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Case Report

Neurendocrine tumor of common hepatic duct: an uncommon site tumor

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ABSTRACT

The neuroendocrine tumor of extrahepatic biliary tract is a rare neoplasm of the gastrointestinal tract. We present a case of 16 year old male presenting with epigastric pain and jaundice with a well-defined lesion in common hepatic duct on imaging. The patient underwent tumor resection. Histopathology examination revealed thickened common hepatic duct infiltrated by tumor cells with expression of Pan CK, Synaptophysin & Chromogranin with Ki- 67 proliferation index of 5%. The final diagnosis of Neuroendocrine tumor of Common Hepatic Duct, grade 2 was rendered. The patient showed no recurrence to date without intravenous chemotherapy.

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INTRODUCTION

Neuroendocrine tumor of a biliary tract is a rare malignant tumor of gastrointestinal neuroendocrine tumors constituting about 0.2 – 2 percent.[1,2] The tumor most commonly arises from a common bile duct followed by hilar confluence, cystic duct, common hepatic duct and left hepatic duct. The average age of presentation of neuroendocrine tumor is about 47 years with a female predominance. The present case is a rare neuroendocrine tumor arising from a common hepatic duct (CHD) in a 16 year old male with extension into loco-regional lymph nodes.

CASE REPORT

A 16- year average-build male patient presenting with pain in the epigastrium and mild yellowish discoloration of sclera and urine for 6 months. There was a history of the passage of black coloured stools along with loss of appetite. There was no history of previous surgery, pancreatitis, gastric outlet obstruction or gastrointestinal bleed. On examination, the abdomen was soft on palpation and no lump was palpable.

