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CASE REPORT

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Primary hepatic functional neuroendocrine tumor in an elderly female: Case report

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Key Clinical Message

Primary hepatic neuroendocrine tumor, an exceptionally rare subtype, poses a diagnostic challenge. Oncological resections should be considered, even in elderly patients after following protocolized pre-operative optimizations.

Abstract

Neuroendocrine tumors (NETs) are rare tumors that primarily develop in the gastrointestinal and respiratory tracts. While the liver is commonly affected by NET metastases, primary hepatic neuroendocrine tumors (PHNETs) are an exceptionally rare subtype. The characteristic slow growth and nonfunctional nature of PHNETs pose challenges in their diagnosis. Furthermore, PHNETs often exhibit a lack of unique radiological characteristics that differentiate them from other liver tumors, leading to frequent misdiagnosis as hepatocellular carcinoma. We performed left hepatectomy for PHNET in an elderly lady with prolonged stormy postoperative course. This case report of a PHNET highlights the importance of histopathology and immunohistochemistry in the diagnosis and emphasizes that oncological resection, if feasible, is the preferred treatment even in the elderly population.

KEYWORDS

functional neuroendocrine tumor, immunohistochemistry, liver neoplasms, primary hepatic

1 | INTRODUCTION

Primary neuroendocrine tumors (NETs) originating in the liver are extremely uncommon, with only around 200 reported cases documented globally.[1–3] Determining the precise incidence of primary NETs in the liver remains challenging due to the prevalence of neuroendocrine liver lesions that mainly develop from metastases, commonly originating from the gastroenteropancreatic system.[4]

In this case report, we present a distinctive occurrence of a functional primary NET in the left lobe of the liver in an elderly woman, who underwent a left hepatectomy and experienced an extended period of postoperative recovery. The aim of reporting this case is to share our experience of dealing with an extremely uncommon clinical entity and highlight the importance of histopathology and immunohistochemistry in the diagnosis and emphasize that oncological resection, if

feasible, is the preferred treatment even in the elderly population.

2 | CASE DETAILS

A 73-year-old female presented with a history of recurring episodes of diarrhea and abdominal discomfort over the past 3 months. She also had anorexia and significant weight loss with no significant past medical and surgical history. Clinical examination was unremarkable and she had good performance score.

The initial abdominal ultrasound examination revealed a solid lesion in the left lobe of the liver, specifically in segments IVa and IVb with no background cirrhosis. The patient's laboratory tests, including viral-markers and tumor-markers like alpha feto-protein, carcinoembryonic antigen and carbohydrate antigen 19–9 were within normal ranges. A contrast-enhanced CT scan of the chest, abdomen and pelvis showed a heterogeneous hypodense lesion measuring 5.8 × 6 × 6.2 cm in segments IVa and IVb of the liver. The lesion exhibited arterial phase enhancement, followed by washout in the venous and delayed phases, suggestive of hepatocellular carcinoma without any other lesions elsewhere (Figure 1A, B). Subsequent 18-Fluoro-deoxy Glucose (FDG) PET imaging did not reveal any areas of increased FDG uptake (Figure 1C). To establish a definitive diagnosis, a USG-guided biopsy of the lesion was performed, which identified a Grade 2 neuroendocrine tumor, positive for synaptophysin and chromogranin, but negative for Hep-par1 and CK20. The Ki-67 index was 5%. Elevated levels of serum chromogranin A and 24-h urinary 5-HIAA (HydroxyIndoleAcetic Acid) were also observed.

Further investigations, including upper gastrointestinal endoscopy and colonoscopy, did not reveal any lesions. A whole-body DOTANOC PET-CT was conducted to search for a potential primary origin, but no other lesions were found apart from a 6.9 × 5.5 × 5.5 cm lesion in segments IVa and IVb of the liver (Figure 1D). As a result, the patient was diagnosed with a nonmetastatic, functional Grade 2 primary hepatic neuroendocrine tumor involving segments IVa and IVb. A left hepatectomy was planned, and the patient underwent brief prehabilitation, routinely followed at our centre.

She underwent open left hepatectomy with resection of segments II, III, and IV preserving the middle hepatic vein along with cholecystectomy and regional lymph nodal resection. The left hepatic duct was sutured with 4–0 polydioxanone suture. Per-operatively a 6 × 6 cm mass was found involving the left lobe of liver (Figure 2A–D) with normal right lobe and multiple gallstones with normal gallbladder mucosa. A few sub-centimetric lymph nodes were found at the porta and Hepato-duodenal ligament, which were resected. Final histopathology confirmed Grade 2 neuroendocrine tumor with presence of lympho-vascular invasion and involvement of common hepatic artery lymph node but without perineural spread. The immunohistochemistry confirmed synaptophysin and chromogranin positivity with negative Hep-par1 and CDX2 markers and Ki-67 of 8%–10% (Figure 3A–C).

