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CASE REPORT | BILIARY

Recurrent Cardiac Tamponade: An Unusual Presentation of Intrahepatic Cholangiocarcinoma

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Abstract

A 48-year-old Egyptian woman presented with 8 months of sharp right upper chest pain and weight loss. She was discovered to have an enlarged cardiac silhouette on chest x-ray, and an echocardiogram revealed a large pericardial effusion with diastolic right atrial collapse. Pericardial window was done, and epithelial membrane antigen-positive neoplastic cells were identified in the pericardial fluid. Computed tomography showed a 6-cm hypermetabolic lesion on the liver segment IV, confirmed on biopsy to be a moderately differentiated adenocarcinoma consistent with intrahepatic cholangiocarcinoma.

Introduction

Cholangiocarcinoma is the second most common primary hepatic neoplasm after hepatocellular carcinoma (HCC), accounting for 5–30% of all primary hepatic malignancies. Intrahepatic cholangiocarcinoma (ICC) is a relatively unusual tumor, representing only 10% of all cholangiocarcinomas.[1] ICC is associated with poor survival due to a lack of symptoms and unspecific clinical findings reflected in presentation with advanced local involvement. Patients present with abdominal pain (30–50%), weight loss (30–50%), and fever (up to 20%)[2-4]; the remaining cases are recognized after an incidental mass is discovered on abdominal imaging.

Extrahepatic bile duct cholangiocarcinomas may not be visualized on imaging, especially if small, but features of biliary obstruction may suggest the diagnosis. ICC, contrarily, rarely causes jaundice or biochemical obstruction, and rarely present with symptoms of metastatic disease or evidence of metastatic disease on imaging. Distant metastases occur late in the course of ICC and are most often found in other segments of the liver, lungs, and peritoneum.

Case Report

A 48-year-old Egyptian woman presented with 8 months of sharp right upper chest pain that was initially intermittent, but in the recent 3 months had become more persistent, especially at night. She had also developed exertional dyspnea in the prior few weeks. She denied fever, chills, night sweats, cough, tobacco, or illicit drugs use, but had lost 13 pounds in 3 months. Vital signs, laboratory values, physical exam, and cardiovascular evaluation were all normal. Thyroid-stimulating hormone was elevated 5.3 mIU/L, but free T4 was normal at 1.25 ng/dL.

Chest x-ray revealed an enlarged cardiac silhouette and a left basilar airspace opacity with air bronchogram. Electrocardiogram showed normal sinus rhythm with left atrial enlargement, low-voltage QRS, and prolonged QT inter-

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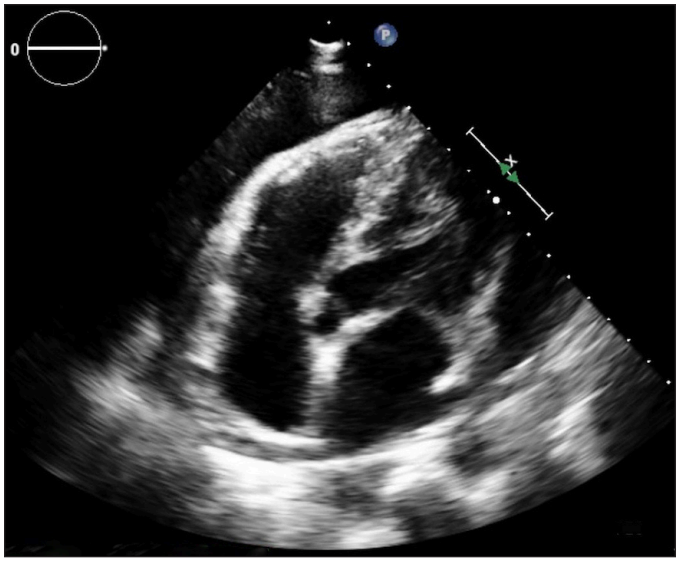

Figure 1. Echocardiogram showing a normal left ventricle with normal wall thickness and an ejection fraction of 55%. A large pericardial effusion with diastolic right atrial collapse is seen.

