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CASE REPORT

Pancreatic schwannoma: Case report and an updated 30-year review of the literature yielding 47 cases

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Abstract

Pancreatic schwannomas are rare neoplasms. Authors briefly describe a 64-year-old female patient with cystic pancreatic schwannoma mimicking other cystic tumors and review the literature. Databases for PubMed were searched for English-language articles from 1980 to 2010 using a list of keywords, as well as references from review articles. Only 41 articles, including 47 cases, have been reported in the English literature. The mean age was 55.7 years (range 20-87 years), with 45% of patients being male. Mean tumor size was 6.2 cm (range 1-20 cm). Tumor location was the head (40%), head and body (6%), body (21%), body and tail (15%), tail (4%), and uncinate process (13%). Thirty-four percent of patients exhibited solid tumors and 60% of patients exhibited cystic tumors. Treatment included pancreaticoduodenectomy (32%), distal pancreatectomy (21%), enucleation (15%), unresectable (4%), refused operation (2%) and the detail of resection was not specified in 26% of patients. No patients died of disease with a mean follow-up of 15.7 mo (range 3-65 mo), although 5 (11%) patients had a malignancy. The tumor size was significantly related to malignant tumor (13.8 ± 6.2 cm for malignancy *vs* 5.5 ± 4.4 cm for benign, $P = 0.001$) and cystic formation (7.9 ± 5.9 cm for cystic tumor *vs* 3.9 ± 2.4 cm for solid tumor, $P = 0.005$). The preoperative diagnosis of pancreatic schwannoma remains difficult. Cystic pancreatic schwannomas should be considered in the differential diagnosis of cystic neoplasms and pseudocysts. In our case, intraoperative frozen section confirmed the diagnosis of a schwannoma. Simple enucleation may be adequate, if this is possible.

Key words: Pancreatic schwannoma; Pancreas; Schwannoma; Neurinoma; Resection; Imaging; Enucleation; Prognosis; Cystic

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INTRODUCTION

Pancreatic schwannomas are rare neoplasms that originate from Schwann cells. The Schwann cells line the nerve sheath and can generate either schwannoma or neurofibroma[1]. Schwannoma usually occur in the extremities, but can also be found in the trunk, head and neck, retroperitoneum, mediastinum, pelvis and rectum[2,3]. Pancre-

atic schwannomas are even more unusual neoplasms that affect adults with an equal gender distribution[4,5]. These tumors vary considerably in size and approximately two-thirds are reported to undergo degenerative changes including cyst formation, calcification, hemorrhage, hyalinization and xanthomatous infiltration[4,5]. As a result, they may radiographically mimic cystic pancreatic lesions (e.g., mucinous cystic neoplasms, solid and pseudopapillary neoplasms, serous cystic neoplasms, and pseudocysts).

Only 47 cases have been reported in the English literature in the last three decades[2-42]. In this report, we present a case of pancreatic schwannoma and provide a pertinent review of literature with emphasis on clinical presentation, diagnosis, treatment options, and outcome.

