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ORIGINAL ARTICLE

Pancreatic Nerve Sheath Tumors: a Single Institutional Series and Systematic Review of the Literature

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Abstract

Introduction Improvement in imaging has resulted in frequent diagnosis of benign and premalignant pancreatic tumors. Pancreatic nerve sheath (PNS) tumors are one of the rarest pancreatic tumors. Literature on PNS is limited and their biology is poorly understood. Here, we report the largest series of PNS tumors to date and review the literature to evaluate the current data available on PNS tumors.

Methods An institutional database was used to identify patients who underwent resection for PNS tumors. Clinicopathological characteristics and outcomes of these patients were reported. Furthermore, a review of literature was performed.

Results From January 1994 through December 2016, seven patients underwent resection for PNS tumors. The median age was 57.7 years (IQR, 44.9–61.9) and the sex was approximately equally distributed (male = 4; 57.1%). Three (42.9%) patients were diagnosed incidentally and six (85.7%) were misdiagnosed as having other pancreatic tumors. The median tumor size was 2.1 (IQR 1.8–3.0) cm and six (85.7%) had no nodal disease. At a median follow-up of 15.5 (IQR 13.7–49.3) months, six patients were alive without evidence of disease and one patient was lost to follow-up. The literature review identified 49 studies reporting 54 patients with PNS tumors. Forty-six were misdiagnosed as having other pancreatic tumors. The median tumor size was 3.6 (range 1–20) cm, nodal disease was present in six patients (22.2%), and no patient had distant metastatic disease. At the time of last follow-up, all patients were free of disease.

Conclusion This is the largest single institution series on PNS tumors reported to date. These tumors are rare and are often misdiagnosed, given their radiological characteristics. PNS tumors have a benign course of disease and surgical resection results in favorable long-term outcomes.

Keywords Pancreatic surgery · Schwannoma · Nerve sheath tumor · Hepatobilliary surgery · Pancreatic neoplasm · Pancreatic tumor

Introduction

Recent improvements in imaging techniques have led to an increase in the diagnosis of premalignant and benign tumors of the pancreas. One of the rarest reported type of pancreatic tumors is pancreatic nerve sheath (PNS) tumor, more commonly known as pancreatic schwannomas (PS).

Schwanommas are tumors that arise from the Schwann cells surrounding nerves and are commonly found in the periphery of the upper and lower extremities, head and neck, peritoneum, and retroperitoneum.[1] Schwann cells surrounding the vagus nerve that courses through the pancreas can lead to the formation of pancreatic schwannomas or neurofibromas.[2] These, in addition to paragangliomas arising in the pancreas are collectively referred to as PNS tumors. These tumors were

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first described by Moller-Pedderson et al. in 1982, and to date, 49 articles have reported 54 cases in the literature; the largest series of three patients being reported by Ferrozi et al.[1–49] These tumors are predominantly solid but can present with a variety of degenerative changes, including cystic features, calcification, hemorrhage, hyalinization, and xanthomatous infiltration.[1] Given their rarity and the wide range of their radiological appearance, these tumors are often misdiagnosed. Furthermore, due to the lack of literature, the biology of PNS tumors is poorly understood.[17] In this study, we report the largest series reported to date on PNS tumors and present the current literature available on this disease.

Methods

Study Design and Data Collection

A prospectively maintained, institutionally approved database on all patients undergoing pancreatic resection at the Johns Hopkins Hospital was reviewed to identify patients who underwent surgical resection for PNS tumors between 1994 and 2016. Clinicopathological data were extracted from the database, and missing data were collected from the patients' electronic medical records. Continuous variables were reported as means and standard deviations or medians and ranges as deemed appropriate, while all categorical variables were reported as frequencies and percentages. All analyses were performed using STATA version 14.1 (StataCorp, College Station, TX).

