Case Report

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Primary Neuroendocrine Tumour of Extrahepatic Bile Duct: A Rarity

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Abstract

Extrahepatic bile duct Neuroendocrine Tumour (NET) is uncommon, and hence a pre-operative diagnosis is rare. The definite diagnosis depends on post-operative histopathology examination and immunohistochemistry studies. Complete excision of the lesion is considered as a curative treatment. We report a case of 39 year old male who presented with obstructive jaundice and imaging suggested Cholangiocarcinoma involving the hepatic ducts. He underwent a right hepatectomy and cholecystectomy with hepatoduodenal lymphadenectomy. The histopathological examination revealed a Neuroendocrine Tumour.

Keywords: Extrahepatic bile duct (EHBD); RHD; LHD; CHD; NET.

INTRODUCTION

Neuroendocrine tumours (NETs) arise from Kulchitsky cells (Enterochromaffin cells), which are derived from the endoderm. These cells are most frequent in the small intestine and uncommon in the hepatobiliary tract, which explains the rarity of neuroendocrine tumours at this site.[1] Adenocarcinomas are the most frequent neoplasms originating from the biliary tree, they represent upto 80% of all bile duct tumours. Extrahepatic bile duct (EHBD) NETs are extremely uncommon, make up 0.2% to 0.3% of all the tumours arising at this site, and occur more frequently in younger women.[2]

Pre-operative diagnosis of EHBD NET is rare and majority of the cases are diagnosed intra-operatively or post-operatively on the histological examination, as they are presumed to be Cholangiocarcinoma which is a more common malignancy at this site.

Here we present a case of NET originating at the confluence of right and left hepatic ducts and involving common hepatic duct.

CASE REPORT

A 39 year old male presented with dull aching abdominal pain and jaundice. His lab investigations showed increased Bilirubin (Total) of 2.91 mg/dl, of which Bilirubin (Direct) was 2.41 mg/dl. His

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serum Gamma Glutamyl Transferase (GGT) was 152.00 U/L.

On further evaluation, Computed tomography (CT) abdomen showed a hilar lesion involving the confluence of right and left hepatic ducts, suggested possibility of Hilar Cholangiocarcinoma (Klatskin tumour). Magnetic resonance imaging (MRI) also suggested Klatskin tumour and no other lesions were detected on imaging.

He underwent a right hepatectomy and cholecystectomy with hepatoduodenal lymphadenectomy. On gross examination, the right lobe of liver measured 16x16x8 cm and weighed 810 grams. The right anterior hepatic duct (7mm in length) and right posterior hepatic duct (RHD) (5 mm in length) were identified with labelling sutures at the hilum. Left hepatic duct (LHD) and common hepatic duct (CHD) were also identified and each measured 8 mm in length. The portal vein measured 3.5 x 1.5 cm. The cut surface of the liver at the hilum showed a well circumscribed, grey white, firm tumour measuring 3.2x2.8x2.6cm.

We had also received gall bladder measuring 7x2 cm, the mucosa was bile stained and showed yellowish streaks.

Microscopic examination of the hilar tumour showed tumour cells arranged in nests, islands, trabeculae, and organoid pattern, exhibiting round to ovoid nuclei with salt and pepper chromatin (Fig. 1A, B, D). Perineural and intraneural invasion were seen multifocally (Fig. 1C). The tumour was seen mainly centered at the confluence of the right and left hepatic ducts with the common hepatic duct, and involved all the ducts, predominantly the RHD – posterior.

