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CASE REPORT | BILIARY

Rare Collision Tumor of the Biliary Tract

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ABSTRACT

Malignancies of the gallbladder are uncommon in the developed world. Collision tumors are also extremely rare neoplastic phenomena. Given their scarcity, there are no guidelines for treatment, and prognosis is based on the more aggressive tumor type. We present a patient with a collision tumor consisting of signet-ring cholangiocarcinoma and large-cell neuroendocrine gallbladder carcinoma of the biliary tract, and we review the literature pertaining to biliary tract collision tumors and their management.

INTRODUCTION

Malignancies of the gallbladder are extremely rare, accounting for 0.5% of all cancers in the developed world.[1,2] The highest prevalence of these malignancies is observed in Latin America and Asia, and they are attributed to genetic predisposition and environmental factors, including parasite-induced chronic inflammation.[3] These malignancies are categorized by their embryological origin: epithelial, mesenchymal, and neuroendocrine. Collision tumors are a rare neoplastic phenomenon wherein 2 histologically distinct tumors occur in the same organ with a clear area of transition between them.[4] Although cases of collision tumors involving the gallbladder are described in the literature, our case appears to be unique in that the collision tumor was composed of signet-ring cell cholangiocarcinoma and large-cell neuroendocrine gallbladder carcinoma in the biliary tract.[2,5-15]

CASE REPORT

A 35-year-old Nigerian woman without any significant medical history presented with acute-onset, constant, sharp, right upper quadrant abdominal pain exacerbated by food. She denied prior episodes of pain or history of gallstones. Review of symptoms was unremarkable, and she denied a family history of gastrointestinal or biliary malignancy. A computed tomography (CT) scan of the abdomen and pelvis showed a complex mass (8.5 × 7.2 × 10.8 cm) within the gallbladder fossa with intrahepatic extension concerning for malignancy (Figure 1). Her laboratory findings were significant for hemoglobin 11.1 g/dL, mean corpuscular volume 81 fL, iron deficiency, and elevations in CA-125 and CA19-9 at 33.8 U/mL and 40.77 U/mL, respectively.

Endoscopic ultrasound revealed a heterogeneous, hypoechoic mass involving the inferior portion of the gallbladder and abutting the second portion of the duodenum. Biopsies obtained with fine-needle aspiration were fixed in formalin for hematoxylin and eosin (H&E) stain and immunohistochemistry stain (Figure 2). The H&E-stained sections showed small clusters of cells with a high nuclear-to-cytoplasmic ratio, a predominance of small to medium cells, and occasional large cells with rare clusters forming micro-rosettes. Immunohistochemistry revealed cells positive for synaptophysin and CD56, with a Ki67 > 90%, and negative for chromogranin, CD45, and CD20, suggesting a high-grade neuroendocrine carcinoma (Figure 3). Upon review by the multidisciplinary tumor board, the

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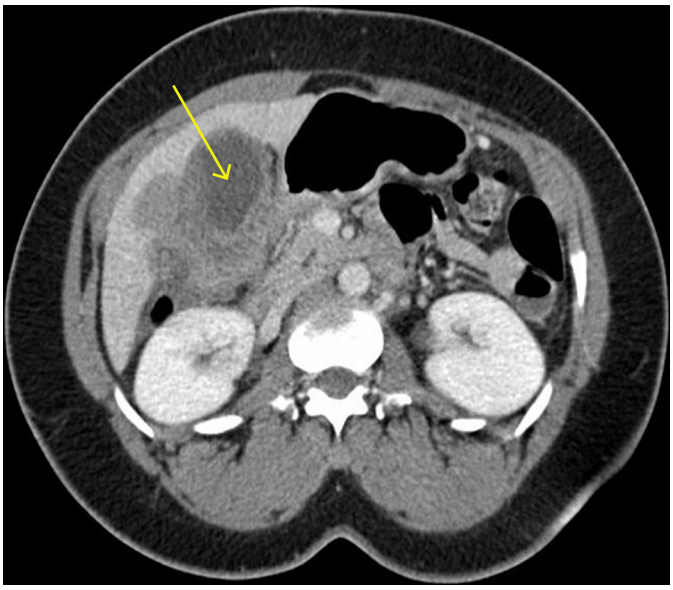

Figure 1. Abdominal and pelvic computed tomography showing a complex gallbladder mass with extension into the right hepatic segment (arrow).

tumor was deemed unresectable. The patient underwent cisplatin and etoposide with concurrent radiation, which resulted in disease stabilization.