CASE REPORT

A 64-year-old previously healthy woman was incidentally discovered to have a cystic tumor in the pancreas during an ultrasound examination for a health check. She was referred to our institution for further investigation. The abdominal physical examination did not detect any marked finding and all laboratory data were normal, including tumor markers. The computed tomography (CT) scan demonstrated a well-encapsulated tumor, which was composed of solid and cystic areas (Figure 1), and neither liver mass nor peripancreatic lymph node swelling was detected. Magnetic resonance imaging (MRI) showed a mass, with hypointensity on T1-weighted images and hyperintensity on T2-weighted images. Magnetic resonance cholangiopancreatography (MRCP) showed a hyperintense mass in the pancreatic head with no dilatation of the main pancreatic duct. Endoscopic retrograde cholangiopancreatography revealed no communication between cystic tumor and pancreatic duct. Endoscopic ultrasonography showed that the tumor was composed of cystic part and solid part. We performed surgery under the diagnosis of cystic tumor of the pancreas as mucinous cystic tumor, solid pseudo papillary tumor or gastrointestinal stromal tumor. The laparotomy disclosed a well-encapsulated 4-cm mass in the uncinate process of the pancreas that had no signs of inflammation. Intraoperative ultrasound confirmed a solitary mass composed of solid and cystic components (Figure 2). The mass was enucleated and an intraoperative frozen section demonstrated a benign schwannoma. No further resection was performed based on these findings. The tumor was 4 cm × 4 cm × 3 cm in size, and was composed of a mixture of solid and hemorrhage areas. On microscopic examination, the tumor was composed of spindle cells strongly positive for S-100 proteins and foci of hemorrhage (hematoxylin and eosin, × 100) (Figure 3). The tumor cells were negative for smooth muscle actin and CD-34. The tumor was therefore histologically diagnosed as benign schwannoma. The patient was discharged uneventfully on postoperative day 17. At a 65-month follow up after resection, the patient is doing well without any recurrent disease.

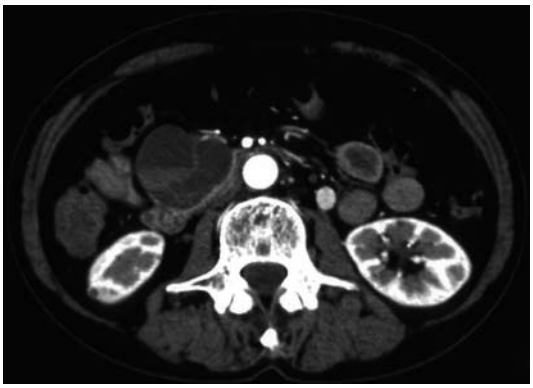

Figure 1 Contrast-enhanced computed tomography scan obtained in the arterial phase showing a multilocular cystic mass in the uncinate process of the pancreas. No pancreatic ductal dilatation or invasion into adjacent arteries or portal vein are identified.

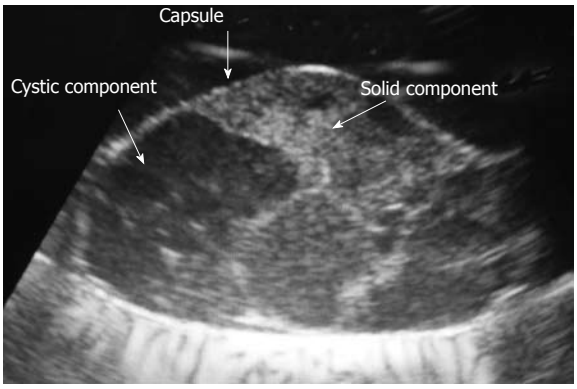

Figure 2 Intraoperative ultrasound showing the well-encapsulated pancreatic mass that is composed of solid and cystic components.

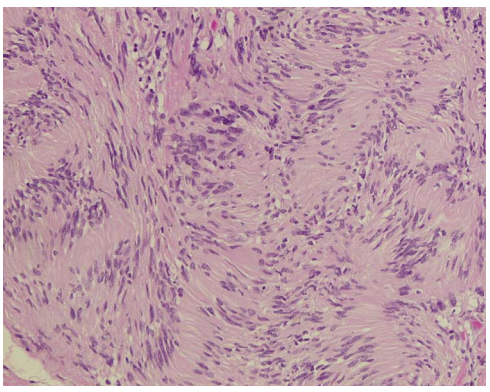

Figure 3 Microscopic examination demonstrating spindle cells without nuclear atypism (HE x 100). Immunohistochemical staining for S-100 protein was positive. HE: Hematoxylin and eosin.

