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CASE REPORT

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Misdiagnosed cystic pancreatic neuroendocrine tumor with bilobar hepatic metastasis managed with single-stage resection — a case report

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Abstract

Background Pancreatic neuroendocrine tumors (PNET) account for less than 2% of all pancreatic tumors, while cystic PNETs account for only 10–18% of all resected PNETs. The most common site for metastasis is the liver. Few detailed guidelines currently exist for management of stage 4 cystic PNETs. This is a unique case that was managed with complete surgical resection in one sitting.

Case presentation Our report is on a young male patient who was initially misdiagnosed as having a pancreatic pseudocyst and treated accordingly. He was finally diagnosed with PNET but was reluctant to undergo surgery until he developed bilobar hepatic metastasis. We performed a pylorus-preserving pancreaticoduodenectomy with a Roux-en-Y hepaticojejunostomy and wedge resection of both hepatic metastatic deposits.

Conclusion Cystic PNETs are rare and commonly misdiagnosed as pancreatic pseudocysts. Surgical resection is considered ideal, but sparse literature exists on the management due to a paucity of cases. We have reported this case as it was successfully managed with single-stage surgery for both the primary tumor as well as bilobar hepatic metastatic deposits, and no similar cases have been reported in literature. The follow-up scan revealed no residual disease.

Keywords Cystic pancreatic neuroendocrine tumor (PNET), Case report, Metastatic pancreatic neuroendocrine tumor (PNET), Complete resection of metastatic pancreatic neuroendocrine tumor (PNET), Wedge resection of bilobar liver metastasis, Surgical management of metastatic pancreatic neuroendocrine tumor (PNET), Single-stage resection of metastatic pancreatic neuroendocrine tumor (PNET), Pancreaticoduodenectomy for pancreatic neuroendocrine tumor (PNET), Pancreatic pseudocyst

Introduction

Pancreatic neuroendocrine tumor (PNET) is a rare neoplasm of the pancreas, accounting for less than 2% of all pancreatic tumors [1]. The incidence of PNETs has been increasing due to advancements in diagnostic imaging techniques. At the time of diagnosis, PNETs have already metastasized in 40–80% of cases, with the liver being the most common site of metastasis (40–93%) [2]. Liver metastasis is a crucial prognostic factor in PNETs.

Neuroendocrine tumors typically present as solid masses, and cystic PNETs are infrequent, often resulting from degeneration of a solid tumor. Cystic PNETs can mimic other pancreatic lesions, posing a diagnostic challenge for radiologists and surgeons. In this article, we present a case of a patient with a solid plus cystic PNET with liver metastasis, initially misdiagnosed as a pseudocyst and managed accordingly. To our knowledge, there

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is no similar reported case in which the primary pancreatic NET lesion as well as the hepatic metastasis of both lobes was resected in the same surgery.

