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Case Report

Primary neuroendocrine tumor of the liver: a rare case report

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ABSTRACT

The primary neuroendocrine tumor of the liver (PNET) is an exceptionally rare diagnosis, representing only 0.3% of all neuroendocrine tumors (NET). Due to its infrequency, accurate differentiation from other hepatic masses and exclusion of occult primary NETs are imperative. Establishing a definitive diagnosis of liver PNET often requires a comprehensive follow-up to rule out alternative primary causes. The liver is a frequent site for neuroendocrine metastases, and notably, primary neuroendocrine liver tumors typically demonstrate a more favorable prognosis compared to hepatocellular carcinoma and other malignant hepatic lesions. This paper reports on the case of a 74-year-old female patient who presented with pain in the right upper quadrant of the abdomen for two months. Following a triphasic CT scan and liver mass biopsy, the diagnosis of PNET was confirmed based on biopsy reports and immunohistochemistry (IHC). The patient underwent multimodality treatment; however, further intervention was deferred due to the patient's poor general condition. Instead, the patient was placed on the best supportive care.

Keywords: Neuroendocrine tumor; Liver tumor; Synaptophysin

INTRODUCTION

Neuroendocrine tumors (NETs) constitute a diverse group of malignancies characterized by distinct clinical presentations and heterogeneous pathogenesis. These tumors share a common origin from diffuse neuroendocrine cells, and they can manifest in various organs. The most prevalent occurrences are observed in the Gastro-entero-pancreatic tract (GEP-NETs) and the lungs, although NETs have the potential to arise in any organ.[1]

Tumors originating from neuroendocrine cells typically exhibit a histologic appearance that mirrors the characteristics of the site of origin. However, diagnostic challenges emerge in rare instances where the morphology deviates from the typical presentation, posing difficulties in accurate identification. NETs occurring in the liver are considered a rare entity. Among this group of uncommon diseases, PHNET account for only 0.3% of all NETs.[2]

CASE REPORT

A 74-year-old female presented in surgery OPD (out-patient department) and later referred to Radiation oncology OPD, RIMS (Regional Institute of Medica Sciences) with complaints of right upper abdominal pain for a period of one month which is gradual in onset, progressive in nature, not radiating and associated with decreased appetite. The patient also had non-insulin dependent diabetes mellitus (NIDDM) and is on oral medication for the past 20 years. There is no history of cigarette smoking, alcohol consumption, or tobacco chewing. There is no significant history of any other chronic disease. On examination, the patient had an average build with good general condition. His body surface area (BSA) was 1.5 m^2, and he had a Karnofsky performance score (KPS) of 80%. On per-abdomen examination, liver was palpable 5cm below the right costal margin and no other mass/lymph node was clinically palpable in any other parts of body. Routine baseline investigations are done and found to be within normal

limits. USG abdomen is done and shows mixed echogenicity in right lobe of liver. Triphasic CT of liver shows multiple hypodense peripherally enhancing nodular lesions seen on all segments of liver, largest measuring 32×19×22 mm in segment IV A. The patient underwent endoscopic ultrasound guided biopsy from liver and it shows Neuroendocrine tumor favouring squamous cell carcinoma. IHC study, CK 7 is positive, TTf1 and CK 20 are negative. Synaptophysin and chromogranin are positive and Ki 67 is positive in about 98% of cells.

After routine blood test investigations, patient was started on chemotherapeutic regime IE (Ifosfamide + Etoposide). Inj Ifosfamide 2 g/m^2 (day 1-5) and Inj Etoposide 100 mg/m^2 (day 1-4) every three-weekly. Patient was given three cycles of chemotherapy and assessed clinically and radiologically with CECT whole abdomen. On assessment, patient showed partial response according to RECIST criteria v1.1 and advised to continue three more cycles of same chemotherapy. However, patient's general condition deteriorated after fourth cycle and patient was placed on best supportive care and succumbed to illness.