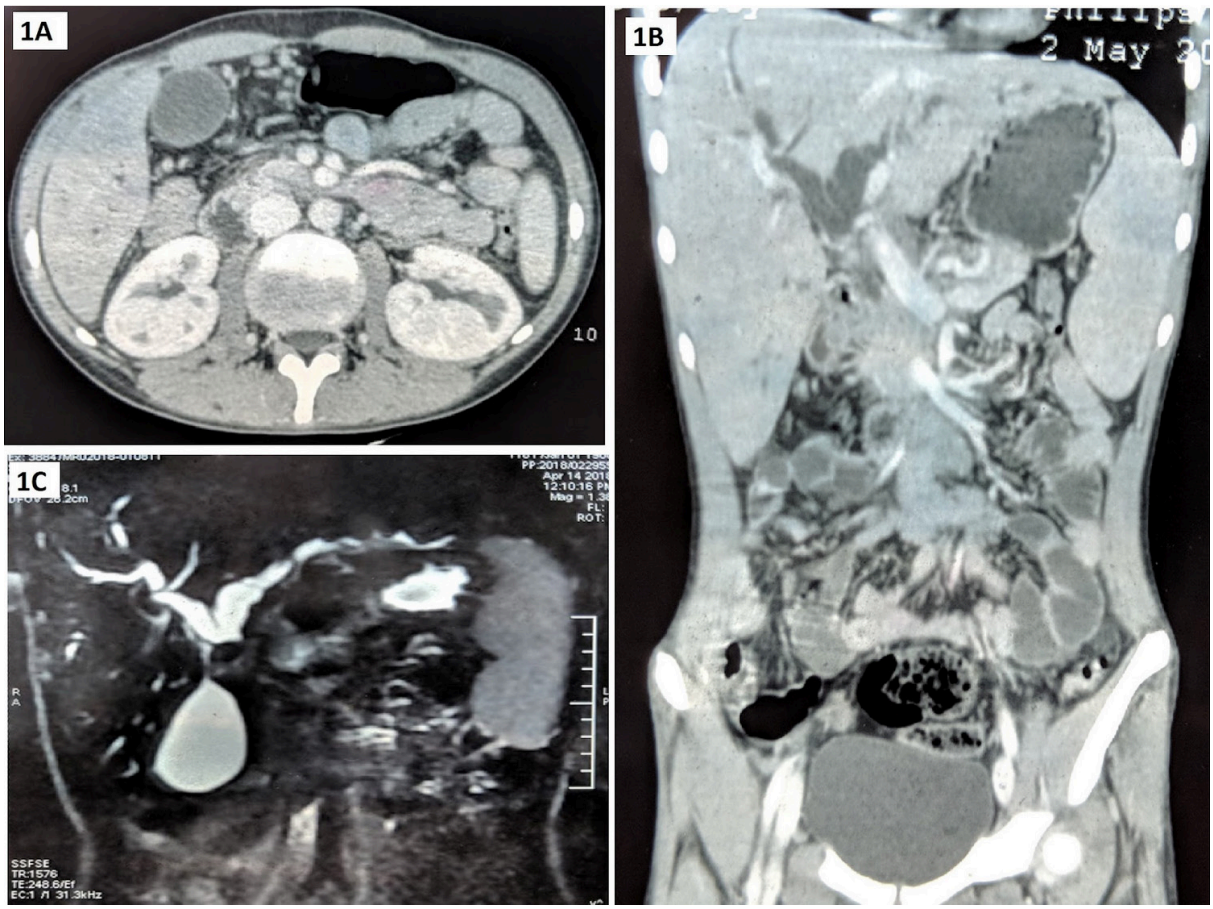

Figure 1: : *Contrast-enhanced abdominal computed tomography scan showing dilation of the biliary tree and an ill-defined mass, approximately 14.5 mm in diameter in common hepatic duct with heterogenous post contrast dilatation of rest of CHD and bilobar intrahepatic biliary radicle dilatation.* ***(A,B)*** *MRCP showing a filling defect in the common hepatic duct* ***(C).***

Serological test were performed the per-operative findings were Bilirubin(total): 5.89 mg/dl, Bilirubin(direct): 3.5 mg/dl, SGOT: 87 U/l, SGPT: 25 U/l, Alkaline Phosphatase: 250U/l, Urine bilirubin: Present, Gamma glutamy transferase: 301U/l & CA 19.9: 158.92 U/ml.

A triple phase contrast enhanced computarised tomography (CECT) revealed ill-defined rounded soft tissue attenuated lesion, minimally hypo to iso dense in common hepatic duct (CHD). The lesion was seen arising from the wall projecting into the lumen, measuring 14.5 x 12.8 x 10.8 mm showing nearly heterogenous post contrast dilatation of the rest of CHD and bilobar intrahepatic biliary radicle dilatation with circumferential enhancing wall thickening of CHD. Multiple subcentrimetric lymph nodes were seen at the porta, peripancreatic region, precaval, a celiac group with the largest in the perihepatic region measuring approximately 16 mm. (fig. 1A and B). A Magnetic resonance cholangiopancreatography (MRCP) was also performed which confirmed the CECT findings, showing focal wall thickening with intraluminal hypointense areas seen in CHD causing abrupt cut-off of CHD. Upstream biliary dilatation was seen. fig.1C)

The primary biliary confluence was well formed. The lesion was seen closely abutting the cystic duct and neck region of the gall bladder. The clinical and radiological diagnosis of cholangiocarcinoma was made. The patient underwent a laparatomy and cholecystectomy, with CHD tumor resection, lymph node biopsy, and Roux-en-Y hepaticojejunostomy reconstruction. The post-operative period was uneventful and the patient was discharged with abdominal in situ in view of high output serous fluid. The specimen was sent for hisopathological examination. Grossly specimen comprised of gall bladder with an attached part of CHD and common bile duct. CHD showed a solid white mass measuring 1.5 x 1.0 x 1.0 cm in size. The sections from the resection margins including proximal and distal part of the bile duct were also taken. Regional lymph node including celiac artery lymph node, common hepatic artery lymph nodes, proper hepatic artery lymph nodes, and right and left hepatic artery lymph nodes, periportal, peripancreatic, retropancreatic and gastroduodenal artery lymph nodes were also sent for histopathological examination. Microscopically, the thickened common hepatic duct was infiltrated by islands and nests of cells. The tumor was confined within the wall of the hepatic duct. Individual tumor cells were small to medium sized with eosinophilic to amphophilic, finely granular cytoplasm. The nuclei are mildly pleomorphic with "salt and pepper" (finely stippled) chromatin, inconspicuous

