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Case Report

Extrahepatic Biliary Neuroendocrine Tumors Presented as Liver Mass

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Abstract

Extrahepatic biliary neuroendocrine tumors (EBNETs) are a rare group of neoplasms with varying characteristics, with 223 cases documented since their discovery. In this case report, an EBNET is described as a result of vague abdominal pain and significantly elevated liver function tests in a 41-year-old woman who presented with vague abdominal pain and elevated liver function tests. Despite the challenges faced in preoperative diagnosis, including the need to differentiate from cholangiocarcinoma, surgical intervention was successful. Due to the tumor's complex nature, meticulous dissection and reconstruction were required, leading to crucial insights into surgical management. In addition to highlighting the rarity of EBNETs, this case emphasizes the importance of early detection and customized surgical approaches.

More Information

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Background

Neuroendocrine Tumors (NETs) are heterogeneous clinical entities with a wide spectrum of grades, pace of disease, functional status, and primary sites of involvement [1]. NETs can arise in various organs, including the bronchopulmonary tree, the gastrointestinal tract, and even the liver or the biliary tree [1-3]. Particularly, NETs affecting the gastrointestinal system are relatively common, with the small intestine and rectum the most common primary sites [4]. The incidence of NETs among all gastrointestinal tumors is approximately 2 per 100,000 cases per year [5]. In recent decades, the incidence of gastro-intestinal (GI-NETs) has been steadily increasing, partly due to the expansion of the indications for endoscopy [6].

Extrahepatic Biliary Neuroendocrine Tumors (EBNETs) are exceptionally rare, with fewer than 200 cases reported in the literature since their initial description by Pilz in 1961 [1,7,8]. As of 2017, this number has increased to 223 documented cases. Histological and Immunohistochemical (IHC) evaluation of the specimen is the most common method of detection postoperatively. The majority of reported cases proceed to surgery with the presumption that the disease is cholangiocarcinoma, a much more common cancer of the extrahepatic duct. Surgery is the standard treatment of care and offers prolonged disease-free survival [9,10].

This case report presents an unusual presentation of a tumor located within the Common Hepatic Duct (CHD) and its branches, which may provide a differential diagnosis for lesions located in segment 4 of the liver. This case highlights the importance of recognizing such tumors as potentially metastatic Neuroendocrine Tumors (NETs). Considering the rarity of this presentation, it is imperative to consider this differential diagnosis when evaluating similar cases, as it can significantly impact treatment decisions and patient management.

Case presentation

On February 14, 2024, a 41-year-old woman presented to the clinic with a two-month history of nonspecific abdominal pain. Ultrasound imaging revealed enlargement of the intrahepatic bile ducts and the presence of a tumor in segment 4 of the liver. The patient was alert and stable, with mild right upper quadrant tenderness on abdominal palpation. No rebound tenderness, guarding, or palpable masses were noted. Bowel sounds were normal. Skin examination revealed no jaundice. Cardiovascular and respiratory systems were unremarkable. The results of routine laboratory tests indicated that Liver Function Tests (LFTs) were significantly elevated, with aspartate aminotransferase (AST) at 780 U/L and alanine aminotransferase (ALT) at 871 U/L (normal range: 0-51 U/L), along with elevated Alkaline Phosphatase (ALP). A Complete Blood Count (CBC) revealed mild leukocytosis, while urine analysis results were normal. Moreover, tumor markers such as Carcinoembryonic Antigen (CEA), Alpha-fetoprotein (AFP), and carbohydrate antigen 19-9 (CA19-9) were positive.

Neither the patient nor any members of his family had any significant medical history related to liver disease.

A Computed Tomography (CT) scan was performed following the laboratory tests. In segment 4 of the liver, an imaging study revealed a mass measuring 38 x 40 mm, with findings suggesting benign lesions, possibly hepatic adenomas (Figure 1). As a result of the mass exerting pressure on the Common Bile Duct (CBD), there was a widening of the portal right and left branch vein and mild intrahepatic biliary ectasia. As a result of a percutaneous biopsy, a neuroendocrine tumor was identified. Despite the decrease over time, the elevated AST and ALT levels were consistent with the initial findings. To identify the source of the mass, comprehensive evaluations, including endoscopy and colonoscopy, were conducted; however, no primary source was found, leading to the conclusion that this was a primary tumor. Due to the patient's symptoms, an endoscopic evaluation was conducted to determine whether the duodenum had Gastrointestinal Stromal Tumors (GISTs). A normal endoscopy result ruled out the presence of any mass.

