Clinics in Oncology

Case Series
Published: 25 Mar, 2024

Pancreatic Schwannoma, a Rare Entity: Management of Two Cases with Review of Literature

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Abstract

Pancreatic schwannoma is rare clinical entity with less than 80 cases reported in literature. These are usually benign with no specific clinical and radiological features and may present as solid and or cystic lesion on imaging. Diagnosis is usually established by histopathological examination. There is no clarity in the literature about its diagnosis and management. Accurate diagnosis before surgery, is mandated for its preoperative management strategy. We herein discuss the management of the two cases of Schwannomas with review of literature.

Keywords: Pancreatic Schwannoma; Cystic and solid pancreatic neoplasm; Clinical signs and symptoms; Diagnostic imaging-CT/MRI; Treatment; Surgical options

Introduction

Pancreatic schwannomas originate from the nerve sheaths in and around the pancreas are extremely rare with less than 80 case reports in the literature. There are no characteristics clinical features. As imaging masquerades with other benign or malignant pancreatic pathologies, diagnosis is often made postoperatively on histopathology or pre-op biopsy. Radiological features mimic those of other benign cystic neoplasms and malignant pancreatic tumors. In the absence of characteristic findings on imaging, very few patients have been diagnosed pre-operatively mostly based on biopsy findings [1]. Von Recklinghausen's disease is usually associated with schwannoma which are malignant and none of the benign pancreatic schwannomas have association with it [2,3]. Involvement of surrounding organs including adjacent vascular structures have also been reported in some cases [4]. There is no unanimity regarding its surgical management. We report two cases of benign pancreatic schwannoma, one of them having vascular involvement. Both were managed successfully by resection.

Case Series

Case 1

A 45-years-old male was found have a thin-walled cystic lesion on sonography in the body of pancreas during routine evaluation for hypertension. A triple phase Computed Tomography (CT) revealed a calcified lesion seen in body of pancreas measuring 74 mm × 79 mm × 77 mm with extra features of internal enhancing irregular thick septations, with few enhancing soft tissue nodules. Patient was clinically asymptomatic without any abdominal sign. The lesion was abutting, on Gastroduodenal Artery (GDA), Common Hepatic Artery (CHA) and widely splaying the spleno-portal junction. Right hepatic artery was replaced, arising from Superior Mesenteric Artery (SMA) and replaced left hepatic artery originating from left gastric Artery. There was no evidence of calcification and MPD or CBD dilatation. MRI of the abdomen was also done and the findings were like those of CT scan. MRI impression was mucinous cystic neoplasm of the body of pancreas (Figure 1).

Patient underwent open central pancreatectomy. Intraoperatively, a 10 cm × 10 cm cystic mass found arising from pancreatic body. There were no obvious lymph nodes. Splenic vein and artery were splayed under the mass with maintained plane. Common hepatic artery was involved by the mass at superior aspect near its origin. Patient underwent tumor resection with en-block excision of CHA after confirming flow in the Hepatoduodenal ligament and there was replaced right hepatic artery arising from superior mesenteric artery. Proximal and distal transection was done with 1 cm margin. Proximal pancreatic stump was suture closed and reconstruction of the distal stump was done with dunking type pancreatic-jejunal anastomosis with PDS 5/0 (interrupted) (Figure 2).

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Received Date: *05 Mar 2024*
Accepted Date: *19 Mar 2024*
Published Date: *25 Mar 2024*

Citation:
Rakesh R, Somnath M, Ashok K II, Ashok K. Pancreatic Schwannoma, a Rare Entity: Management of Two Cases with Review of Literature. Clin Oncol. 2024; 9: 2065.

