Case study

Primary hepatic neuroendocrine tumor with Hepatocellular carcinoma- a rare case report.

Abstract

Aim: Hepatocellular carcinoma is the most common primary liver malignancy followed by intrahepatic cholangiocarcinoma. The diagnosis of primary hepatic neuroendocrine tumor, a rare liver lesion, generally occurs during histological examination.

Case report: A 48 year old male patient presented with a lesion in the segment 5/6 of liver clinically and imaging features suggestive of Hepatocellular carcinoma. He underwent resection of the lesion. Final histopathological analysis of the lesion showed combined Hepatocellular carcinoma and neuroendocrine tumor. DOTANAC scan was done postoperatively which confirmed primary hepatic neuroendocrine tumor by ruling out primary neuroendocrine tumor elsewhere. He is currently on adjuvant chemotherapy.

Discussion and Conclusion: Primary hepatic neuroendocrine tumor is a rare malignancy. It is mandatory to search for primary neuroendocrine tumors in rest of the gastrointestinal system before making the diagnosis. Combined Hepatocellular carcinoma and primary hepatic neuroendocrine tumor is a rare tumor which needs multidisciplinary team discussion to formulate treatment plan.

Keywords

Hepatocellular carcinoma, Hepatic neuroendocrine tumor, Ki 67, HepPar, CD 56, Synaptophysin, Arginase

Introduction

Primary hepatic neuroendocrine tumor (PHNET) is a rare tumor. It occurs in about 0.3% of all neuroendocrine tumors[1]. These tumors arise from neuroendocrine cells capable of producing functional peptides. Majority of these tumors occur in small bowel constituting about 44.7% of all the lesions[2]. PHNET must be histologically confirmed to be NETs for the diagnosis. Imaging studies are not specific for PHNET; most of them mimic hepatocellular carcinoma (HCC) or cholangiocarcinoma[3]. The definitive diagnosis is frequently made once the tumor has been removed and after confirming that there are no primary lesions elsewhere. Being a rare lesion, staging and treatment guidelines have not been formulated. However, surgical resection plays a crucial role[3]. Here we present a case of combined HCC and PHNET because of its rarity.

Case Presentration

A 48 year old male presented to us with a history of vague upper abdomen pain and loss of appetite for duration of 1 month. He was recently diagnosed to be a diabetic when evaluated as a part of routine health check. He was evaluated with ultrasound abdomen which showed a fatty liver with an irregular mixed echoic lesion in the right lobe of liver. We have evaluated him with routine blood investigations and imaging studies. His complete blood picture, renal and liver function tests were within normal limits. His tumor markers showed elevated Alfa feto protein (AFP) of 196ng/ml, Carcinoembryogenic antigen (CEA) and Carbohydrate antigen 19-9 (CA19-9) were within normal limits. Hepatitis viral markers were negative. Contrast enhanced CT of abdomen was suggestive of 10.7 x 6.1 cm partly exophytic mass lesion in segment 5/6 of liver with contrast enhancement features suggestive of hepatocellular carcinoma. There were multiple enlarged lymph nodes in the periportal area largest measuring 1.9*2.1cm. PET scan showed an SUV of 4.0 in the liver lesion and 3.3 in the lymph nodes. Figure 1 and 2 showing the pictures of CT abdomen and PET scan.

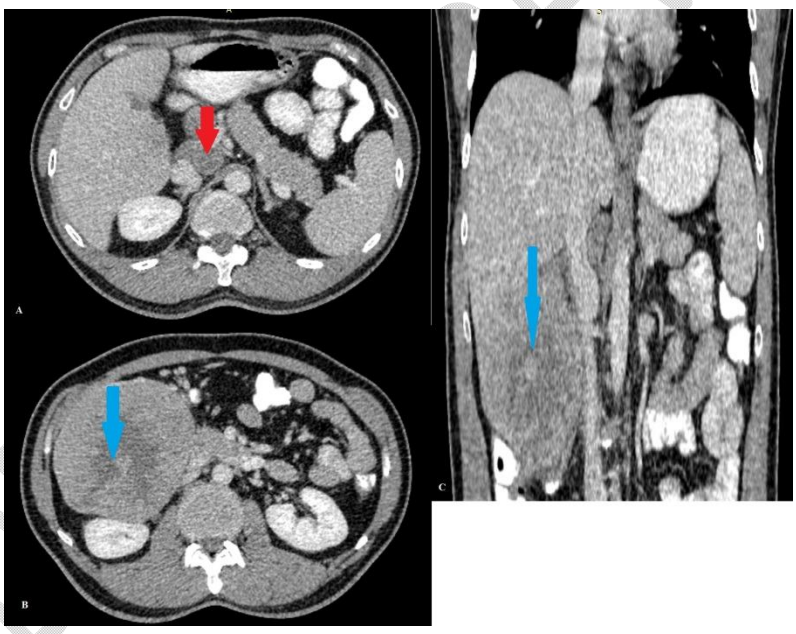

Figure 1: CT abdomen pictures showing the lesion, Red arrow marking lymph nodes and blue arrow marking the liver lesion.

