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Case Report

Surgery Section

Neuroendocrine Tumour in a 37-Year-Old Female: A Diagnostic Challenge

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ABSTRACT

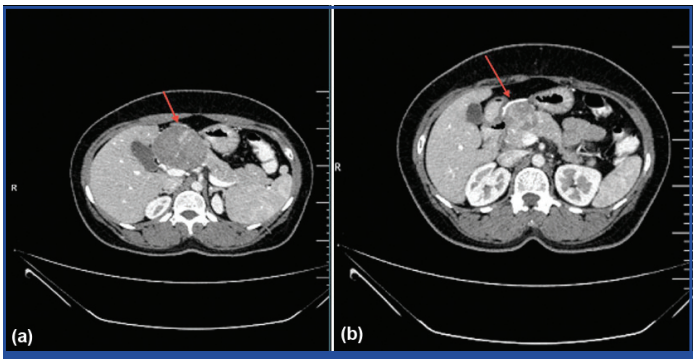
Pancreatic Neuroendocrine Tumours (PNETs) are a rare group of neoplasms arising from hormone-producing cells in the pancreas. Unlike the more common pancreatic adenocarcinomas, PNETs often grow more slowly and may produce hormones, leading to distinct clinical symptoms. We present a rare and diagnostically challenging case of a PNET in a 37-year-old female who presented with a three-month history of epigastric pain. Initial imaging studies revealed a mass in the liver, mimicking Hepatocellular Carcinoma (HCC), while subsequent investigations, including Positron Emission Tomography-Computed Tomography (PET-CT) and ultrasound-guided Fine-Needle Aspiration Cytology (FNAC), suggested a PNET. A Whipple procedure was performed, and histopathological examination confirmed the diagnosis. This case highlights the importance of a multidisciplinary approach in managing rare and challenging malignancies, emphasising the need for clinical vigilance, advanced imaging, and histopathological evaluation to confirm the diagnosis. The successful management of this case underscores the critical role of timely surgical intervention and personalised treatment strategies in achieving favourable outcomes.

Keywords: Case report, Malignancy, Pancreatic mass, Surgical management, Whipple procedure

CASE REPORT

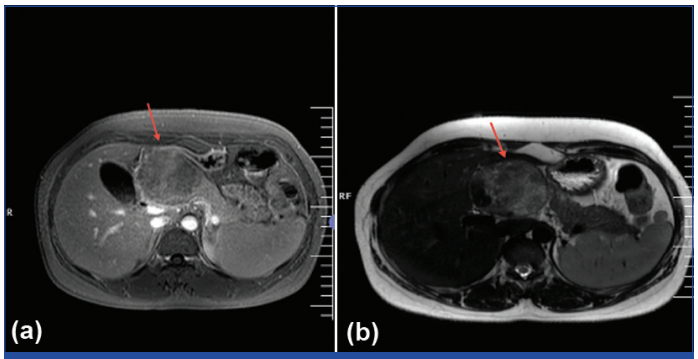
A 37-year-old female presented with a three-month history of epigastric pain. The pain was not associated with nausea, vomiting, fever, weight loss, reduced appetite, jaundice, or altered bowel habits. She had no known comorbidities such as diabetes mellitus, hypertension, ischaemic heart disease, tuberculosis, asthma, or epilepsy. There was no significant family history, and the patient denied any addictions or substance abuse. Physical examination revealed a scaphoid-shaped, soft, and non-tender abdomen with no signs of ascites; abdominal findings were otherwise unremarkable.

Initial investigations included an Ultrasound (USG) of the abdomen and pelvis, which revealed a mass measuring 7.5×6 cm with internal vascularity in segment 4b of the liver. A Contrast-Enhanced CT (CECT) of the abdomen and pelvis showed a well-defined, encapsulated, heterogeneously enhancing lesion located at the anteroposterior portion of the pancreatic head. This finding was suggestive of either a pancreatic mass with exophytic extension or a hepatic mass with exophytic extension [Table/Fig-1]. Magnetic Resonance Imaging (MRI) of the abdomen further identified a mass in the caudate lobe of the liver indenting the superior aspect of the pancreatic body, raising the possibility of Hepatocellular Carcinoma (HCC) [Table/Fig-2].



[Table/Fig-1a,b]: Axial view of Contrast Enhanced CT (CECT) scan of abdomen and pelvis showing well-defined, encapsulated, heterogeneously enhancing lesion located at the anteroposterior portion of the pancreatic head.

