Current Science
CS 5 (1), 1061– 1065 (2025)
Received 16 Oct 2024 | **Revised** 27 **Nov.** 2024 | **Accepted** 15 **Dec**. 2024 | **Online Available** 12 **Jan** 2025
https://doi.org/10.52845/CS/2025-5-1-8

Current Science

Current Science

OPEN ACCESS

ISSN (O) 2795-8639

ORIGINAL ARTICLE

A Case of Mixed Serous Neuroendocrine Tumor of the Pancreas

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Abstract

Pancreatic Mixed Serous Neuroendocrine Neoplasm (MSNN) is a rare type of pancreatic tumor characterized by the coexistence of serous cystic and neuroendocrine tumor features. This neoplasm typically produces excessive amounts of serous fluid and neuroendocrine hormones, leading to pancreatic dysfunction and endocrine imbalance. This article retrospectively analyzes the diagnostic and therapeutic process of a rare case of pancreatic MSNN, reviews the relevant literature, and explores its clinical features and treatment strategies to provide insights for clinical practitioners.

Keywords: Pancreatic Mixed Serous Neuroendocrine Neoplasm; Surgical

Introduction

Pancreatic serous cystic neoplasms (PSCNs) account for only 1%–2% of all pancreatic tumors [1]. In the 2010 World Health Organization (WHO) classification of tumors of the digestive system, PSCNs were categorized into five subtypes: serous microcystic adenoma (SMA), serous oligocystic adenoma (SOA), solid serous adenoma, serous cystic tumors associated with Von Hippel-Lindau (VHL) syndrome, and mixed serous-neuroendocrine neoplasms (MSNN)[2]. Serous microcystic adenoma of the pancreas (SMAP) is defined as a benign tumor composed of numerous small cysts arranged around a central stellate scar. The cysts are lined with uniform, glycogen-rich cuboidal epithelial cells. This subtype was first described by Compagno et al. in 1978[3]. In patients with SMAP, loss or mutation of the Von Hippel-Lindau tumor suppressor gene, located on chromosome 3, is commonly observed. SMAP represents approximately 1%–2% of all pancreatic exocrine tumors[4]. It predominantly occurs in middle-aged and elderly women (approximately 70%), with an average age of 66 years (range: 34–91 years)[5].

MSNN is a rare pancreatic tumor that comprises both serous cystic components and neuroendocrine tumor cells, exhibiting the combined characteristics of serous cystadenomas and neuroendocrine neoplasms, thereby posing significant challenges for clinical diagnosis and treatment. These tumors often produce excessive serous fluid and neuroendocrine hormones, resulting in pancreatic dysfunction and endocrine imbalance. Patients may present with symptoms such as pancreatitis, abdominal pain, nausea, vomiting, and jaundice.Due to its rarity and hybrid nature, the diagnosis and treatment of MSNN are often complex, requiring a combination of imaging studies, tumor marker evaluations, and tissue biopsies for confirmation. Given its uncommon nature, treatment plans are typically tailored to the individual patient's condition. The prognosis depends on factors such as tumor size, degree of differentiation, and extent of spread. Early diagnosis and prompt, aggressive treatment are critical for improving patient survival rates.

In summary, pancreatic MSNN is a rare tumor with mixed characteristics and endocrine dysfunction, posing significant challenges for clinical diagnosis and management.

Clinical Data

A 50-year-old female patient was admitted with a history of diabetes for five years and worsening fatigue for over a month. On physical examination, the abdomen was soft and flat, with no palpable masses. Mild tenderness was noted in the epigastric region, bowel sounds were normal, and no vascular bruits were detected. Routine blood tests, biochemical tests, and urinalysis showed no significant abnormalities. Endocrine evaluation revealed fasting C-peptide at 95.0 pmol/L and glycated hemoglobin (HbA1c) at 14.1%. Tumor marker CEA was elevated at 9.79 ng/mL.

Abdominal ultrasound suggested multiple pancreatic cysts and possible other cystic lesions, along with abdominal interstitial fluid accumulation. A further contrast-enhanced CT scan of the abdomen revealed the following findings (Figures A and B):1.Pancreatic enlargement with main pancreatic duct dilation and multiple cystic low-density areas within the parenchyma, predominantly in the head and neck region, suggesting intraductal mucinous neoplasm (mixed type).2.A hypervascular nodule in the uncinate process of the pancreas, highly suggestive of a neuroendocrine tumor.

After completing relevant evaluations and excluding significant surgical contraindications, the patient underwent “exploratory laparotomy and total pancreatectomy” under general anesthesia on November 22, 2021. Intraoperative findings revealed firm cystic-solid masses in the pancreatic head and body, measuring approximately 3 × 4 cm, with multiple surface cysts observed on the pancreatic body. The solid masses were tightly adhered to the surrounding tissues. The duodenum, gallbladder, spleen, and surrounding ligaments and vessels were mobilized. Due to tight adhesion between the pancreas and spleen, a "total pancreatectomy with splenectomy" was performed. The surgery was completed successfully, and the patient had an uneventful postoperative recovery.