Following a comprehensive evaluation and diagnosis of a neuroendocrine tumor, the treatment plan was determined to include surgical intervention. Intraoperatively, the mass was found not in segment 4, but rather at the anterior aspect of the liver hilum, involving a portion of the proximal common hepatic duct (Figure 2). To achieve complete excision of the tumor, we performed a total resection of the Common Bile Duct (CBD) and Common Hepatic Duct (CHD), along with a complex lymphadenectomy of the left and right branches in the liver hilum and around the celiac artery (Figure 3). The mass was excised with free margins. Subsequently, a Roux-en-Y hepatojejunostomy was performed, with the Roux limb anastomosed to the remaining segmental ducts, resulting in a total of four anastomoses within the liver. The histological evaluation confirmed the neuroendocrine nature of the tumor. Figure 4 provides detailed pathological findings, including diffuse and strong expression of synaptophysin and chromogranin, confirming the neuroendocrine nature of the tumor. The Ki-67 index indicated a low proliferation rate (< 2%), consistent with a well-differentiated grade. Following surgery, the patient was prescribed a wide range of antibiotics, serum and electrolyte therapy, and injected vitamins to support recovery.

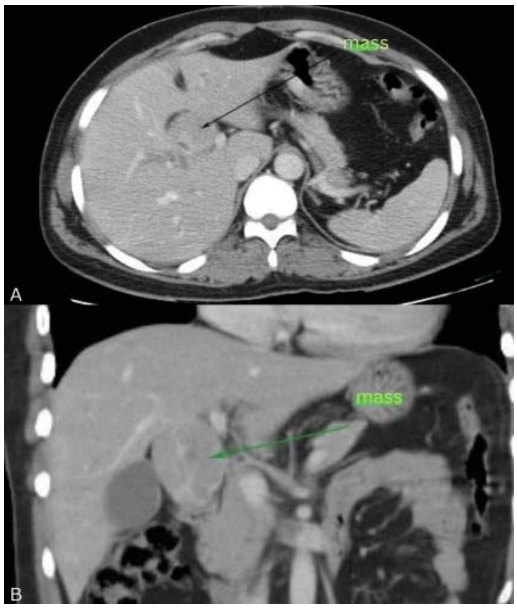

Figure 1: Ultrasound imaging demonstrating a mass with a suspicious origin from the liver.

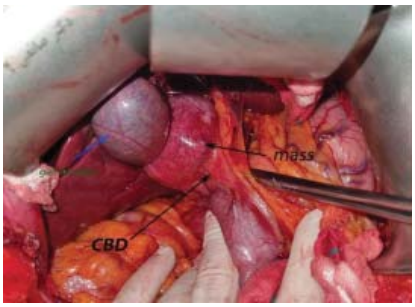

Figure 2: Preoperative imaging highlighting the mass's location (indicated by an arrow) before resection.

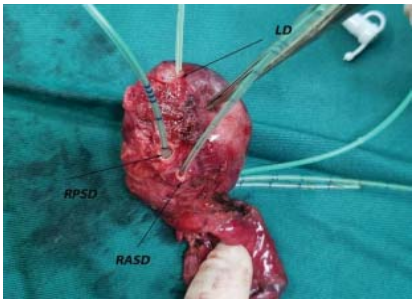

Figure 3: Postoperative imaging showing catheters (arrows) inserted through the biliary tree.

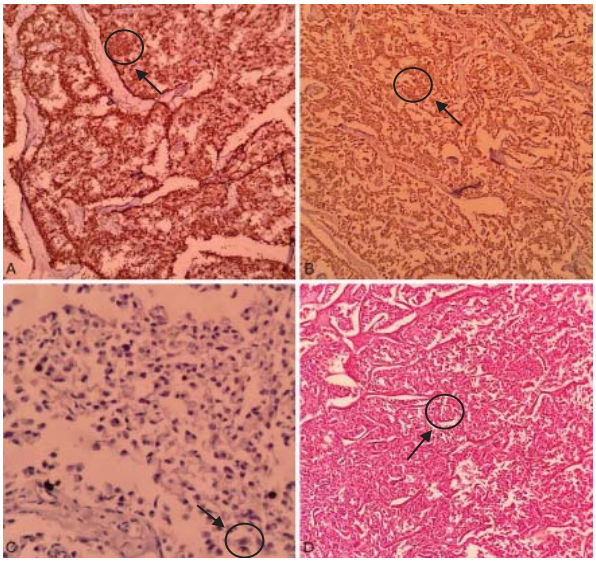

Figure 4: A) Synaptophysin, diffuse and strong expression confirming neuroendocrine nature of cells. B) Chromogranin, diffuse and strong expression confirming the neuroendocrine nature of cells. C) Ki67: positive in less than 2% of cells. D) H&E staining shows monotonous regular cells arranged in nests with salt & pepper chromatin.

