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Case Report

A case report of primary hepatic neuroendocrine tumour (VIPoma) of liver

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ABSTRACT

Rare cancers that start in the cells of the neuroendocrine system are called neuroendocrine tumors (NETs). The gastrointestinal and respiratory systems are among the organs where they are most frequently detected. Due to their rarity and sluggish growth rate, primary hepatic neuroendocrine tumors (PHNETs) are frequently difficult to identify until the disease has advanced to a later stage. A case of 22-year-old male patient with history of chronic diarrhoea for two years, large volume (700–1000 ml/day), watery, yellow colour, frequency of 6-7 times/day, not associated with abdomen pain or blood and mucus in stools. He had lost 9 kg weight over 2 years with preserved appetite. He was evaluated in multiple hospitals as infective diarrhoea or irritable bowel syndrome (IBS). Routine investigations revealed dehydration related acute kidney injury, hypokalaemia and compensated normal anion gap acidosis. Ultrasound and magnetic resonance imaging (MRI) identified a liver lesion suggestive of hemangioma. PHNETs are uncommon liver tumors that can be difficult to differentiate from other liver tumor types since they frequently exhibit vague symptoms. For PHNETs, hepatectomy is the recommended course of treatment. However, different strategies need to be taken into account when there are several intrahepatic lesions or when surgery is not an appropriate treatment for vascular invasion.

Keywords: Neuroendocrine tumors, Primary hepatic neuroendocrine tumor, Serum VIP, Serum chromogranin, CA19-9, Ga68 DOTA PET

INTRODUCTION

Rare cancers that start in the cells of the neuroendocrine system are called neuroendocrine tumors (NETs).[1] Although NETs are found in many vital organs in the human body, the gastrointestinal tract accounts for around 50% of NETs, while the bronchopulmonary tree accounts for about 30%.[2] The liver is rarely the site of NET descriptions, and those that are found there are usually the consequence of metastases from other organs. A very uncommon hepatic lesion is primary hepatic NET (PHNET).[3] Edmondson published the first description of this illness in 1958. Only about 150 instances of PHNET have been recorded, according to a study of the literature by Li et al till 2009.[4] Lesions typically manifest as a solid mass in adulthood and show no discernible sex preference.[5] Due to their rarity and sluggish growth rate, PHNETs are frequently difficult to identify until the disease has advanced to a later stage.[6] It can be difficult to diagnose PHNETs because of their vague radiographic characteristics, which frequently cause them to be confused with other kinds of liver lesions. Nonetheless, immunohistochemistry and histopathology can help with PHNET diagnosis. Due to their lack of distinctive imaging characteristics, PHNETs are frequently misidentified as other hepatic tumors such cholangiocarcinoma (CCC) or hepatocellular carcinoma (HCC). There is no difference in the pathological outcomes of PHNETs and other NETs.[7] However, the diagnosis of PHNET is especially alarming because pathology and imaging investigations cannot distinguish between a primary PHNET lesion and a subsequent metastatic NET.[8]

CASE REPORT

A case of 22-year-old male patient with history of chronic diarrhoea for two years, large volume (700–1000 ml/day), watery, yellow colour, frequency of 6-7 times/day, not

associated with abdomen pain or blood and mucus in stools. He had lost 9 kg weight over 2 years with preserved appetite. He was evaluated in multiple hospitals as infective diarrhoea or IBS. Routine investigations revealed dehydration related acute kidney injury, hypokalaemia and compensated normal anion gap acidosis. Ultrasound and MRI identified a liver lesion suggestive of hemangioma. On further evaluation was found to have elevated serum VIP (834 pg/ml). CA 19-9 8.51u/ml, AFP 1.82 ng/ml, and other blood investigations were normal in range. He was referred to MGE department of GMC Kottayam for further management. Serum chromogranin was elevated (>1156). Ga68 DOTA PET scan showed uptake in liver lesion (SUVmax 48) with no uptake elsewhere in the body. Upper and lower GI endoscopy showed no obvious primary lesion for diagnosis. The case was discussed in multi-disciplinary meet involving MGE, endocrinology and oncology and was decided to go ahead with resection of liver lesion.