Postoperative pathology (Figures C, D, and E) confirmed:1.Mixed serous-neuroendocrine neoplasm of the pancreas, with diffuse serous cystadenoma involvement across the pancreatic head, body, and tail, and neuroendocrine tumor (NET, G2) localized in the head region.2.Negative tumor margins at the gastroduodenal junction, with no lymph node metastases (0/4).

The patient has been followed up for three years postoperatively, with good recovery. Repeat abdominal CT and MRI scans have shown no tumor recurrence, anastomotic thickening, or other significant abnormalities.

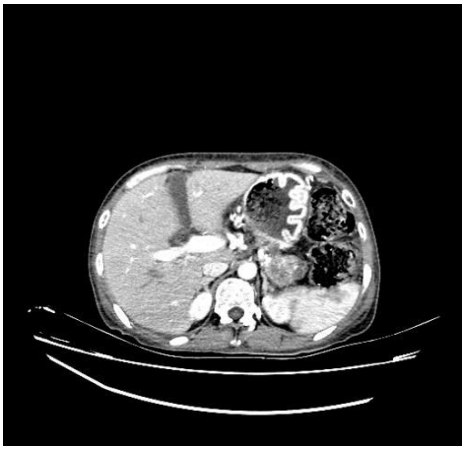

Figure A: Enhanced CT scan reveals a solid mass in the tail of the pancreas, measuring 4x3 cm.

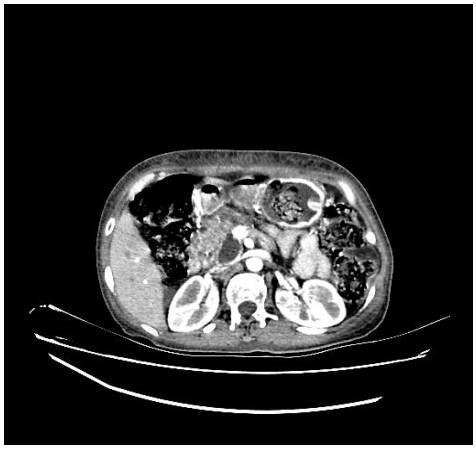

Figure B: A cystic lesion is present in the head of the pancreas, measuring 2x3 cm.

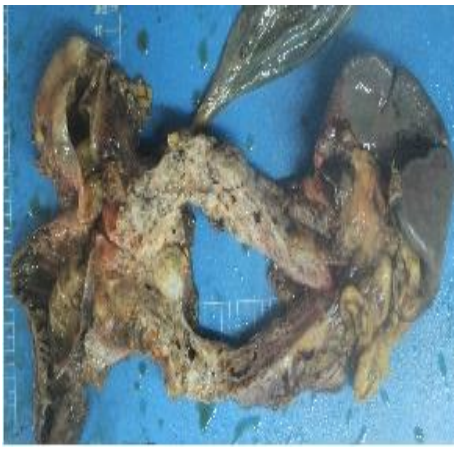

Figure C: Gross specimen showing masses in both the head and tail of the pancreas.

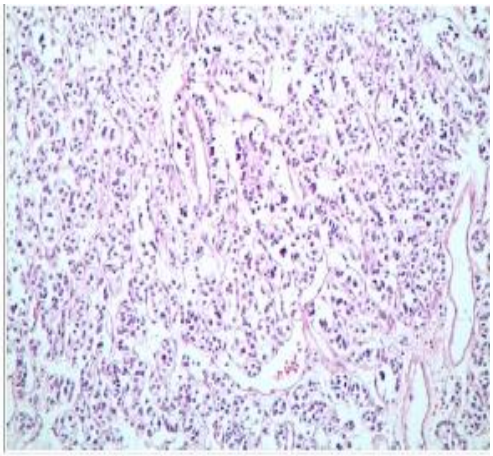

Figure D: Result of pathological slice processing - Part 1.

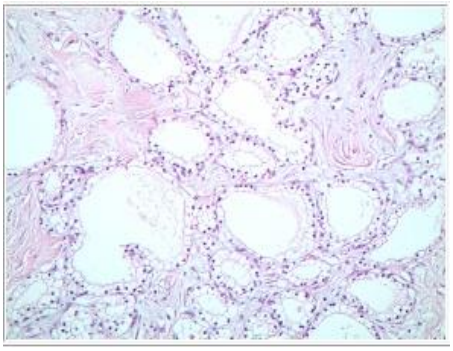

Figure E: Result of pathological slice processing - Part 2.

