

Management of obstructive jaundice in stage IV cholangiocarcinoma with peritoneal carcinomatosis and history of gastrointestinal stromal tumor

Samuel B. Reynolds, Alexander C. Podlaski, Areeb Zamir

ABSTRACT

Introduction: Biliary obstruction can cause a state of hyperbilirubinemia in patients, which is characterized by a total bilirubin level of >1.0 mg/dL. Possible causes of obstructive jaundice include biliary stone impaction, presence of tumor, and parasitic infection among others. When initial diagnosis is not known, a multidepartment treatment approach can be initiated. **Case Report:** A 73-year-old female presented with obstructive jaundice and history of gastrointestinal stromal tumor (GIST) who required biliary drainage using an external/internal catheter as well as endoscopic stenting through the ampulla of Vater and common bile duct. A diagnosis of cholangiocarcinoma with metastases, rather than recurrence of GIST, was ultimately made following analysis of a biopsy taken from the diaphragm. **Conclusion:** Combined radiologic intervention with percutaneous intrabiliary stenting as well as endoscopic stenting through the gastrointestinal tract and subsequent intestinal drainage can provide adequate therapy for obstructive jaundice secondary to an infiltrative mass by preventing further increase of total bilirubin and decreasing total bilirubin level through

biliary drainage. Patients with additional cancer history, such as those with GIST, should undergo further evaluation to determine whether their obstructive mass is a new primary tumor or recurrent disease.

Keywords: Cholangiocarcinoma, Cholangiogram, Esophagogastroduodenoscopy, Hyperbilirubinemia

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INTRODUCTION

Obstructive jaundice is a disease state characterized by a physical obstruction to either the intra-hepatic or extrahepatic biliary tree resulting in elevated blood levels of conjugated bilirubin. Causes of obstructive jaundice can include biliary stone impaction, presence of primary or malignant tumor, parasitic infection, AIDS cholangiopathy, and primary sclerosing cholangitis, to name a few. A multidisciplinary diagnostic approach can be undertaken when an obvious cause of the condition cannot be immediately identified in order to aid and direct critical initial management. Departmental consults can often be placed to hematology–oncology, interventional radiology, gastroenterology, rheumatology, and infectious

disease specialists. We present a case of obstructive jaundice for which initial management involving multiple departments was implemented before a definitive diagnosis was reached.

CASE REPORT

A 73-year-old female with a past medical history of gastrointestinal stromal tumor resected with partial gastrectomy three years prior to admission presented to the hospital with a three-day history of jaundice, first noticed by her family physician during a routine visit. Outside laboratory studies also revealed an elevated AST and ALT, alkaline phosphatase and bilirubin. Further discussion with the patient revealed a three-month history of unintended weight loss, decreased appetite and intermittent epigastric and right upper quadrant abdominal pain. Abdominal pain was only occasionally brought on by eating but severely interfered with sleep, as patient was unable to lie on her left side, and had been unable to sleep beyond short bursts of 3–4 hours at a time. Patient did not describe a personal history of smoking but did endorse substantial secondhand smoke exposure. Family history included stomach cancer of unspecified type and breast cancer in the maternal aunt and grandmother, respectively.

Laboratory studies performed on admission confirmed the finding reported by the outside physician: AST/ALT of 457/551 U/L, alkaline phosphatase of 1035 U/L and total bilirubin of 17.8 mg/dL. A CT scan of the abdomen and pelvis with contrast (Figure 1) revealed the presence of infiltrative tumor along common bile duct and intrahepatic dilation and encasement of biliary ducts, likely representative of intrahepatic and extrahepatic strictures.

Given her history and exam along with laboratory and imaging findings, our patient was preliminarily diagnosed with obstructive jaundice secondary to an infiltrative tumor. Management considerations would now include input from gastroenterology, interventional radiology (IR), and additional specialists as needed. Gastroenterology agreed with the primary care team's diagnosis, and suggested the patient undergo esophagogastroduodenoscopy (EGD) with endoscopic ultrasound and endoscopic retrograde cholangiopancreatography (ERCP). These procedures were performed, and included placement of a biliary stent through the ampulla of Vater and into the common bile duct.

While initially successful at lowering the total bilirubin (22.9–11.6 mg/dL), the levels continued to climb over the next several days, and IR was consulted accordingly. Interventional radiology, while in agreement with the diagnosis of the primary care team and gastroenterology, felt the patient required management that would address her intrahepatic biliary strictures as well. The patient, now five days post-EGD and ERCP, underwent percutaneous

transhepatic cholangiography (PTC) with placement of an internal/external biliary drain. Imaging during her PTC as shown in Figure 2.