Six months after completion of treatment, the patient presented with obstructive jaundice. CT scans showed increased intrahepatic biliary duct dilation and persistent gallbladder mass without suggestion of other masses. Endoscopic retrograde cholangiopancreatography revealed a Bismuth type IIIa stricture involving the primary branch of the right

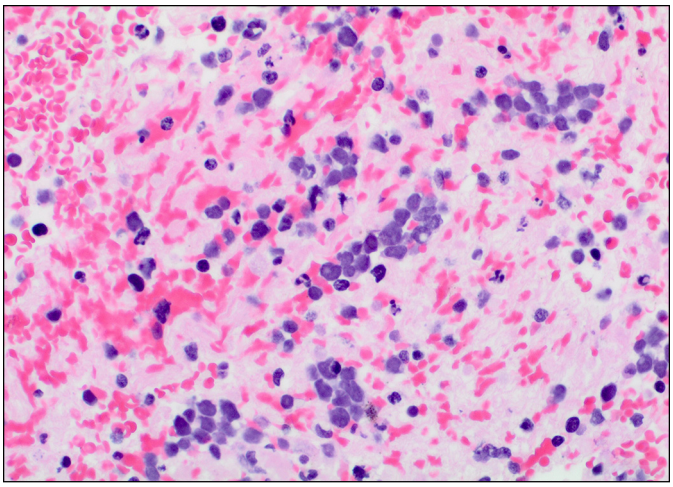

Figure 2. Hematoxylin and eosin (H&E) stain of fine-needle aspiration cytology and cell block showing small to large cells with a high nuclear-to-cytoplasmic ratio and round nuclei with an open, salt-and-pepper chromatin pattern present singly or forming rare clusters or micro-rosettes (×400).

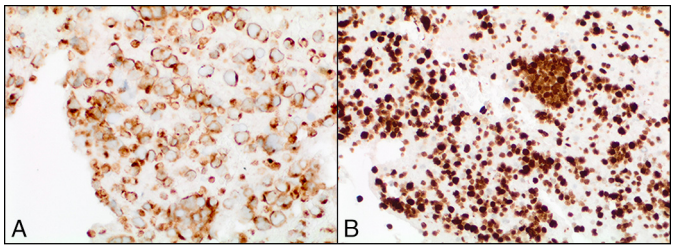

Figure 3. Tumor cells showing cytoplasmic positivity for (A) synaptophysin (×400) and (B) Ki67 (×200) with high Ki67 index (>90%) and nuclear positivity for Ki67.

intrahepatic duct and extending to mid-common bile duct (CBD) (Figure 4). This stricture appeared to be malignant. Cholangioscopy revealed abnormal ductal epithelium consisting of villous projections, friability, and neo-vascularization extending from the right intrahepatic duct to the mid-CBD (Video 1). Biliary duct biopsies revealed clusters of infiltrative tumor cells, mostly signet-ring cells; there were no visualized features of neuroendocrine carcinoma (Figure 5), and the biopsies were negative for synaptophysin and chromogranin. The patient was diagnosed with collision tumor of the biliary tract consisting of neuroendocrine carcinoma of the gallbladder and signet-ring cell cholangiocarcinoma. The second malignancy was also deemed unresectable, and a self-expanding uncovered metal stent was placed.

After multiple admissions with cholangitis and obstructive cholestasis, and with increasing disease burden in the biliary system, the goals of care shifted and the patient was discharged home with hospice.

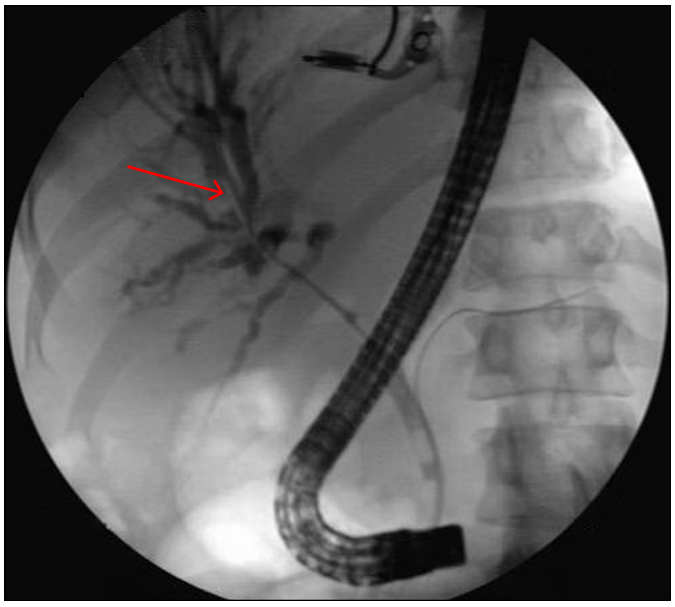

Figure 4. Endoscopic retrograde cholangiopancreatography showing a Bismuth type IIIa stricture (arrow).