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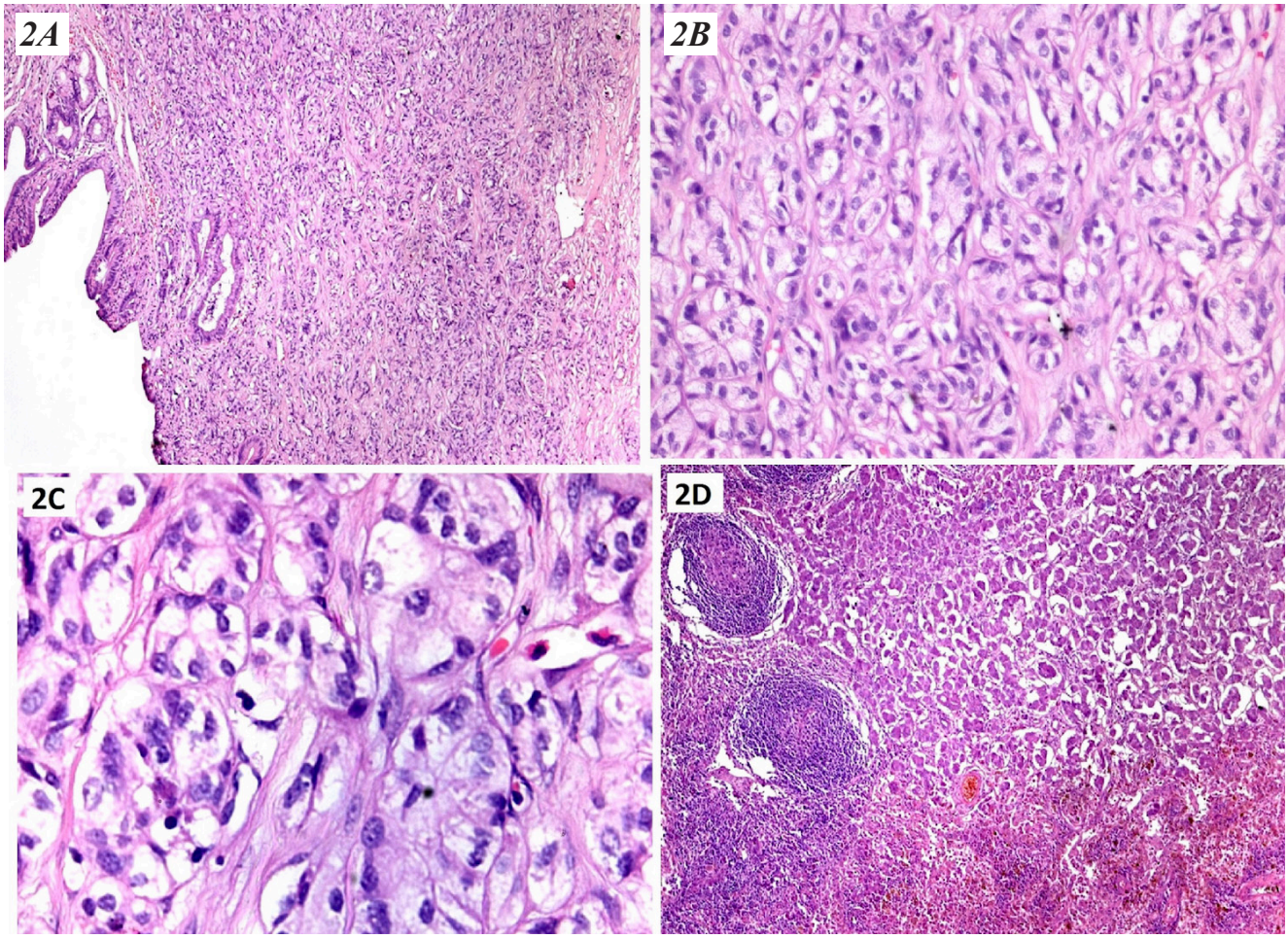