Review of Literature

A review of literature through July 2016 was performed to identify studies reporting patients with PNS tumors. A comprehensive search was performed using PubMed, EMBASE, and Medline using the terms "Pancreatic nerve sheath tumors," "Pancreatic schwannoma," "Pancreatic paraganglioma," "pancreatic neurinomas," and "pancreatic neurilemomas." Two authors (AAJ and KC) performed independent reviews and then compiled a comprehensive list of available literature. The references in the studies identified during the initial review were screened to identify more articles reporting patients with PNS tumors. In cases where multiple pancreatic tumors were reported, data relevant to patients with PNS were extracted. When applicable, data that reappeared in the review were cross verified across multiple articles for data accuracy. Studies in languages other than English were excluded. Studies were limited to publication through July 2016 to allow for adequate reporting. Data on the clinicopathological features (including age, gender, symptoms, tumor location, initial diagnosis, surgery type, tumor size, nodal status, and distant metastasis) and outcomes (postoperative complications, recurrence of disease, and overall survival) were collected. A complete list of variables can be seen in Tables 1, 2, 3 and 4.

The study was approved by the Institutional Review Board for Human Research and complied with all Health Insurance Portability and Accountability Act regulations.

Results

During the study period, seven patients underwent surgical resection for primary PNS tumors (Table 1). The median age was 57.7 years (IQR, 44.9–61.9) and sex was approximately equally distributed ($N = 4$ males, 57.1% vs. $N = 3$ females, 42.9%), while a majority were white ($N = 6$, 85.7%). The most common presenting symptoms included abdominal pain ($N = 4$, 57.1%) and jaundice ($N = 2$, 28.6%). Two (28.6%) patients were diagnosed incidentally on routine medical evaluation or imaging done for other diseases. A majority ($N = 5$, 71.4%) had no history of smoking. The patients' past medical history was significant for hypertension ($N = 3$, 42.9%), hyperlipidemia ($N = 2$, 28.6%), and pancreatitis ($N = 1$, 14.3%). One (14.3%) patient had a history of prior bladder cancer and one patient (14.3%) had a family history significant for colorectal cancer. The patient with bladder cancer underwent surgical resection prior to the diagnosis of the PNS tumor.

All patients were initially evaluated using a pancreas protocol computed tomography. (Table 2). Imaging demonstrated cystic features in six patients (85.7%) (Fig. 1). Specifically, nodularity was observed in two (28.6%) patients (Fig. 2), hypodensity was observed in two (28.6%) patients, central necrosis was observed in two (28.6%) patients (Fig. 3), while three (42.9%) patients had rim enhancement. The presumed diagnosis based on cross-sectional imaging included pancreatic cystic neoplasm ($N = 3$, 42.9%), intraductal papillary mucinous neoplasm (IPMN) ($N = 1$, 14.3%), pancreatic neuroendocrine tumor ($N = 1$, 14.3%), carcinoid tumor ($N = 1$, 14.3%), and lymphoma ($N = 1$, 11.1%). Subsequently five patients (71.4%) underwent evaluation via endoscopic ultrasound (EUS) and fine needle aspiration. The suggested diagnosed based upon histopathological review of the cytology included malignant neoplasm ($N = 1$, 14.3%), carcinoid tumor ($N = 1$, 14.3%), and PNS tumor ($N = 1$, 14.3%), and two (28.6%) patient's biology was deemed to be inconclusive.

A majority ($N = 4$, 57.1%) of the tumors were located in the head of the pancreas. Six patients (85.7%) underwent pancreaticoduodenectomy while one patient (14.3%) underwent a central pancreatectomy. The final histopathological examination confirmed a diagnosis of PNS tumors in seven patients (100%) (Table 3). The median size of the tumor was 2.1 cm (IQR 1.6–3.5), and a majority had no nodal disease ($N = 6$, 85.7%). The one-node-positive patient (14.3%) was found to have metastatic granulocytic paraganglioma in