DISCUSSION

A review of the patient's chart was performed along with a review of English-language articles using a PubMed search for the last three decades. We found 41 articles including 47 patients with pancreatic schwannoma. Details of the cases are summarized in Table 1 along with the current patient. Table 2 summarizes the important

Table 1 Summary of cases with pancreatic schwannoma

Author	Year	Sex	Age	Presenting symptoms	Size (cm)	Location	Solid/cystic by image	Treatment	Histology	Follow-up (mo)
Current case	2010	F	64	Asymptomatic	4.0	Uncinate	Solid and cystic	Enucleation	Benign	65
Dorsey *et al*[6]	2010	F	54	Abdominal pain, weight loss	1.4	Head	Solid	NA	Benign	NA
Stojanovic *et al*[7]	2010	F	24	Abdominal pain, dyspepsia, weight loss, palpable tumor	18.0	Body/tail	Cystic	DP + transverse colon	Malignant	28
Suzuki *et al*[8]	2010	F	66	Asymptomatic	3.0	Body	Solid and cystic	DP	Benign	24
Aggarwal *et al*[9]	2010	M	20	Upper abdominal discomfort	3.0	Head	NA	Enucleation	Benign	NA
Ohshima *et al*[10]	2010	F	32	Back pain	4.0	Head	Solid and cystic	PD	Benign	NA
Mummadi *et al*[11]	2009	M	35	Epigastric pain	7.0	Body	Solid and cystic	NA	Benign	6
Gupta *et al*[5]	2009	F	56	Asymptomatic	8.3	Head/body	Cystic	PD	Benign	NA
Li *et al*[12]	2009	M	37	Asymptomatic	16.0	Head	Solid and Cystic	PD	Benign	NA
Tafe *et al*[13]	2008	M	46	Abdominal pain	11.0	Body/tail	Cystic	DP	Benign	NA
Hirabayashi *et al*[14]	2008	M	51	Asymptomatic	6.0	Tail	Cystic	DP	Benign	NA
Okuma *et al*[15]	2008	F	71	Epigastric pain	4.0	Body	Solid and cystic	DP	Benign	NA
Tofigh *et al*[16]	2008	M	54	Epigastric pain, weight loss, nausea, intermittent jaundice	3.0	Head	Solid (by specimen)	PD	Benign	
Fasanella *et al*[17]	2007	M	36	Abdominal discomfort	3.6	Uncinate	Cystic	NA	Benign	NA
Di Benedetto *et al*[18]	2007	M	42	Asymptomatic	2.5	Body	Solid	DP	Benign	NA
Yu *et al*[19]	2006	M	72	Upper abdominal pain	1.0	Head/body	Solid	NA	Benign	NA
Wu *et al*[20]	2005	M	71	Epigastric pain, decreased appetite	1.5	Head	Cystic	Enucleation	Benign	10
Novellas *et al*[21]	2005	F	46	Asthenia, weight loss, empyema	3.0	Head	Solid	PD	Benign	24
Soumaoro *et al*[22]	2005	F	64	Asymptomatic	2.5	Head	Solid	Enucleation	Benign	24
Bui *et al*[23]	2004	F	69	Abdominal pain	5.0	Head	Solid	Unresectable	NA[1]	NA
Akiyoshi *et al*[24]	2004	F	67	Asymptomatic	5.0	Head	Cystic	PD	Benign	43
Von Dobschuetz *et al*[25]	2004	F	55	Asymptomatic	8.0	Head	Cystic	PD + PV reconstruction	Benign	10
Paranjape *et al*[4]	2004	F	77	Upper abdominal pain, weight loss	3.5	Body	Solid	Enucleation	Benign	3
Tan *et al*[26]	2003	F	46	Right upper quadrant pain	2.2	Head	Solid and Cystic	PD	Benign	NA
Almo *et al*[2]	2001	F	73	Abdominal pain, nausea, vomiting	3.0	Head	Cystic	PD	Benign	17
Almo *et al*[2]	2001	F	47	Abdominal pain, back pain	5.5	Head	Solid	PD	Benign	14
Lee *et al*[27]	2001	F	63	Upper abdominal pain	10.0	Tail	Cystic	DP	Benign	6
Morita *et al*[28]	1999	F	50	Upper abdominal pain	9.5	Body/tail	Cystic	DP	Benign	7
Brown *et al*[29]	1998	M	52	Asymptomatic	5.5	Body	Cystic	Resection[2]	Benign	NA
Brown *et al*[29]	1998	M	69	Asymptomatic	6.0	Head	Cystic	PD	Benign	NA
Hsiano *et al*[30]	1998	F	70	Palpable tumor	18.0	Body/tail	Cystic	Resection[2]	Benign	24
Feldman *et al*[31]	1997	M	63	Asymptomatic	2.5	Body	Solid	Enucleation	Benign	NA
Feldman *et al*[31]	1997	F	54	Abdominal pain	2.0	Uncinate	Solid	Enucleation	Benign	22
Ferrozzi *et al*[32]	1995	M	47	Right-sided abdominal pain	3.5	Body	NA	DP	Benign	48
Ferrozzi *et al*[32]	1995	M	63	Abdominal pain	NA	Body	Cystic	NA	Benign	NA
Ferrozzi *et al*[32]	1995	F	68	Upper abdominal pain	NA	Head/body	Cystic	NA	Benign	6
Sugiyama *et al*[33]	1995	M	41	Asymptomatic	1.5	Uncinate	Cystic	PD	Benign	NA
Steven *et al*[34]	1994	M	59	Asymptomatic	4.0	Uncinate	Solid	PD	Benign	10
Melato *et al*[35]	1993	M	87	Upper abdominal pain	20.0	Body/tail	Cystic	NA	Benign	NA
David *et al*[3]	1993	M	46	Right sided abdominal pain	6.0	Uncinate	Cystic	NA	Benign	NA
Urban *et al*[36]	1992	F	56	Right sided hip pain	4.0	Body	Cystic	DP	Benign	NA
Burd *et al*[37]	1992	M	73	Right upper quadrant abdominal pain	2.0	Body/tail	Solid	NA	Benign	NA
Coombs *et al*[38]	1990	F	74	Anemia, melena	7.0	Head	Solid with necrotic center	NA	Malignant	NA
Liessi *et al*[39]	1990	F	75	Abdominal pain	7.0	Head	Solid	Not resected	Benign	7
Walsh *et al*[40]	1989	F	35	Abdominal pain, melena, anemia	NA	Head	NA	PD	Malignant	24
Eggermont *et al*[41]	1987	F	40	Upper abdominal pain, jaundice, weight loss	10.0	Head	Solid with necrotic center	PD	Malignant	9
Moller-Pederson *et al*[42]	1982	M	60	Back pain, weight loss	20.0	Body/tail	Cystic	Unresectable	Malignant	4