ISSN: 2474-1663

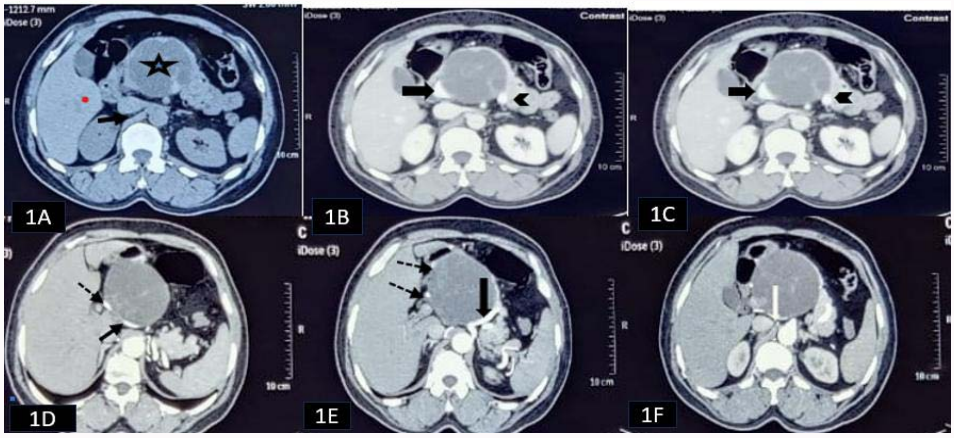
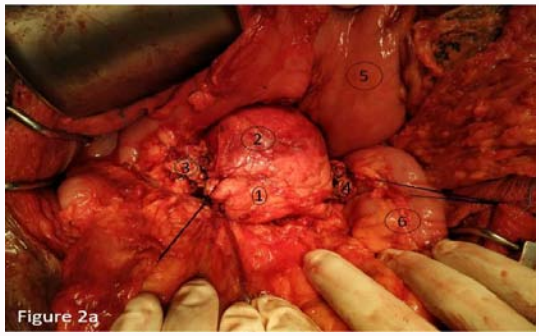


Figure 1: Triple Phase Contrast enhanced Computed Tomography.
1A) Non contrast image showing 7.4 cm × 7.9 cm × 7.7 cm cystic lesion (*).
1B, 1C) Venous phase showing lesion with enhancing thick septation and few enhancing soft tissue nodule arising from pancreatic body. Lesion is abutting main Portal Vein (solid thick arrow), splenic vein (thick arrow head) and close to SMA shown in venous phase.
1D, 1E, 1F) Arterial phase showing common hepatic artery (solid black arrow) being close to mass (found to be involved intra-operatively) and continuing as Gastroduodenal artery (dotted arrow) and splenic artery (long and thick black arrow) and replaced right hepatic artery from SMA (white arrow). Patient had replaced left hepatic artery from left gastric artery (not shown).



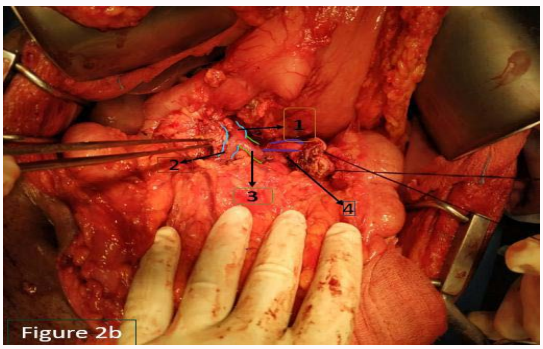


Figure 2: Intraoperative Pictures.
Figure 2a: Showing pancreatic SOL (2) originating from pancreatic body in (1) situ being divided from head (3) and tail (4) with retracted stomach (5) and transverse colon (6).
Figure 2b: Mass was in close relation to SMV (2), splenic vein (3), Portal vein (1) and splenic artery (4) and was dissected safely. CHA (not shown) continuing as GDA (gastroduodenal artery) was divided near its origin.

Postoperatively patient developed Grade A postoperative pancreatic fistula (ISGPS classification) which was managed conservatively and patient was discharged on postoperative day 10. Histopathology of the specimen revealed tumor composed of spindle cells in vague fascicles having cellular and hypocellular areas vaguely alternating with each other with areas of hemorrhage, cystic change, foamy macrophages and hyalinized blood vessels were noted. Focal areas of myxoid degeneration and necrosis were also seen. There was no evidence of atypia or mitotic activity noted. Immunohistochemistry done was strongly positive for S100 (Figure 3).

Case 2

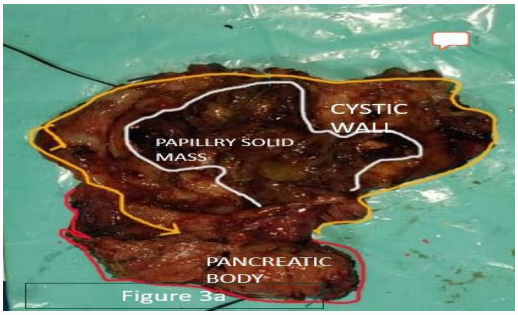
A 36-year male patient presented with mild upper abdominal pain for 9 months. There no other bowel symptom and abdominal examination was unremarkable ultrasound abdomen revealed a lesion in the pancreatic head and uncinate process.