Table 1 General demographics of study population

Present case series	Age	Gender	Race	Past medical history	Smoking status
Case 1	62.6	Male	White	HTN, HLD, BPH, GERD	Former
Case 2	57.7	Female	White	None	Former
Case 3	61.3	Female	White	HLD	Never
Case 4	65.4	Male	African-American	HTN	Never
Case 5	37.4	Male	White	Hematuria, pancreatitis	Never
Case 6	43.5	Female	White	Carcinoma of the bladder, rhabdomyosarcoma	Never
Case 7	46.3	Male	White	HTN	Never

HTN hypertension, *HLD* hyperlipidemia, *BPH* benign prostate hypertrophy, *GERD* gastroesophageal reflux disease

one lymph node. A negative margin was achieved in all seven (100%) patients. Three patients (42.9%) each had a T1 and T2 tumor while one patient (14.3%) had a T3 tumor. No patients were found to have metastatic disease. The patients were classified as having AJCC stage IA ($N = 1$, 14.3%), IB ($N = 3$, 42.9%), IIA ($N = 1$, 14.3%), and IIB ($N = 2$, 28.6%) disease as defined by the AJCC 7th edition.[50]

The median length of hospitalization was 7 days (IQR 7–10), and three patients (42.9%) developed postoperative complications. One patient (14.3%) experienced delayed gastric emptying, while one patient (14.3%) developed a postoperative pancreatic fistulae (POPF) (Table 3).

The median follow-up was 15.5 months (IQR 13.7–49.3). At the time of most recent follow-up, six patients (85.7%) were alive without evidence of disease and one patient (14.3%) was lost to follow-up.

Review of Literature

The review of literature yielded 1526 potential articles. After excluding those reporting PNS of origin other than the pancreas, and those with overlapping patients, a total of 49 studies reporting 54 patients with PNS tumors were identified. (Table 4) The patient population was approximately equally distributed with regard to sex (31 females, 57.4% vs. 23 males, 42.6%) and the median age was 55 years (range 20–87). The presenting symptoms included abdominal pain ($N = 28$, 51.9%), weight loss ($N = 10$, 18.5%), dyspepsia ($N = 4$, 7.4%), and jaundice ($N = 1$, 1.8%), while 24 patients (44.4%) were diagnosed incidentally. The tumor was more commonly located in the head of the pancreas ($N = 23$, 42.6%), while 15 patients (27.8%) had tumors in the body of the pancreas.

The presumed diagnosis was reported for 46 patients (85.2%), of whom only three (5.6%) had a presumed diagnosis of PNS. For the remaining patients, it varied from pancreatic cystic neoplasm ($N = 19$, 35.2%) to pancreatic ductal adenocarcinoma ($N = 3$, 5.6%), MCN ($N = 6$, 11.2%), microcystic adenoma ($N = 1$, 1.9%), pancreatic neuroendocrine tumor (PNET) ($N = 8$, 14.8%), and pseudocyst ($N = 4$, 7.4%).

Type of surgery was reported for 48 patients (88.9%) of whom 19 (35.2%) underwent pancreaticoduodenectomy, 11 (20.4%) underwent distal pancreatectomies, nine (16.7%)

Table 2 Presentation and workup of study population

Present case series	Presenting symptoms	Tumor location	Biopsy	Biopsy result	Radiology suggested diagnosis
Case 1	Asymptomatic	Head	1	Non-diagnostic (hypocellularity)	Indraductal papillary mucinous neoplasm
Case 2	Abdominal pain, weight loss	Neck	1	Malignant neoplasm	Cystic neoplasm
Case 3	Asymptomatic	Head	0	–	Pancreatic neuroendocrine tumor
Case 4	Abdominal pain, jaundice	Head	1	Carcinoid tumor	Carcinoid tumor of the ampulla
Case 5	Abdominal pain	Body	1	Pancreatic schwannoma	Pancreatic schwannoma
Case 6	Asymptomatic	Uncinate	1	Non-diagnostic (hypocellularity)	Indraductal papillary mucinous neoplasm
Case 7	Abdominal pain, jaundice	Head	0		Cystic neoplasm