M: Male; F: Female; NA: Not available. [1]Unresectable because of encasing the superior mesenteric artery and the portal vein, although the malignant finding was not confirmed by histopathology; [2]No specific operation documented.

Table 2 Summary of clinicopathological data from all 47 cases of pancreatic schwannoma

	n (%) or mean ± SD (range)
Age (yr)	55.7 ± 15.1 (20-87)
Sex (male/female), (male %)	21/26 (45%)
Symptoms[1]	
Asymptomatic	14 (30%)
Symptomatic	
Abdominal pain	27 (57%)
Weight loss	6 (13%)
Back pain	3 (6%)
Nausea/vomiting	2 (4%)
Abdominal mass	2 (4%)
Anemia	2 (4%)
Melena	2 (4%)
Jaundice	1 (4%)
Location	
Head	19 (40%)
Head/body	3 (6%)
Body	10 (21%)
Body/tail	7 (15%)
Tail	2 (4%)
Uncinate process	6 (13%)
Mean size (cm), (*n* = 44)	6.2 ± 5.1 (1-20)
Operation	
Pancreaticoduodenectomy[2]	15 (32%)
Distal pancreatectomy[3]	10 (21%)
Enucleation	7 (15%)
Unresectable	2 (4%)
Refused	1 (2%)
Not specified	12 (26%)
Histology	
Malignant	5 (11%)
Benign	41 (87%)
Not specified	1 (2%)
Nature of tumor	
Solid	16 (34%)
Cystic	28 (60%)
Not specified	3 (6%)
Mean follow-up months (*n* = 23)	18.9 ± 15.7 (3-65)
Died of disease	0 (0%)

[1]Patients had several symptoms; [2]One patient underwent resection of portal vein; [3]One patient underwent resection of transverse colon.

