

CASE REPORT

Enlarging Pancreatic Schwannoma – A Case Report and Review of the Literature

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ABSTRACT

Context Schwannomas are rare neoplasms that typically occur in the peripheral nerve of the extremities. Visceral localization of these tumors is particularly rare. We present a unique case of a pancreatic schwannoma presenting as long-lasting dyspepsia and intermittent epigastric pain. **Case report** Seventy-two-year-old female presented with dyspepsia for 2 years and an incidental mass in the head of the pancreas on abdominal CT scan. Patient had multiple negative endoscopic ultrasound guided biopsies and a non-diagnostic open core biopsy. She was followed up for 3 years with serial imaging until an abdominal CT scan showed an increase in size of the pancreatic mass from 1.9x2.2 cm to 3.1x2.7 cm. Physical examination was unremarkable. Laboratory tests including tumor markers were normal. Given the enlarging size of the mass and its impingement on the portal vein, the consensus was to proceed with surgery. Patient underwent a non-pylorus preserving pancreaticoduodenectomy. Histology revealed a 3.5 cm mass showing a spindle cell neoplasm with mild atypia. The lesion was well defined and nerve tissue was noted at the periphery. On immuno stains, the spindle cells were positive for S-100 protein and negative for pancytokeratin, CD-34, CD-117, smooth muscle actin and Melan A, consistent with the diagnosis of a pancreatic schwannoma. **Conclusions** Pancreatic schwannomas arise from branches of the vagus nerve which courses through the pancreas. Pre-operative diagnosis of pancreatic schwannomas is difficult even with multiple imaging modalities. The final diagnosis of these tumors is often made only after operative excision and histological studies.

INTRODUCTION

Schwannomas (also called neurilemmomas) are encapsulated tumors made entirely of benign neoplastic Schwann cells [1-2]. They are the most common peripheral nerve tumors. They grow from peripheral nerves or nerve roots in an eccentric fashion with the nerve itself usually incorporated into the capsule [3]. Schwannomas usually grow, in descending order of frequency, in the lower extremity, upper extremity, trunk, head and neck, retroperitoneum, mediastinum, and pelvis [4].

Pancreatic schwannomas are very rare neoplasms. Based on a recent study in 2012, less than 50 cases of pancreatic schwannoma have been described in the English literature over the past thirty years [5]. This tumor is believed to arise from either autonomic sympathetic or parasympathetic branches of the Vagus nerve [6-7]. 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 [8-9]. Preoperative diagnosis of pancreatic schwannoma can be challenging as the radiographic findings are similar to other more common pancreatic tumors such as pancreatic adenocarcinoma, neuroendocrine tumors or cystic neoplasms. Herein, we present a case of an enlarging pancreatic head schwannoma in a 72 year old woman who presented with a long standing history of dyspepsia and intermittent epigastric pain.

CASE REPORT

The patient is 72 year old Caucasian female with a past medical history of hypertension, hyperlipidemia, cervical stenosis and depression. She originally presented with worsening dyspepsia and intermittent epigastric pain for 2 years for which she sought medical attention. During the initial evaluation, a solid, enhancing mass in the anterolateral surface of the head of the pancreas was found on abdominal CT scan. There was no associated dilatation of the main pancreatic or common bile duct. Upper endoscopy revealed no lesions in the stomach or duodenum. During the following two years, the patient had multiple endoscopic ultrasound guided fine needle aspiration biopsies of the mass which were either non-diagnostic or resulted in benign appearing pancreatic tissue. She then underwent an open pancreatic biopsy with removal of a peri-pancreatic lymph node. These all revealed benign pancreatic tissue with fibrosis and no obvious evidence of malignancy. Her CEA and CA19-9 levels were within normal limits. She was followed closely for 3 years with serial imaging and endoscopic

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ultrasounds, until an abdominal CT scan showed a substantial increase in the size of the pancreatic mass from 1.9 x 2.2 cm to 3.1 x 2.7 cm (**Figure 1**). The pancreatic mass was described as a well-encapsulated tumor, without any cystic component. There were no other intra-abdominal lesions or pathologic lymphadenopathy noted. Magnetic resonance cholangiopancreatography showed normal caliber of the biliary tree and pancreatic duct. Endoscopic ultrasound confirmed a heterogeneous solid pancreatic head mass without pancreatic duct dilation (**Figure 2**). Her serum CEA and CA19-9 levels remained within normal limits throughout. Physical examination did not reveal any concerning findings, although the patient reported ongoing intermittent epigastric discomfort. Given the patient's ongoing epigastric pain, and the enlarging size of the mass, a decision was made to proceed with surgery due to the concern that this may represent either a well-differentiated pancreatic neuroendocrine tumor or a low grade pancreatic neoplasm (e.g. solid pseudopapillary neoplasm).