Figure 2: *Histopathology images showing unremarkable hepatic duct lining epithelium with tumor infiltrating the wall disarranged in islands and nests of cells.(A,B) Individual tumor cells are moderately pleomorphic with eosinophilic to amphophilic, finely granular cytoplasm. The nuclei are mildly pleomorphic with "salt and pepper" (finely stippled) chromatin, inconspicuous nucleoli.(C) Lymph node architecture effaced by metastatic tumor nests.(D) [Original magnification x50 (A,D), x200 (B), x400(C)]*

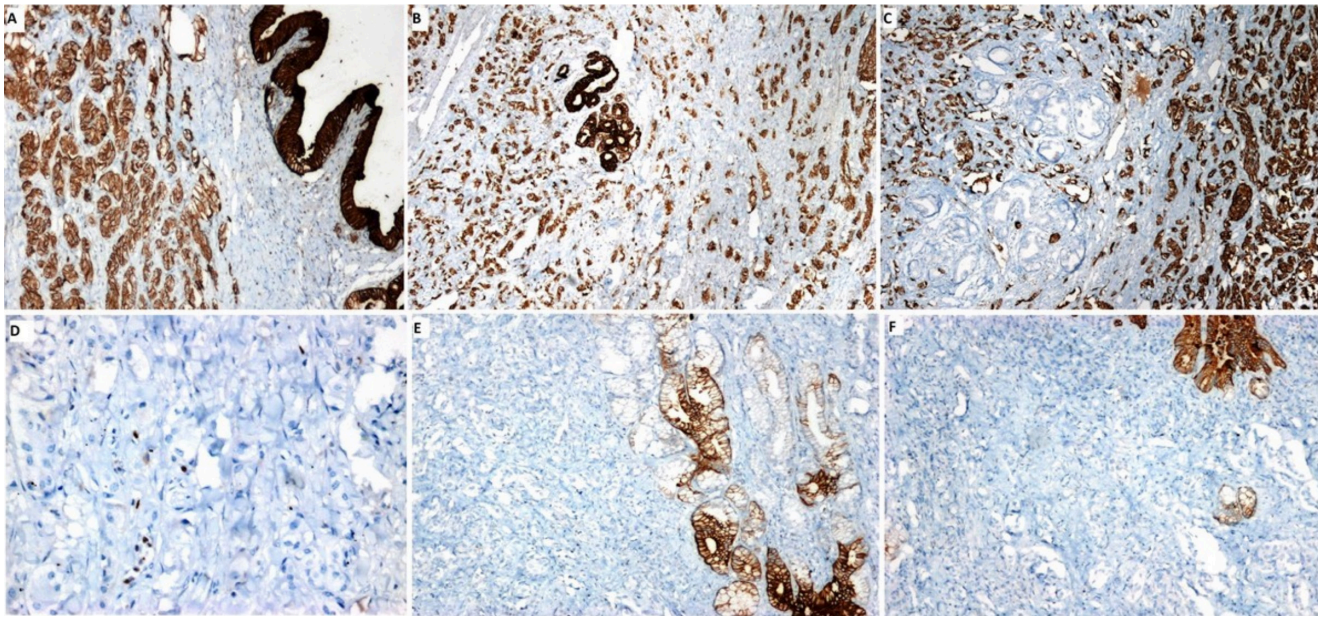

Figure 3: *Immunohistochemistry markers: Tumor cells showing diffuse positivity for Pan Cytokeratin, Synaptophysin & Chromogranin**(A-C)**, Ki 67 proliferation index~5%**(D)**. CK7 & CK19 are highlighting the lining epithelium with negative expression in tumor cells. **(E,F)** [Original magnification x50(A-C), x200 (D), x50(E,F)]*

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nucleoli. Occassional mitotic figures were present. (fig. 2A-C)

Immunohistochemical studies showed the tumor cells were positive for Pan-cytokeratin, synaptophysin, and chromogranin (fig. 3A-C), and Ki-67/MIB-1 Labelling Index was 5 % (fig. 3D).

