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Solid pseudopapillary epithelial neoplasm of the pancreas: an audit of 29 cases operated in a tertiary Indian centre

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Abstract

Background Solid pseudopapillary epithelial neoplasm (SPEN) of the pancreas is an indolent tumor of rare occurrence seen predominantly in young females in the 2nd to 4th decade. These tumors tend to grow large, producing a mass effect, or may show local invasiveness.

Methods This is a retrospective analysis of a prospectively maintained database of SPEN cases operated at a tertiary care hospital in India from 2011-2023.

Results The cohort consisted of 29 patients with a male: female ratio of 1:8.6, and a median age of 24 years. The majority of the lesions were in the body and tail of the pancreas (65.5%). Mean tumor diameter was 6.1±1.9 cm. Pancreatic resection (9 distal pancreatectomies, 7 Whipple'spancreatic oduodenectomies, 2 central pancreatectomies) was undertaken in the majority of cases (62.1%), while 11 patients (37.9%) underwent enucleation. Additional resections included splenectomy (n=4), segmental colonic resection (n=2), and 1 non-anatomical liver wedge resection for solitary liver metastasis. Mean operative time and blood loss were 222.1±106.1 minutes and 115.5±85.9 mL, respectively. Minor complications were seen in 7 (24.1%) patients, while 1 patient had a major complication. At a median follow up of 37 months, 28 (96.6%) patients were alive, 1 of whom had local recurrence.

Conclusions SPEN represents an indolent, low-grade malignant tumor that is reasonably diagnosed preoperatively by cross-sectional imaging. The majority of cases are cured by surgical resection, the extent of which is dictated by the location of the tumor and its relation to surrounding structures. Excellent outcomes, both short- and long-term, can be achieved.

Keywords Solid pseudopapillary epithelial neoplasm, pancreatic resection, enucleation

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Introduction

Solid pseudopapillary epithelial neoplasm (SPEN) of the pancreas is an indolent tumor of rare occurrence, described alongside cystic neoplasms of the pancreas. It was first described by Virginia Frantz in 1959, who called it "papillary tumor of the pancreas—benign or malignant" [1]. The histological characteristics were further described by Hamoudi *et al*, which is why SPEN is sometimes also referred to as a Hamoudi tumor [2]. A literature search will also yield various other terminologies, such as papillary-cystic tumor, solid cystic tumor, solid and cystic acinar cell tumor, papillary epithelial neoplasm, solid and papillary neoplasm, and papillary tumor of the pancreas [3]. The entity was named "solid pseudopapillary epithelial neoplasm" by the World Health Organization in 1996 [4].

The true incidence of SPEN is not known, although it is believed to represent 1-2% of all pancreatic tumours [5]. It tends to occur predominantly in young females in the 2nd to 4th decade. Most patients develop symptoms only after the lesion has grown significantly in size. These tumors may produce a mass effect, or show local invasiveness, but their malignant potential is quite low [3,6,7]. Surgical resection remains the only curative option, and many series have shown excellent outcomes [8-11]. This audit highlights

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Conflict of Interest: None

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our experience in the surgical management of patients with SPEN.

Methodology

This study is a retrospective analysis of a prospectively maintained database of patients with pancreatic neoplasms managed from January 2011 to December 2023 in a single unit in the Department of Gastrointestinal Surgery in a tertiary care hospital in New Delhi, India. Patients across all age groups operated for pancreatic tumors with a histology consistent with SPEN were included. Patients with other cystic neoplasms, neuroendocrine tumors, adenocarcinoma, or any other pancreatic tumors were excluded. Patients' demographic parameters, symptomatology, clinical examination findings, laboratory and radiological data were collected. For the radiological assessment, contrast-enhanced computed tomography (CECT) was the preferred imaging modality. Magnetic resonance imaging (MRI) and endoscopic ultrasound (EUS) with fine-needle aspiration cytology (FNAC) were used selectively when other differential diagnoses were being considered. Tumor markers CEA and CA 19-9 were obtained in all patients.

Operative procedures were performed either laparoscopically or by open surgery, and consisted of enucleation, or pancreatic resection in the form of Whipple's pancreaticoduodenectomy (WPD), central or distal pancreatectomy, as deemed appropriate intraoperatively. Enucleation was preferred for lesions away from the main pancreatic duct (MPD). However, in cases where the MPD was accidentally injured, pancreatic resection was undertaken. Pancreatic reconstruction, when indicated, was either through pancreaticojejunostomy (PJ) by the modified Blumgart technique [12], or pancreaticogastrostomy (PG) by the double U-stitch technique [13], depending on the surgeon's preference. A drain was placed in all cases. Intraoperative findings, duration of surgery, blood loss, postoperative events and hospital stay were recorded. Postoperative complications were graded according to the Clavien-Dindo classification [14]. Pancreatectomy-specific complications, such as postoperative pancreatic fistula (POPF), and post-pancreatectomy hemorrhage (PPH) were described as per the International Study Group of Pancreatic Surgery guidelines [15]. Follow-up data were collected from outpatient records and/or telephone interviews. Investigations (blood tests, ultrasonography, CECT) were tailored according to the patient's clinical presentation. Survival was calculated from date of surgery to date of last follow up, or death from any cause. This study was conducted in accordance with the Declaration of Helsinki; the need for written informed consent was waived in view of the study's retrospective nature.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation. The median was used for variables that showed a skewed distribution. Categorical variables were reported as numbers and percentages.