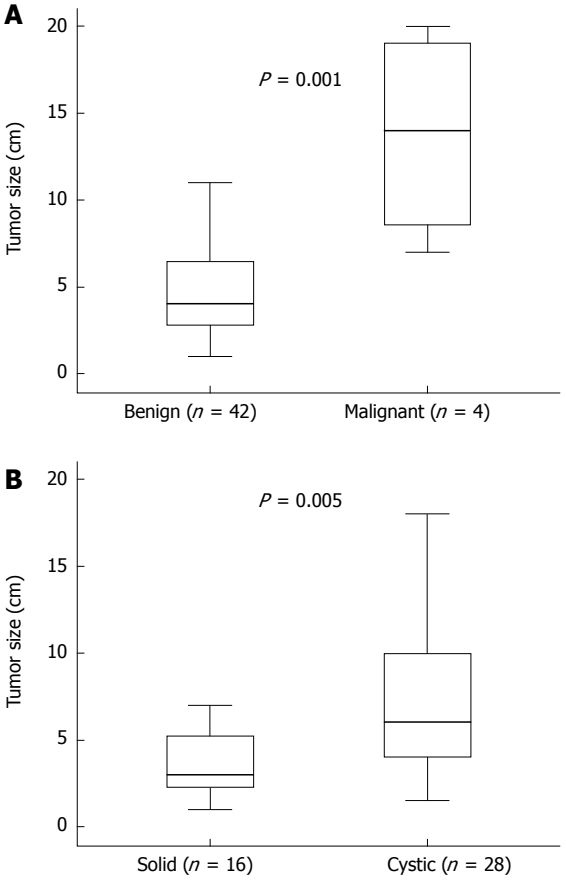

Figure 4 Analysis for relation between tumor size and malignant potential and tumor nature (solid or cystic) in all 47 cases of pancreatic schwannoma. A: Relationship between tumor size and malignancy. Larger tumor size is related to malignant tumor (13.8 ± 6.2 cm for malignancy *vs* 5.5 ± 4.4 cm for benign, $P = 0.001$); B: Relationship between tumor size and nature of tumor. Larger tumor size is related to cystic degeneration (13.8 ± 6.2 cm for cystic tumor *vs* 5.5 ± 4.4 cm for solid tumor, $P = 0.005$).

available facts regarding all patients. We examined the correlation between tumor size and malignancy, as well as tumor size and cystic degeneration. Continuous data are presented as mean ± standard deviation and range. Student *t*-test was used for all comparisons among continuous variables. A $P < 0.05$ was considered statistically significant.

A PubMed search of the literature indicated 41 reports including 47 patients with pancreatic schwannoma in the English literature. Details of all the 47 cases are summarized in Table 1. Table 2 summarizes the important available clinicopathological factors. The mean age of the patients was 55.7 ± 15.1 years (range 20-87 years) and the male-female ratio was 21:26. Thirty percent of patients were asymptomatic and 70% of patients were symptomatic. Symptoms included abdominal pain (57%), weight loss (13%), back pain (6%), nausea/vomiting (4%), abdominal mass (4%), melena (4%), and jaundice (4%). The symptoms did not correlate with tumor size and tumor location. The lesion was located in the pancreas head in 19 patients (40%), head and body in 3 patients (6%), body in 10 patients (21%), body and tail in 7 (15%), tail in 2 patients (4%), and uncinate process in 6 patients (13%). Mean tumor size was 6.2 ± 5.1 cm (range 1-20 cm). Treatment included pancreaticoduodenectomy for 15 patients (32%) including one portal vein reconstruction, distal pancreatectomy for 10 patients (21%) including combined transverse colon resection, enucleation for 7 patients (15%), unresectable for 2 patients (4%), refused operation for 1 patient (2%) and the detail of resection was not specified in 12 patients (26%). Enucleation was performed for 7 patients, and out of these, 3 lesions were located in the head, 2 lesions were in the uncinate process and 2 lesions were in the body. The mean tumor size in the patients who underwent enucleation was 2.7 cm (range 1.5-4.0 cm). Regarding gross appearance, 34% of patients exhibited solid tumors and 60% of patients exhibited cystic tumors. No patient died of disease with a follow-up of 15.7 mo (range 3-65 mo), although 4 (9%) patients had a malignancy. The tumor size was related to malignant tumor (13.8 ± 6.2 cm for malignancy *vs* 5.5 ± 4.4 cm for benign, $P = 0.001$) (Figure 4A) and cystic for-

