Biliary neuroendocrine tumor (BNET) of hepatic hilum: An interesting presentation with obstructive jaundice

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ABSTRACT

Biliary neuroendocrine tumour (BNET) are rare tumours of the biliary system. They may present with obstructive jaundice and resemble cholangiocarcinomas. However, they have good prognosis if resected completely. The aim of this article is to show the presentation of BNET in a young female, its biological behavior, its newer immunotyping for precise diagnosis and possibility of complete surgical excision which can result in excellent prognosis.

Keywords: Biliary neuroendocrine tumor, Hilar mass, Neuroendocrine tumour, Obstructive jaundice

INTRODUCTION

Biliary neuroendocrine tumours are rare tumours of the biliary hilum and can present clinically just like hilar cholangiocarcinomas. These are seen in middle aged females more commonly involving the common hepatic duct and proximal ducts and have an insidious and less aggressive clinical course when compared to cholangiocarcinoma [1]. These tumours should be differentiated from other hilar tumors as they are associated with markedly better prognosis on R0 resection.

CASE REPORT

Thirty year old female presented with jaundice, pruritus and clay colored stools for three months. Contrast enhanced Computerised Tomography (CECT) (Figure 1) and Magnetic Resonance CholangioPancreatography (MRCP) revealed a non cirrhotic liver with abrupt cut off of the common hepatic duct with Intrahepatic Biliary Radicle Dilatation (IHBR), right and left hepatic duct dilatation with hilar mass of size 3×3 cm suggestive of Type 1 cholangiocarcinoma (Figure 2). Fine Needle Aspiration Cytology (FNAC) of the mass lesion was suggestive of malignancy. As the patient developed features of cholangitis and had increased bilirubin, Percutaneous transhepatic biliary drainage (PTBD) of the left system was done. After PTBD, the laboratory investigations showed normalization of liver function (Total Bilirubin-1.2 mg%, Direct bilirubin-0.6 mg%, Alkaline Phosphatase- 80 IU/ml) and tumor markers (Alpha-FetoProtein level (AFP)-3.5 ng%, CA 19-9- 25 IU/ml and CEA- 2.5 ng%). After normalization of liver function, patient was planned for elective surgery. The hilar mass was in close proximity to the portal vein and carefully delineated and then resection of the hilar mass with roux en y hepaticojejunostomy was done. HPE of the
specimen was suggestive of low grade neuroendocrine tumour of the hilum with clear margins (Figure 3). Immunohistochemistry (IHC) done showed cytokeratin 7, chromogranin positive, neuron specific enolase strong immunoreactivity (70%) and CK 20, CD 34 negativity (Figures 4 and 5).

Figure 1: MRCP showing dilated Bilateral IHBR with abrupt cut off.

Figure 2: CECT showing hilar mass (arrow) with upstream bilateral dilated IHBR.

Figure 3: Cords and nests of tumour cells with moderate eosinophilic cytoplasm, round to oval nuclei and stippled chromatin with moderate pleomorphism and prominent nucleoli (H&E stain, x100).

Figure 4: IHC tumour cells diffusely staining for Chromogranin (H&E stain, x100).

The patient had an unremarkable postoperative course and was discharged home on postoperative Day 11 after free flow of contrast was seen through the hepaticojejunostomy site when contrast was given through the retained PTBD in the left hepatic duct. The case is described to emphasize that BNET (Biliary Neuro Endocrine Tumours) can present as hilar masses and it must be thought as a entertained diagnosis in spite of its rarity.
DISCUSSION

World Health Organization (WHO) system distinguishes well-differentiated neuroendocrine tumors (NETs) from poorly differentiated neuroendocrine carcinomas (NECs) [2, 3]. Well differentiated NETs, or carcinoid tumors, are those with mild or no atypia, ≤1 cm in size, with ≤2 mitoses/10 HPFs and without angioinvasion. Poorly differentiated neuroendocrine carcinomas (NECs) have high grade metastatic potential and are composed of highly atypical, small to intermediate sized tumor cells with necrosis and prominent angio and/or perineural invasion.

The European Neuroendocrine Tumor Society (ENETS) grades NET into three categories (G1-3) that dependent upon the tumor's proliferation status. 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% [2, 3].

NETs arising from the biliary tract are extremely rare (0.32%) [4]. In an analysis of 150 cases, most are found in the common hepatic duct and proximal bile duct (19.2%), followed by the middle of the common bile duct (17.9%) and cystic duct (16.7%) [1]. Symptoms related to hormone or peptide secretion are seen in <10% of cases. BNET are more common in females (F:M ratio of 1.6:1) at a mean age of approximately 47 years (range 6-79 years) where the most common symptoms were jaundice (60.3 %) and pruritus (19.2%) [1]. Cholelithiasis co-existed in 15 cases (19.2%). Surgical management was considered the main treatment for extrahepatic BNETs, where excision of extrahepatic biliary tree (62.82%) with portal vein lymphadenectomy (43.6%) was the most popular procedure [1]. BNETs are extremely rare which makes their characterization particularly difficult. Biliary NET are diagnosed if it fulfilled the following diagnostic criteria: (1) radiologically primary tumour in the extrahepatic biliary apparatus (2) classic pathology of neuroendocrine tumour with the histology of trabecular rosette, nesting, insular, or ribbon-like cell clusters, variable mitotic activity with small cell or large cell cytological features (3) positive expression of more than one type of immunohistochemical stain, such as chromogranin A, synaptophysin, CD 56 (CD56) or neural cell adhesion molecule [5].

In clinical practice, these lesions are difficult to diagnose and distinguish from cholangiocarcinoma preoperatively. Certain clinical features like propensity for young age, benign local invasion or distant metastatic disease can be useful but these are not absolute in distinguishing BNET from adenocarcinoma. Well-circumscribed hypervascular tumor during the arterial phase may help to differentiate them from other biliary neoplasms [6].

A pre-operative diagnosis can be made by examining brush cytology [7] Somatostatin analogues such as octreotide, have been shown in clinical trials cause symptomatic improvement [8]. Prognostic data for BNETs are limited due to their rarity [9].

It is to be noted that BNETs were previously classified as small cell carcinoma[SCC] and their prognosis shows marked heterogeneity. Albores-Saavedra et al., [10] analyzed the demographics and 10-year relative survival rates of carcinoids and small cell carcinomas [SCCs] of the gallbladder and ExtraHepatic Bile Duct(EHBD) according to histologic type and stage. There were 31 carcinoid tumors and 17 SCCs of the EHBD. The 10-year survival rate was 80% for carcinoid tumors of the EHBD And 0% for SCC of the EHBD. Almost all patients with SCC in the biliary system died within one year after diagnosis implying that carcinoids have better prognosis.

The optimal treatment for patients with NET or NEC is controversial as most of the current literature available comes from case reports and small case series, without comparable control groups [11]. Options for the management of localized biliary NETs include complete surgical resection, systemic therapy and multivisceral transplant.

CONCLUSION

BNETs are rare tumors in the biliary tract which may mimic cholangiocarcinoma. However, these have good prognosis when identified early and resected. Further developments in the techniques of immunohistochemistry is in order to precisely diagnose and treat these rare neoplasms.
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Conflict of Interest

Authors declare no conflict of interest.

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