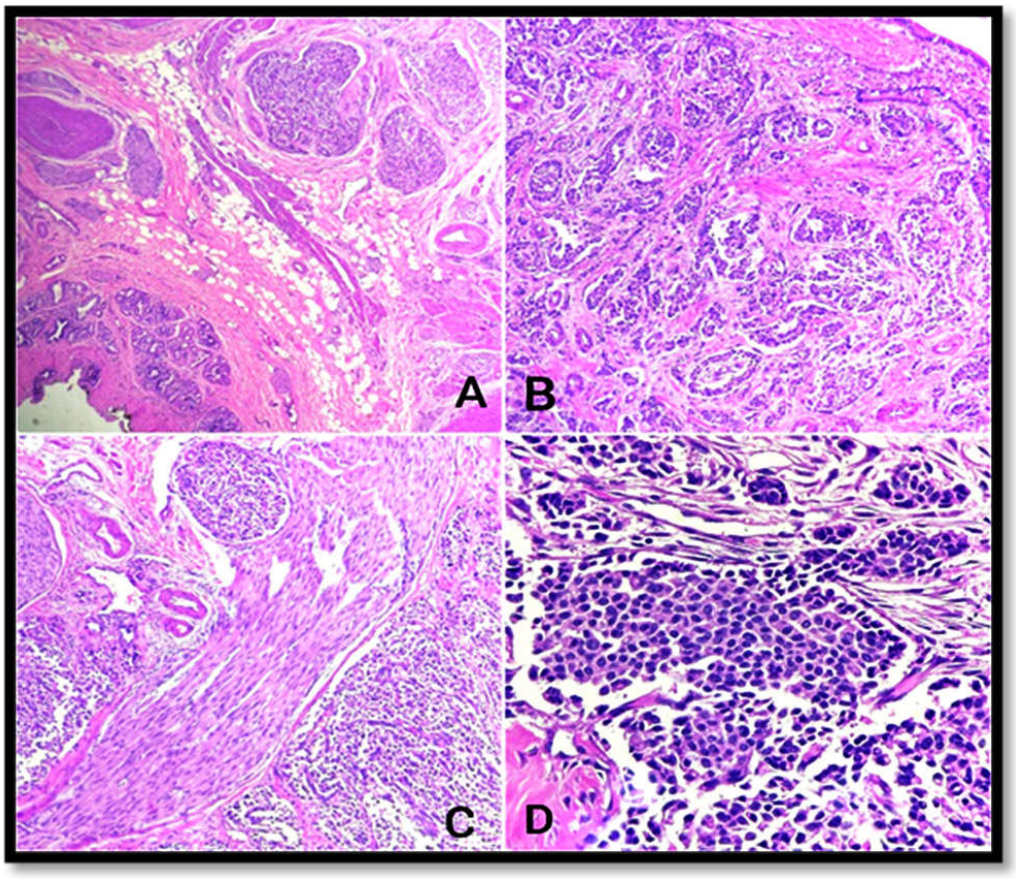

Fig. 1: A – Tumour cells arranged in lobules (H&E stain 40x), B – Tumour cells arranged in nests, islands, trabeculae, and organoid pattern (H&E stain 100x), C - Perineural and intraneural invasion (H&E stain 100x), D – Tumour cells exhibiting round to ovoid nuclei with salt and pepper chromatin (H&E stain 400x)

Portal vein was free of tumour. The non neoplastic liver showed portal to portal and portal to central bridging fibrosis with occasional nodules (Fibrosis stage – 4-5/6).

The gall bladder showed mild cholecystitis with cholesterolosis and was free of tumour. Two tiny hepatoduodenal lymph nodes isolated (2mm each) were free of tumour.

On Immunohistochemistry (IHC) studies, the tumour was positive for Synaptophysin, Chromogranin and CK (Fig. 2A, B, C) confirming Neuroendocrine Tumour (NET). CK7, CK20 and CEA were negative which ruled out Adenocarcinoma. The proliferation index (Ki67) was 8 to 9%, confirming a Grade 2, NET (Fig. 2D).

