

Contents lists available at [ScienceDirect](#)

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

Extrahepatic biliary obstruction secondary to neuroendocrine tumor of the common hepatic duct



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ARTICLE INFO

Article history:

Received 3 November 2016

Received in revised form

21 November 2016

Accepted 21 November 2016

Available online 23 November 2016

Keywords:

Biliary obstruction

Neuroendocrine tumor

Extrahepatic bile duct

Cholangiocarcinoma

Unusual biliary tumors

ABSTRACT

INTRODUCTION: Primary neuroendocrine tumors (NET) of the extrahepatic biliary tree are a rare entity with less than 100 reported cases in the literature.

PRESENTATION OF CASE: Here, we report a case of NET of the extrahepatic bile duct in a 64-year-old male patient presenting with painless jaundice, direct hyperbilirubinemia, and mildly elevated transaminases. Diagnostic workup with an ultrasound revealed dilation of the intrahepatic biliary ducts, without cholelithiasis or choledocholithiasis. Additional cross sectional imaging identified a stricture at the confluence of the common hepatic and cystic duct junction. Given lack of additional findings presumptive diagnosis of localized Klatskin's tumor was made. The patient subsequently underwent resection of the common bile duct and roux-en-y hepaticojejunostomy reconstruction. Final pathologic diagnosis showed G2 well-differentiated NET of the extrahepatic bile duct, measuring $1.3 \times 1.1 \times 1$ cm.

DISCUSSION: When a patient is evaluated for a primary bile duct neoplasm, differentiation between cholangiocarcinoma and an unusual bile duct tumor, such as a NET is very difficult before surgical resection and histologic review.

CONCLUSION: NET of the extrahepatic biliary tree are a rare entity. Typical presentation is with painless jaundice and other symptoms related to obstruction of the biliary tree and the diagnosis is usually made post-operatively.

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1. Introduction

Neuroendocrine tumors (NETs) are thought to originate from enterochromaffin, or Kulchitsky cells, of the gastroenteropancreatic tract. These cells presumably undergo a pre-malignant intestinal metaplasia from inflammation. Enterochromaffin cells are found in highest proportion in the small intestine, and rarely within the biliary ducts. This low proportion of precursor cells corresponds with the low incidence of extrahepatic biliary neuroendocrine tumors (NET) [1,2,9]. The presenting signs and symptoms of extrahepatic NETs are secondary to the obstruction of the normal flow of bile, thereby causing hyperbilirubinemia and jaundice. Here we report case of a patient with extrahepatic NET in line with the SCARE criteria [3].

2. Presentation of case

64-year-old male presented with 2-week history of jaundice, pruritus, acholic stools, and tea colored urine. He also noted poor oral intake and approximately 16-pound weight loss during that time. He denied any abdominal pain, nausea, or vomiting and had no family history of hepatopancreatobiliary malignancy. On examination, the patient's skin was jaundiced, his abdomen was soft, non-tender, non-distended and no masses were palpable. Laboratory test were suggestive of obstructive jaundice with Total and Direct Bilirubin elevated at 1.6 and 1.1 mg/dL respectively. Right upper quadrant ultrasound showed dilation of the intrahepatic biliary ducts, without cholelithiasis or choledocholithiasis. The patient subsequently underwent computerized tomography (CT) scan of the abdomen and pelvis with intravenous and oral contrast, which showed diffuse mild to moderate intrahepatic biliary ductal dilatation, with a distended gallbladder. The common bile duct (CBD) at the level of the gallbladder measured 1.4 cm, with a distal abrupt caliber change and a soft tissue density mass measuring 1.3 cm was noted in the hepatic duct (Fig. 1). These findings were considered concerning for a Klatskin tumor/cholangiocarcinoma, without

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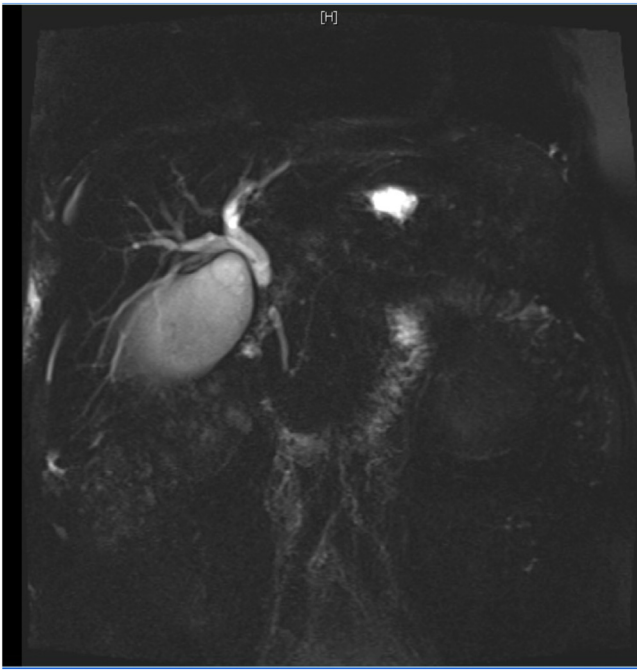


Fig. 1. CT scan demonstrating distal abrupt caliber change and a soft tissue density mass measuring 1.3 cm was noted in the hepatic duct.

evidence of lymphadenopathy or metastasis. Magnetic resonance cholangiopancreatography (MRCP) validated the same findings.