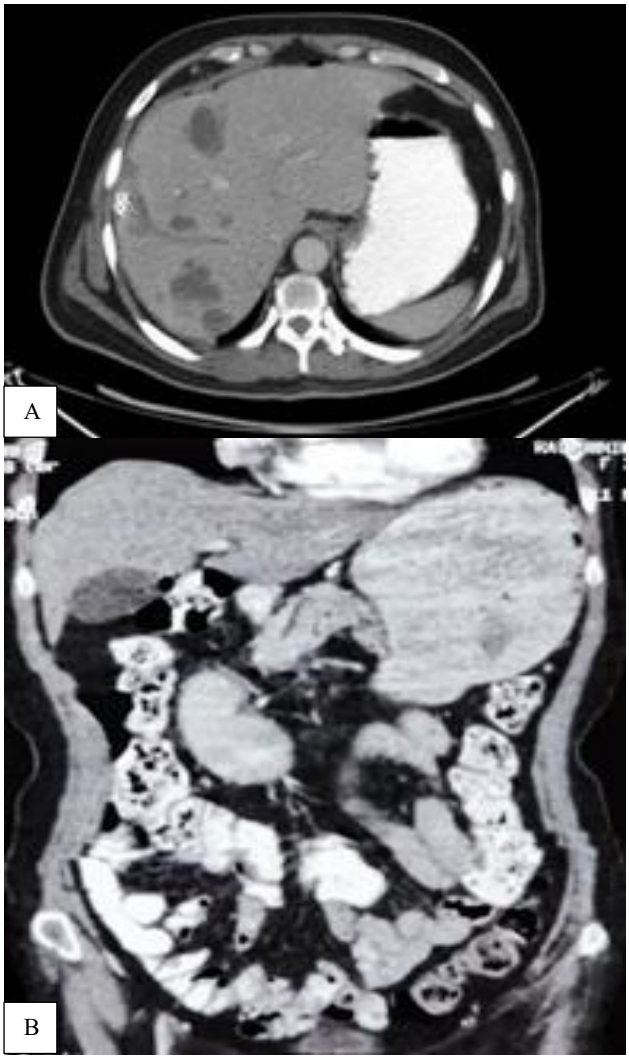

Figure 1 (A and B): CECT W/A showing multiple hypodense peripherally enhancing lesions on liver.

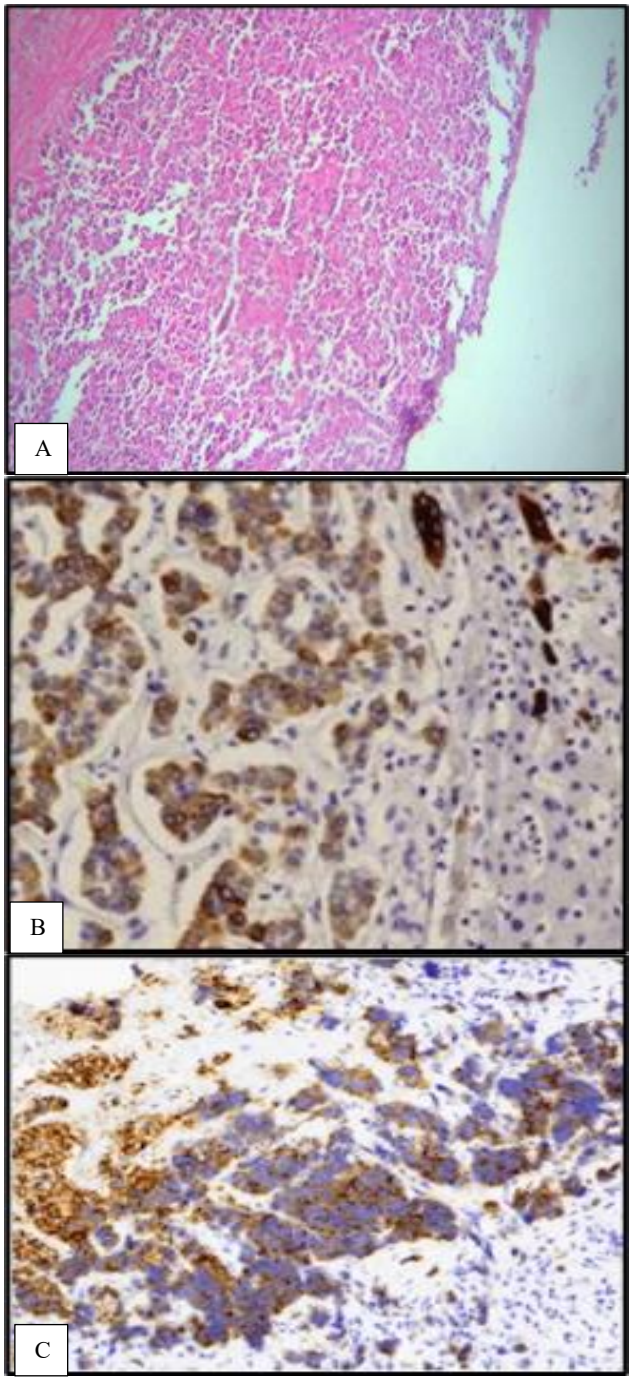

Figure 2 (A-C): A-NET of liver showing sheets of uniform small and bland tumor cells. B-Synaptophysin positive C-CK 7 positive.