mation (7.9 ± 5.9 cm for cystic tumor *vs* 3.9 ± 2.4 cm for solid tumor, $P = 0.005$) (Figure 4B).

In 1910, Verocay reported a schwannoma as a true neoplasm which originated from Schwann cells, and which did not contain neuroganglion cells[1]. Since then, schwannomas have become well known as benign spindle cell tumors derived from Schwann cells that line the nerve sheaths. Schwannomas usually occur in the extremities, but can also be found in the trunk, head and neck, retroperitoneum, mediastinum, pelvis and rectum[2-4]. Pancreatic schwannomas are rare neoplasms that arise from either autonomic sympathetic or parasympathetic fibers, both of which course through the pancreas as branches of the vagus nerve[2-4].

Microscopically, a typical schwannoma is composed of 2 areas, namely Antoni A and Antoni B areas. The Antoni A area is hypercellular and characterized by closely packed spindle cells with occasional nuclear palisading and Verocay bodies, whereas the Antoni B area is hypocellular and is occupied by loosely arranged tumor cells[43]. Most of the pancreatic schwannomas reported had both Antoni A and Antoni B areas in various proportions. Degenerative or cystic changes such as calcification or hemorrhage are often recognized in the Antoni B area. These changes result from vascular thrombosis and subsequent necrosis[43]. Cystic pancreatic schwannomas can mimic the whole spectrum of cystic pancreatic lesions including: intraductal mucinous-papillary neoplasms, mucinous cystic neoplasms, serous cystic neoplasms, solid and pseudo-papillary neoplasms, lymphangiomas, and pancreatic pseudocysts. Immunohistochemically, schwannomas stain strongly positive for S-100 protein, vimentin and CD 56, while negative for other tumor markers including cytokeratin AE1/AE3, desmin, smooth muscle myosin, CD 34 and CD 117[43].

The symptoms of the reported patient cases of pancreatic schwannoma vary. Seventy percent of patients were symptomatic. Abdominal pain was the most common symptom reported (57%). Symptoms such as back pain (6%), nausea/vomiting (4%), weight loss (13%), melena (4%) and jaundice (4%) have been also reported. Thirty percent of patients were asymptomatic and the lesions were incidentally discovered on CT scans performed for other reasons.

The preoperative diagnosis of pancreatic schwannoma is very difficult, especially in cystic schwannomas. Suzuki *et al*[8] reviewed imaging features of pancreatic schwannomas. The most characteristic feature on CT scan was the presence of an area of low density and/or cystic images reflecting the Antoni B component or degenerative cystic areas of the schwannoma. Contrast-enhanced CT scan showed the difference between the Antoni A and the Antoni B areas based on their vascularity, i.e., well-enhanced areas corresponding to Antoni A, and unenhanced areas corresponding to Antoni B. The CT findings correlated well with pathological features[8,19]. The MRI findings usually showed hypointensity on T1-weighted images and hyperintensity on T2-weighted images[21]. However, other pancreatic tumors often share those imaging features, and differential diagnoses should always be considered. Ultrasound-guided Fine Needle Aspiration (EUS-FNA) biopsy has been used increasingly commonly at many institutions. This procedure may be useful for accurate preoperative diagnosis. Cytologically, schwannomas are characteristically composed of spindle-shaped cells, which possess indistinct cytoplasmic borders and wavy nuclei embedded in a fibrillary and occasionally myxoid or collagenous matrix. The Antoni A (cohesive cellular clusters) and Antoni B (loosely cohesive or poorly cellular sheets) areas are occasionally found. Immunohistochemical staining is useful for accurate diagnosis of schwannoma[12,14]. It is diffusely and strongly positive for S-100 protein. There has only been one previous report of pancreatic schwannoma diagnosed preoperatively by EUS-FNA cytology combined with immunohistochemistry[12].

