CASE REPORT | BILIARY

Cholangiocarcinoma Presenting as Linitis Plastica with Unusual Metastases to the Psoas Muscle and Urinary Bladder

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ABSTRACT
Cholangiocarcinoma offers poor prognosis. Infrequent sites of metastasis are poorly described and often diagnostically delayed or missed. Bile duct brush cytologies provide poor diagnostic sensitivity/specificity. We present an unusual case of cholangiocarcinoma in a 34-year-old woman with rare distant metastasis to the psoas muscle and urinary bladder. It is the first case of metastatic cholangiocarcinoma presenting as linitis plastica, and our patient is the youngest to be described with metastatic cholangiocarcinoma to the psoas muscle leading to diagnosis. We conclude that seemingly idiopathic biliary strictures that fail to respond to testing should prompt alarm and referral for cholangioscopy, where available.

INTRODUCTION
Cholangiocarcinoma (CCA) is a tumor of the bile duct, which carries a poor prognosis because of the large tumor burden and advanced disease at presentation. Patients with a CCA present with biliary obstruction and with local and distant metastases. The most common sites of metastasis include the liver, gallbladder, and stomach.

CASE REPORT
A 34-year-old woman presented with new-onset ascites and worsening jaundice. A cholestatic liver profile demonstrated total bilirubin 17 mg/dL, direct bilirubin 10 mg/dL, aspartate aminotransferase 224 U/L, alanine aminotransferase 219 U/L, and alkaline phosphatase 822 international U/L. Ascitic fluid revealed a serum-ascites albumin gradient <1.1 g/dL. Fluid cytology was negative for malignancy, fluid cultures were negative, and fluid cell count was normal. She had presented to an outside small community facility 6 months prior with similar symptoms. Endoscopic retrograde cholangiopancreatography (ERCP) performed there revealed a common hepatic duct stricture with negative brush cytology. She underwent biliary stenting. Labs at our facility revealed an improved cholestatic liver profile with total bilirubin 11.9 mg/dL and alkaline phosphatase 614 IU/L. Magnetic resonance cholangiopancreatography (MRCP) showed diffuse gastric wall thickening, left psoas muscle fullness with left hydronephrosis, bladder mucosal enhancement, and intrahepatic dilatation despite biliary stenting (Figure 1). CA 19-9 was normal.
A second ERCP with stent exchange was performed; however, biliary biopsies were not obtained due to previous negative cytology and the unavailability of an endoscopic ultrasound-guided cholangioscope (Figure 2). Repeat brush cytology was negative. Percutaneous biopsy of the psoas muscle revealed tumor cells expressing CCA-specific cytokeratin (CK) 7 and CK19 (Figure 3). Cystoscopy demonstrated trigonal fluffy tissue obscuring the left ureteral orifice, with pathology consistent with CCA. Based on a fluoroscopy image, the CCA was classified as Bismuth-Corlette type II.

The patient’s hospital course was complicated by hematemia 2 months after the most recent ERCP. Esophagastroduodenoscopy showed a rigid stomach creating a challenging duodenal intubation (Figure 4). Gastric biopsies revealed another discrete location of metastatic CCA, confirming linitis plastica.

**DISCUSSION**

Skeletal muscle and gastric metastases from primary cholangiocarcinoma are exceedingly rare. Metastatic cholangiocarcinoma is postulated to occur hematogenously. Although well-vascularized, skeletal muscle is a rare site of secondary tumors due to specific tumor suppressor-like factors, such as fluid mobility, reactive hyperemia, lactate-rich environment, and local antineoplastic immune mediators (i.e., natural killer cells and lymphocytes). Skeletal muscle metastases may be overlooked and consequently may be under-diagnosed due to patients being relatively asymptomatic or having nonspecific symptoms.

To date, there have been 5 reports in the English literature of skeletal muscle metastasis from a primary cholangiocarcinoma. Our case represents the youngest patient described to date, diagnosed at 34 years of age. Although traditionally
thought of as a tumor that presents in the elderly, cholangiocarcinoma has been known to be sporadic. The age of patients in previous studies exploring distant skeletal muscle metastasis ranges from 44 to 72 years.

The stomach is also a rare site of metastatic cholangiocarcinoma. In 2009, Kim et al. described the only published case of cholangiocarcinoma metastasizing to the stomach and mimicking primary gastric cancer.8 This is the first presentation of metastatic cholangiocarcinoma as linitis plastica. There have been no reports of cholangiocarcinoma metastasizing to the urinary bladder. With respect to the genitourinary system, no published cases involve the urinary components of the genitourinary system; the current literature regarding metastatic cholangiocarcinoma include only the penis, uterus, and ovary.9–11 Bladder metastasis along with infiltration of the left psoas muscle may have contributed to hydronephrosis and acute kidney injury.

Our case is the first report of cholangiocarcinoma within the urinary bladder that presented as linitis plastica. It is also unique in the additional involvement of skeletal muscle. The disease skipped the common sites of lymphatic and hematogenous spread, including the lungs and liver. The unexplained refractory biliary stricture should prompt further investigations for a malignant etiology. Diagnosis was additionally difficult due to limitations in obtaining adequate biopsies. Bile-duct brush cytology has a low sensitivity of 9–24%, which improves marginally to 47% with the addition of fluorescence in situ hybridization to detect aneuploidy.12 Digital cholangioscopy with targeted biopsy from strictured locations offers potential early diagnoses and a higher sensitivity of 66% and specificity of 97%.13 However, the tissue yield is still sub-optimal due to the miniature forceps used. A specific pathological marker for cholangiocarcinoma is not available; however, dual positivity for CK7 and CK19 with clinical correlation (including radiologic/endoscopic techniques) can rule out competing differentials. With respect to cholangiocarcinoma, CK7 has a sensitivity of 90–96%, while that of CK19 is 84%. CK19 distinguishes cholangiocarcinoma from a hepatocellular malignancy. Fluoroscopy-guided pediatric forceps biopsy samples and brush cytology samples were negative on both occasions from the outside hospital where our patient was initially seen.

Unusual distant sites of tumor spread may explain a patient’s atypical presentation and should prompt a search for undiagnosed cholangiocarcinoma in the setting of a refractory biliary stricture. Our case highlights the very rare metastases to organs such as the bladder, stomach, and skeletal muscle, altogether skipping the liver and lungs, which may be partly attributable to limitations in her early diagnosis. As a result,
therapies that may have been offered to potentially hinder otherwise localized cholangiocarcinoma were not offered. Therefore, we recommend the referral of patients with unexplained biliary strictures to a facility where cholangioscopy is available.

DISCLOSURES

Author contributions: All authors contributed equally to the manuscript. S Raghavapuram is the article guarantor.

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Informed patient consent could not be obtained as the patient is deceased and next of kin was unreachable.

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