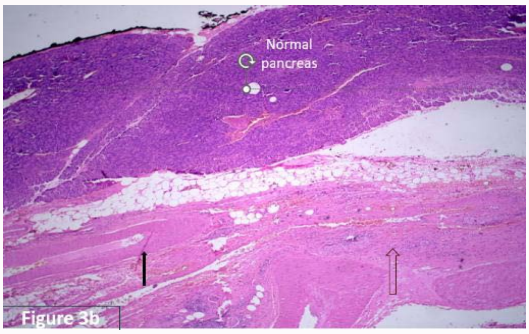
On further evaluation with CECT abdomen a well-defined enhancing hypodense lesion measuring approximately 2.7 cm × 2.3 cm was noted involving the uncinate process, abutting and displacing the superior mesenteric artery and vein. Preoperatively a provisional diagnosis of a cystic pancreatic neoplasm was made.

On MRI, a focal well-defined space occupying lesion of size 30 mm × 27 mm was found in the region of uncinate process of pancreas, predominantly T2 hyperintense signal intensity with patchy hypointense foci lesion with thin T2 hypointense capsule. Lesion was hypointense on T1W images with peripheral enhancing capsule and internal enhancing areas on dynamic post Gd T1W images with non-enhancing cystic/necrotic areas. Lesion was located caudal to the spleno-portal axis and posterior to superior mesenteric vessels and displacing it anteriorly, indenting it with preserved intervening fat planes. Pancreatic duct was normal in diameter (2 mm) with no communication of main duct to lesion. Based on MRI a differential diagnosis of either Solid Pseudopapillary Neoplasm (SPEN) or Branch Duct Intra-Ductal Papillary Mucinous Neoplasm (BD-IPMN) was made.

Further to know the character of the lesion, EUS was performed which showed a well-defined hypo- to hetero- echoic SOL of 3 cm × 2.8 cm in the uncinate process of pancreas. EUS guided FNAC of the lesion revealed atypical cells with suspicion of malignancy.

Patient underwent classical pancreaticoduodenectomy. Postoperatively, he developed POPF grade B fistula and intrabdominal collection (bile mixed with blood). In view of the blood collection, Digital Subtraction Angiography (DSA) was performed which revealed bleeding from GDA for which he underwent coil





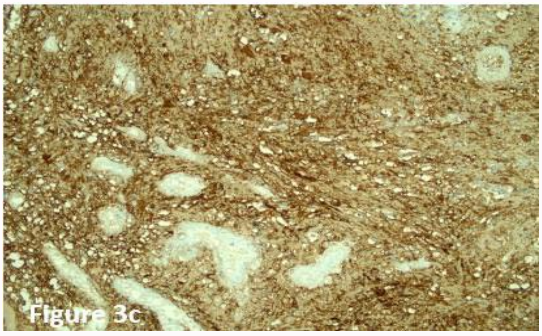


Figure 3: Histopathology features and Immunohistochemistry.
Figure 3a: Resected specimen- showing resected cystic tumor with cyst wall having intrapapillary growth with in it and pancreatic body attached.
Figure 3b: Histopathology- tumor composed of spindle cells in vague fascicles having cellular and hypocellular area vaguely alternating with each other having ovoid to elongated nuclei (black arrow). Areas of hemorrhage, cystic change (myxoid degeneration), foamy macrophages and hyalinized blood vessels (solid black arrow) are noted. There is no evidence of atypia, mitotic activity, or necrosis. Section from adjacent pancreas show unremarkable pancreatic parenchyma (outlined above).
Figure 3c: Immunohistochemistry – showing diffuse S-100 positivity.