Gastroenterology would see the patient again four days later for EGD and removal of their earlier-placed stent, as, in theory, the intrahepatic and extrahepatic stenting performed by IR would provide adequate biliary drainage. When the patient's total bilirubin did not substantially decrease, however, it became clear that her strictures were too extensive to be managed with stenting alone, and that only management of her likely cancer would provide relief, as it was causative of this biliary ductal compression. Two brush biopsies were taken from the mass, but neither yielded a definitive cytological diagnosis. These results prompted diagnostic laparoscopy with abdominal lavage, during which peritoneal and diaphragmatic implants were discovered. Biopsy of a diaphragmatic lesion is shown in Figure 3. While the biopsy results were pending, the patient developed culture-positive anaerobic bacteremia requiring management with intravenous ampicillin/sulbactam and ciprofloxacin. Biopsy results returned and were analyzed to identify a cholangiocarcinoma with metastases to the diaphragm and peritoneum. The difficulty in discerning an exact primary was due to widespread involvement of the hepatobiliary system on initial presentation. Cholangiocarcinoma was staged using the TNM staging system as TxNxM1. Specialists from hematology-oncology performed a comprehensive assessment and determined the patient to be an unlikely candidate for chemotherapy, in light of the active sepsis and poor performance status. The patient was transferred to an inpatient hospice unit and passed away several days later.

DISCUSSION

Occurrences of gastrointestinal stromal tumor (GIST) and intrahepatic cholangiocarcinoma have seldom been reported in literature. One such case was reported in a recent 2015 study, which described a patient with known GIST who underwent surgical exploration and discovered to have what were thought at the time to be liver metastases of the stromal tumor. Biopsy, however, revealed intrahepatic cholangiocarcinoma. The study went on to discuss GIST, and how given the liver is the most common metastatic site, clinicians often diagnose liver lesions as metastases, thereby delaying timely diagnosis and treatment of what could in fact be a primary cholangiocarcinoma [1]. Our case, while comparable to this study in the sense that the patient was diagnosed with both tumors, is unlikely to represent an example of the diagnostic dilemma of metastatic GIST versus primary intrahepatic cholangiocarcinoma, as her GIST was resected three years prior to admission. It would also be unusual to observe GIST in this location anatomically according to data available in the current literature. In an article published in 2015, retrospectively examined

anatomic locations of GISTs in 4411 patients: 2658 were found in the stomach, 1463 in the small intestine, 135 rectal, 126 colonic and 29 esophageal [2]. Recall from earlier that our patient's tumor ran along her common bile duct and resulted in intrahepatic biliary dilation secondary to strictures; which was not observed in a single patient of over 4,000 studied in the paper above, thus almost definitively ruling out a GIST recurrence even prior to return of her biopsy results. It can be reasonably

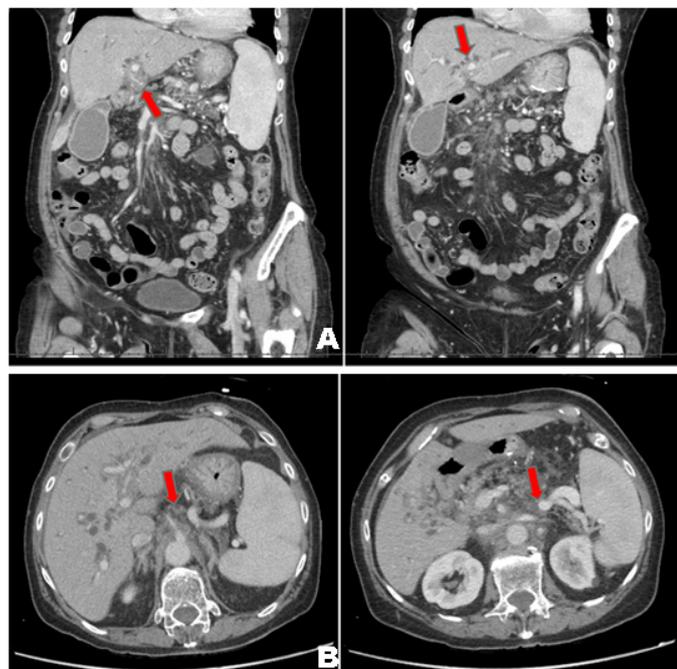


Figure 1: (A) Computed tomography scan of abdomen and pelvis with contrast. Note the presence of infiltrative tumor along common bile duct (left) and intrahepatic dilation and encasement of biliary ducts (right), likely representative of intra and extrahepatic strictures. (B) CT of the abdomen and pelvis with contrast showing lesions in the areas of the liver, celiac trunk, and splenic vein.



Figure 2: Intrahepatic stenting following biliary duct drainage.