Table 3 Surgical, pathological, and outcome details of study population

Present case series	Surgery type	Surgical approach	Pathology	Tumor size (cm)	Nodal status	Metastasis	ICU days	Postoperative course	Follow-up (months)	Recurrence	Death
Case 1	PD	Open	Schwannoma	3.50	0/10, N0	M0	1	DGE*, Wound complication	77.6	No	No
Case 2	PD	Open	Schwannoma	2.10	0/12, N0	M0	2	Uncomplicated	20.9	No	No
Case 3	PD	Open	Schwannoma	9.50	0/16, N0	M0	1	Anastomotic ulcer	15.5	No	No
Case 4	PD	Open	Paraganglioma	2.00	1/10, N1	M0	1	Uncomplicated	13.1	No	No
Case 5	CP	Open	Schwannoma	1.30	0/0, Nx	M0	1	Uncomplicated	5.0	No	No
Case 6	PD	Robotic MIS	Schwannoma	1.60	0/12, N0	M0	1	DGE*	14.3	No	No
Case 7	PD	Open	Schwannoma	2.50	0/10, N0	M0	1	Uncomplicated	198.8	No	No

MIS minimally invasive surgery, *DGE* delayed gastric emptying, *PD* pancreaticoduodenectomy, *CP* central pancreatectomy

received enucleations, and one (1.9%) received a central pancreatectomy. Seven patients (13.0%) underwent nonspecific pancreatectomies, while one was deemed to have unresectable disease and underwent a palliative gastrojejunostomy.[8]

On histopathological review, the median size of the tumor (reported on 54 patients) was 3.6 cm (range 1–20). Nodal disease was present in six patients (22.2%) (reported on 27 patients), while no patients had distant metastatic disease. At a median follow-up of 15.5 (range 6–24) months, no patients had recurrence of disease.

Discussion

PNS tumors represent an exceedingly rare tumor of the pancreas.[2]They are generally benign neoplasms of pancreatic nerve sheaths originating on the vagus nerve and are often misdiagnosed as cystic pancreatic tumors.[2] On gross histopathological examination, these tumors are generally well-differentiated, tan-yellow colored, round, and encapsulated, and can undergo degenerative changes such as hyalinization, cystic degeneration, hemorrhage, and xanthomatous infiltration. These tumors stain strongly for the S100 protein, vimentin, and CD56 + .[12,51] Additionally, they stain for CD34-, CD117-, DOG1-, and AE1-/AE3-.[12] Commonly, PNS tumors are negative for cytokeratin, c-kit, desmin, alpha smooth muscle actin, and smooth muscle myosin.[1,30] Furthermore, cytogenetic studies have shown that most PNS tumors generally have mutations resulting in monosomy 22 or loss of 22q.[1,20]

To date, only 54 cases have been documented in English literature with the largest series reporting three cases.[2] Together with our present series, which is the largest to date, a total of 63 cases of PNS tumors have been identified. The combined cohort demonstrates that PNS tumors show no preference for age or gender. Patients are typically asymptomatic or present with generalized symptoms including abdominal pain and weight loss. The median tumor size for all 61 cases was 2.9 cm and a majority ($N = 27$, 44.3%) were located in the head of the pancreas. Nodal disease was present in 4 (6.6%) of these patients. This is a clinically relevant finding given that while it is thought that all PNS tumors are benign, in fact, some of them may have malignant potential as evident by the nodal involvement, which warrants surgical resection rather than observation. Furthermore, if patients are symptomatic from their tumor, or the tumor growth is observed on subsequent scans, surgical resection is recommended.