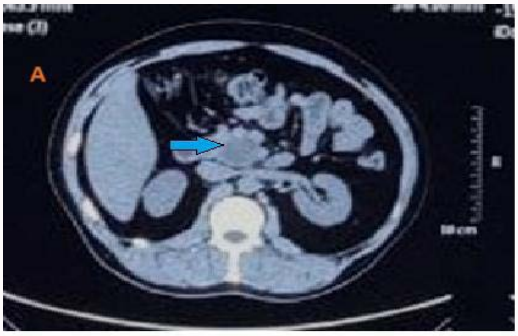


FIGURE4a

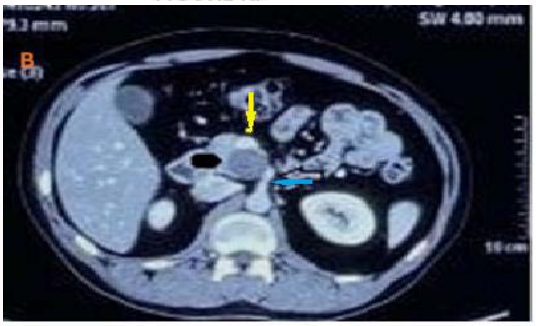


Figure 4b

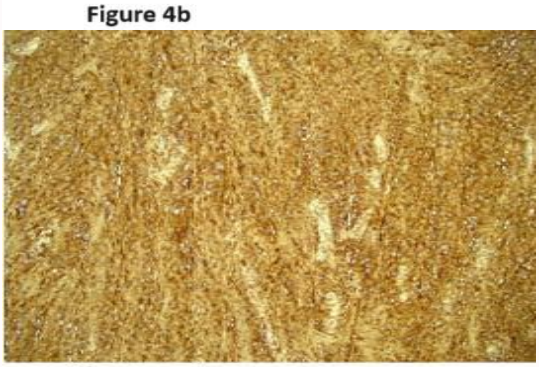


Figure 4c

Figure 4: Contrast enhanced computed Tomography (CECT) and Immunohistochemistry (CASE 2).
Figure 4a: Non contrast phase showing hypodense lesion originating from uncinate process of pancreas.
Figure 4b: Contrast phase showing well defined enhancing hypodense lesion abutting superior mesenteric artery (blue arrow) and vein (yellow arrow).
Figure 4c: Immunohistochemistry done was strongly positive for S100.

embolization. Percutaneous drainage of intrabdominal collection was done. He was discharged on post operative day 40 off intraabdominal tube. Histopathological study revealed schwannoma. Immunohistochemistry done was strongly positive for S100.

In Follow up after 3 months, he developed stricture of the hepaticojejunostomy and managed with percutaneous transhepatic dilation. However, he later required surgical intervention in the form of RYHJ (Figure 4).

Discussion

Schwannomas are usually benign well circumscribed tumors originating from peripheral nerve sheath consisting of clonal proliferation of Schwann cells, first described by the Uruguayan pathologist Dr. Jose Juan Vero cay in 1910. Pancreatic schwannomas probably originate from the epineurium of either the autonomic sympathetic or parasympathetic nerve fibers that travels the pancreas through its interconnecting net like perivascular, peri-acinar, and peri-insular plexus. However, it is not known from which type of nerve fibers the pancreatic schwannomas originate [5].

In a literature review of previously published series [5-7], Pancreatic schwannomas have been noted to be distributed equally among both men and women, occurring usually in middle age (at mean age of 55.7 years). However, in our report patients were young 45 years and 36 years respectively. Most common mode of presentation of pancreatic schwannoma is abdominal pain or abdominal discomfort. Weight loss, jaundice, pancreatitis (high risk feature of pancreatic malignancy) usually absent (Table 1).

In previously published series the most common location for schwannoma has been described in the head of pancreas (38.2%); followed by pancreatic body (20.6%), body and tail (10.3%), uncinate process (11.8%) (Table 2).

Table 1: Demographic profile and clinical feature of published series.

Author et al (in year)/ Parameters	Number of cases	Age (year) (mean)	Sex (M/F) (M %)	Asymptomatic	Abdominal pain	Abdominal mass	Jaundice	Anemia	Weight loss	Dyspepsia	Nausea And vomiting
Xiaoming et al. [6]	77	55.2	32/43	23 (31%)	33 (44%)	9 (12%)	5 (7%)			6 (8%)	12 (16%)
Yuntong Ma et al. [5]	68	55.7	30/38	23 (34%)	34 (50%)	3 (4.40%)	2 (2.90%)	2 (2.90%)	12 (18%)	5 (7.40%)	6 (8.8%)
Moriya et al. [7]	47	55.7	21/26 (45%)	14 (30%)	27 (57%)	2 (4%)	1 (2%)	2 (4%)	6 (13%)	NA	2(4%)

Table 2: Reported location and nature of lesion in published series.