DISCUSSION

PHNETs are exceedingly rare neoplasms, a fact that piques the professional curiosity of medical professionals. Their rarity, nonspecific clinical presentation, and radiologic overlap with more common hepatic lesions pose a significant diagnostic and therapeutic challenge. The need to reliably exclude an extrahepatic primary further complicates the situation. Published series and case reports estimate that PHNETs account for a tiny fraction of

neuroendocrine tumours involving the liver, with many series emphasising the rarity and citing fewer than a few hundred documented cases overall.[3]

Epidemiology and presentation

Most patients present in middle to late adulthood with vague symptoms-abdominal pain, weight loss, or an incidentally detected liver mass-and only a minority show classical carcinoid syndrome, making clinical suspicion low at first encounter. However, due to the uncommon nature of PHNETs, clinicians play a crucial role in prioritising a thorough search for an occult extrahepatic primary (gastroenteropancreatic tract or bronchopulmonary sites) before assigning a primary hepatic origin. Functional nuclear imaging (e.g., somatostatin-receptor imaging such as 68Ga-DOTATATE PET/CT when available) and endoscopic evaluation are valuable complements to cross-sectional imaging in this diagnostic workup.[3,4]

Radiology and differential diagnosis

On ultrasound, CT and MRI, PHNETs frequently appear as well-demarcated lesions with variable enhancement patterns; they can mimic hepatocellular carcinoma (HCC), cholangiocarcinoma, or metastatic NETs. Contrast-enhanced imaging and diffusion-weighted MRI add diagnostic value but are not definitive. Given the predominance of hepatic involvement by metastases from extrahepatic NETs, imaging alone cannot confirm a primary hepatic origin; instead, imaging guides the extent of disease evaluation and surgical planning.[4]

Pathology and immunohistochemistry

Definitive diagnosis rests on histopathology with neuroendocrine morphology and corroborative immunohistochemistry: chromogranin A and synaptophysin are consistently used markers, while cytokeratins and additional lineage markers help exclude other hepatic neoplasms. Grading is performed according to mitotic count and Ki-67 index (WHO classification), strongly influencing prognosis and therapeutic decisions. Careful sampling and correlation with clinical/imaging exclusion of extrahepatic primaries are essential to reduce the risk of misclassifying metastases as primary lesions.[4]

Treatment strategies and outcomes

Surgical resection with curative intent (anatomic liver resection) is the preferred treatment for localised PHNETs when feasible and offers the best chance for long-term survival. Multiple case series and institutional reports support favourable outcomes after complete resection compared with non-surgical management. For multifocal or unresectable hepatic disease, orthotopic liver transplantation (OLT) has been reported to have durable disease-free intervals in carefully selected patients. However, patient selection criteria and timing remain debated; recent comparative series suggest improved long-term disease-free survival with transplantation in highly selected cohorts. Locoregional therapies (transarterial chemoembolization or radioembolization), peptide receptor radionuclide therapy (PRRT), and systemic therapies (somatostatin analogues, targeted agents, platinum-based chemotherapy for high-grade disease) have roles in controlling tumour burden, palliation, or as bridges to surgery/transplantation. Treatment should be individualised by tumour grade, burden, functional status, and patient comorbidities, ideally discussed in a multidisciplinary tumour board.[5,6]

Prognosis and prognostic factors

Prognosis correlates strongly with tumour grade, completeness of resection, and extent of hepatic involvement. Low- and intermediate-grade PHNETs that are completely resected show substantially better outcomes than high-grade neuroendocrine carcinomas. Even after resection, recurrence may occur, necessitating long-term surveillance. Comparisons of resection versus transplantation indicate that transplantation may yield superior disease-free survival for selected patients with unresectable but liver-confined disease, but this must be weighed against organ availability and recurrence risk.[7]

Challenges, limitations, and recommendations

The principal diagnostic pitfall is confusing metastatic NETs to the liver with a primary hepatic NET. This underscores the need for exhaustive endoscopic and imaging searches (including somatostatin-receptor PET where available) and long-term follow-up to ensure no occult primary emerges. Reporting bias (many published data are case reports or small retrospective series) limits strong evidence-based recommendations; multicenter registries or pooled analyses would improve understanding of natural history and optimal management. Furthermore, the heterogeneity of NET biology (from indolent low-grade tumours to aggressive NEC) argues that histologic grading is central to treatment planning. Researchers should standardise clinical, imaging, pathologic, and outcome data reporting to permit meaningful comparisons.[3,6]

CONCLUSION

PHNETs are rare and diagnostically challenging entities. Histopathologic confirmation plus rigorous exclusion of extrahepatic primaries is required to establish the diagnosis. Surgical resection remains the cornerstone for resectable disease, while transplantation and systemic/locoregional therapies serve important roles in unresectable or advanced cases. Given the scarcity of high-quality prospective data, the responsibility of making individualised treatment decisions in a multidisciplinary setting falls heavily on the shoulders of medical professionals. Broader collaborative data collection is

needed to refine diagnostic algorithms and treatment guidelines.

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