The patient had prolonged postoperative course because of bile leak through the intraabdominal drain. Ultrasound guided pigtail drainage did not help, even after up-sizing the same and CECT abdomen revealed large peri-hepatic collection with a controlled biliary fistula (Figure 3D). A hepatobiliary Iminodiacetic acid (HIDA) scan revealed right hepatic duct leak and hence, Endoscopic Retrograde Cholangiography (ERC) with a plastic stent placement was done. Despite the stent, the bile leak did not resolve, but rather increased in quantity.

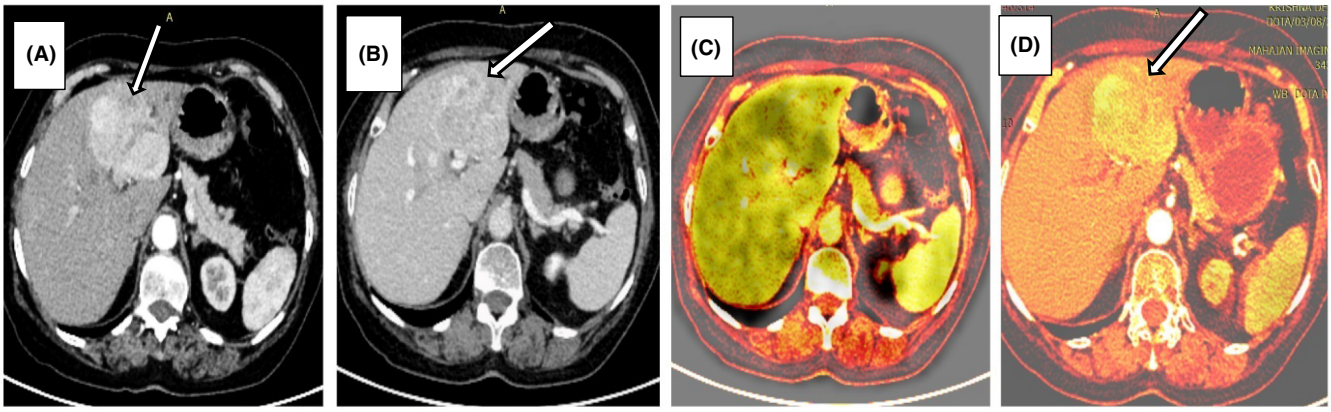

FIGURE 1 Preoperative images. (A, B) Triple phase CECT abdomen revealed a 5.8 × 6 × 6.2 cm heterogeneous hypodense lesion involving segments IVa and IVb of liver (white arrow) with nodular enhancement on arterial phase, early washout in venous and delayed phases. (C) 18-FDG PET-CT did not reveal any focus of increased FDG uptake. (D) DOTANOC PET CT showed a SSTR-expressing lesion in left lobe of liver (white arrow) with no disease elsewhere.

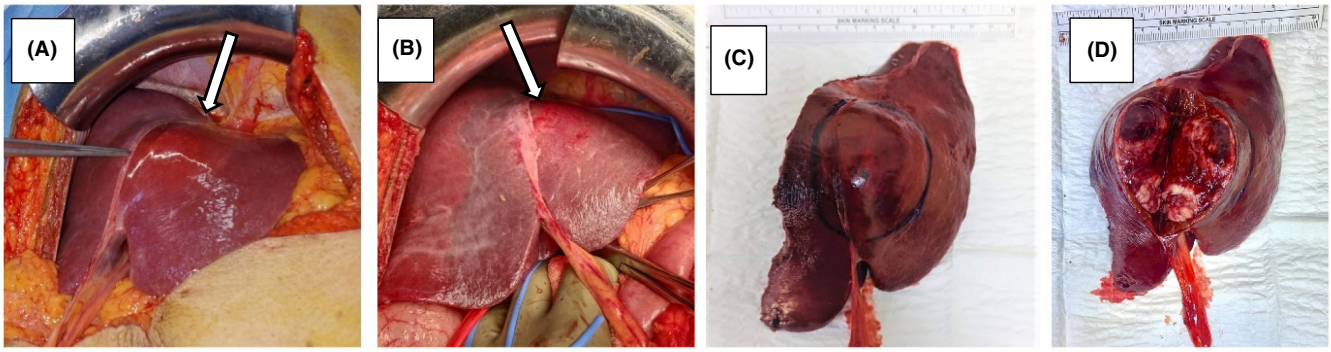

FIGURE 2 Intraoperative images. (A, B) 5×5 cm mass (white arrow) was found involving the left lobe of liver with normal right lobe (C, D) Left hepatectomy gross specimen showing a 6×6 cm growth (black marker on specimen) with variegated appearance with intact capsule.