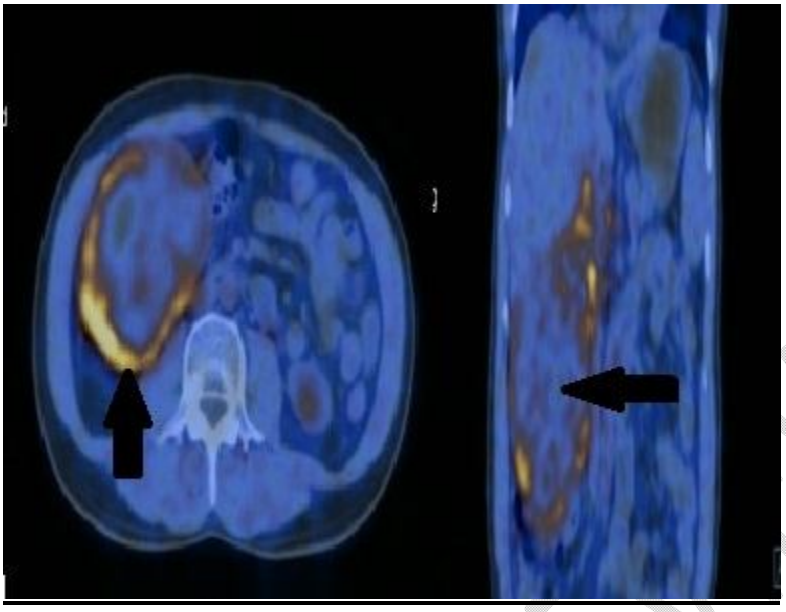

Figure 2: PET scan images. Arrow showing the lesion in segment 5, 6 of liver with PET uptake.

With a working diagnosis of hepatocellular carcinoma, we planned for diagnostic laparoscopy followed by resection of the tumor. On diagnostic laparoscopy, we found liver was non cirrhotic, no evidence of ascites or peritoneal metastasis. Large irregular mass arising from liver segment 5/6 was noted. We proceeded with laparotomy; greater omentum adherent to the liver mass was released. Lymph nodes in the periportal area were dissected. Fundus down cholecystectomy performed after ligating the cystic artery and duct. The lesion was resected with a 5cm margin from the tumor. Postoperative period was uneventful; patient was discharged on post-operative day 5. Figure 3, 4 showing intraoperative picture and specimen images.

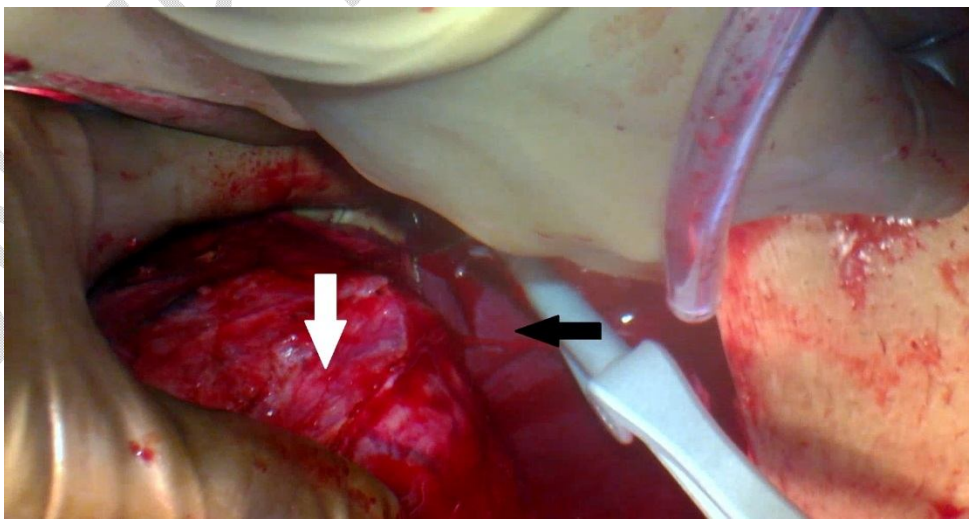

Figure 3: Picture showing liver lesion. Black arrow- Liver surface, White arrow-lesion.