Case presentation

A 21-year-old male patient visited our clinic complaining of abdominal discomfort and early satiety persisting for 7–8 years. He denied weight loss, diarrhea, flushing, fainting, hypoglycemic spells, steatorrhea, or jaundice. The examination of the patient was also unremarkable. His weight at presentation was 58 kg with a body mass index (BMI) of 19.3 kg/m^2. Initial imaging studies, including a CT scan, revealed dilation of the pancreatic duct (PD) with atrophy of the pancreatic body and tail. The head and uncinate process appeared enlarged, with a well-defined cystic lesion measuring 9×6 mm in the uncinate process. Magnetic resonance cholangiopancreatography (MRCP) performed in January 2018 showed dilation of the PD and common bile duct (CBD) without any filling defects. The possibility of a mass lesion in the pancreaticoduodenal groove was also considered. Subsequently, the patient underwent two endoscopic retrograde cholangiopancreatography (ERCP) procedures, 3 months apart, which both confirmed the dilated PD and CBD without any other pathological findings. Based on these findings, the patient was advised to undergo either a diversion procedure (e.g., pancreaticojejunostomy) or a resection procedure (pancreaticoduodenectomy) if a lesion was identified per-operatively. However, the patient declined further intervention and was subsequently lost to follow-up. A few years later, the patient experienced a recurrence of symptoms and resumed follow-up. His serum amylase levels were significantly raised to 18,300 IU/L. Repeat MRCP revealed the presence of a cystic lesion with debris, leading to the diagnosis of a pseudocyst following pancreatitis. Subsequently, the patient underwent an endoscopic ultrasound (EUS)-guided cystogastrostomy 3 months later, during which two stents were placed. The aspirated fluid showed an amylase level of approximately 2000 units (Fig. 1). However, following the procedure, the patient developed massive pneumoperitoneum, necessitating an exploratory laparotomy. During the surgery, both stents were removed, and the posterior wall of the stomach was repaired. A tru-cut biopsy of the pancreatic head mass was obtained. The biopsy results revealed a grade 1 neuroendocrine tumor, positive for the following immunohistochemical markers: CKAE1/AE3, synaptophysin, CD56, and Ki-67 (highlighting low proliferation < 3%). Chromogranin staining was dimly positive. Subsequently, the patient was again lost to follow-up for 1 year before presenting to our clinic.

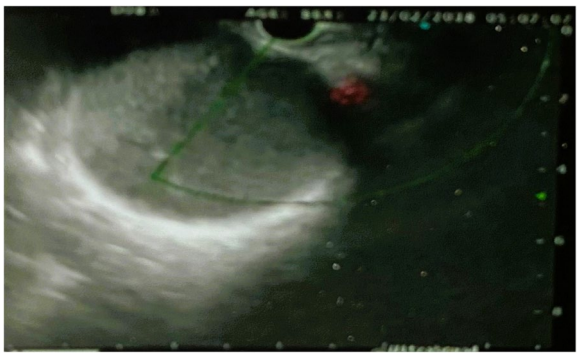

Fig. 1 Image of the pseudocyst on EUS

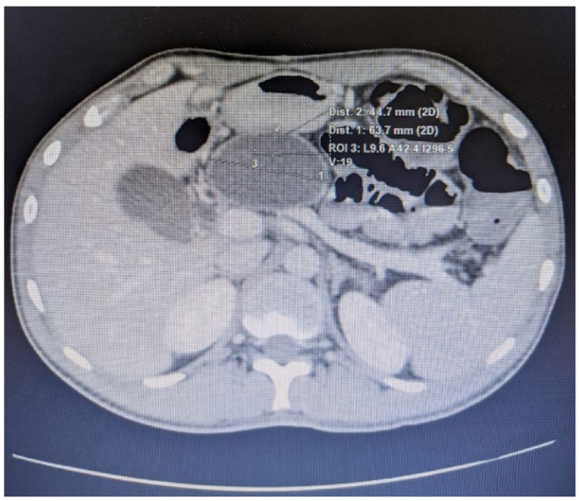

Fig. 2 Axial view showing the cystic component of PNET

A repeat CT scan revealed an enhancing lesion in the pancreatic head and uncinate process, measuring 6.4×5 cm, abutting the duodenum, CBD, inferior vena cava, and portal vein. A cystic area measuring 6.7×4.1 cm was also observed in the body of the pancreas, with the remaining pancreas appearing atrophic. A dotatate scan revealed two metastatic liver lesions (Figs. 2 and 3). A multidisciplinary team meeting was held, and surgical resection was decided (Figs. 2 and 3).