On cross-sectional imaging, these tumors often mimic pancreatic cystic lesions with calcifications.[1] Typically, imaging demonstrates encapsulated and well-defined lesions while endoscopic ultrasound (EUS) demonstrates hypoechoic masses. Unfortunately, fine-needle aspiration (FNA) is unreliable for PNS tumors, in part, due to the hypocellularity.[42] Only a small minority ($N = 4$, 6.6%) of cases were diagnosed as PNS tumors preoperatively using EUS-guided FNA.[8,15,25] Diagnostic challenges also stem from the heterogeneity of samples, as PNS tumors may contain epithelioid, inflammatory, or reactive cells.[42] Microscopically, PNS contain two areas: Antoni A areas and Antoni B areas. Antoni A areas are characterized by hypercellular regions of tightly packed, monomorphic, spindle-shaped Schwann cells. The cells in Antoni A areas notably display nuclear palisading.[51] Antoni B areas are characterized by hypocellular regions where the aforementioned degenerative changes are generally observed.[51] Further, the Schwann cells in Antoni B areas tend to appear with nuclei that are suspended in a myxoid, microcystic matrix. There are multiple cases in the literature that have shown varying proportions of Antoni A and B areas in PNS tumors.[51] Tumors with a high Antoni A/Antoni B ratio appear nonhomogenous due to increased lipid content, while tumors with a low ratio appear hypodense, cystic, and multiseptated. With contrast imaging, Antoni A areas will show enhancement due to increased vascular involvement, while Antoni B areas will

Table 4 Comprehensive literature review

Author and year of publication	Age	Gender	Symptoms	Tumor location	Original diagnosis	Surgical type	Tumor size (cm)	Nodal status	Metastasis	Postoperative course	Follow up (mo.)	Recurrence
Abu-Zaid et al. 2013	44	Male	Abdominal pain	Tail	Pancreatic mass	DP	7.2	N0	M0	Uneventful	6	No recurrence
Agarwal et al. 2010	20	Male	Abdominal pain	Head	Pancreatic mass	En	3	N0	M0	Uneventful	NR	NR
Akiyoshi et al. 2004	67	Female	Assymptomatic	Head	Cystic neoplasm	PD	5	NR	NR	Delayed gastric emptying	43	No recurrence
Alma et al. 2001	73	Female	Abdominal pain	Head	Cystic neoplasm	PD	3	N0	M0	Uneventful	17	No recurrence
Almo et al. 2001	47	Female	Assymptomatic	Head	PNET	PD	3	N0	M0	Uneventful	14	No recurrence
Brown et al. 1998	52	Male	Assymptomatic	Body	Cystic neoplasm	Panc, nos	5.5	NR	NR	NR	NR	NR
