Foresee Your Next Patient

Unusual Metastasis of Intrahepatic Cholangiocarcinoma to the Esophagus

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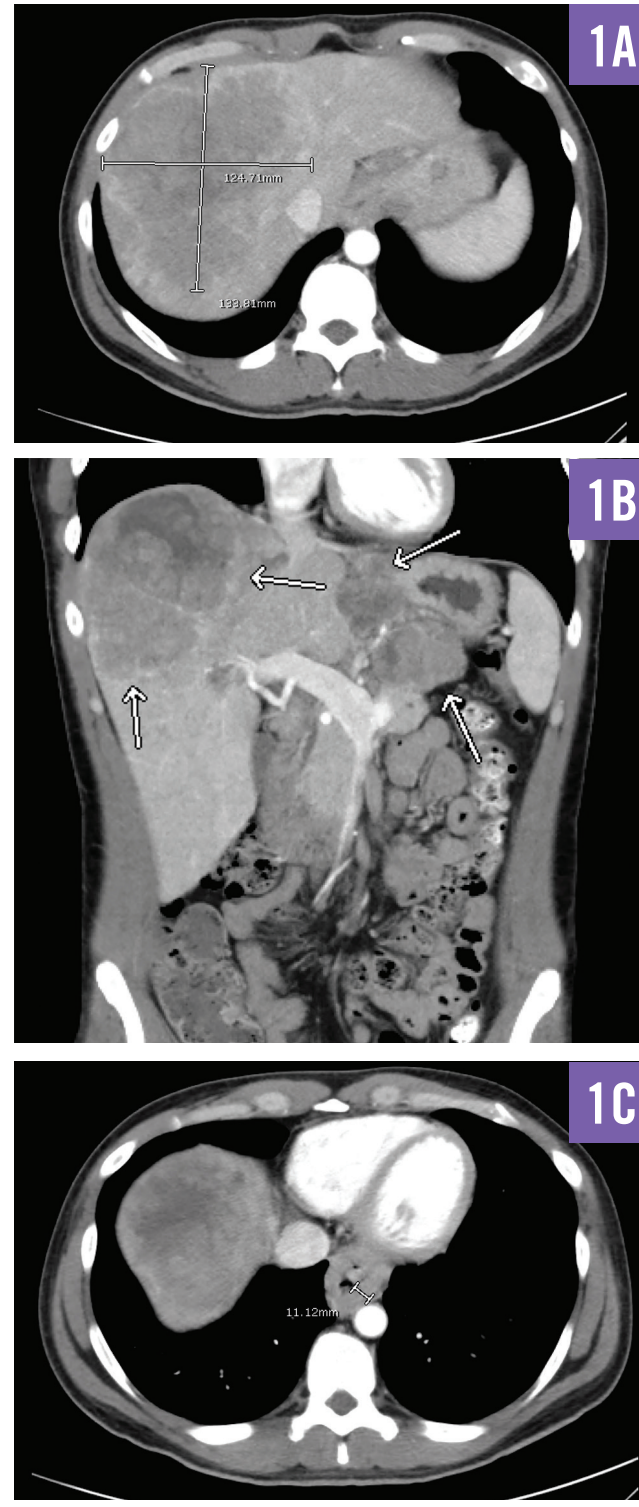
A 41-year-old man presented to our hospital for evaluation of progressive dysphagia. The patient had had an unintentional weight loss of 9 kg over 3 months. He had a 20 pack-year history of smoking and no significant medical history. His family history was notable for several maternal relatives with pancreatic, lung, or breast cancer, as well as for lung cancer in his father. Physical examination findings were noncontributory.

Computed tomography (CT) scans of the chest, abdomen, and pelvis revealed large hepatic and esophageal masses associated with bulky lymphadenopathy and thrombosis of the distal right main portal vein and multiple branches in the right lobe (**Figure 1**).



CT scans revealed large hepatic (**1A**, top, and **1B**, middle) and esophageal (**1C**, bottom) masses associated with bulky lymphadenopathy and thrombosis of the distal right main portal vein and multiple branches in the right lobe.