Moreover Carbohydrate antigen 19-9 (CA 19-9) was checked and found to be elevated at 50U/mL.

The patient was then referred to the Department of Surgical Oncology at a teaching hospital and offered surgical resection. The patient underwent resection of the CBD, cholecystectomy, end to side roux-en-y hepaticojejunostomy, and portal lymphadenectomy, with a presumed pre-operative diagnosis of hilar cholangiocarcinoma. Intraoperative frozen sections of resection margins were negative for tumor. Dissected lymph nodes in the porta hepatis were normal appearing. The patient's immediate postoperative course was uncomplicated and he was discharged home on POD 4. The final pathologic results showed a G2 neuroendocrine tumor of the extrahepatic CBD, measuring 1.3 × 1.1 × 1 cm (Fig. 3). Histologically, the tumors cells were well differentiated (Fig. 2A) with 13–15 mitoses per 10 high power fields (Fig. 2B). The tumor showed perineural invasion but was negative for lymphovascular invasion. Immunohistochemical staining showed all the tumor cells were strongly positive for chromogranin, synaptophysin (Fig. 2C), and CD 56. Immunohistochemistry for Ki-67 showed a proliferation index of approximately 5 (Fig. 2D). The histologic findings and the immunoprofile of the neoplasm were consistent with neuroendocrine tumor, well differentiated, G2 (grade 2). Given the rarity of the clinical diagnosis verbal informed consent was obtained from the patient to publish this case in a scientific journal.

3. Discussion

Less than 100 cases of extrahepatic biliary NET have been reported in the literature to date. A review of the recent literature

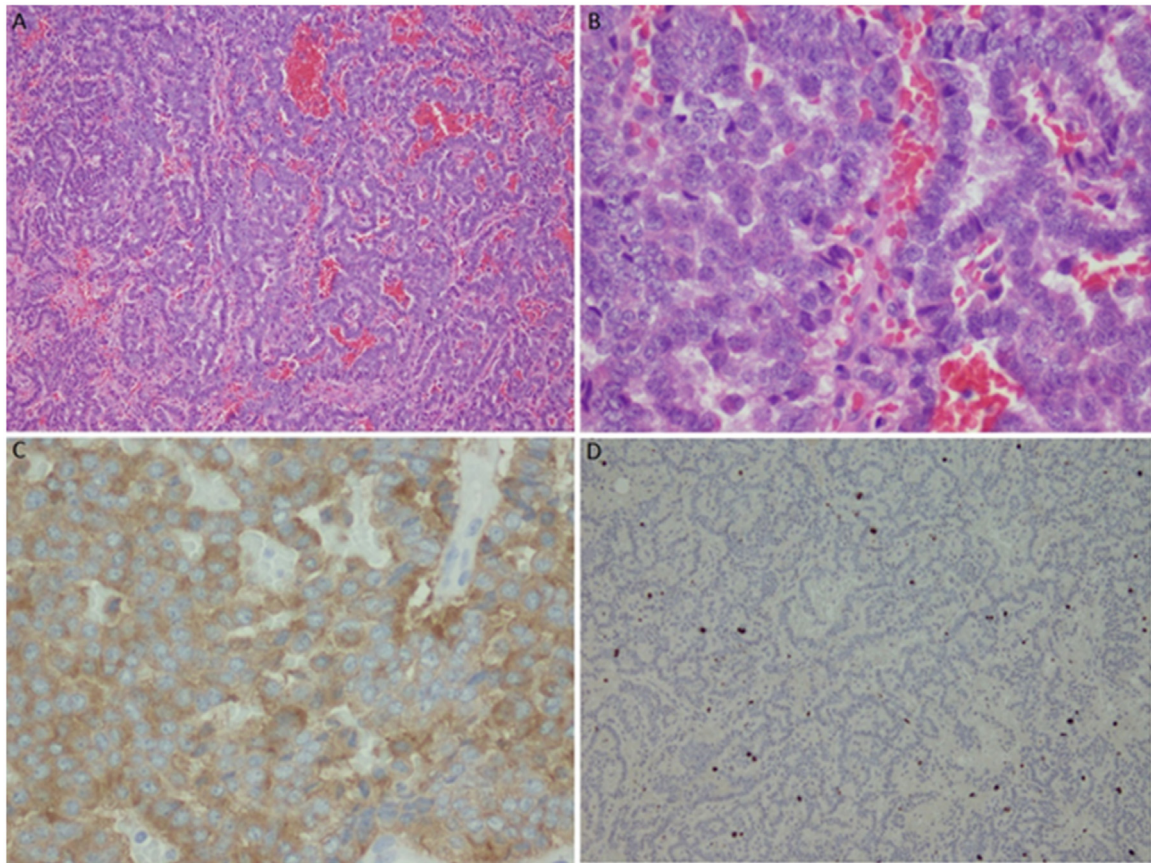


Fig. 2. A: Histologic findings of the gallbladder neoplasm: Tumor cells arranged in a trabecular pattern with scant intervening fibrovascular stroma (Hematoxylin and eosin (HE), ×10); B: The tumors cells showed medium to large hyperchromatic nuclei with coarse granular chromatin, occasional nucleoli, small to moderate amphophilic cytoplasm, and scattered mitotic figures (HE, ×40); C: The tumor cells were strongly positive for synaptophysin (×40); D: 5% of the tumor cells were positive for Ki-67 (×10).