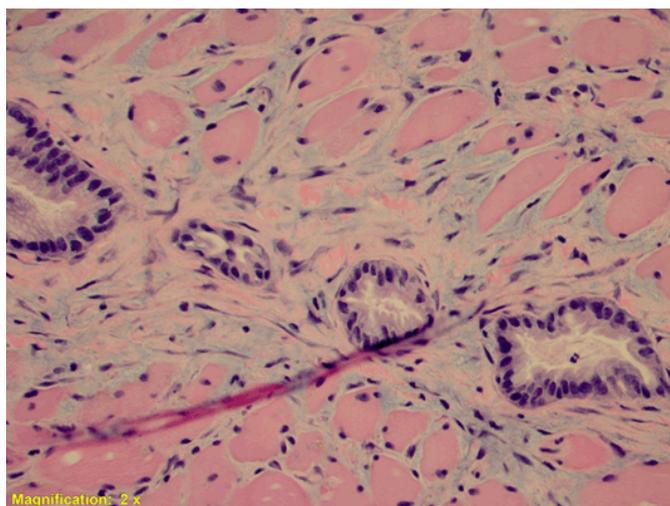


Figure 3: Biopsy obtained from patient's diaphragm, showing skeletal muscle interspersed with several gland acini. Correlated clinically, this histological finding is consistent with metastatic adenocarcinoma secondary to pancreatobiliary primary tumor. Stain performed with Hematoxylin-Eosin.

concluded, therefore, that her GIST and adenocarcinoma were independent occurrences, rather than a continuum of one unified cancer progression.

Despite ruling out GIST as causative of the patient's clinical picture, we still had a differential diagnosis to consider in our case: cholangiocarcinoma versus lymphoma versus primary sclerosing cholangitis. The first two were more likely in our patient, given her sudden weight loss and absent history of autoimmune condition(s), and histology allowed us to definitively narrow down the diagnosis to cholangiocarcinoma. One important consideration for clinicians, however, is that not every patient has such a straightforward picture, and the diagnosis often comes down to a biopsy. Cholangiocarcinoma, for example, is classically characterized by adenocarcinoma with a mix of acini, nests, trabeculae and tubules sitting within stroma [3]. Lymphomas have more varied presentations depending on subtype (Reed/Sternberg cells, for instance, are characteristic of Hodgkin's lymphoma) [4]. Primary sclerosing cholangitis is entirely different entity from cancer, and represents its own histopathologic dilemma, as "onion skin fibrosis" is seen in under 40% of patients on biopsy [5] and is beyond pathology,

Our case serves as an example of the recommended initial management of obstructive jaundice due to a space occupying tumor, specifically cholangiocarcinoma. Treatment for cholangiocarcinoma, if localized only to the biliary ductal system, is surgery followed by radiation and adjuvant chemotherapy. If more advanced to neighboring and/or distant organs or if directly involving vascular structures, focused radiation with chemotherapy is preferred. In the event, none of surgery, radiation, or chemotherapy is likely to provide

any mortality benefit, however, palliative measures are often considered. Endoscopic biliary stenting is an accepted palliative management approach to reduce hyperbilirubinemia when due to obstructive lesions, as noted by Grimm and Baron [6]. This stenting can be accomplished during an ERCP. If this original stenting fails to lower bilirubin levels, as occurred in our patient, a percutaneous transhepatic biliary drainage can be attempted [7]. While both of these interventions were performed in this patient, neither accomplished adequate bilirubin reduction. A compounding factor proved to be the multitude of intrahepatic and extrahepatic structures that were present due to her advanced disease.

Cholangiocarcinomas can be classified by their anatomic location within the liver. This particular case represented a type IV cholangiocarcinoma due to its multifocal location incorporating regions of the extrahepatic bile ducts, superior mesenteric vessels, splenic vein, and diaphragm [8]. One of the primary methods of curative intervention would be surgical resection. In order for resection to be possible the patient would need to have good performance status with localized disease represented by clear margins [8]. Additionally, evidence of metastasis should not be present. Metastasis is found in up to one-third of patients undergoing staging laparoscopy for cholangiocarcinoma and 80% of patients present with disease considered to be unresectable [8, 9]. Our patient's advanced tumor stage with metastasis precluded her from surgical resection. A 1996 study showed that the mean survival time was seven months among patients with cholangiocarcinoma who did not receive surgical resection [10]. Other non-curative interventions that have been associated with extrahepatic cholangiocarcinoma (ECC) include portal vein embolization, systemic chemotherapy with 5-fluorouracil, and chemoradiation therapy although none these were determined to be viable treatment courses for our patient due to the inability to reduce her hyperbilirubinemia.

CONCLUSION

Patients with metastatic cholangiocarcinoma often present with obstructive jaundice, evidenced clinically by diffuse jaundice with scleral icterus, elevated alkaline phosphatase, liver enzymes and total bilirubin. Although difficult candidates for both surgical and cytotoxic therapy, patients can still be provided relief through radiologic intervention, with percutaneous intrabiliary stenting, and through the assistance of gastrointestinal specialists with endoscopic stenting of bile ducts and subsequent biliary drainage into the intestine. Patients with concomitant history of additional cancer, such as gastrointestinal stromal tumor (GIST) should be evaluated for whether or not their presentation is consistent with a new primary or a metastasis. Biopsy becomes a valuable tool here, as providers can discern on

a cellular level which subtype of tumor is present, which then guides the appropriate management to ensure the best possible clinical outcomes.

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Author Contributions

Samuel B. Reynolds – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Alexander C. Podlaski – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Areeb Zamir – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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