To confirm the diagnosis, ultrasound-guided FNAC of the mass was performed, which was positive for malignancy. The differential

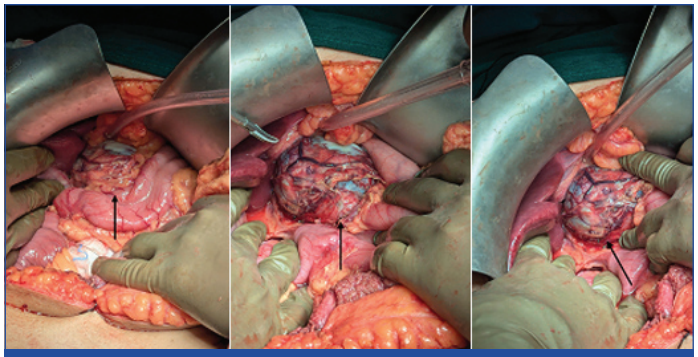


[Table/Fig-2a,b]: Axial view of MRI abdomen and pelvis showing a mass in the caudate lobe of the liver.

diagnoses included a Neuroendocrine Tumour (NET), metastatic deposits from pancreatic carcinoma, or round-cell HCC. Tumour markers, including Carcinoembryonic Antigen (CEA), Carbohydrate Antigen 19-9 (CA 19-9), Alpha-Fetoprotein (AFP) were all within normal limits. Chromogranin A was elevated at 375 ng/mL, indicating a significant increase. A PET-CT scan conducted subsequently revealed a metabolically active lesion involving and abutting segments 3 and 4 of the liver, with no evidence of metastatic spread elsewhere.

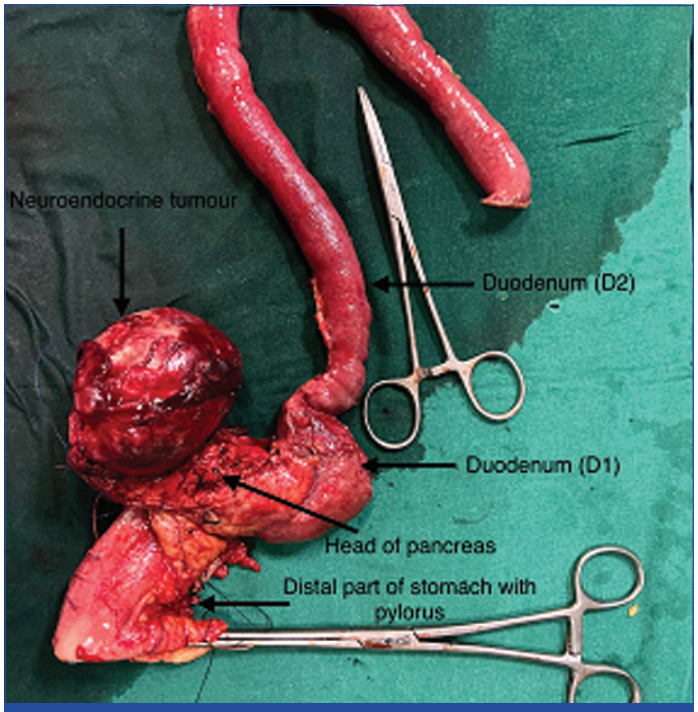
Given the diagnostic uncertainty, a Whipple procedure (pancreaticoduodenectomy) and, if required, left hepatectomy were planned, as imaging studies showed that the left hepatic artery was abutting the mass. If the left hepatic artery had to be compromised, perfusion to the left lobe could not solely rely on the portal blood supply, which would increase the chances of biliary strictures, sclerosing cholangitis, and necrosis. During surgery, the Kocher manoeuver was performed to mobilise the duodenum and the head of the pancreas, after which a mass arising from the neck of the pancreas was identified, surrounded by dense vasculature. The left hepatic artery was found to arise from the mass, with the coeliac plexus adherent to it. The left hepatic artery was ligated distally, and no bleeding was noted at the distal end, suggesting well-developed collaterals; thus, left hepatectomy was avoided [Table/Fig-3a-c].

The dissection was performed with significant technical difficulty but was completed successfully without intraoperative complications.

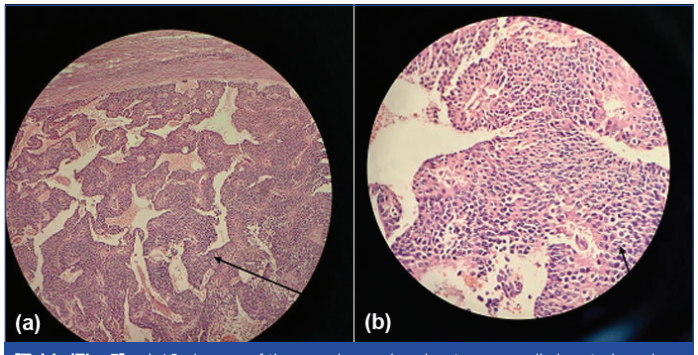


[Table/Fig-3]: Mass arising from the pancreas abutting liver.