		Location					Nature of lesion		
Author et al (in year)/ Parameters	Number of cases	Head	Uncinate	Head and body	Body and tail	Tail	Solid	Cystic	Solid + Cystic
Xiaoming et al. [6]	77	33 (44%)	7 (9%)	3 (4%)	5 (7%)	6 (8%)	8 (11%)	30 (52%), not specified 28 (37%)	
Yuntong Ma et al. [5]	68	27 (40%)	9 (13%)	3 (4.5%)	21 (31%)	6 (9.0%)	19 (28%)	29 (43%)	15 (22%)
Moriya et al. [7]	47	19 (40%)	6 (13%)	3 (6%)	17 (36%)	2 (4%)	16 (34%)	28 (60%)	

Table 3: Published preoperative diagnosis in previously reported series.

Author et al. (in year)/ Parameters	Number of cases	Pre-operative diagnosis	Correct	Incorrect*	Cystic neoplasm	SCN	MCN	SPEN	Acinar cell carcinoma	Pseudocyst	Adenocarcinoma Mucinous	tumour Neuroendocrine
Xiaoming et al. [6]	77 cases	40 FNA - 25 IFS -15	18 (23%)	59 (76%)	19/34 (56%)	2/34 (6%)	13/34 (38%)	8/34 (24%)	3/34 (9%)	2/34 (6%)		
Yuntong Ma et al. [5]	68 cases		9 (20%)	35 (80%)	17 (49%)	3 (8.60%)	8 (23%)	7 (20%)	3 (8.60%)	2 (5.70%)	6 (17%)	8 (23%)
Moriya et al. [7]	47 cases	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

*SCN: Serous Cystic neoplasm; MCN: Mucinous Cystic Neoplasm; SPEN: Solid Pseudopapillary Neoplasm *Inclusive of radiology, EUS, FNA and frozen section

Pancreatic schwannomas associated with von Recklinghausen disease have a high risk for malignancy [8].

In 1920, Nils Ragnar Eugene Antoni (1887–1968), a Swedish neurologist first described histologically that Schwannomas show areas of nuclear palisading, often forming parallel nuclear arrays called as Verocay bodies and usually consist of two distinct patterns of cellular arrangement of Schwann cells called Antony 'A' and Antony 'B' areas. Antoni A pattern contain areas composed of fascicles of Schwann cells that have a spindle cell morphology, intensely polar and are highly cellular, whereas Antoni B pattern is more loosely textured and microcystic spaces filled with basophilic mucin areas. Usually, these two cellular patterns coexist within same tumor in variable amount with larger tumors having more amount of Antoni B pattern and smaller tumor with Antony 'A' areas.

Probably because of this histological architecture of pancreatic schwannoma are solid in initial phase and later changing to solid cystic to predominantly cystic in larger tumors as size increase due degenerative changes which has been reported in up to 66% of cases i.e., hemorrhage, necrosis, calcification resulting in misdiagnosis of other pancreatic neoplasms based on their overlapping imaging features easily, despite the use of multiple non-invasive imaging modalities [9,10]. In literature review correct preoperative diagnosis was done in only 20% to 23% of cases inclusive of preoperative FNA and intraoperative frozen section [6,7]. Preoperative differential diagnosis in decreasing order of frequency as reported in literature are serous cystic neoplasm, mucinous cystic neoplasm, solid pseudopapillary neoplasm, acinar cell carcinoma, pseudocyst and pancreatic neuroendocrine tumor (Table 3). This makes preoperative diagnosis of pancreatic schwannoma a clinical challenge.

Computed Tomography (CT) features of pancreatic schwannoma consist of solid and cystic lesion. Solid masses (usually small <3 cm, and corresponding to Antony 'A areas) are well circumscribed, hypodense and shows homogenous/inhomogeneous enhancement on contrast phase. Large masses (usually 3-20 cm, with Antony 'b areas having cystic degeneration, hemorrhage, necrosis, and solid areas having Antony 'A' areas) usually are well circumscribed, hypodense, solid cystic lesion predominantly cystic lesion with enhancing septa and mural nodule is present [10,11]. In our case series one patient has cystic while other had solid lesion.