Brown et al. 1998	69	Male	Assymptomatic	Head	Cystic neoplasm	PD	6	NR	NR	NR	NR	NR
Bui et al. 2004	69	Female	Abdominal pain	Head	Pancreatic mass	Palliative bypass*	5	N0	M0	Uneventful	NR	NR
Ciledag et al. 2014	30	Male	Abdominal pain, weight loss	Head	Pancreatic mass	PD	9	NR	NR	NR	NR	NR
Coombs et al. 1990	74	Female	Assymptomatic	Head	Cystic Neoplasm	PD	7	NR	NR	NR	NR	NR
D Benedetto et al. 2007	42	Male	Assymptomatic	Body	Pancreatic mass	DP	2.5	N0	M0	Uneventful	NR	NR
David et al. 1993	46	Male	Abdominal pain	Uncinate	Pancreatic mass	Panc, nos	6.5	NR	NR	Uneventful	NR	No recurrence
Devi et al. 2014	63	Female	Abdominal pain, weight loss	Tail	PDAC	DP	1	NR	NR	NR	NR	NR
Dorsey et al. 2013	54	Female	Abdominal pain, weight loss	Head	Pancreatic mass	NR	1.4	NR	NR	NR	NR	NR
Duma et al. 2015	72	Female	Abdominal pain, dyspepsia	Head	Pancreatic mass	PD	3.5	N0	M0	Uneventful	12	No recurrence
Eggermont et al. 1987	40	Female	Abdominal pain, jaundice, weight loss	Head	Pancreatic mass	PD	10	NR	NR	Uneventful	9	No recurrence
Fasanella et al. 2007	36	Male	Abdominal pain	Uncinate	Pancreatic Schwannoma	En	4	N0	M0	Uneventful	NR	NR
Feldman et al. 1997	63	Male	Assymptomatic	Body	Pancreatic mass	En	2	N0	M0	Uneventful	24	No recurrence
Feldman et al. 1997	54	Female	Abdominal pain, weight loss	Body	Pancreatic mass	En	2	N0	M0	Uneventful	24	No recurrence
Ferrozzi et al. 1995	47	Male	Abdominal pain, dyspepsia	Body	MCN	DP	3.5	NR	NR	Uneventful	48	No recurrence
Ferrozzi et al. 1995	63	Male	Abdominal pain	Body	Cystic neoplasm/hemangioma	Panc, nos	3.5	NR	NR	NR	NR	NR
Ferrozzi et al. 1995	68	Female	Abdominal pain, dyspepsia	Body	Cystic neoplasm	NR	3.5	NR	NR	Uneventful	6	No recurrence
Gupta et al. 2009	56	Female	Assymptomatic	Body-head	Cystic neoplasm	PD	8.9	NR	NR	Uneventful	NR	NR
Hirabayashi et al. 2008	51	Male	Assymptomatic	Tail	Cystic neoplasm	DP	6	NR	NR	Uneventful	NR	NR
Hsiao et al. 1998	70	Female	Assymptomatic	Body-tail	MCN	Panc, nos	18	N0	M0	Uneventful	24	No recurrence
Kameyama et al. 2012	50	Female	Assymptomatic	Body	PNET	Panc, nos	1.7	NR	NR	Uneventful	1	No recurrence
Kim et al. 2011	45	Female	Assymptomatic	Uncinate	PNET	PD	2.5	NR	NR	NR	NR	NR
Kinhal et al. 2010	55	Male	Abdominal pain	Body-head	Cystic neoplasm	En	6.8	N0	M0	Uneventful	3	No recurrence
Lee et al. 2001	63	Female	Abdominal pain	Tail	Cystic neoplasm	DP	10	NR	NR	NR	6	No recurrence
Li et al. 2009	37	Male	Assymptomatic	Body	Pancreatic schwannoma	Panc, nos	1.3	NR	NR	NR	NR	NR