Although malignant pancreatic schwannomas have been reported in 5 articles[7,38,40-42], in 3 of 5 the methods of diagnosing malignancy were inconsistent, as some previous reports pointed out[4,5]. Immunohistochemical examination was not used or was not available in these 3 patients. Walsh and Bradspigel[40] described a case of pancreatic schwannoma eroding into the bowel wall and presenting with gastrointestinal bleeding that mimicked a recurrently bleeding duodenal ulcer. Another two patients reported had disease associated with von Recklinghausen's disease[41,42]. These could represent misdiagnosed neurofibromas that underwent malignant degeneration[4,5]. Stojanovic *et al*[7] reported malignant pancreatic schwannoma with node metastasis and infiltrating serosa of transverse colon. This tumor was confirmed using immunohistochemical examination. This may be the first definite report of malignant schwannoma with subsequent radical resection.

Since malignant transformation of pancreatic schwannomas is uncommon, simple enucleation is usually sufficient. A review of the treatment showed that the most common resection was pancreaticoduodenectomy (32%), followed by distal pancreatectomy (21%) and enucleation (15%). This result may account for the difficulty in accurate diagnosis of pancreatic schwannoma and relate to larger size of this tumor. Enucleation was performed for 7 patients for whom 3 lesions were located in the head, 2 lesions were in the uncinate process and 2 lesions were in the body. The mean tumor size of the patients who underwent enucleation was 2.7 cm (range 1.5-4.0 cm). Intraoperative consultation with the pathologist was carried out in most of the enucleated cases. An intraoperative frozen section should be performed, as it helps to establish the diagnosis of a benign schwannoma and avoid more radical resection. Large tumors, tumors involving portal vein, ampulla, or splenic hilum, may require a more radical resection than simple enucleation.

The present report shows the correlation between tumor size and malignant formation (Figure 4A), and tumor size and cystic degeneration (Figure 4B). Malignant schwannomas were more likely to be larger-sized compared to many other tumors. On the other hand, the par-

ticular feature of pancreatic schwannoma was that larger tumor size was related to cystic degeneration, as shown in Figure 4B. Cystic degeneration could make it difficult to diagnose pancreatic schwannoma preoperatively, because of mimicking other cystic neoplasms. Caution should be applied when diagnosing cystic neoplasm. An intraoperative frozen section may help to establish the diagnosis of a schwannoma and avoid more radical resection. To our knowledge, the present report is the first to analyze the relation among tumor size, malignant formation and cystic degeneration. Our results suggest that pancreatic schwannoma might be resected even though diagnosed preoperatively, because if schwannomas are smaller, enucleation should be oncologically adequate. However, when tumors become larger with associated bleeding risk, more invasive resection such a PD or DP might be necessary. In particular, in cases of tumors more than 10 cm in size, we should pay special attention to malignant degeneration and should perform a more extended resection. To avoid extended resection, earlier resection and accurate diagnosis are very important.

In conclusion, pancreatic schwannomas deserve attention with regard to the differential diagnosis of pancreatic lesions. Preoperative diagnosis is very difficult. Simple enucleation is adequate if this is possible to achieve. Intraoperative frozen section is useful to diagnose schwannoma.

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