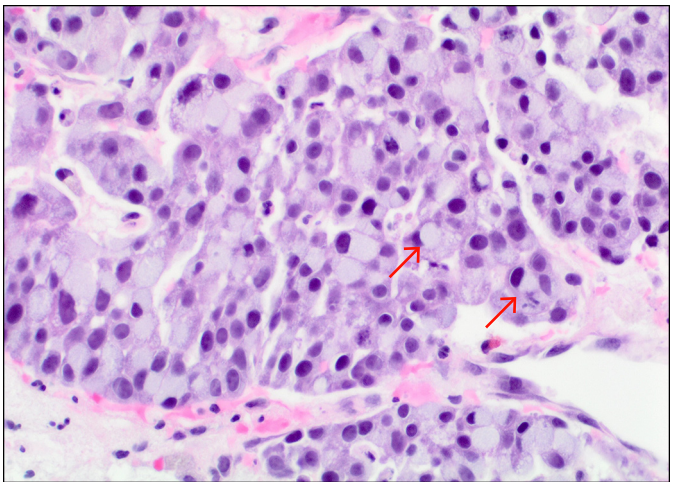

Figure 5. H&E stain of tumor cells with intracytoplasmic mucin showing signet-cell morphology (arrows; ×400).

Video 1. Single-operator cholangioscopy within the right intrahepatic duct. The ductal epithelium is markedly abnormal with villous projections, nodularity, and friability. The abnormal epithelium extends from the right intrahepatic duct to the proximal common bile duct. Watch the video: http://s3.gi.org/media/links/Millien_Video.mp4.

DISCUSSION

Synchronous malignant neoplasms are described as 2 distinct primary tumors occurring in the same organ, both displaying malignant characteristics and not representing metastases from other locations.[4] These tumors are known as collision tumors if the exocrine and endocrine neoplasms occur at the same time within the same organ, but with a distinct transition zone. This contrasts with combined tumors that have exocrine and endocrine neoplasms mixed in the same area without distinction, and amphicene tumors that contain both exocrine and endocrine features within the same neoplastic cell.[2,16,17]

Collision tumors are extremely rare.[4,17] The histopathologic origin of these malignancies is unknown, and there are 2 competing hypotheses: either both neoplasms occur simultaneously from 2 different precursors, or both neoplasms originate from a common progenitor with an area of transition between them. Their incidence is unknown, but more cases have been diagnosed with advancements in imaging studies and increased access to healthcare.[17] Given their rarity, there are no guidelines for treatment, and prognosis is based on the more aggressive tumor type. Mortality is highest in patients with collision tumors consisting of predominantly large-cell neuroendocrine neoplasms.

Our patient was initially diagnosed with large-cell neuroendocrine carcinoma in the gallbladder, which is a rare entity. This diagnosis was determined with immunohistochemical analysis, and chemotherapy stabilized the mass. The development of intrahepatic dilation treatment led to the diagnosis of a second primary malignancy, a signet-ring carcinoma of the bile duct. This second diagnosis was determined by way of an endoscopic technique using single-operator, per-oral cholangiopancreatoscopy, which allows direct visualization of biliary ducts and has revolutionized the diagnosis and management of pancreatobiliary disease.[18] The technique has been described as a "mother-baby" system, in which a "mother" duodenoscope is inserted orally, and a "baby" cholangioscope is fed through the duodenoscope to access the CBD. Cholangioscopy with newer platforms has been shown to have biopsy-directed sensitivity and specificity of 71% and 100%, respectively.[18,19]

In our extensive review of the literature, our case represents the first collision tumor in the biliary system involving signet-ring and large neuroendocrine cells. Despite identification of 2 distinct malignant entities, it is difficult to determine whether both malignancies occurred synchronously or metachronously given different biopsy locations at diagnosis. Lessons from other collision tumors within the biliary system have shown decreased survival of 2–36 months in patients with a neuroendocrine neoplasm component, whereas collision tumors without a neuroendocrine component have shown survival of more than 3 years.[8-5] As a result, it is important to recognize collision tumors to determine the prognosis and to tailor therapy.

DISCLOSURES

Author contributions: All authors contributed equally to the preparation of the manuscript. R. Sealock is the article guarantor.

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