Discussion

Neuroendocrine tumors (NETs) are a relatively rare group of neoplasms, with the pancreas being one of their most common sites of origin. In recent years, the incidence of pancreatic neuroendocrine neoplasms (PNENs) has risen significantly, making them the most prevalent subtype among gastroenteropancreatic neuroendocrine tumors. The majority of PNEN patients are asymptomatic at diagnosis, with sporadic (approximately 90.3%) and non-functional tumors (around 65.6%) being the most common. Functional PNENs (about 34.4%) are predominantly insulinomas, accounting for roughly 94.8% of cases[6,7]. Among pancreatic neuroendocrine tumors (PNETs), the incidence of G1, G2, and G3 tumors is approximately 49.2%, 45.7%, and 5.1%, respectively[15]. Notably, the differential diagnosis between PSCNs and PNETs can be challenging, particularly in small biopsy specimens. However, a key distinction lies in the lack of reactivity to neuroendocrine markers, such as chromogranin A, in PSCNs[12]. Instead, PSCNs exhibit positivity for epithelial markers, such as CK19 and CK7, and may also express other markers, including alpha-inhibin and calretinin [13,14].

In the 2010 WHO classification of pancreatic tumors, the concept of mixed serous-neuroendocrine neoplasm (MSNN) was explicitly introduced as a new subtype of serous cystadenomas[7]. Two hypotheses have been proposed regarding the origin of MSNN: (1) a common progenitor cell; and (2) distinct progenitor cells.The first hypothesis suggests that PSCNs and PNETs may originate from a shared multipotent stem cell[8], supported by observations of biphasic differentiation in pancreatic lesions[9], such as nesidioblastosis—a non-neoplastic condition characterized by simultaneous epithelial and endocrine differentiation. Additionally, Kakkar et al.[10] identified neurosecretory granules, glycogen, and intermediate filaments within the same tumor cells through ultrastructural examination. This could explain cases where the two tumor components are closely intermingled but fails to account for lesions where the components are spatially distinct.The second hypothesis posits that the two components of MSNN arise from two distinct cell types,

potentially triggered by a predisposed genetic condition, such as Von Hippel-Lindau (VHL) syndrome[11]

The primary indications for total pancreatectomy include chronic refractory pancreatitis, pancreatic head carcinoma, neuroendocrine tumors, intraductal papillary mucinous neoplasm (IPMN), and multiple metastatic pancreatic cancers[15]. In this case, the patient was admitted due to a five-year history of diabetes and over a month of worsening fatigue. Upon comprehensive examination, a pancreatic mass was identified, and a total pancreatectomy was performed. Postoperative pathology confirmed a diagnosis of mixed serous-neuroendocrine tumor (MSNN) of the pancreas, with a pathological grade of G2 neuroendocrine tumor.It is noteworthy that due to the extremely low incidence of mixed-type MSNN, insufficient awareness often leads to misdiagnosis or missed diagnosis[16]**.** Greater efforts are needed to enhance understanding of this rare disease. In this case, preoperative CT suggested intraductal mucinous carcinoma of the pancreas, with no consideration of pancreatic cystadenoma. The limitations of preoperative imaging in diagnosing pancreatic tumors ultimately resulted in clinical misdiagnosis.

Conclusion

MSNN represents a distinct clinicopathological tumor entity, rather than a coincidental concurrence of serous cystadenoma and neuroendocrine tumor as two separate neoplasms. This case contributes to a deeper understanding of MSNN, which may provide insights into its prognosis, including its malignant potential, appropriate therapeutic strategies, and the necessity for long-term follow-up.

However, due to the rarity of reported MSNN cases, our knowledge of this disease remains limited. Further research is essential to better elucidate its etiology, pathogenesis, clinical manifestations, diagnostic criteria, treatment approaches, and prognostic factors. By accumulating more case reports and conducting comprehensive studies, we can enhance our understanding of MSNN and offer patients more accurate diagnoses and improved treatment options.

Funding

This work was supported by the Military Logistics Scientific Research Plan Project (20BJZ23) and the Internal Research Project of No. 940 Hospital of Joint Logistics Support Force of Chinese People's Liberation Army (2022yxky016).

Data Availability Statements

The data generated in the present study may be requested from the corresponding author.(E-mail:qinjianwei940@163.com)

The data generated in the present study are included in the figures and/or tables of this article.

Authors' Contributions

LYS and SYH analyzed the data and were the primary author of the manuscript. PYP acquired the CT scan images. MBW analyzed patient data. SYH and XSL confirm the authenticity of the data. XSL and QJW assisted in writing the manuscript. All authors have read and approved the final manuscript.

Patient Consent for Publication

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Competing Interests

The authors declare that they have no competing interests.

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