On magnetic resonance imaging pancreatic schwannomas are heterogeneously hyperintense on T2-weighted images and hypointense on T1-weighted images when compared with normal pancreas, hyperintense on DWI, and hypointense on ADC (Apparent Diffusion Coefficient) maps. There is presence of progressive hyperenhancement in the portal venous or delayed phase images which is more than that of the surrounding pancreatic parenchyma seen in cases of pancreatic schwannoma [12]. This finding would be against the enhancement patterns of pancreatic ductal adenocarcinoma, mucinous cystic neoplasms and solid pseudopapillary neoplasms. However, imaging features of pancreatic schwannoma may overlap with non-functioning neuroendocrine neoplasms. On CT and MRI; findings of an ill-defined tumor boundary, metastatic lymph nodes, and the presence of upstream pancreatic ductal dilatation and parenchymal atrophy are absent in benign schwannoma and are more representative of adenocarcinoma/malignant schwannoma. Around 30% to 40% of tumors are found to be in close relation to major surrounding vessels leading to splaying of vessels, however; infiltration into vessels has been reported in malignant schwannoma. In our first case common hepatic artery was found to be involved.

The diagnostic efficacy of EUS (endoscopic ultrasound) has been only 52.9%, which is considerably lower than that of other pancreatic tumors. The role of EUS-guided FNA in diagnosing pancreatic schwannoma is controversial as of now due to its inadequate amount of specimen, high false-negative rate and low diagnostic accuracy [13]. Newer Fine-Needle Biopsy (FNB) needles such as Franseen needle can increase the amount of tissue obtained for analysis while preserving its architecture. Small pancreatic schwannomas whose

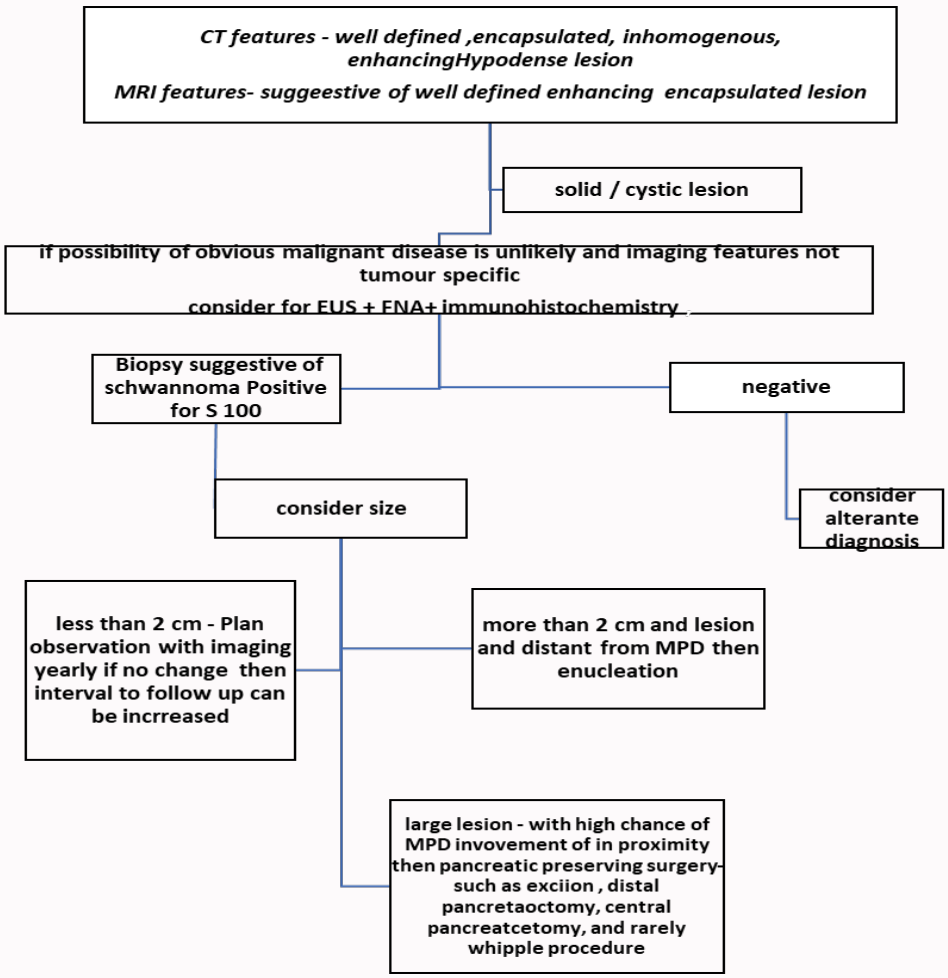


Figure 5: A proposed algorithm for management of pancreatic Schwannoma is mentioned.

diagnosis can be achieved by EUS-FNA can facilitate observation, enucleation, and selection of minimally invasive surgery. However, in recent years EUS FNA for evaluation of pancreatic SOL is on the rise and sensitivity for preoperative diagnosis is on rise, probably due to better experience, increased availability, and better targeting for biopsy.