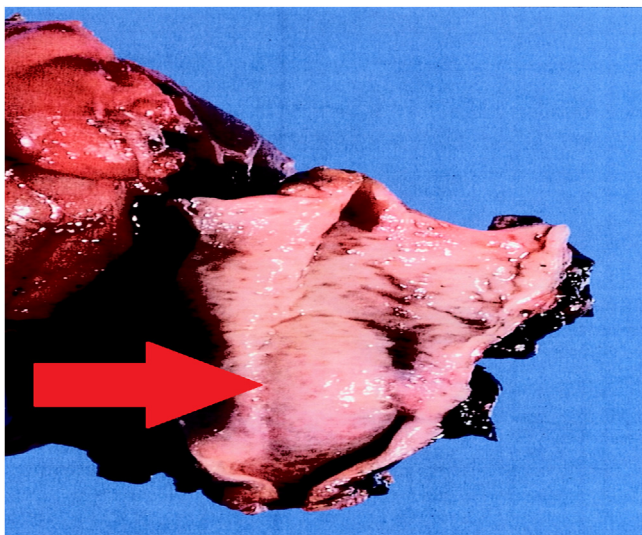


Fig. 3. Macroscopic photograph of the cut surface of the lesion with arrow depicting the lesion.

showed that in most cases the presenting symptom was related to local invasion of the tumor [4]. These symptoms included jaundice (most common), abdominal pain, pruritus, nausea, vomiting, and weight loss. These tumors are most commonly located in the common hepatic duct, and distal common bile duct [10]. When a patient is evaluated for a primary bile duct neoplasm, differentiation between cholangiocarcinoma and an unusual bile duct tumor, such as a NET is very difficult before surgical resection and histologic review. Percutaneous needle biopsies and endoscopic brush biopsies are reliable only if they identify a malignancy [11]. Consequently NET are typically identified following surgical resection as seen in the case presented. Of note, NETs are being diagnosed at increasing frequency due to the growing number of endoscopies performed and to advances in our understanding and detection of these tumors [8].

Surgical resection is the corner stone of treatment for biliary NET, and the only potential curative treatment [12,13]. Previously reported patients who underwent curative resection had favorable long term disease free survival and long term survival, even in the setting of metastatic liver disease [7]. Similar to NET located outside the biliary tree the biologic behavior likely is related to the degree of differentiation. NET can be classified using the World Health Organization (WHO) system that distinguishes between well-differentiated neuroendocrine tumors (NETs) and poorly differentiated neuroendocrine carcinomas (NECs) of small or large cell type [5,6]. Well differentiated NETs, or carcinoid tumors, are those with mild or no atypia and are considered benign if they do not demonstrate angioinvasion, are ≤ 1 cm in size, with ≤ 2 mitoses/10HPFs. Tumors with low grade malignant potential are >1 cm, mitotic index of >2 mitoses/10 HPFs, or proliferation index $>2\%$ Ki-67-positive cells. Poorly differentiated neuroendocrine carcinomas (NECs) have high grade malignant potential, and are composed of highly atypical, small to intermediate-sized tumor cells often with necrosis and prominent angio and/or perineural invasion.

The European Neuroendocrine Tumor Society (ENETS) is a simpler classification system proposing three categories (G1-3) that is exclusively dependent upon the tumor's proliferation status. In this system, G1 tumors have <2 mitoses/10 HPFs, or a Ki-67 index less than 2%. G2 tumors have 2–20 mitoses/10 HPFs, or a Ki-67 index between 3 and 20%. G3 tumors have >21 mitoses/10 HPFs, and a Ki-67 index greater than 20%.

4. Conclusion

NET of the extrahepatic biliary tree are a rare entity. Typical presentation is with painless jaundice and other symptoms related to obstruction of the biliary tree. Surgical resection is the mainstay of therapy, and the diagnosis is usually made post-operatively after analysis by pathology.

Conflict of interest

All authors declare no conflict of interest relevant to this report.

Funding

No external source of funding.

Ethical approval

Given that this is a case report with no identifiable information included in the manuscript ethical approval was not obtained.

Consent

Verbal informed consent was obtained from the patient for publication of this case report and accompanying images.

Author contribution

FK conceptualized the study and finalized the manuscript.
 ASC collected data and drafted the initial manuscript.
 RC collected data and drafted the initial manuscript.
 AH collected data, reviewed and approved the final manuscript.
 DE conceptualized the study and approved the final manuscript.
 DW conceptualized the study and approved the final manuscript.

Guarantor

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