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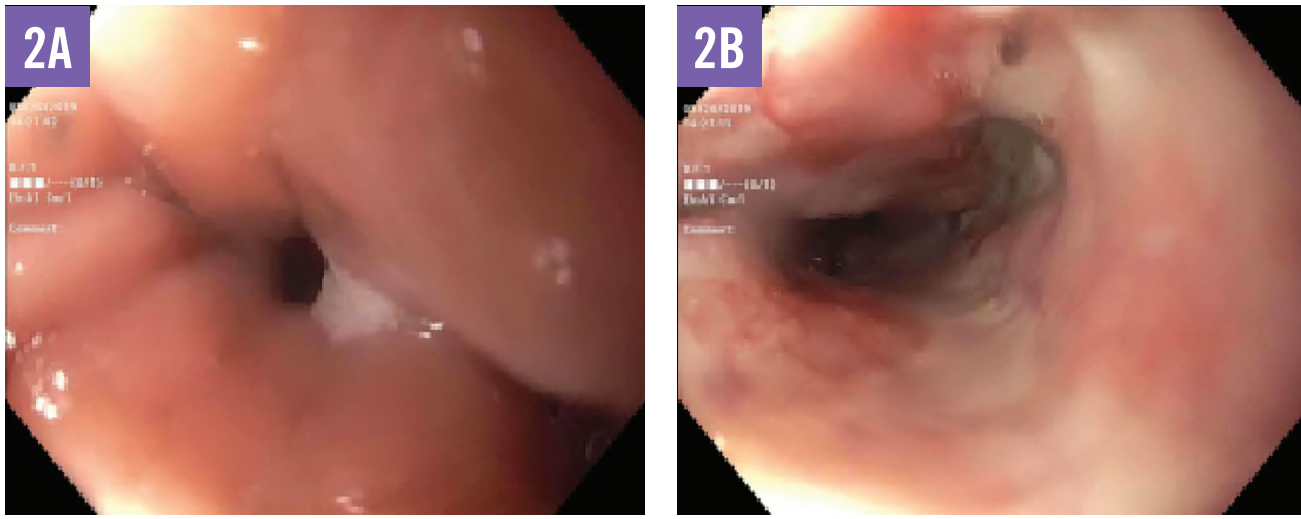
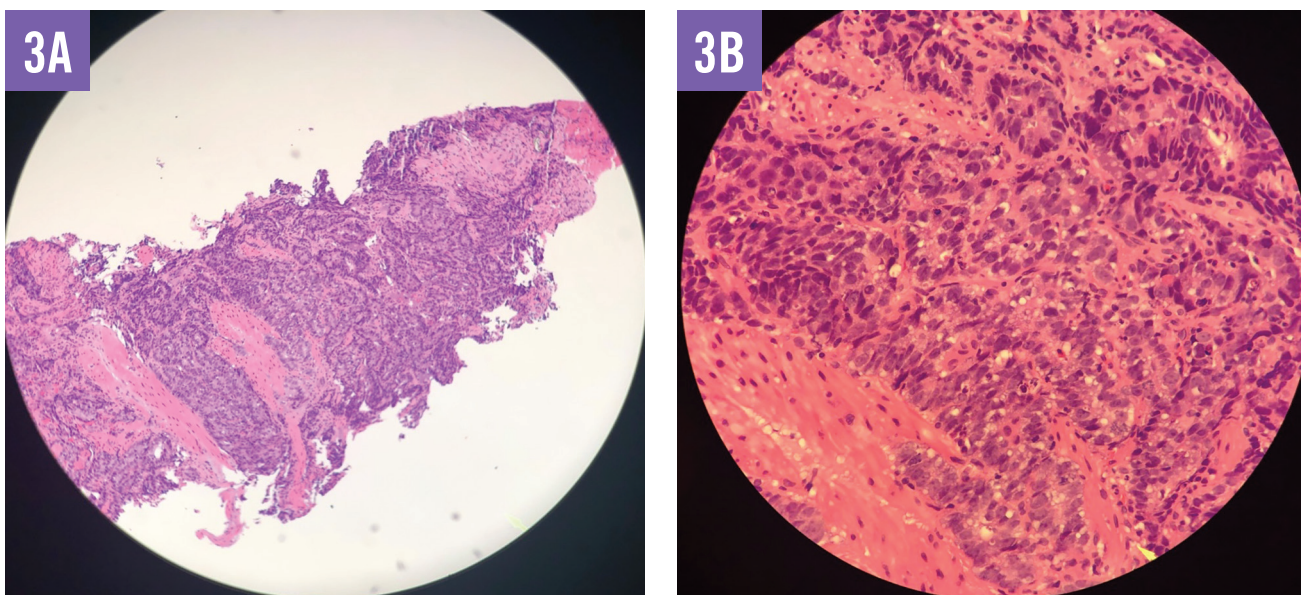


Upper gastrointestinal tract endoscopy revealed a partially obstructive, circumferential fungating mass at the gastroesophageal junction.