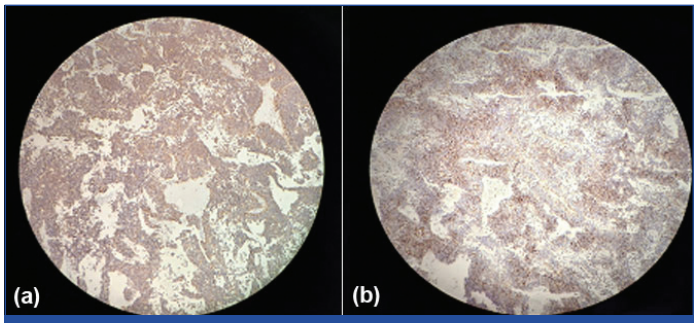
Intraoperatively, Doppler ultrasound of the portal vein demonstrated normal flow, excluding any injury. A cholecystectomy was performed, and the Common Bile Duct (CBD) was dissected and divided. The stomach was partially resected, and the duodenum was transected distal to the pylorus. Reconstruction was done using end-to-side pancreatic jejunostomy, hepaticojejunostomy, and gastrojejunostomy. A gross specimen of the pancreatico-duodenectomy (Whipple's resection) with the gallbladder was obtained. The external surface of the pancreas showed encapsulation with a grey-white appearance. The cut surface revealed variegated areas and hemorrhagic regions [Table/Fig-4]. Histopathological examination confirmed the diagnosis of a well-differentiated NET of the head of the pancreas, Grade 2, with metastasis to a single regional lymph node [Table/Fig-5]. Immunohistochemistry (IHC) markers were positive for synaptophysin and chromogranin [Table/Fig-6], and negative for beta-catenin and CD10, with Ki67 (5-6%) in multiple hot spots.



[Table/Fig-4]: Gross image of the specimen.



[Table/Fig-5]: a) 10x image of the specimen showing tumour cells in a trabecular pattern; b) 40x image of the tumour showing medium sized tumour cells with eosinophilic cytoplasm and "salt-and-pepper" chromatin.



[Table/Fig-6]: a) Synaptophysin {(Immunohistochemistry (IHC) marker}; b) Chromogranin (IHC Marker).

Postoperatively, the patient's recovery was uneventful; she was transferred from the intensive care unit to the surgical ward on Postoperative Day (POD) 2. The nasogastric tube was removed on POD 3, following the return of bowel function, and a soft oral diet was initiated and well tolerated. Surgical drains were removed on POD 6 after output was minimal, and amylase levels were within normal limits. Liver function tests were repeated on POD 9 and were well within acceptable limits. The patient's postoperative recovery was uneventful, and she was discharged.

At the two-week outpatient follow-up, the patient was recovering well. Wound healing was satisfactory with no signs of infection or dehiscence. She reported good oral intake, adequate pain control with oral analgesics, and no gastrointestinal symptoms. Stool frequency was normal, and there were no signs of steatorrhoea or malabsorption. Her weight was stable. Initial blood tests, including liver function tests and fasting glucose, were within normal limits.

At six weeks, a CECT scan of the abdomen and pelvis was performed as a baseline for surveillance, showing no evidence of residual disease. Chromogranin A levels were within the reference range. The patient remained asymptomatic, with stable weight and no signs of endocrine or exocrine insufficiency. Pancreatic enzyme replacement therapy was initiated. Follow-up was scheduled at three-month intervals for the first year, including physical examination, routine blood tests (including liver function, fasting glucose, and chromogranin A), and imaging every six months or as clinically indicated. At the latest follow-up, three months postoperatively, the patient remained clinically well with no evidence of disease recurrence.

DISCUSSION

PNETs are rare neoplasms that account for approximately 1-2% of all pancreatic tumours [1]. They arise from the islet cells of the pancreas and can be classified as functional or non-functional based on hormone production. Functional tumours present with specific clinical syndromes, while non-functional tumours often remain asymptomatic until they grow large or cause local complications [2]. The majority of PNETs are diagnosed in individuals aged 50-60 years [3]. Our case is notable for the relatively young age of presentation (37 years), highlighting the need for awareness of PNETs even in younger patients.