The patient underwent an uneventful non-pylorus preserving pancreaticoduodenectomy. A well-encapsulated 3.5 cm mass was found arising from the superior aspect of the pancreatic head. Intraoperative ultrasound confirmed a solitary solid mass, with no evidence of lesions in the liver or remainder of the pancreas. She had an unremarkable post-operative course and was sent home on post-operative day 6.

On microscopic examination, sections of the 3.5 cm mass revealed a cellular spindle cell neoplasm with mild atypia and focal cystic degenerative changes (**Figure 3**). The lesion was relatively well defined and nerve tissue was noted at the periphery. On immunohistochemistry, the spindle cells were strongly positive for S-100 protein (**Figure 4**) and negative for pancytokeratin, CD-34, CD-117, smooth muscle actin and Melan A. These findings were consistent with the diagnosis of a pancreatic schwannoma. At 12 months follow up, the patient is doing well without recurrent disease and resolution of her epigastric pain and dyspepsia.

DISCUSSION

Pancreatic schwannomas are extremely uncommon neoplasms. The majority of these tumors are benign, with only 5 cases of malignant pancreatic schwannomas reported in the English literature [9-10] (**Table 1**). These tumors commonly affect adults (range: 20-87 years) without gender or race preference [5, 11, 12]. Pancreatic schwannomas vary in size (1-20 cm) and location. In a previous study, an association between tumor size and malignant potential has been suggested with larger tumors having more malignant potential [11]. They generally grow slowly but the incidence of degenerative changes including cyst formation, calcification, hemorrhage and lipid infiltrates is directly proportional to the size of the tumor.

The pancreatic head is the most common location representing 40% all of tumors, followed by the body (20%),

and tail (15%). The uncinete process is the least common location (15%) [13-14]. There is a direct association with tumor location and symptoms. Tumors located in the head of the pancreas tend to be more symptomatic when compared with tumors in the periphery of the gland. In recent studies, up to 70% of the patients are symptomatic at the time of diagnosis [5-11], but most of the symptoms are vague and no specific including: dyspepsia, epigastric or back pain, and nausea. Jaundice is rare as the biliary tree is seldom occluded [15-16]. About 30% of the patients are asymptomatic and the lesions are found incidentally on abdominal imaging. Laboratory tests in the diagnosis of pancreatic schwannoma are not usually helpful; most of the patients have normal values and negative tumor markers.

Pre-operative diagnosis of pancreatic schwannomas is difficult even with multiple imaging modalities. Computed tomography (CT) scan can be helpful in distinguishing solid from cystic lesions and help in determining



Figure 1. Contrast enhanced computed tomography (CT) scan of the abdomen showing a pancreatic head mass (arrow), with heterogeneous enhancement.



Figure 2. Endoscopic ultrasound reveals a solid heterogeneous mass (24 mm by 23 mm maximal cross-sectional diameter), with a spiculated appearance.

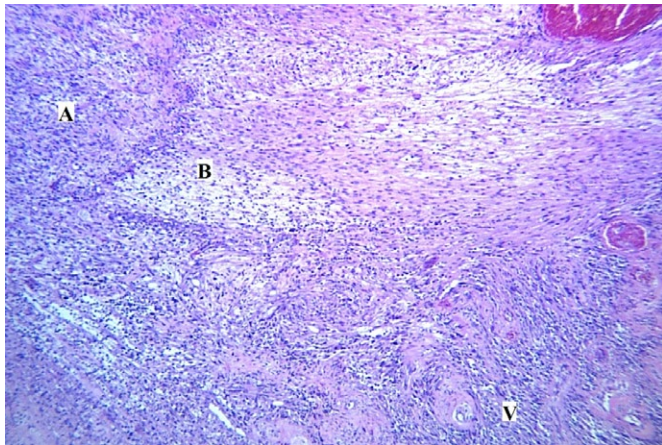


Figure 3. The tumor also showed alternating areas of hypercellularity with edematous, myxoid, hypocellular foci, Antoni A (a.) and B (b.) areas. No mitoses or necrosis are present. Associated hyalinized vessels (V) are prominent.

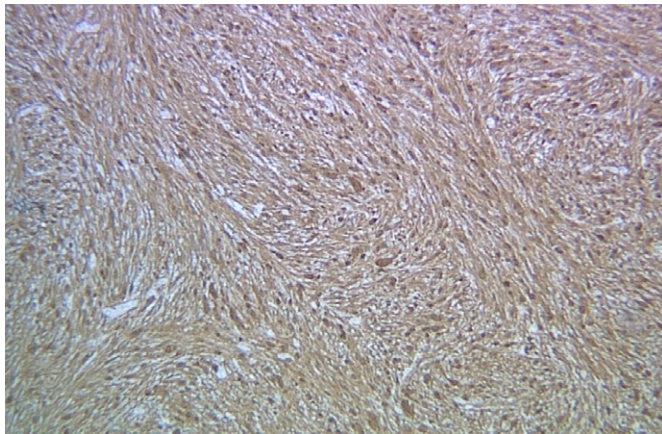


Figure 4. Immunohistochemical examination of the pancreatic head tumor shows diffuse and strong positivity to S100 protein (brown staining), and negative for pancytokeratin, CD34, CD117, smooth muscle actin and Melan-A.