Table 4 (continued)

Author and year of publication	Age	Gender	Symptoms	Tumor location	Original diagnosis	Surgical type	Tumor size (cm)	Nodal status	Metastasis	Postoperative course	Follow up (mo.)	Recurrence
Liegl et al. 2011	62	Male	Assymptomatic	Head	PDAC	PD	5	N1	M0	Postoperative mortality	–	–
Liessi et al. 1990	75	Female	Abdominal pain	Head	Pseudocyst	Patient refused surgery	7	NR	NR	NR	NR	NR
Melato et al. 1993	87	Male	Abdominal pain	Body-tail	Pseudocyst	NR	20	NR	NR	NR	NR	NR
Moller-Pederson et al. 1982	60	Male	Abdominal pain, weight loss	Body-tail	Cystic neoplasm	Unresectable	20	NR	NR	NR	4	No recurrence
Moriya et al. 2010	64	Female	Assymptomatic	Uncinate	MCN/GIST	En	4	N0	M0	Uneventful	65	No recurrence
Mourra et al. 2015	64	Female	Assymptomatics	Body	PNET	CP	4.2	N0	M0	NR	NR	NR
Mummadi et al. 2009	35	Male	Abdominal pain	Body	Pseudocyst	NR	7	NR	NR	Uneventful	6	No recurrence
Novellas et al. 2005	46	Female	Weight loss	Head	PNET	DP	3	NR	M0	Uneventful	24	No recurrence
Ohbatake et al. 2014	40	Female	Assymptomatic	Head	PNET/pseudocyst	PD	3.6	NR	NR	NR	NR	NR
Okuma et al. 2008	71	Female	Abdominal pain	Body	PNET	DP	2	N0	M0	NR	NR	NR
Oshima et al. 2010	32	Female	Assymptomatic	Head	Pseudocyst	PD	3.5	N0	M0	Uneventful	36	No recurrence
Paranjape et al. 2004	77	Female	Abdominal pain, weight loss	Body	Cystic neoplasm	En	3.5	N0	M0	Uneventful	3	No recurrence
Poosawang et al. 2013	46	Female	Dyspepsia, weight loss	Head	Cystic neoplasm	PD	5.8	NR	NR	Uneventful	18	No recurrence
Soumaoro et al. 2005	64	Female	Assymptomatic	Head	Cystic neoplasm	En	2.5	N0	M0	Uneventful	24	No recurrence
Stojanovic et al. 2010	24	Female	Abdominal pain, dyspepsia, weight loss	Body-tail	Cystic Neoplasm	DP	18	N1	M1	Uneventful	28	No recurrence
Suzuki et al. 2010	66	Female	Assymptomatic	Body	MCN	DP	3	N1	M1	Uneventful	24	No recurrence
Tafe et al. 2008	46	Male	Abdominal pain	Body-tail	Cystic neoplasm	DP	9.3	NR	NR	NR	NR	NR
Tan et al. 2003	46	Male	Abdominal Pain	Head	MCN	PD	2.2	NR	NR	NR	NR	NR
Tofigh et al. 2008	54	Male	Abdominal pain, jaundice, weight loss	Head	Pancreatic mass	PD	3	NR	NR	Uneventful	NR	NR
Urban et al. 1992	56	Female	Assymptomatic	Body	MCN	DP	3.5	N0	M0	NR	NR	NR
Von Dobschuetz et al. 2004	55	Female	Assymptomatic	Head	Pancreatic mass	PD	8	NR	NR	Pleural effusion/POPF	10	No recurrence
Wu et al. 2005	71	Male	Abdominal pain	Head	Cystic neoplasm	En	1	N0	M0	Uneventful	10	No recurrence
Yu et al. 2005	72	Male	Abdominal pain	Head-body	Pancreatic mass	Panc, nos	1	NR	NR	NR	NR	NR

PNET pancreatic neuroendocrine tumor, *MCN* mucinous cystic neoplasm, *GIST* gastrointestinal stromal tumors, *NR* not reported *PD* pancreaticoduodenectomy, *DP* distal pancreatectomy, *CP* central pancreatectomy, *Panc*, *nos* pancreatectomy, not otherwise specified, *En* enucleation

*Palliative bypass—gastrojejunostomy

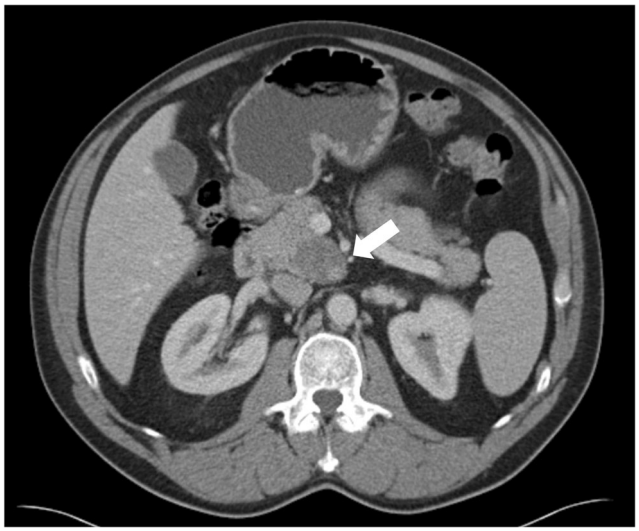

Fig. 1 CT scan of a 62-year-old male demonstrating a 3.8-cm mass arising off the medial aspect of the uncinate process. No intrahepatic or pancreatic duct dilatation was observed. The mass was well defined but had cystic features. Furthermore, there was peripheral enchantment of the lesion. Presumed diagnosis was a pancreatic cystic lesion

