CASE REPORT | LIVER

Siblings Diagnosed With Primary Neuroendocrine Tumor of the Left Hepatic Duct

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ABSTRACT

Primary left hepatic duct neuroendocrine tumors are extremely rare. We describe 2 cases of siblings, a 51-year-old brother and a 48-year-old sister, who were both diagnosed with primary left hepatic duct neuroendocrine tumor. Both patients underwent successful left hepatectomy and are both alive with no recurrence. For this rare malignancy, while definitive diagnosis is made only by histopathology, a margin-free surgical resection remains the only curative treatment modality to date.

INTRODUCTION

Primary biliary tract neuroendocrine tumors (NETs) are rare with a range from 0.2% to 2% of all gastrointestinal NETs.1,2 The final diagnosis requires always the chromogranin A (CgA) determination with immunohistochemistry in the specimen. A MEDLINE search for the literature has identified just 2 reports of NETs that arose clearly from within the right or left hepatic duct, hereby intrahepatic bile ducts are the most uncommon site of neuroendocrine malignancy in the biliary tract.

CASE REPORT

Case 1: A 48-year-old woman presented with abdominal pain mainly referred to the right upper quadrant. Her father had prostate cancer. Physical examination revealed no remarkable findings. Abdominal ultrasonography (US) presented a hyperechoic lesion measuring 4 cm in the left liver. Laboratory workup showed carbohydrate antigen 19-9 65.3 U/mL and cancer antigen 72-4 17.70 U/mL, without any other abnormalities. Total body contrast computed tomography (CT) showed a hypodense formation in the fourth hepatic segment with a thick peripheral portion, measuring 3.8 × 3.2 × 3 cm (Figure 1). Abdominal contrast magnetic resonance imaging showed a lesion measuring 4 × 3 × 3.5 cm in the fourth hepatic segment (Figure 2).

The patient underwent left hepatectomy with cholecystectomy. Intraoperative ultrasonography (USG) confirmed a lesion arising from the left hepatic duct. The operation was successfully performed, and after an uneventful recovery, our patient was discharged in good condition. Histopathology with immunohistochemistry reported NET cell appearance and positivity for Pan-cytokeratin, low-molecular-weight cytokeratin, CgA, and cluster of differentiation 56 (CD 56), with a Ki67 index of <2%, thus confirming diagnosis of NET G1 of the left hepatic duct. After 39 months of follow-up, included serial laboratory tests, abdominal USG, chest and abdomen CT, and an octreotide scan scintigraphy, the patient had good health without recurrence (Figure 3).
Case 2: A 51-year-old man presented with vomiting and abdominal pain to the right upper quadrant. The patient’s sister had been diagnosed and operated for NET G1 of the left hepatic duct, and his father had been diagnosed with prostatic cancer. Laboratory workup revealed no remarkable findings. Abdominal US showed a hyperechoic lesion measuring 6 × 7 cm in the left liver. Abdominal CT and magnetic resonance imaging confirmed a lesion in the left liver (Figure 4). Contrast-enhanced ultrasound were suggestive for cholangiocarcinoma with suspected involvement of the pancreaticoduodenal lymph nodes.

The patient underwent left hepatectomy with cholecystectomy and locoregional lymphadenectomy. Intraoperatively, USG confirmed a lesion arising from the left hepatic duct.

The operation was successfully performed, and after an uneventful recovery, our patient was discharged in good condition. Pathological examination with immunohistochemistry postoperatively of the mass revealed NET cell appearance and positivity for CgA, homeobox protein CDX-2, and somatostatin receptors-2A,5 with a Ki67 index of 2.3%, thus confirming diagnosis of NET G1 of the left hepatic duct. Three months after surgery, positron emission tomography–68Ga-DOTANOC revealed hypercaptation areas in proximity to the head of the pancreas, along the pancreas body, and in proximity to the cutting surface of the liver (Figure 5).

The patient was started on lanreotide treatment. Follow-up endoscopic ultrasound confirmed highly vascularized formation, of size 28 mm in contiguity to the head of the pancreas, suggesting a malignant duodenal NET with nodal metastasis near the pancreas. After multidisciplinary operations, the patient was discharged in good condition.
discussions, the patient underwent total pancreasectomy with splenectomy and hepatic resection. Intraoperative extemporaneous analysis of the masses in contiguity to the pancreas (head and body) confirmed them as metastatic NET lymph nodes (Figure 6). The operation was successfully performed, and after an uneventful recovery, our patient was discharged in good condition. Histopathology of the surgical specimen reported that the pancreas parenchyma was tumor-free with 2 positive metastatic lymph nodes in contiguity to the head and the body, the lesion in the liver was chronic xanthogranulomatous inflammation mimicking tumor nodule, and the duodenum was positive for primitive multifocal NET G1 and partially positive for gastrin (<30%).

DISCUSSION

Primary biliary tract NETs are rare, and intrahepatic bile duct NETs are further rare, with only 2 cases reported in the literature. In 1998, a right hepatic duct NET was diagnosed in a 74-year-old asymptomatic man as an incidental finding and was successfully treated by surgery. In 2002, a NET in the left hepatic duct was diagnosed in a 69-year-old woman with right upper quadrant pain. Initially the tumor was not resectable and somatostatin analogue was administered with evidence of radiological tumor regression.

We present the first case of 2 sibling patients, brother and sister, who were both diagnosed with primary left hepatic duct NET and were successfully treated by surgery with no local recurrence. Although the presence of NETs in the sibling is highly suspicious for hereditary endocrine syndrome, a genetic test for multiple endocrine neoplasia type 1 resulted negative.

Nevertheless, an unknown hereditary endocrine syndrome or multiple endocrine neoplasia type 1 mutation could play a role in the genesis of the 3 tumors (2 hepatic and 1 duodenal) in 2 siblings.

There are a small number of intrahepatic bile duct NET cases reported in the literature, making it difficult to define a unique treatment strategy. Our cases represent 50% of the world literature, and we urge consideration of radical removal of lesions as a curative treatment.

DISCLOSURES

Author contributions: A. Dayan and C. Ricci wrote the manuscript. D. Santini completed the pathological study. D. Campana, P. Fughelli, F. Minni, and B. Nardo edited the manuscript. B. Nardo is the article guarantor.

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Figure 5. Positron emission tomography shows the hypercaptation area (A) in close proximity to the head of the pancreas and (B) in proximity to the cutting surface of the liver.

Figure 6. Enlarged metastatic neuroendocrine tumor lymph node near the pancreas head.
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