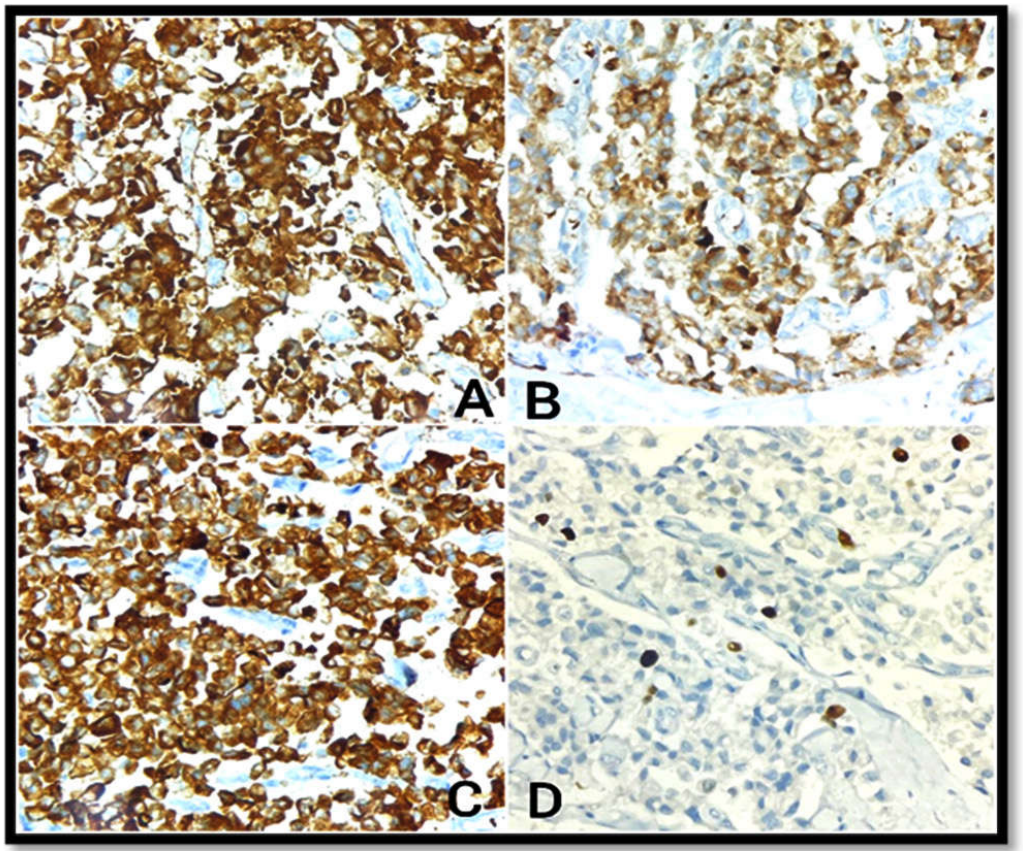

Fig. 2: On Immunohistochemistry, the tumour is positive for Synaptophysin (A), Chromogranin (B), CK (C) and Ki67 showed 8 to 9% proliferation index (D).

DISCUSSION

Bile duct NETs represent 0.2% to 2.0% of all digestive tract neuroendocrine tumours, and thus extremely uncommon.[3] Although the exact mechanism by which NET develops in bile duct is unknown, the generally accepted notion is that chronic inflammation of the bile duct leads to subsequent metaplastic changes of the endocrine cells, and then transformation into NET.[3] Among the extrahepatic bile duct NETs, the most frequent sites are common hepatic duct and distal CBD (19.2%) followed by mid CBD (17.9%), the cystic duct (16.7%) and the proximal CBD(11.5%).[4]

Although NETs have the capacity to secrete various hormonal substances such as gastrin, glucagon, insulin, serotonin, somatostatin and vasoactive intestinal peptide, these are often not detected during the pre-operative phase, as hormonal symptoms and detectable serum markers are often lacking.[5] Our patient presented with jaundice and otherwise was asymptomatic.

Noronha *et al.*[1] proposed that pre-operative confirmation of NET can be established by brush cytology smears obtained using ERCP, percutaneous transhepatic cholangiography (PTC) or endoscopic ultrasound guided fine needle aspiration. Because the NET is often submucosally situated, these techniques may at times produce false negative results.[5]

The neuroendocrine neoplasms of digestive tract are categorized into three subtypes according to World Health Organization (WHO) classification, 2019 Well differentiated neuroendocrine tumour (NET), poorly differentiated neuroendocrine carcinoma (NEC) and mixed neuroendocrine non-neuroendocrine neoplasm (MiNEN).[6] These neoplasms are graded according to histomorphology and proliferation index (Table 1).

Table 1: Classification and grading criteria for neuroendocrine neoplasms (NENs) of the GI tract and hepatopancreatobiliary organs.

Terminology	Differentiation	Grade	Mitotic rate (Mitoses/2mm²)	Ki67 index
NET, G1	Well differentiated	Low	<2	<3%
NET, G2		Intermediate	2-20	3-20%
NET, G3		High	>20	>20%
NEC, small cell type (SCNEC)	Poorly differentiated	High	>20	>20%
NEC, large cell type (LCNEC)			>20	>20%
MiNEN	Well or poorly differentiated	Variable	Variable	Variable

The widely accepted surgical approach to EBNETs is hepatic duct resection enbloc with the mass, with hepaticojejunostomy reconstruction.[7]

The level of aggression among EBNETs varies greatly. Given the rarity of these cases and the lack of long term follow up, determining the prognosis of these tumours is challenging.[8] However, the size of the tumour, lymphovascular invasion and proliferation (Ki67) index helps in determining the prognosis.[9] These tumours appear to have a better prognosis than bile duct carcinomas following surgical treatment, based on the data that is currently available.[8]

CONCLUSION

Extrahepatic biliary duct Neuroendocrine tumours are uncommon tumours. The rarity and the submucosal location of the NETs at this site, makes the diagnosis difficult preoperatively. Histopathological examination with IHC studies remain the mainstay for the diagnosis of EBNETs.

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