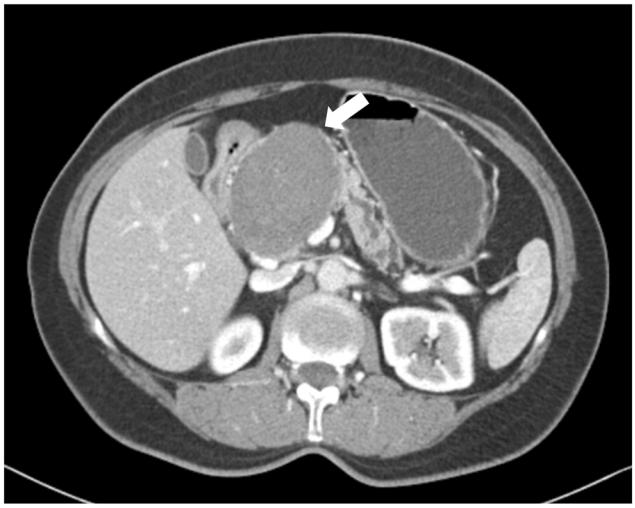

Fig. 3 CT scan of a 61-year old female demonstrating a 8.4-cm well-circumscribed, homogenous mass arising from the head of the pancreas, with upstream pancreatic duct dilatation. The mass had several smaller foci of internal cystic changes with central necrosis. Presumed diagnosis was a pancreatic cystic neuroendocrine tumor

be non-enhancing due to less vascularity. Importantly, the diagnosis of PNS tumor does not preclude other cancer diagnoses, as concurrent PNS tumor and PDAC have been observed.

In both our institutional experience and literature, all cases of resected PNS tumors achieved good long-term outcomes; none of the patients developing recurrence at the last follow-up. PNS tumors are generally benign, and are believed to be relatively indolent tumors. A diagnosis of PNS tumor should be considered in the setting of heterogeneous masses of the pancreas particularly with calcification, hemorrhage, or hyalinization. Accurate diagnosis of pancreatic cystic lesions remains inexact; in fact, up to 25% of IPMNs are misdiagnosed preoperatively.[52] As such, improved diagnostic imaging remains a need for accurate diagnosis of pancreatic tumors. Future studies may seek to rely on mutational analysis of preoperative FNA biopsies of these tumors. This study has several limitations, as is common with all retrospective analyses, including the potential for inaccurate data reporting and missed studies for inclusion.

In conclusion, PNS tumors are exceptionally rare tumors of the pancreas that are often misdiagnosed as other cystic pancreatic tumors. Surgical resection remains the treatment of choice and can help achieve excellent long-term outcomes.

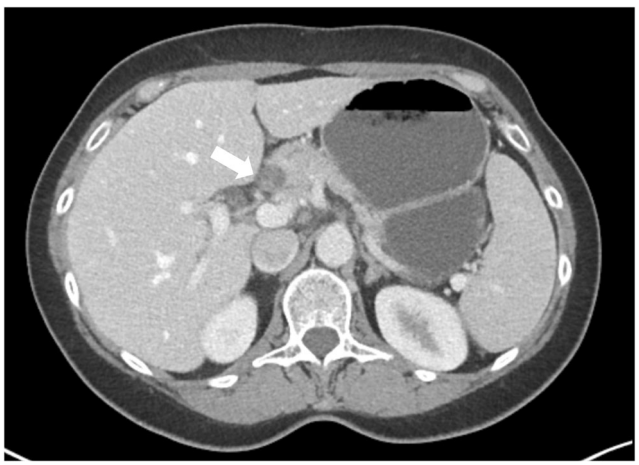

Fig. 2 CT scan of a 57-year-old female demonstrating a 1.9-cm hypodense, cystic mass arising from the neck of the pancreas. This lesion was slightly denser than simple cyst, and had mural nodularity. Presumed diagnosis was a pancreatic cystic neoplasm

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