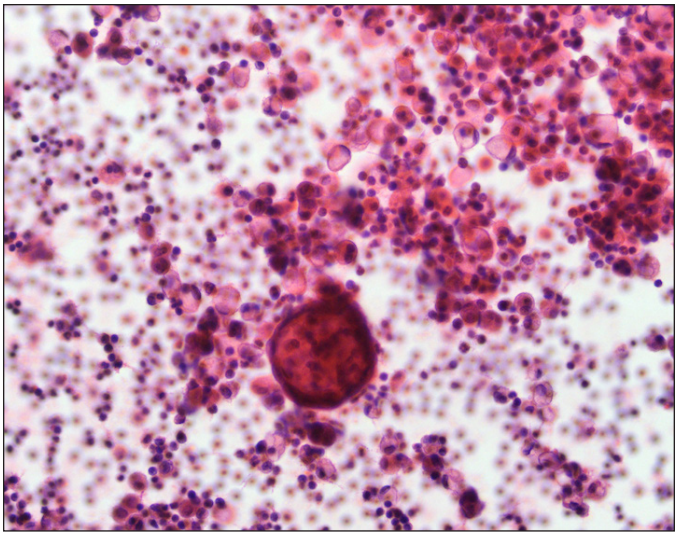

Figure 2. Pericardial fluid showing carcinoma cells isolated and forming 3-dimensional groups (Pap stain).

val (525 msec). Cardiac enzymes were negative (Troponin-T <0.01 ng/mL) and pro-BNP was minimally elevated (157.1 pg/mL). Chest computed tomography (CT) with contrast showed numerous bilateral pulmonary nodules up to 4.5 mm with an upper and mid-lung zone predominance. Although these lesions were of concern, they were not considered an explanation for her chest pain.

An echocardiogram revealed a normal left ventricle with normal wall thickness, ejection fraction of 55%. There was diastolic right ventricular compression, but right ventricular systolic pressure was normal. A large pericardial effusion with diastolic right atrial collapse was seen (Figure 1). Chest CT with contrast confirmed the large pericardial effusion. No mediastinal adenopathy or masses were seen, but a 7.1-cm hypodense mass in the right lobe of the liver was found. Abdominal CT precontrast showed a 6.0 x 5.3-cm hypoattenuating lesion, and mild enhancement of its peripheral margins with gradual centripetal enhancement was seen with contrast. Enhancement was heterogeneous and did not parallel the blood pool.

A pericardial window was performed with pericardial, xiphoid cartilage, and mediastinum lymph node biopsies. Bacterial, fungal, and mycobacterial smears and cultures were negative. Mycobacteria were not detected by polymerase chain reaction. The lymph node biopsy showed non-caseating granulomatous inflammation, but angiotensin-converting enzyme (ACE) levels were normal and there was no hiliar adenopathy. Anti-nuclear antibody was positive (speckled pattern 1:40). Auto-antibodies, viral hepatitis panel, and coxsackievirus, Echovirus, and *Brucella* serologic tests were negative. The patient's clinical status stabilized after drainage of the pericardial effusion.

The patient was readmitted 1 month later with similar symptoms and was found to have recurrent cardiac tamponade. A second pericardial window was created with drainage of 600 mL of fluid. The pericardial biopsy showed pericardial tissue with fibrinous deposition and few inflammatory cells. The pericardial fluid was discohesive and showed clusters of carcinoma cells (Figure 2), which were positive for epithelial membrane antigen (EMA). Triple-phase CT revealed a hepatic mass in segment IV A and IV B measuring approximately 5.8 x 6.4 x 6.8 cm. A continuously enhancing inner rim was visible on arterial phase images, which was noted to increase in enhancement on portal venous and delayed images. Increased patchy enhancing areas within the mass were visible on delayed images (Figure 3). Findings were suggestive of ICC or a single metastatic lesion.

Work-up for adenocarcinoma of unknown primary was undertaken, including bone scan, breast ultrasound, mammogram, upper endoscopy, and colonoscopy. Alpha-fetoprotein, CA-19-9, and carcinoembryonic antigen were normal (1.1 ng/mL, 6.6 U/mL, and 0.81 ng/mL, respectively). PET/CT showed a hypermetabolic lesion on the liver segment IV, as well as diffuse, nonspecific perihilar, and suprahilar fluoro-D-glucose uptake. Finally, a CT-guided biopsy of the liver mass confirmed moderately differentiated adenocarcinoma (Figure 4). Immunohistochemistry was positive for keratin and DPC-4, and negative for CD31, ERG, and CDX2, confirming adenocarcinoma, morphologically compatible with ICC. (Figure 4). Ki67 immunohistochemistry showed low proliferative index. IDH1/IDH2 mutation was not detected.