The patient underwent a pylorus-preserving pancreaticoduodenectomy with Roux-en-Y hepaticojejunostomy and a wedge resection of the two hepatic metastatic lesions. Intraoperatively, a large cystic mass measuring approximately ~ 6×6 cm was observed arising from the pancreatic head with a bulky uncinate process. It did not resemble a pseudocyst but rather a solid-cystic mass. The remaining pancreas displayed atrophy. During the mobilization of the cystic lesion, adhesions from the previous surgery were encountered. After mobilizing the head, uncinate process, and cystic mass, a stapler was used

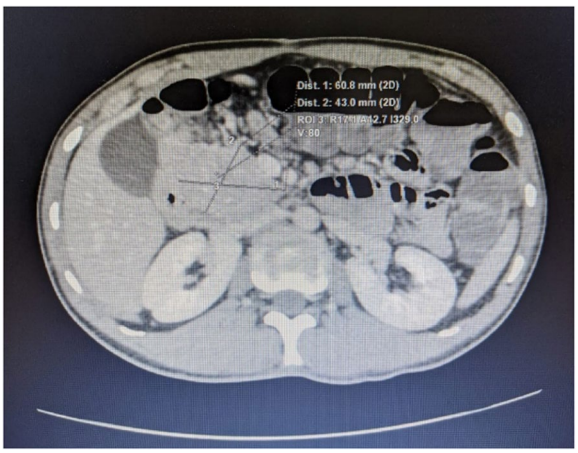

Fig. 3 Axial view showing the solid component of PNET

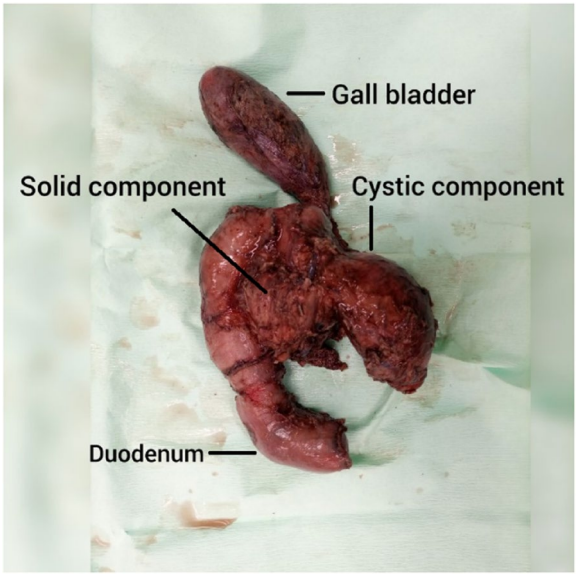

Fig. 5 The specimen after en bloc resection of the gall bladder, CBD, duodenum, and the solid cum cystic mass involving the proximal pancreas

distally, leaving behind only a small residual piece of pancreas. The tumor and cystic mass were removed en bloc with the duodenum, distal CBD, and gallbladder. A Roux loop was mobilized for hepaticojejunostomy.

The segment VI lesion in the liver was visible on the liver surface, while the lesion in segment III was palpable. Both lesions were resected using a harmonic scalpel. Postoperatively, the patient had a smooth recovery (Figs. 4 and 5). A per-operative drain placed had minimal output with normal amylase levels; hence, it was removed on postoperative day 3. The patient was discharged after 1 week.

