation-based disorder that occurs in patients with underlying liver disease and is characterized by hepatic and extrahepatic organ failure. Morbidity and mortality are high in patients with ACLF, and therefore prevention and early identification are critical to improve outcome. The purpose of this article is to define ACLF, describe ways to identify the expected outcome of ACLF after development, and illustrate interventions to prevent it and when it is not preventable reduce associated morbidity and mortality.