Frozen section analysis can rule out the diagnosis of endocrine and other cystic pancreatic lesion, but it cannot establish the type of spindle cell tumor which requires histopathologic examination and immunohistochemical staining as of now [14,15]. In a study by Hirabayashi et al. of the cytological and histological materials were analyzed through immunohistochemistry for S-100 protein which can lead to the diagnosis of pancreatic schwannoma [16]. This can form one of the methods of preoperative or intraoperative diagnosis of schwannoma by using FNA for obtaining cytological materials from cyst for immunohistochemistry which if positive for S-100 can impact management. As schwannomas arise from nerve cells which express glucose transporter type 3, and FDG uptake is increased. Zhang et al. in a study on 5 patients noted significant FDG uptake which went on to have pathologically confirmed schwannomas. Benign schwannoma shave shown to be FDG avid while there is no correlation between malignant schwannoma and FDG activity [6].

As pancreatic schwannoma is mainly a benign tumor and risk of recurrence after surgery is rare. Management options can range from observation, enucleation, and pancreatic resection. Management of pancreatic schwannoma depends on various factors. If a preoperative diagnosis of benign pancreatic schwannoma can be established through EUS guided biopsy, small lesions less than 2 cm to 3 cm can be placed on observation. Enucleation of the lesion can be undertaken when schwannoma is preoperatively diagnosed with certainty or when it is strongly believed to be a benign lesion on evaluation. Schwannomas are usually well encapsulated, slowly growing benign tumors, so enucleation is a safe option; however, there is 10% documented recurrence in incomplete resections and continuous follow-up is recommended [17]. When in doubt whether to do a radical resection or enucleation intraoperative frozen section analysis can be done however the histological diagnostic accuracy of intraoperative frozen section analysis of pancreatic lesions is just 83%. Pathological review during the operation has limitations and can potentially be misleading.

As is the case most of the times, patient is taken up for surgery with diagnostic uncertainty or a based on a diagnosis of cystic neoplasm of pancreas. Various resection surgeries have been done in literature from pancreaticoduodenectomy, central pancreatectomy, and distal pancreatectomy to en-bloc resections of surrounding involved organs mainly for malignant schwannomas. Vascular involvement by pancreatic schwannoma is one of the features of malignancy, however as noted in one of our case the cystic lesion was

involving CHA requiring its resection during central pancreatectomy. Literature review of surgical procedures for Pancreatic schwannoma yielded two cases of central pancreatectomy done. Uncinate process pancreatic schwannoma is an uncommon site and in the literature 9 cases have been reported.

In the literature review by Ma et al. on pancreatic schwannomas it was noted that vascular compression and displacement was seen in 9 patients and encasement was seen in 4 patients [18,19]. Vascular resections have not been documented for pancreatic schwannomas. As vascular displacement was seen in both of our cases, in one of cases where the CHA was involved by tumor, we could carry safe resection of CHA as the collateral flow was confirmed through GDA and there was replaced RHA form SMA.

Conclusion

Pancreatic schwannoma although being a rare lesion possess diagnostic challenge, it should be assessed preoperatively clinically, and radiologically. Patient with no or vague abdominal symptoms with lack of jaundice, weight loss, and anemia usually points toward a benign pathology, may be suspected to have Schwannoma. A solid or cystic lesion on CT/MRI in these patients, a differential diagnosis of pancreatic Schwannoma may be entertained. The management will depend on the size and site of the lesion. The surgical treatment varies from observation for smaller lesions, enucleation (if MPD not involved), parenchymal preserving surgery such as Central Pancreatectomy, distal pancreatectomy either by open or minimally invasive procedure. A proposed algorithm for management of pancreatic Schwannoma is mentioned below (Figure 5).

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