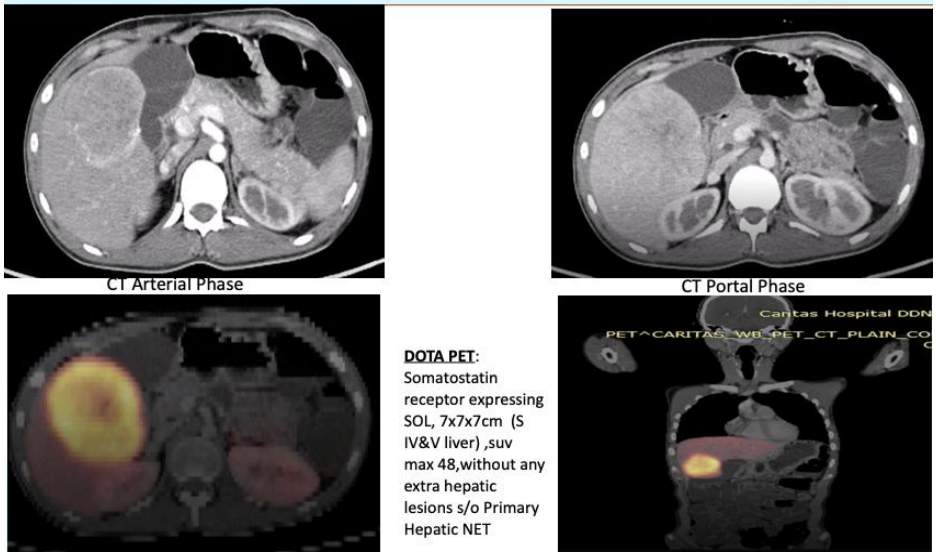

Figure 1: CECT scan.

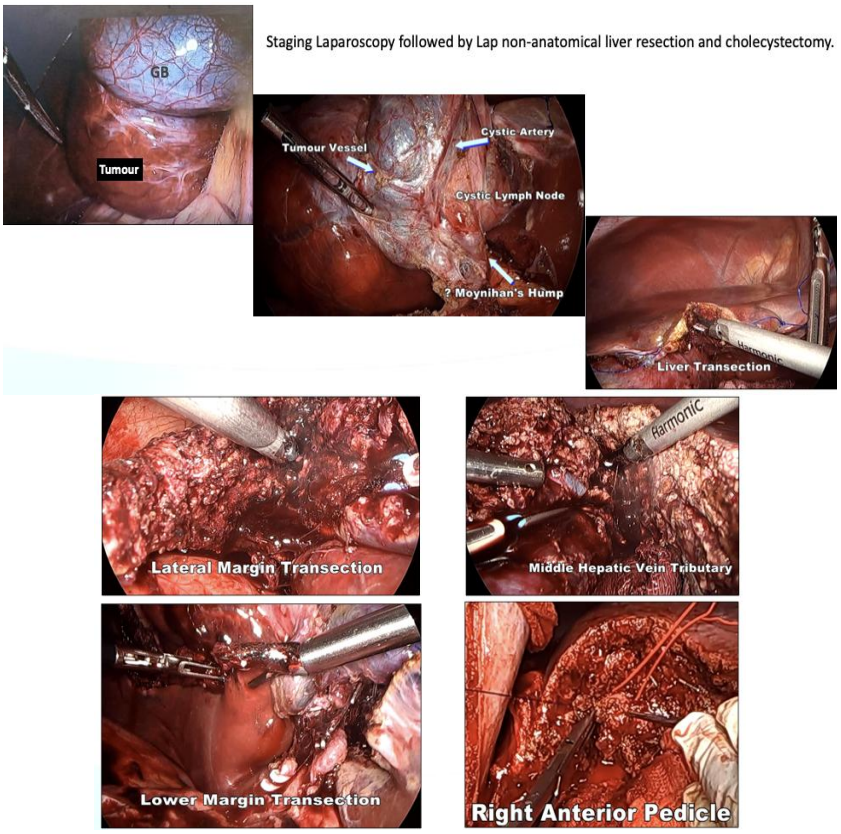

Figure 2: Intraoperative procedure in patient.

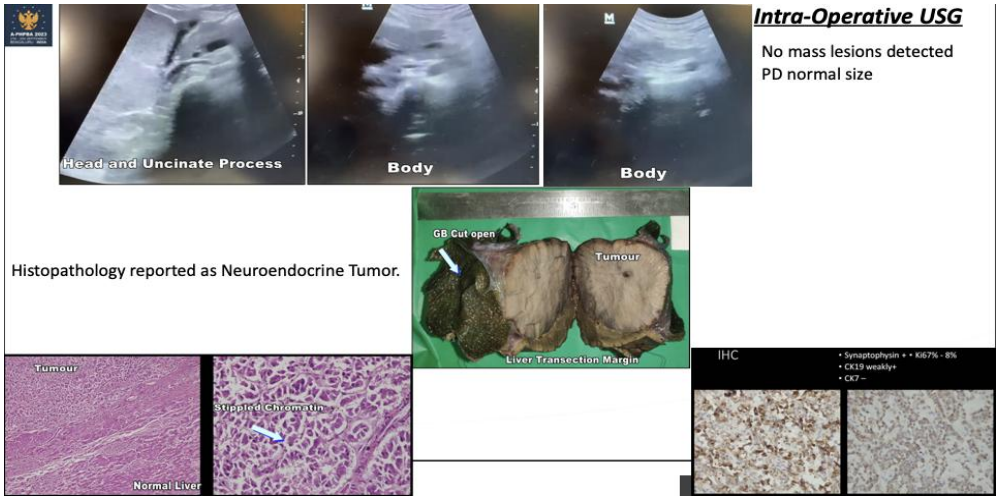

Figure 3: USG, specimen, and histology of lesion.