pancreatic duct dilation, the precise location of the mass, and its relation to mesenteric vessels. Certain pancreatic schwannoma characteristics on CT scan include; Antoni A and B components of the tumor that can be seen as low density and/or cystic degenerative areas [17, 18]. The more vascular Antoni A areas are usually enhancing lesions whereas Antoni B areas are frequently non-enhancing lesions [17, 18]. Magnetic resonance imaging (MRI) usually shows hypointensity on T1-weighted images and hyperintensity on T2-weighted images but like the CT features, these findings are non-specific.

The use of ultrasound-guided fine needle aspiration (FNA) in diagnosing pancreatic schwannomas remains controversial due to its high false negative rate. Based on previous literature reports only 1 out of 8 pancreatic schwannomas were diagnosed with ultrasound-guided FNA [19]. As was seen in our patient, multiple FNAs and even an open core biopsy did not confirm the diagnosis. The real challenge in the diagnosis of pancreatic schwannomas is the presence of cystic formation within the tumor. Lesions can often be misdiagnosed as benign pancreatic cysts. The definitive diagnosis can often only be made with histologic examination of a resected specimen and immunohistochemical staining.

Macroscopically, pancreatic schwannomas commonly appear cystic but they can also have a complete solid structure or a mixed pattern of solid and cystic formations throughout the tumor. Usually, they are well-demarcated, well-encapsulated, homogenous nodules that can have degenerative changes including hemorrhagic areas and xanthomous infiltrations that could give the tumor a yellow-tan coloration.

Microscopically, a typical pancreatic schwannoma is composed of hypercellular and hypocellular areas. Hypercellular or the Antoni A area consists of monomorphic spindle shaped Schwann cells full of poorly defined eosinophilic cytoplasm and pointed basophilic nuclei, in a variably collagenous stroma. These cells in the Antoni A areas show nuclear palisading, and parallel arrays of such palisades with intervening cell processes called Verocay bodies. Antoni B areas or hypocellular areas are also composed of Schwann cells with inconspicuous cytoplasm and nuclei appearing to be suspended in a copious myxoid, often microcystic matrix. The degenerative changes are usually recognized in the Antoni B areas. Normally, less than five mitotic figures per 10 high power fields can be seen in a benign schwannoma. Very rarely, pancreatic schwannomas can undergo malignant transformation, with only 5 cases described in the English literature. Malignant schwannomas are characterized by rapid growth, infiltration of adjacent structures, and multiple necrotic and hemorrhagic changes within the tumor [20, 21].

Immunohistochemically, pancreatic schwannomas are positive for S 100, Vimentin and CD 56. Conversely, spindle cells in pancreatic schwannomas stain negative for cytokeratin, CD117, desmin, CD34, AE1/AE3, alpha smooth muscle actin, and smooth muscle myosin. Cytogenetic analysis studies show that most schwannomas show either monosomy 22 or loss of 22q material [22, 32, 35].

The management of pancreatic schwannoma is strictly guided by the histologic results. With most of the tumors having a benign histology, tumor enucleation is the most common surgical procedure performed [23]. In cases where the tumor is showing malignant behavior (infiltration of tissue or close proximity to important vessels) or the frozen section is inconclusive, an oncologic, margin negative resection is recommended.

Although malignant peripheral nerve sheath tumors can be treated with Doxorubicin based chemotherapy, there are no data on the use of chemotherapy for pancreatic schwannomas. Other therapeutic options like radiation therapy, have not been studied for pancreatic schwannomas. Nonetheless, neurogenic schwannomas have been managed with radiation therapy for decades suggesting that radiation could be used in the future for the treatment of pancreatic schwannoma in patients that are not suitable for surgical resection [11].

In conclusion, we present a case of a 3.5 cm pancreatic schwannoma, which presented as intermittent epigastric pain and persistent dyspepsia and was followed by serial

Table 1. Summary of cases of pancreatic schwannoma over the last 20 years..