In postupdate 4, the patient experienced abdominal pain. Follow-up sonography and CT imaging revealed a fluid collection in the subhepatic region, suspected to be a biloma, measuring 29 x 80 x 130 mm. A percutaneous drainage catheter was inserted, and a small duct in segment 1 was monitored, resulting in the cessation of leakage within one week.

Discussion

Gastrointestinal NETs are primarily derived from Kulchitsky cells. Only 0.32% of digestive NETs are EBNETs, and their immunohistochemical profiles are distinct [1,2].

In a recent study of 223 patients with EBNETs, the median age was 61, with the majority of the patients being male. It is noteworthy that 18.3% of the patients had synchronous distant metastases, primarily affecting the liver. There was a median tumor size of 17.5 mm, which is smaller than in our patient. The majority of tumors presented with neuroendocrine histology without a specific extrahepatic biliary location, which is consistent with our findings of no identifiable primary source.

EBNETs have diverse macroscopic characteristics, such as nodular and infiltrating growth patterns, and histologically resemble intestinal neuroendocrine tumors, often invading ductal walls [4,5]. Ki-67 serves as a critical prognostic factor for tumor grade: 2% indicates G1 (well-differentiated), 3% - 20% indicates G2 and > 20% indicates G3 (poorly differentiated) [6,8]. Despite the limited specific data on EBNETs, this grading system is useful for assessing EBNETs' biological behavior and aggressiveness [8].

Some cases have shown elevated urinary 5-hydroxyindoleacetic acid (5-HIAA) and gastrin levels preoperatively; however, the majority of diagnoses are made intraoperatively or postoperatively based on pathology reports. Improved preoperative diagnosis could potentially be achieved by routine use of brush cytology specimens during procedures like ERCP or endoscopic ultrasound-guided fine needle aspiration. To date, only two EBNETs have been diagnosed preoperatively via histological biopsy results, and our case represents the third instance of such a diagnosis [9].

Distinguishing Neuroendocrine Tumors (NETs) from carcinomas, particularly extrahepatic bile duct tumors, can be challenging preoperatively. EBNETs typically show less aggressive local invasion and lower metastatic rates. Complete surgical resection is often feasible for EBNETs [10,11]. Prognosis varies significantly based on tumor size and the Ki-67 index, although many diagnoses are made postoperatively due to preoperative differentiation difficulties [6,12].

An aggressive surgical resection is the only possible treatment for EBNETs, which have a slow growth pattern. Hepatic duct resection with mass followed by hepatojejunostomy reconstruction is the most common surgical approach [13-15].

Contrary to this, patients who did not undergo surgery were more likely to receive chemotherapy or radiation therapy [2]. Although the National Comprehensive Cancer Network guidelines recommend lymph node dissection, its exact extent is not clear; however, in our patient, we performed liver hilum lymphadenectomy CHA was done to the body of celiac [15].

Debulking should be attempted for inoperable tumors [16]. Young patients with localized tumors without distal metastases may benefit from liver transplantation when traditional curative resection is not possible, with a comprehensive evaluation of the Ki-67 index conducted before the procedure. A variety of medical treatment options are available for advanced EBNETs, including systemic chemotherapies, targeted therapies, somatostatin analogs, liver-directed therapies, and radionuclide therapies targeting peptide receptors [5,17,18]. An endoscopic ultrasound-guided biopsy revealed a preoperative diagnosis of EBNET in a patient, demonstrating the feasibility of a preoperative diagnosis of EBNET [11].

To conclude in tumors located in segment 4 of the liver involving the portal confluence, the differential diagnosis should include CHD. There is a need for further comprehensive studies and surgical reports, given the complexity of EBNETs and the variability in treatment outcomes. Our understanding of EBNET pathogenesis and surgical approaches may be enhanced by such investigations, which may lead to improved patient management and outcomes in the future.

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