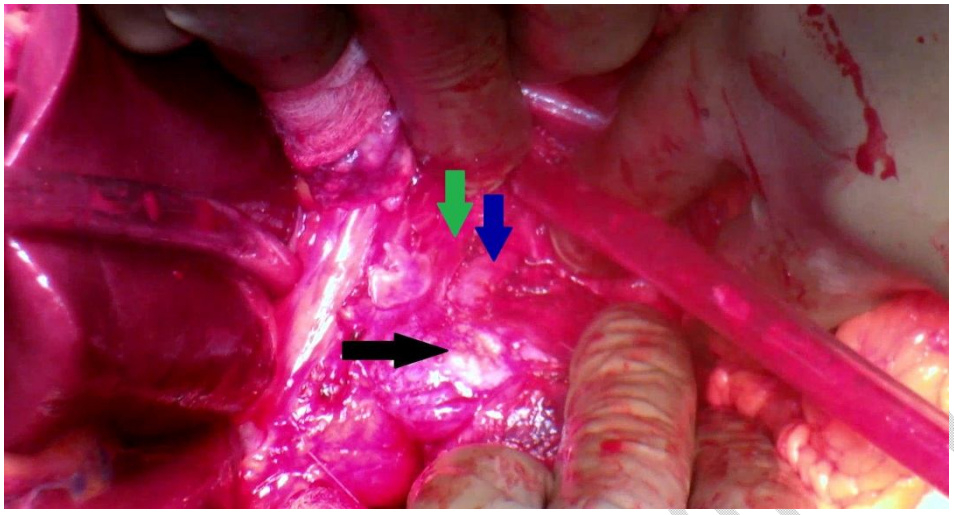

Figure 4: Picture showing portocaval lymph nodes. Green arrow- bile duct, blue arrow portal vein, black arrow- lymph nodes.

Histopathological examination of the lesion showed features suggestive of both hepatocellular carcinoma and large cell neuroendocrine carcinoma. The large lymph nodal mass also contained cells of large cell neuroendocrine cell carcinoma. Immunohistochemistry (IHC) markers were done to confirm the diagnosis using clone technique. Liver lesion contained 80% of the tissue suggestive of HCC which were positive for HepPar and Arginase; 20% of the tissue with large round cells positive for Synaptophysin and CD 56 suggestive of large cell NET. Tissue from lymph node was positive for Synaptophysin and CD 56. Figure 5, 6 showing microscopic picture of the lesion and IHC.

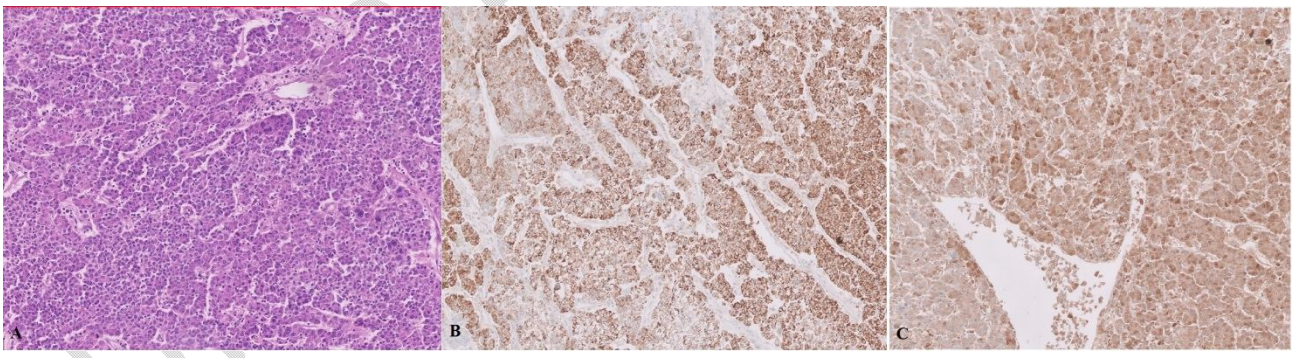

Figure 5: Images of HCC. A- High power magnification showing neoplastic hepatocytes with high Nuclear: Cytoplasmic ratio arranged in trabecular pattern, B- HepPar staining, C- Arginase staining.