Intra-op transabdominal USG showed no obvious primary lesions in pancreas. Staging laparoscopy followed by non-anatomical liver resection and cholecystectomy later converted to open due to technical reasons. Post-operative period was uneventful. Histopathology reported suggestive of NET and on IHC examination, synaptophysin positive and Ki67 was 8%. Patient is free of symptoms and is on regular follow-up. We present for the diagnostic dilemma of a primary liver NEN (VIPoma) or secondary in the liver with unidentified or regressed primary leisons.

DISCUSSION

NETs can arise from cells in the neuroendocrine system and can occur in a variety of organs; the gastrointestinal tract accounts for 54 to 90% of all NET cases.[9] Since primary hepatic neuroendocrine tumors are extremely uncommon, hardly much study has been done on their features and available treatments. Hormone-secreting tumors and non-hormone-secreting tumors are the two broad categories into which NET lesions fall. PHNETs are usually tumors that do not secrete hormones. The World Health Organization (WHO) developed a classification system for NET in 2010 that is based on pathological findings, such as cell shape, the number of mitotic cells found in ten high-power fields of view, and the Ki67 index. This categorization approach allows NET tumors in the gastrointestinal tract and pancreas (GEP-NETs) to be divided into three categories: low malignancy (grade 1), moderate malignancy (grade 2), and high malignancy (grade 3). As grade increases, the prognosis becomes worse. Grade 3 NET has poorly differentiated cells, including two small-cell types and one large-cell type, and is categorized as neuroendocrine carcinoma (NEC).[10]

For PHNET, no classification scheme has yet been developed. However, the previously reported NET classification, which is highly helpful for assessing the prognosis and malignancy potential of tumors, can be used to classify PHNET. PHNET presents with different clinical symptoms than other NETs. Since PHNETs do not secrete hormones and usually grow slowly, they are usually only found by accident and only show up in the clinic in their late stages. Although they can be multifocal and are more prevalent in the right lobe (46.8%), PHNETs are mostly solitary (76.6%).[11]

Long-term follow-up for the identification of primary extra-hepatic lesions is usually part of the pre-operative to post-operative approach for diagnosing PHNET. Images of PHNET lesions producing portal thrombosis have been published in multiple papers, and Wang et al noted that all PHNET lesions exhibit arterial phase enhancement and can be mistaken for other hypervascular liver lesions.[12] Huang et al described a patient who had high AFP, portal vein tumor thrombus, and a large PHNET in the left lobe.[13] In this instance, the AFP value was within the normal range, but the tumor's growth resulted in portal venous thrombosis more than a year after PHNET was discovered.

The diagnosis of PHNET is aided by pathology and PHNET's histopathology is comparable to that of other NET tumors, showing masses with a combination of solid and cystic components, either with or without necrotic hemorrhage on gross pictures. The tumors typically have a nested, trabecular, or microacinar architecture on microscopic images. They are made up of small, homogeneous tumor cells with round nuclei, granular chromatin, and frequently stromal hyalinization. Chromogranin, synaptophysin, neuron-specific enolase, and CD56 have all been found to be positive in NETs on immunohistochemistry. The ratio of positive tumor nuclei is assessed by calculating the Ki67 index.[14]

Imaging and pathological characteristics linked to NET in the liver cannot differentiate between metastasized secondary tumors or primary PHNET from NETs in other tissues.[15] Therefore, using CT, MRI, somatostatin scans, PET, gastroscopy, colonoscopy, bronchoscopy, and surgical probes, thorough tests are necessary to rule out the presence of extra-hepatic NET. Long-term patient follow-

up is essential to identify any potentially overlooked extra-hepatic lesions, even after PHNET has been detected.[16]

Although there is currently no formal, internationally recognized treatment guidance for PHNET, surgery is nevertheless a common therapeutic option because it may result in a full recovery. The 10-year survival rate following liver resection is 68%, and the rate of PHNET resection is 92%, according to Knox et al.[17] Transarterial chemoembolization (TACE), chemotherapy, and liver transplantation are among the alternate treatment options accessible to individuals who cannot get surgery.[18] According to Huang et al, the 5-year survival percentage for patients treated with TACE who either had relapse or were not eligible for surgery was between 74 and 78 percent.[19]

CONCLUSION

PHNETs are uncommon liver tumors that can be difficult to differentiate from other liver tumor types since they frequently exhibit vague symptoms. For PHNETs, hepatectomy is the recommended course of treatment. However, different strategies need to be taken into account when there are several intrahepatic lesions or when surgery is not an appropriate treatment for vascular invasion. Interventions such as TAE combined with endocrine therapy or chemotherapy and targeted therapy may not be as effective as liver transplantation, but they can still slow the growth of PHNETs.

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