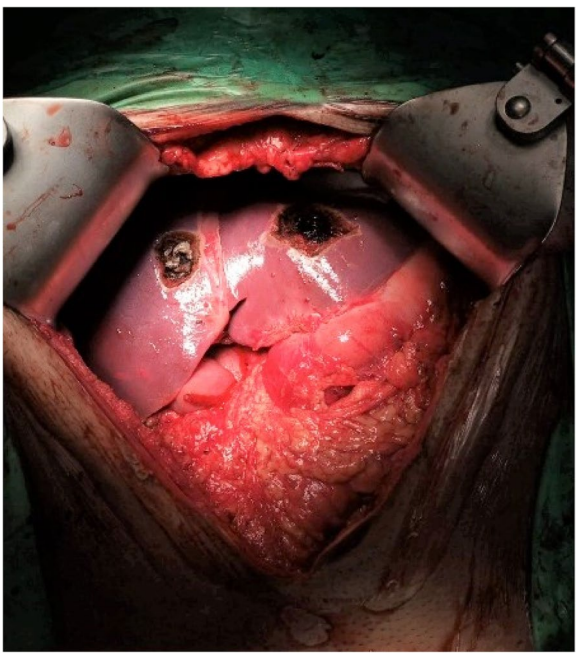

Fig. 4 After pancreaticoduodenectomy + wedge resection of liver deposits

Histopathological examination revealed a pancreatic tumor measuring 6×4×3 cm in size, classified as a WHO (World Health Organization) grade 1 NET tumor. It displayed both solid and cystic components, with the solid component measuring 6.4×5.0 cm and the cystic component measuring 6.7×4.1 cm. Focal invasion of the adjacent peripancreatic soft tissue was observed, with the tumor located 0.2 cm away from the resection margin. The tumor extended up to the muscularis layer of the duodenal wall. Perineural and lymphovascular invasion were present. The proximal and distal resection margins were free of tumor, as was the CBD and gallbladder. The hepatic artery lymph node and 13 additional lymph nodes were also tumor-free. The segment III liver wedge measuring 2.5×2×1 cm contained a metastatic tumor measuring 0.7×0.3 cm, located 0.6 cm away from the resection margin. The segment VI liver wedge measuring 3.5×2×1 cm was involved by a metastatic deposit measuring 0.6×0.3 cm, located 0.4 cm away from the resection margin. The pathological staging was pT3, pN0, and pM1a (Fig. 6).

The patient has been regularly followed up since then and has experienced favorable overall progress, with the exception of steatorrhea managed by oral pancreatic enzyme replacement with meals. Surveillance imaging at 6 months after resection revealed no evidence of recurrent disease or metastasis.

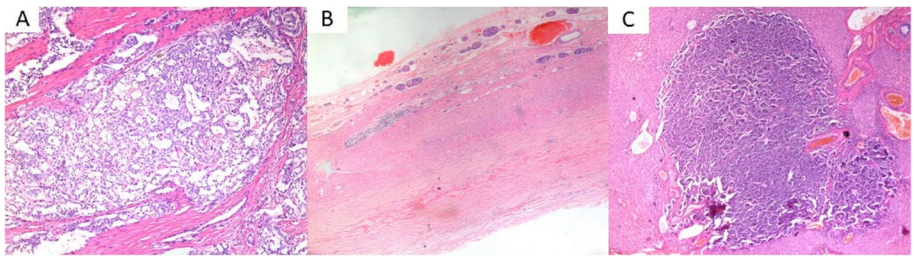

Fig. 6 **A** Medium-power view showing large, solid nests of tumor cells with pseudoglandular spaces (H&E (hematoxylin and eosin) stain, × 200). **B** Low-power view showing cyst wall containing small islands of neoplastic cells embedded in the wall (H&E stain, × 100). **C** Low-power view of liver specimen showing a well-circumscribed nest of tumor arranged in trabecular pattern (H&E stain, × 100)

We report a rare case of a solid cum cystic pancreatic NET which preoperatively was thought to be a pancreatic pseudocyst on imaging with a mass in the uncinate process. The patient was also lost to follow-up intermittently and hence had interval development of hepatic metastasis. He had also undergone two procedures prior with the intention of treating the cystic lesion as a pancreatic pseudocyst. Per-operatively, the challenge was the adhesions around the cystic lesion, duodenum, and the lesser sac due to history of a previous laparotomy. The other point of concern was the remaining pancreas being atrophic, so when the pancreas was mobilized, care was taken to fire a stapler very close to the cyst in order to ensure some pancreatic tissue of the proximal body remained while also not rupturing the cyst in order to avoid pancreatic insufficiency.