This case describes a challenging presentation of a well-differentiated NET of the pancreatic head in a 37-year-old female. Her chief complaint was three months of epigastric pain, notably without typical alarm symptoms such as nausea, vomiting, fever, or weight loss. This subtle onset, characteristic of many slow-growing and often non-functional PNETs, contrasts sharply with the more rapid symptom progression seen in pancreatic adenocarcinoma [4].

Initial imaging studies (ultrasound, contrast-enhanced computed tomography, MRI) presented a significant diagnostic puzzle. While

the ultrasound suggested a hepatic mass, the CECT and MRI offered conflicting interpretations, pointing towards either a pancreatic or hepatic mass with exophytic extension, even raising the possibility of Hepatocellular Carcinoma (HCC). Such ambiguity is a recognised hurdle in differentiating PNETs from other pancreatic or liver lesions due to overlapping radiological features [5,6].

Conventional tumour markers (CEA, CA 19-9, AFP) were unremarkable, which is typical as these markers often lack sensitivity for PNETs [7]. However, the significantly elevated Chromogranin A (CgA) level of 375 ng/mL provided a crucial diagnostic clue. This marked elevation strongly suggested a neuroendocrine origin, aligning with CgA's recognised role as a valuable general biomarker for NETs [8]. It's important to acknowledge that CgA can also be elevated by other factors (e.g., proton pump inhibitor use, renal impairment) [9], but in this patient's clinical context, its pronounced increase strongly supported a NET diagnosis.

PNETs arise from specialised neuroendocrine cells within the pancreas. While some are linked to genetic syndromes [10], most, like in this patient, are sporadic. The development of sporadic PNETs is complex and often involves dysregulation of key molecular pathways such as the mTOR pathway (linked to mutations in TSC2 and PTEN) and alterations in DAXX/ATRX or MEN1 genes [11,12]. Chromogranin A, a protein stored in neuroendocrine secretory granules, is released by these tumours, and its elevated serum levels reflect the tumour's secretory activity or overall tumour burden [13].

The epigastric pain likely stemmed from the tumour's mass effect. Intraoperatively, the observed dense vascularity and adherence to the left hepatic artery and celiac plexus are common features of NETs, presenting considerable surgical challenges [14].

Regarding routine population-wide screening for sporadic PNETs, it is generally not recommended. This stance is primarily due to their relatively low incidence, which renders broad screening programs economically impractical and prone to high false-positive rates [15]. Effective, non-invasive, and cost-efficient screening modalities for the general population are currently lacking [16].

However, targeted screening is essential for individuals at high risk, particularly those with inherited genetic syndromes predisposing them to NETs (e.g., MEN1, VHL, NF1, TSC). For these groups, established surveillance protocols involving biochemical tests and regular imaging are crucial for early detection [17]. In our symptomatic patient, the challenge was effective diagnosis rather than screening, underscoring the importance of vigilance and comprehensive investigation when concerning symptoms arise.

In typical practice, somatostatin receptor-based imaging, such as Ga-68 DOTATATE PET-CT, is preferred for accurate staging and assessment of receptor status [18]. However, in this case, due to the unavailability of Ga-68 imaging, Fludeoxyglucose-18 (FDG) PET-CT was performed instead. The tumour exhibited moderate FDG uptake, consistent with prior observations that intermediate to high-grade PNETs may show FDG avidity [19]. While not ideal for well-differentiated tumours, FDG PET provided additional insight into tumour metabolism and informed surgical planning.

Surgical intervention is the mainstay of treatment for resectable non-functional PNETs, particularly those larger than 2 cm or involving adjacent structures. The goal of surgery is complete resection with negative margins, which has been shown to improve overall survival [20]. Current guidelines from the European Neuroendocrine Tumour Society (ENETS) and the National Comprehensive Cancer Network (NCCN) recommend long-term follow-up with periodic imaging and tumour marker surveillance, especially for intermediate-grade tumours like this one [21].

This case contributes to the existing literature by illustrating the unusual presentation of a non-functional PNET in a young female, the challenges of limited imaging resources, and the successful outcome following complex surgical management.

CONCLUSION(S)

This case exemplifies the diagnostic and therapeutic challenges posed by rare NETs. It highlights the need for clinicians to remain vigilant for atypical presentations and underscores the critical role of advanced imaging and histopathological evaluation in confirming the diagnosis. The successful management of this case through the Whipple procedure, despite its complexity, emphasises the importance of a multidisciplinary approach in achieving favourable outcomes. This case serves as a reminder that early identification and individualised treatment strategies are pivotal in managing rare and challenging malignancies like NET.

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