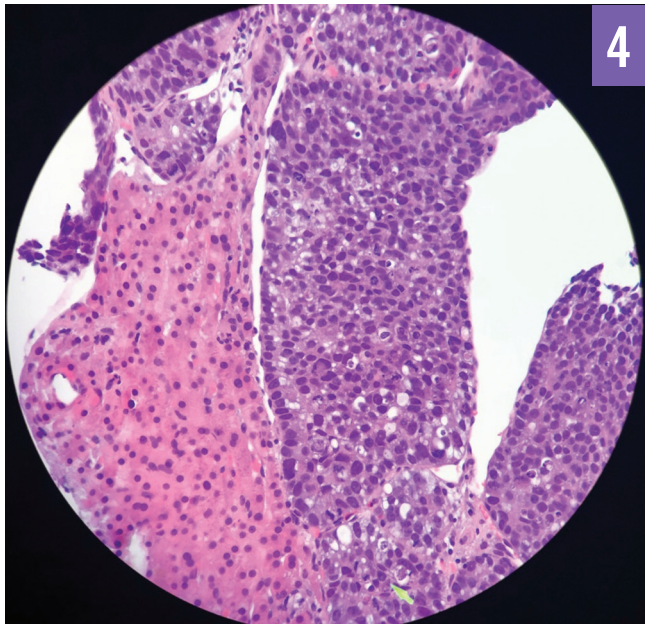


Esophageal biopsy demonstrating multiple fragments of gland-forming, moderate to poorly differentiated neoplasm with necrosis and focal intracytoplasmic mucin vacuoles.

The gastroenterology team was consulted, and the patient underwent upper gastrointestinal tract endoscopy with biopsy, the results of which revealed a partially obstructive, circumferential fungating mass at the gastroesophageal junction (**Figure 2**).

Histopathological analysis of the specimen showed multiple fragments of gland-forming, moderate to poorly differentiated neoplasm with necrosis and focal intracytoplasmic mucin vacuoles (**Figure 3**).

Given the history of a synchronous large liver mass, a panel of immunohistochemical stains was performed on the specimen to further characterize the lesion. The first panel of immunohistochemical stains showed results that could not be differentiated between a primary esophageal adenocarcinoma and a metastatic hepatic neoplasm. There was focal immunoreactivity with α-fetoprotein (AFP) and more extensive immunoreactivity with cancer antigen (CA) 19-9, results which were nonspecific. The tumor was negative for both cytokeratin (CK) 7 and CK20, which is uncommon. Additional immunohistochemical



CT scan-guided core needle biopsy of the hepatic lesion showed moderately differentiated adenocarcinoma. The results of immunohistochemical stains were consistent with intrahepatic cholangiocarcinoma. There was focal aberrant expression of glypican-3, which along with a serum AFP level of 41,551 ng/mL, suggested aberrant hepatocellular differentiation.

stains for intestinal, hepatic, and neuroendocrine antigens showed tumor cells with the following immunoreactivity: positive for CK19, CAM 5.2, monoclonal carcinoembryonic antigen (mCEA), and CDX2; and negative for synaptophysin, chromogranin A, and glypican-3 (weak focal nonspecific immunoreactivity). These results ruled out a neuroendocrine component and supported a biliary tumor origin but could not completely exclude primary esophageal adenocarcinoma. Hence, it was decided to proceed with further workup with CT-guided liver biopsy.

Histopathological study results from the liver biopsy confirmed moderately differentiated adenocarcinoma, with immunohistochemical stains consistent with intrahepatic cholangiocarcinoma (**Figure 4**). Tumor markers were significant for an AFP level of 41,551 ng/mL (reference range, 0-9 ng/mL) and a CA 19-9 level of 192 U/mL (reference value, <34 U/mL).

The biopsy of the liver tumor showed histological features and immunophenotype identical to the esophageal mass. This indicated a primary cholangiocarcinoma metastatic to the esophagus.

After extensive discussion with the patient, including about the prognosis and the available therapeutic options, the patient declined systemic chemotherapy in favor of palliative radiation to the esophagus for relief of the obstruction. He subsequently received external radiation therapy to the esophagus with minimal improvement in the dysphagia. A percutaneous endoscopic gastrostomy tube was placed for enteral nutrition. We had planned for transarterial chemoembolization of his liver lesions; however, the patient's clinical condition continued to decline, and he was eventually transitioned to hospice care given his very poor prognosis.

Discussion. The incidence of esophageal metastasis is very low in primary liver cancers such as hepatocellular carcinoma and intrahepatic cholangiocarcinoma.[1,2] This is likely because lymphatic drainage of the esophagus is uniquely designed such that the lymphatics extend into the lamina propria, unlike the rest of the gastrointestinal tract where lymphatics stop at the submucosal layer. Any obstruction in this lymphatic drainage may act as a portal for metastatic tumors in the esophagus as they drain into the thoracic duct. Dissemination of tumor cells by hepatofugal portal flow to the esophagus seems to be the cause of esophageal metastasis.[3]

As per an extensive literature review, this appears to be only the second reported case of esophageal metastasis from intrahepatic cholangiocarcinoma.[4] Although metastasis to the esophagus is infrequently reported, it is important for clinicians to have a high index of suspicion in patients presenting with progressive dysphagia and multiple tumor masses. For our patient and other patients with esophageal metastasis from intrahepatic cholangiocarcinoma, the overall prognosis is usually very poor. ■

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