#	Author	Year	Sex	Age	Size (cm)	Location	Treatment	Histology	Follow up (months)
1	Current Case	2015	F	72	3.5	Head	Whipple	Benign	12
2	Dorsey <i>et al.</i> ^[24]	2010	F	64	1.4	Head	NA	Benign	NA
3	Stojanovic <i>et al.</i> ^[25]	2010	F	24	18.0	Body/tail	Whipple	Malignant	28
4	Suzuki <i>et al.</i> ^[26]	2010	F	66	3.0	Body	Whipple	Benign	24
5	Aggarwal <i>et al.</i> ^[27]	2010	M	20	3.0	Head	Enucleation	Benign	NA
7	Oshima <i>et al.</i> ^[28]	2010	F	32	4.0	Head	Partial Resection	Benign	NA
8	Mummadi <i>et al.</i> ^[29]	2009	M	35	7.0	Body	NA	Benign	6
9	Gupta <i>et al.</i> ^[13]	2009	F	56	8.3	Head/Body	Partial Resection	Benign	NA
10	Li <i>et al.</i> ^[30]	2009	M	37	16.0	Head	Partial Resection	Benign	NA
11	Tafe and Suriawinata <i>et al.</i> ^[31]	2008	M	46	11.0	Body/Tail	DP	Benign	NA
12	Hirabayashi <i>et al.</i> ^[22]	2008	M	51	8.3	Tail	DP	Benign	NA
13	Okuma <i>et al.</i> ^[33]	2008	F	71	NA	Body	DP	Benign	NA
14	Fasanella <i>et al.</i> ^[34]	2007	M	36	4.0	Uncinate	Enucleation	Benign	NA
15	Di Benedetto <i>et al.</i> ^[9]	2007	M	42	2.5	Body	DP	Benign	NA
16	Yu and Sun ^[18]	2006	M	72	1.0	Head/Body	NA	NA	NA
17	Novellas <i>et al.</i> ^[36]	2005	F	46	3.0	Head	Whipple	NA	24
18	Wu <i>et al.</i> ^[37]	2005	F	71	1.5	Head	Enucleation	Benign	10
19	Soumaoro <i>et al.</i> ^[38]	2005	F	64	2.5	Head	Enucleation	Benign	24
20	Bui <i>et al.</i> ^[39]	2004	F	69	5.0	Head	Not resected	NA	NA
21	Von Dobschuetz <i>et al.</i> ^[40]	2004	F	55	8.0	Head	Whipple	Benign	10
22	Akiyoshi <i>et al.</i> ^[41]	2004	F	67	5.0	Head	Whipple	Benign	43
23	Paranjape <i>et al.</i> ^[42]	2004	F	77	3.5	Head	Enucleation	Benign	3
24	Tan <i>et al.</i> ^[43]	2003	M	46	2.2	Head	Whipple	NA	NA
25	Almo and Traverso ^[6]	2001	F	73	3.0	Head	Whipple	Benign	17
26	Almo and Traverso ^[6]	2001	M	37	5.5	Head	Whipple	Benign	14
27	Lee <i>et al.</i> ^[44]	2001	F	63	10.0	Tail	DP	Malignant	6
28	Morita <i>et al.</i> ^[45]	1999	F	50	9.5	Body	DP	Benign	NA
29	Brown <i>et al.</i> ^[12]	1998	M	52	5.5	Body	NA	NA	NA
30	Brown <i>et al.</i> ^[12]	1998	M	69	6.0	Head	Whipple	NA	NA
31	Hsiao <i>et al.</i> ^[46]	1998	F	70	18.0	Body/tail	NA	NA	NA
32	Feldman <i>et al.</i> ^[47]	1997	M	63	2.5	Body	Enucleation	NA	NA
33	Feldman <i>et al.</i> ^[47]	1997	F	54	2.0	Uncinate	Enucleation	Benign	20
34	Ferrozzi <i>et al.</i> ^[17]	1995	M	47	3.5	Body	DP	Benign	48
35	Ferrozzi <i>et al.</i> ^[17]	1995	M	63	NA	Body	NA	NA	NA
36	Ferrozzi <i>et al.</i> ^[17]	1995	F	68	NA	Head/Body	NA	NA	6
37	Sugiyama <i>et al.</i> ^[48]	1995	M	41	1.5	Uncinate	NA	NA	NA

DP: distal pancreatectomy; NA: not available.

abdominal imaging for approximately two years, until a marked increase in the size of the lesion was observed. Due to its proximity to the portal vessels the consensus was to proceed with surgery, with histology revealing a benign pancreatic schwannoma. Although pancreatic schwannoma is a rare benign disease, it should be included in the list of differential diagnosis of all pancreatic masses with or without cystic changes. The lack of specific symptoms, radiological characteristics and tumor markers from other pancreatic lesions, makes the preoperative

diagnosis challenging with most of the cases diagnosed after surgical excision. Whenever possible the surgical treatment should aim to enucleation of the tumor. When this is not possible due to anatomic location or unclear diagnosis like in our case, more extended resection is justified. Close radiological follow-up is recommended after surgical excision but results from longer follow-up studies are needed in pancreatic schwannoma as there is not clear evidence of the behavior of these tumors after resection.

Conflicting Interest

The authors had no conflicts of interest

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