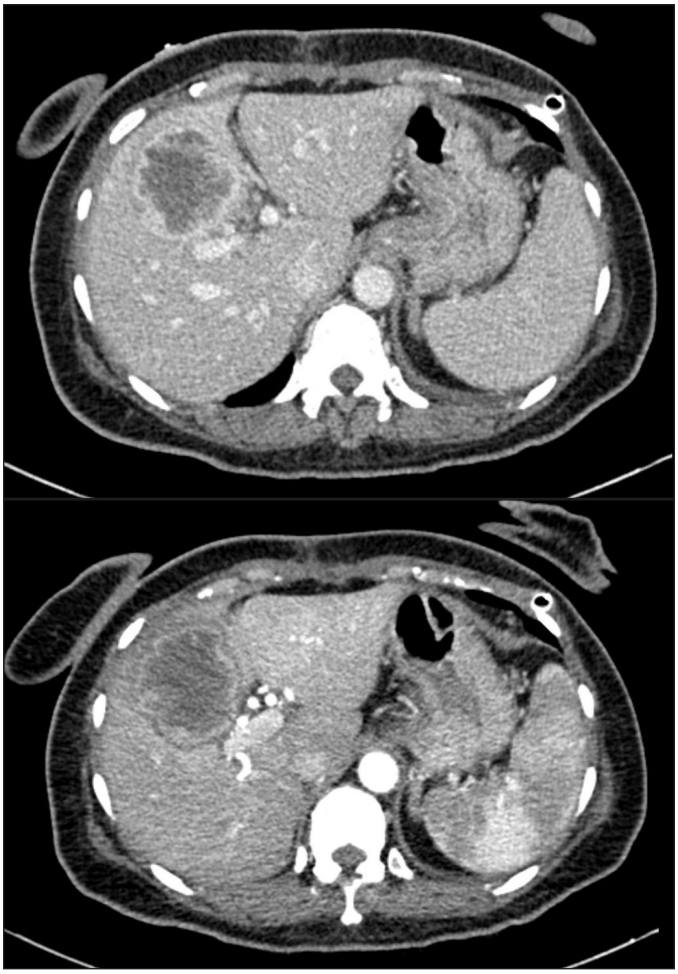

Figure 3. Sequential axial images in the arterial, portovenous, and delayed phases of triple-phase CT contrast enhancement demonstrating gradual centripetal enhancement. Specifically, the central areas of the mass are retaining the contrast, consistent with the fibrous nature of the ICC matrix.