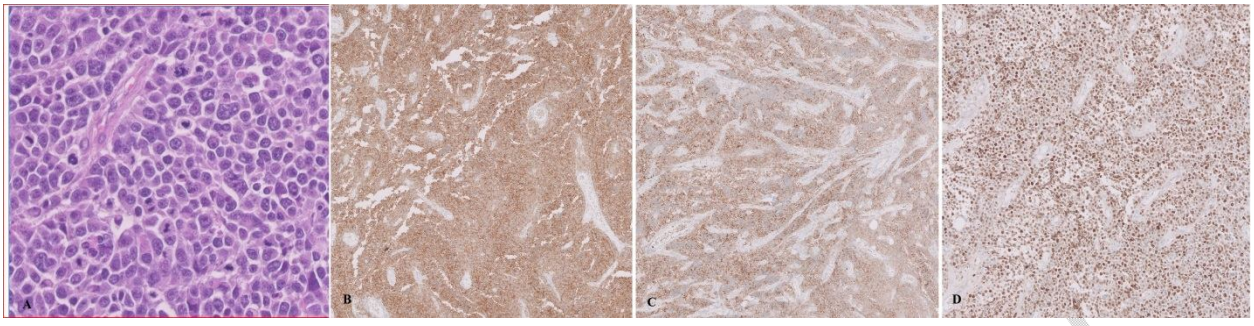

Figure 6: Images of NEC. A- High power magnification image showing large round cells with scant cytoplasm and hyperchromatic nucleus, B- Synaptophysin staining, C- CD 56 staining, D- Ki 67 staining.

Postoperatively, patient underwent DOTONAC scan which ruled out any other primary NET lesions (Figure 7), confirming PHNET. He was started on adjuvant chemotherapy. Six months following resection, patient is under regular follow up with imaging studies and has not developed any recurrence or new lesions.

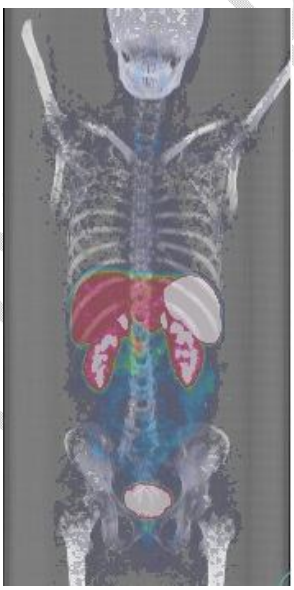

Figure 7: Image of DOTONAC scan showing no active uptake of the tracer in the body confirming the lesion removed as PHNET.

Discussion

HCC of liver is the most common primary liver tumor. It constitutes 75% of all primary liver tumors[4]. Risk factors for HCC include chronic viral hepatitis B/C, aflatoxin and alcohol. Off late, HCC related to nonalcoholic hepatic steatosis and steatohepatitis from obesity, metabolic syndrome and diabetes are increasing[5]. The diagnosis of HCC is mainly by radiological study which shows classical arterial enhancement and washout with delayed

capsular enhancement along with elevated tumor marker AFP[6]. Biopsy is not mandatory for a resectable lesion[7]. Treatment of HCC depends on various factors like performance status, anatomical location, residual liver quality and distant spread. Treatment options include resection, transplantation, ablation, trans arterial chemotherapy and radiotherapy[8].

Combined PHNET and HCC is an uncommon lesion described in the literature. Gyu HC et al have reported similar case in 2016 in a 72 year old male[9]. Jianwei Lan et al have described a similar case in an 39 year old male where the final diagnosis was made only after histopathological examination [10]. Mixed PHNET and HCC reported in literature are limited and few of them are as follows Barsky et al[11], Artopoulos et al[12], Vora et al[13] and Aboelenen et al[14]. All these articles have stressed on the fact that preoperative clinical and radiological picture mimicking as HCC and diagnosis being done by histopathological and immunohistochemistry analysis. In our case we encountered similar picture of lesion appearing as HCC on imaging however large lymph nodes were a distinct finding. A diagnosis of PHNET was arrived after histopathological confirmation of NET in the liver and ruling out primary site outside the liver.

The treatment of such lesions are confusing, guidelines have not be performed due to the rarity of the lesion. Combination chemotherapy of Etoposide and Cisplatin is advised for neuroendocrine tumors. However, we have considered a multidisciplinary team discussion and arrived at a consensus to treat the patient with Cisplatin and Etoposide chemotherapy with Atezolizumab and Bevacizumab combination once in 3 weeks for three cycles and reevaluate with a DOTONAC scan.

Conclusion

PHNET with HCC is a rare tumor of liver. Diagnosis is made only on the final histopathological and immunohistochemistry marker evaluation. Evaluation to find out primary NET elsewhere is essential before further treatment. Multidisciplinary team discussion should be considered in treating these patients, owing to the rarity of the lesions, to formulate treatment plan.

Consent

Informed consent is obtained from the patient for publication of this article.

Ethical Approval:
As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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