Based on these histopathological findings, a pathological diagnosis of Neuroendocrine Tumor Grade 2 was established. Two out of 6 regional lymph nodes were positive for metastatic carcinoma and 1 out of 8 gastroduodenal artery lymph nodes and 2 out of 11 retroperitoneal lymph nodes were positive for metastatic carcinoma,(fig. 2D) rest all other lymph nodes were free from metastatic carcinoma. The tumor was staged according to AJCC 8th edition and pathological staging was given as T1N2. There was no evidence of distant metastasis. Post operative following serological test were performed hemoglobin: 12.4 gm, bilirubin(total):0.51 mg/dl (Normal), bilirubin(direct): 0.15mg/dl (Normal), SGOT:61U/l (Mildly elevated), SGPT: 27U/l (Normal), alkaline Phosphatase: 146 U/l (mildly elevated). A follow up ultrasound whole abdomen was performed showed no evidence of intrahepatic biliary dilatation, however, there was a presence of moderate ascites. Postoperative ultrasonography was performed & there was no evidence of residual tumor and distant metastatic deposits. The cytopathology of the ascitic fluid was also sent for the presence of malignant cells. The cytological smears were prepared and reported as negative for malignant cells.

DISCUSSION

Gastrointestinal tract is a large neuroendocrine system, however the distribution of neuroendocrine cells is not uniform with most of the neuroendocrine tumor occurring in the gut while extrahepatic biliary tract has least number of neuroendocrine cells leading to rare occurrence of neuroendocrine tumor in extrahepatic biliary tract, to best of our knowledge less than 80 cases have been reported in literature. Their distribution in the biliary tract is also variable with most tumors occurring in ampulla followed by the gallbladder, middle CBD, proximal CBD, distal CBD, and hepatic duct/cystic duct.[3,4]

The etiology of the neoplasm is not well known due to the absence of neuroendocrine cells in the biliary tract, however, few cases have been associated with cholelithiasis and congenital malformations which leads to chronic inflammation and metaplasia which further leads to the development of NET.[5] Neuroendocrine tumor of common hepatic duct are rare, constituting only about 3% of neuroendocrine tumor of extrahepatic biliay tract[6]. The neuroendocrine tumor of biliary tract are more frequent in women (ratio 2:1), with an average age of presentation is 47 years (range 10–79), to best of our knowledge less than ten cases of NET of the extrahepatic biliary tract have been reported in children and adolescents. The most common presenting symptoms are painless jaundice followed by abdominal pain. The NET of a biliary tract are most commonly non- functional but few cases having symptoms due to hormones secreted by tumor have been reported, symptoms include diarrhea, recurrent peptic ulcerations due to serotonin and gastrin secretion. Elevated levels of 5-hydroxy indole acetic acid (HIAA) in urine have also been detected in a few cases [3,4]. The NET of bilary tract has a poor prognosis and are difficult to diagnose preoperatively, usually presents with locoregional lymph node involvement and distant metastasis. The most common site of distant metastasis includes liver followed by bone and lung and also associated with lymph node metastasis.[7]

NET are divided into three grades (G1–G3,) based on a number of mitotic figures and the Ki-67 index. The poorly differentiated NETs (Neuroendocrine carcinoma) can be divided into two types according to the tumor cell type: large cell NEC, small cell NEC. Many biomarkers are used for diagnoses, such as Synaptophysin and Chromogranin, in the present case synaptophysin and chromogranin were diffuse positive with Ki-67 about 5%, and finally diagnosed as NET G2 with retropancreatic and gastroduodenal artery lymph node involvement. Due to the rarity of neuroendocrine tumor in the extrahepatic biliary tract, there is no standardized treatment regimen, surgery remains the main stay, however, this tumor usually present with metastasis most commonly liver metastasis which may be treated by excision, embolization/chemoembolization, or ablation. Chemotherapy including somatostatin analogue can be used for carcinoid syndrome since tumor are hypervascular antiangiogenesis factors may be added to the regimen. Tyrosine kinase inhibitor, along with mTOR inhibitors and radiolabeled somatostatin analogs can also be used in metastatic settings, however, chemotherapy regimen still needs to be standardized due to the rarity of the tumor in biliary tract[8,9]

CONCLUSIONS

Large studies are required for a better understanding of the etiology, treatment and survival rates of the patient with NET of the extrahepatic biliary tract. The current case is an addition to the neuroendocrine tumor of common hepatic duct in an adolescent male patient, presenting with locoregional lymph node involvement with no signs of recurrence after 8 months of follow up.

Conflict of Interest: None

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