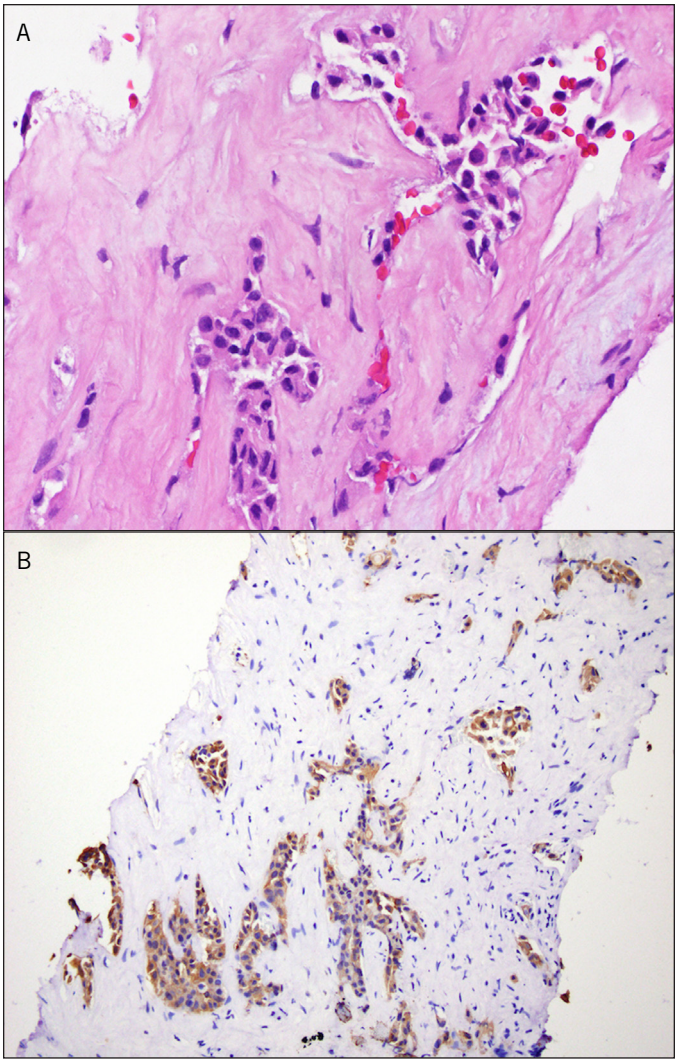

Figure 4. Liver biopsy. (A) H&E stain showing moderately differentiated adenocarcinoma in the background of extensive hyalinized fibrosis, morphologically consistent with ICC. (B) Immunohistochemistry positive for keratin and DPC-4, and negative for CD31, ERG, and CDX2.

Discussion

To our knowledge, this is the first case of ICC with metastasis isolated to the pericardial space presenting with recurrent cardiac tamponade. Intrahepatic cholangiocarcinoma usually does not cause clinical symptoms in the early stage; therefore, the disease is often advanced at the time of diagnosis, and the prognosis is worse than that of extrahepatic cholangiocarcinoma.[5] ICC presents as 3 subtypes: mass-forming, periductal infiltrating, and intraductal growing.[6] Mass-forming ICC (MICC) is most common, accounting for 60% of all ICCs. MICC and periductal-infiltrating cholangiocarcinoma are known to have poorer prognosis than the intraductal-growing type.[7]

The most common findings in patients with extrahepatic cholangiocarcinoma include jaundice, right upper quadrant tenderness, weight loss, and rarely, fever.[2] Patients with cholangiocarcinomas involving only the intrahepatic ducts usually have a history of dull right upper quadrant pain, weight loss, and an elevated alkaline phosphatase, but are unlikely to have jaundice.[8] Some patients are asymptomatic, and the lesions are detected incidentally when imaging is obtained for other reasons or as part of the work-up of abnormal liver blood tests.[9] ICC most commonly metastasizes to other intrahepatic locations, to the peritoneum, and subsequently to the lungs and pleura, and very rarely to the pericardium.

Typical imaging features of cholangiocarcinoma include a hypodense hepatic lesion that can be either well-defined or infiltrative without a capsule, with biliary dilatation. Following contrast administration, there is peripheral (rim) enhancement throughout both arterial and venous phases.[10,11] However, one study reported that these features were only present in 70% of MICCs, while the remaining 30% had an atypical pattern of complete (67%) or partial (33%) enhancement during the

arterial phase.[12] All hypervascular MICCs illustrated complete (87%) or partial (13%) washout in portal and delayed phases.[12] Some small, mass-forming ICC are arterially hyperenhancing and may mimic hepatocellular carcinoma.[13]

The initial CT in our patient showed a 6.0 x 5.3-cm hypoattenuating mass that, following administration of contrast, showed mild peripheral enhancement with gradual enhancement extending centrally. Enhancement was heterogeneous and did not parallel of the blood pool. These enhancement characteristics were atypical for common benign hepatic masses in this age group, so differential diagnostic included atypical hemangioma or atypical adenoma. Triple-phase CT subsequently showed a large hepatic mass within segment IV A and IV B, with a continuously enhancing rim on both arterial and portal venous images, with increased patchy areas of enhancement on delayed images, likely suggesting desmoplastic reaction. This illustrates the importance of performing triple-phase imaging for any suspicious liver lesion, and the value of repeating biopsies and immunohistochemistry when clinically indicated.

Disclosures

Author contributions: LI Diaz collected data, performed the literature review, and wrote the manuscript. JE Corral and L. Arosemena critically reviewed the manuscript. MT Garcia-Buitrago contributed histological information. B. Madrazo interpreted the images. P. Martin critically reviewed the manuscript and is the article guarantor.

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Informed consent was obtained for this case report.

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