Discussion

Cystic nonfunctional PNETs are difficult to diagnose due to lack of specific symptoms and abundance of differentials for cystic lesions in the pancreas. Pancreatic pseudocyst is the most common differential, but pancreatitis in such cases is the consequence of the underlying pathology. Other differential diagnosis to consider in such patients includes serous or mucinous cystadenomas, intraductal papillary neoplasms, or acinar cell cystadenoma. Radiological imaging is recommended including a combination of CT, magnetic resonance imaging (MRI), and EUS with fine needle aspiration (FNA) for cytology [3]. Since diagnosis is difficult, a number of algorithms have been created for early detection of pancreatic cystic lesions with malignant potential, some detailing radiological findings to help differentiate amongst pathologies since these lesions are clinically either asymptomatic or present with nonspecific symptoms [4].

PNETs are rare, arising sporadically in most cases, but 10% of cases are associated with genetic syndromes like multiple endocrine neoplasia (MEN) type 1 and Hippel-Lindau disease [1]. PNETs can be functional or non-functional. Cystic PNETs account for 7–10% of pancreatic neoplasms and 10–18% of resected PNETs [5]. Nonfunctional PNETs predominate with an incidence of 60–90% [6], mostly being discovered incidentally or causing local symptoms due to their compressive effect. Their most frequent site of metastasis is the liver. Surgery remains the curative treatment of choice in resectable disease. Some specialty oncological organizations recommend guidelines for treatment of pancreatic NETs according to stage, and complete surgical resection is recommended if possible for both the primary lesion and the metastatic deposits in low-grade PNETs [7, 8]. If the liver metastasis is un-resectable, then locoregional and pharmacological therapies exist. The treatment strategy is tailored to each patient depending on their performance status and comorbidities.

The 5-year survival is reported to be 40–60% with median survival ranging from 38 to 104 months [9]. Long-term survival in pancreatic neuroendocrine tumors with liver metastases without resection is extremely rare. Hence, treatment of choice is surgical resection; however, for unresectable liver lesions, a number of other options exist. Staged liver segment resections, radiofrequency ablation (RFA), transarterial chemoembolization (TACE), transarterial embolization (TAE), cryoablation, and alkalization are all treatment options for hepatic metastasis of PNETs [10]. Pharmacological therapies are used in cases of unresectable and advanced disease which include conventional chemotherapy, molecular-targeted therapy, and drugs acting on hormone receptors [11].

Conclusion

The management of pancreatic NETs varies from case to case. In our case, we encountered a patient with a history of undergoing treatment with an impression of pancreatic pseudocyst as well as delaying definitive surgery until he had developed hepatic metastasis. Taking advantage of his young age and good health status, we wanted to aim for one major surgery that not only resected the

disease completely but also preserved viable and disease-free pancreatic tissue. He was successfully treated in one procedure for both the solid cum cystic tumor plus the hepatic metastasis while leaving behind enough pancreatic tissue despite his pancreas being largely atrophic to avoid endocrine insufficiency.

Abbreviations

PNET	Pancreatic neuroendocrine tumor
BMI	Body mass index
CT	Computed tomography
PD	Pancreatic duct
CBD	Common bile duct
MRCP	Magnetic resonance cholangiopancreatography
ERCP	Endoscopic retrograde cholangiopancreatography
EUS	Endoscopic ultrasound
H&E	Hematoxylin and eosin
MRI	Magnetic resonance imaging
FNA	Fine needle aspiration
MEN	Multiple endocrine neoplasia
RFA	Radiofrequency ablation
TACE	Transarterial chemoembolization
TAE	Transarterial embolization
WHO	World Health Organization

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Authors' contributions
MNU, manuscript research/writing/editing. MAK, manuscript editing/reviewing. AWK, manuscript editing/reviewing. The authors have read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate
Approved by SIUT-Ethical Review Committee (ERC).

Consent for publication
Informed consent taken from the patient for this case report as well as the accompanying pictures.

Competing interests
The authors declare that they have no competing interests.

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