

Frozen Sections of the Liver

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KEYWORDS

• Liver biopsy • Frozen section • Donor evaluation • Metastatic carcinoma

Key points

- Subcapsular benign biliary proliferations display an even distribution of glands in variably cellular collagenous stroma without significant nuclear atypica or infiltration of adjacent hepatic parenchyma.
- Metastatic adenocarcinoma is characterized by haphazardly arranged glands, fibroinflammatory stroma, nuclear hyperchromasia, size variability, and infiltration of normal hepatic structures, including sinusoids and portal tracts.
- Knowledge of the clinical history is often critical to the correct classification of tumors that features epithelioid cells with eosinophilic cytoplasm.
- Steatosis, fibrosis, inflammation, and necrosis should be documented and quantified when evaluating the suitability of donor liver for transplantation.

ABSTRACT

Intraoperative consultation requires skills in gross examination and histologic diagnosis, as well as an ability to perform rapid interpretations under time constraints. The aim of this review is to provide surgical pathologists with a framework for dealing with hepatic specimens in the frozen section area by covering common clinical scenarios and histologic findings. Differential diagnoses are considered in relation to primary hepatic neoplasia and metastatic diseases. Benign mimics of malignancy and other pitfalls in frozen section diagnosis of lesional tissue are covered. Finally, assessment of donor liver biopsy for organ transplant evaluation is discussed.

OVERVIEW

Despite advances in cross-sectional imaging techniques, intraoperative frozen sections still play an important role in the immediate management of surgical patients. Most frozen sections performed on the liver are intended to evaluate margins for tumors

in partial resection specimens or to assess for hepatic metastases in oncology patients undergoing potentially curative resection of a primary tumor, although frozen sections are also used to determine the suitability of potential donor livers. The purpose of this review is to provide the practicing pathologist with an overview of common issues encountered during frozen section of liver samples, which are organized according to the clinical scenarios in which they are likely to be encountered.

SURGICAL RESECTION OF ADENOCARCINOMA

COLORECTAL CANCER METASTASES

Hepatic metastases are far more common than primary tumors among noncirrhotic patients.¹ Although hepatic metastases were historically treated in a palliative manner, patients with some types of cancer, particularly colorectal cancer, may benefit from surgical resection of isolated hepatic metastases.²⁻⁴ In fact, targeted chemotherapeutic agents in combination with ablative techniques and high-resolution

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imaging have improved surgical management to the point that 5-year survival rates approach 60% among selected patients.⁵

Intraoperative consultation begins with careful gross inspection and identification of vascular and biliary margins, if present. The cauterized parenchymal margin is readily identified and should be assessed for the possibility of visible tumor before the application of ink. Palpation facilitates localization of the mass, and perpendicular sections demonstrating the relationship between the tumor and resection margin can be used to determine the adequacy of resection (**Fig. 1A**). Most surgeons are satisfied with a gross assessment of the distance between the tumor and margin, provided that distance is greater than 0.5 cm. Frozen sections performed on close margins are best assessed with thin perpendicular sections documenting the tumor and margin the same section. Negative resection margins are associated with improved survival.^{6,7}

INTRAHEPATIC CHOLANGIOCARCINOMA

Although intrahepatic cholangiocarcinoma is the second most common primary liver tumor, it remains a rare malignancy. Currently, surgical resection is the only treatment modality that offers curative intent for this malignancy, yet the postoperative 5-year survival remains less than 50%.⁸ As was described for colorectal metastatic disease, resection specimens for intrahepatic cholangiocarcinoma should first be palpated, inked, and sectioned perpendicular to the margin so that the mass can be demonstrated in relation to the inked margin (**Fig. 1B**). Because intrahepatic cholangiocarcinoma may have an infiltrating growth pattern along sinusoids and portal tracts, care should be

taken to identify irregular glands or cytologically atypical cells at the parenchymal, vascular, and biliary margins, where applicable. The histologic appearance of intrahepatic cholangiocarcinoma is discussed in more detail in the section on primary hepatic tumors.

Distinguishing Adenocarcinoma from Primary Hepatic Bile Duct Lesions

Surgeons may request intraoperative consults to evaluate small (<1 cm) nodules that are discovered at laparotomy, particularly when resecting primary adenocarcinomas of the pancreas, extrahepatic bile ducts, gallbladder, esophagus, and stomach. In this situation, the classification of hepatic lesions directly affects immediate patient management. If the hepatic nodule is classified as metastatic carcinoma, then the operative procedure is aborted, whereas a benign diagnosis is usually followed by surgical resection of the primary tumor. The differential diagnosis of metastatic adenocarcinoma includes 3 benign entities: bile duct hamartoma, bile duct adenoma, and ductular reactions that develop as a result of an obstructing mass in the head of the pancreas (**Table 1**).

Clues to a diagnosis of adenocarcinoma are best appreciated at low magnification. Adenocarcinomas are expansile nodules composed of irregularly distributed, angulated glands embedded in fibroinflammatory (desmoplastic) stroma (**Fig. 2A, B**). They tend to overrun preexisting benign elements, including portal tracts, and display an irregular interface with adjacent hepatic parenchyma (**Fig. 2C, D**). Glands vary in size and shape. They may contain mucin, but are usually unassociated with luminal bile, reflecting a lack of communication with the biliary tract. Malignant glands contain

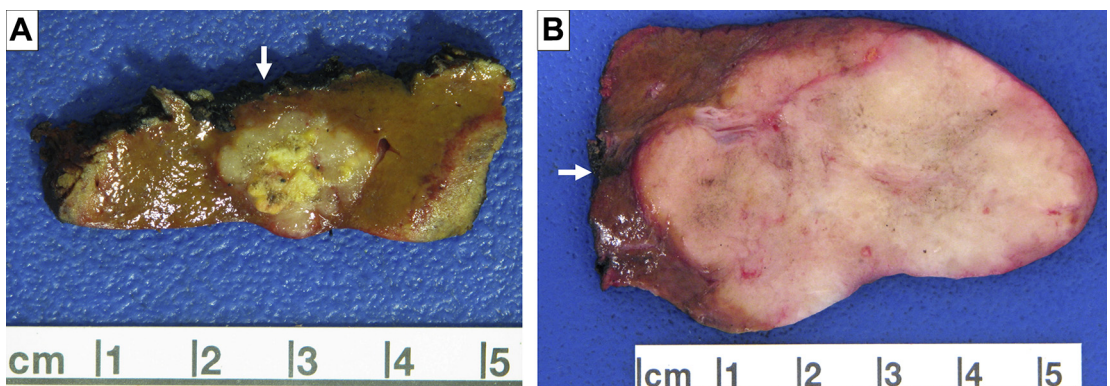


Fig. 1. (A) The parenchymal margin is inked (arrow) and the specimen is sectioned to evaluate the distance from the tumor to the inked margin. Colorectal carcinoma metastases are white, lobulated, and show variable necrosis. (B) An intrahepatic cholangiocarcinoma is close to the inked resection margin (arrow); it has a firm, homogeneous white cut surface.

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