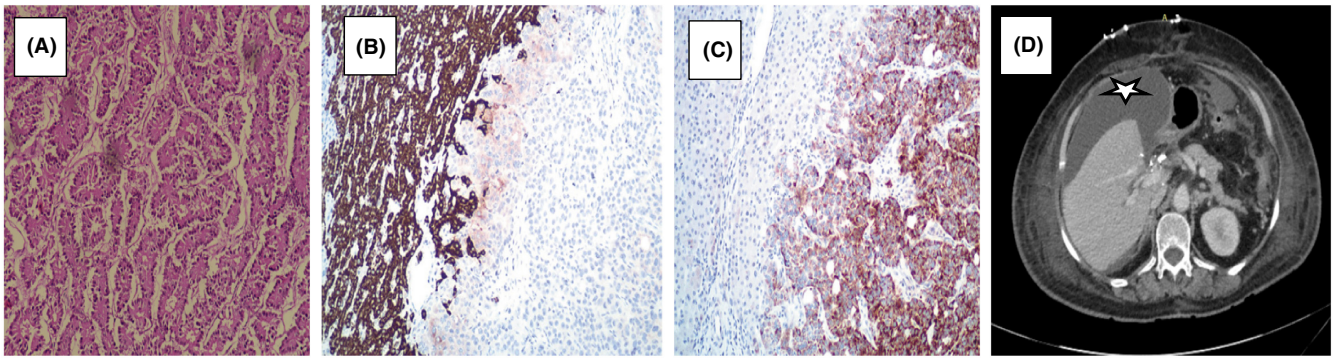

FIGURE 3 Postoperative images. (A) H&E stain, 40× view revealed invasive tumor arranged in nested insular pattern with abundant stroma. Cells show variable morphology with mild to moderate atypia, nuclear pleomorphism. (B, C) IHC showing Synaptophysin and chromogranin positivity (D) POD #9 CECT abdomen revealed large perihepatic collection (white star).

Therefore, she was re-explored on 31st postoperative day and the stent was found to puncture a branch of right duct at the free cut surface of liver, draining freely into the peritoneal cavity. The stent was removed and the leaking duct was closed with 4–0 polydioxanone suture after thorough peritoneal lavage. Thereafter, the patient recovered uneventfully and was discharged in stable condition on 52nd day after the index surgery.

Based on her final histopathology reports, patient did not merit any adjuvant therapy. She is under regular follow-up and disease free at 09 months.

3 | DISCUSSION

NETs constitute less than 1% of primary liver tumors and may be functional or nonfunctional.[5] Unlike other NETs, PHNETs predominantly present as nonfunctional tumors, thus they tend to grow without noticeable symptoms and are often diagnosed at advanced stages. A few patients may experience pain, abdominal distension, or jaundice due to the mass effect. Although uncommon, functional PHNETs can manifest symptoms associated with Zollinger-Ellison syndrome, Cushing's syndrome, or carcinoid syndrome.[4]

Our patient was asymptomatic 3 months ago, but later had functional symptoms. The progression of the tumor over time can account for the transition from being asymptomatic to experiencing these symptoms.

PHNETs lack distinctive radiological features, often leading to misdiagnosis as hepatocellular carcinoma.[6] Histopathology and immunohistochemistry are essential for the diagnosis, especially in a non-cirrhotic liver, as in our case.[1]

DOTANOC PET-CT is preferred over FDG PET due to its higher sensitivity and specificity in detecting NET lesions. DOTANOC PET-CT uses gallium-68 DOTANOC, which binds to somatostatin receptors overexpressed in NETs, enabling accurate visualization of primary tumors as well as metastases. FDG PET relies on cellular metabolic activity and hence may be not be useful in NETs with lower metabolic rates as in our case.[7] Thus, diagnosing, managing, and confirming the primary origin of PHNETs may be challenging, particularly in the absence of metastases. Detailed work up with judicious use of radiological investigations, histopathology examination, and immunohistochemistry are the key.

Surgical management of PHNETs shows the highest effectiveness to date, demonstrating a five-year survival

of 74% with 18% recurrence rate.[8] Medical treatments like Trans-arterial chemoembolization, systemic chemotherapy, local ablation, and somatostatin analogs have not shown long-term survival benefits.[4] Given the rarity of the disease, establishing treatment recommendations or a consensus is challenging.

4 | CONCLUSION

PHNETs pose a distinct challenge due to their rarity, elusive presentation and radiological features, especially in the absence of metastases. Oncological resections should be considered, even in elderly patients after following protocolized preoperative optimizations. Long-term follow-up is crucial to monitor disease progression and detect potential recurrences.

AUTHOR CONTRIBUTIONS

Naveen Kumar Kushwaha: Conceptualization; data curation; investigation; methodology; project administration; resources; software; writing – original draft. **Pradeep Jaiswal:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; software; supervision; validation; visualization; writing – review and editing. **Prashant Gupta:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; software; supervision; validation; visualization; writing – original draft. **Niharika Mishra:** Investigation; methodology; resources; software; writing – original draft. **Shrirang Vasant Kulkarni:** Data curation; formal analysis; investigation; methodology; project administration; software; supervision; validation; writing – review and editing.

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None.

DATA AVAILABILITY STATEMENT

Data is available and can be shared.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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