Results

The database retrieved 29 operated cases of pancreatic SPEN (Table 1). There were 26 females and 3 males, with a mean age of 28.2±9.9 years (median 24 years, range 15-50 years). The majority (65.5%) of the patients were below 30 years of age, while none were above the age of 50 years. Pain was the commonest symptom, experienced by 86.2% of patients. Nine patients (31%) presented with a palpable abdominal lump. The diagnosis was incidental in 3 patients (10.3%), found through radiological evaluation for an unrelated indication. Three patients had jaundice, while 1 of them underwent biliary stenting for severe cholangitis. The median duration of symptoms was 13.5 months. CECT was the most common modality for radiological characterization of the lesion, performed in 90% cases. Three out of 5 patients who underwent EUS-FNAC had cytological findings consistent with SPEN. Mean levels of CEA and CA19-9 were 2.9±1.67 ng/mL and 22.8±8.43 U/mL, respectively.

Table 1 Baseline characteristics of patients (n=29)

Baseline parameter	Observed value (percentage)
Female: male	8.6:1
Age (mean ± SD)	28.2±9.9 years Median 24 years
Stratification by age in years:	
<20	5 (17.2%)
21-30:	14 (48.3%)
31-40:	6 (20.7%)
41-50:	4 (13.8%)
>50	0
Clinical presentation:	
Pain	25 (86.2%)
Palpable lump	9 (31%)
Jaundice	3 (10.3%)
Cholangitis	2 (6.9%)
Others (vomiting, weight loss)	8 (27.6%)
Incidental diagnosis	3 (10.3%)
Median duration of symptoms	13.5 months
Biliary stenting	1 (3.4%)
Radiological investigation*	
CECT	26
MRI/MRCP	6
EUS	5
Tumor markers (mean ± SD)	
CEA (ng/mL)	2.9 ± 1.67
CA 19-9 (U/mL)	22.8 ± 8.43

*Some patients underwent multiple investigations

SD, standard deviation; CECT, contrast-enhanced computed tomography; MRI, magnetic resonance imaging; MRCP, magnetic resonance cholangiopancreatography

Operative findings (Table 2)

The majority of tumors were in the body and tail of the pancreas (65.5%), followed by head/uncinate process (34.5%). The surgical resection was attempted laparoscopically in 16 (55.2%) cases, of which 12 (41.4%) were completed successfully, while 4 required conversion to open surgery. The reason for conversion was either bleeding (n=1), or unclear planes (n=3) due to dense adhesions with adjacent viscera. The remaining 13 (44.8%) were operated by upfront open surgery. Pancreatic resection (9 distal pancreatectomies, 7 WPD, 2 central pancreatectomies) was undertaken in the majority of cases (62.1%), while in 11 patients (37.9%) whose MPD could be preserved enucleation was performed. Additional resections included splenectomy in 4 patients, segmental colonic resection in 2 patients, and 1 non-anatomical liver wedge resection for a solitary liver metastasis in segment 3. None of the patients needed vascular resection. Mean operative time and blood loss were 222.1±106.1 minutes and 115.5 ± 85.9 mL, respectively. Mean tumor diameter was 6.1 ± 1.9 cm (range 3.7-10.4 cm). Histopathology was benign in most cases (n=28), while only 1 patient had a solitary metastatic deposit in segment 3 suggestive of malignancy.

Table 2 Operative details

Operative parameter	Observed value (percentage)
Location of tumor	
Body/neck	12 (41.4%)
Head/uncinate process	10 (34.5%)
Tail	7 (24.1%)
Operative approach	
Completely Laparoscopic	12 (41.4%)
Laparoscopy converted to open	04 (13.8%)
Upfront open surgery	13 (44.8%)
Procedure performed	
Pancreatic resection	18 (62.1%)
Distal pancreatectomy	9
WPD	7
Central pancreatectomy	2
Enucleation	11 (37.9%)
Pancreatic reconstruction	9 (31%)
Pancreaticogastrostomy	6 (20.7%)
Pancreaticojejunostomy	3 (10.3%)
Additional resection	
Splenectomy	4 (13.8%)
Colonic segment	2 (6.9%)
Metastatectomy (liver wedge)	1 (3.4%)
Vascular resection	0
Operative time in minutes (mean ± SD)	222.1 ± 106.1
Blood loss in mL (mean± SD)	115.5 ± 85.9
Tumor diameter (mean ± SD)	6.1 ± 1.9 cm
Histopathology	
Benign	28 (96.6%)
Malignant	1 (3.4%)

WPD, Whipple's pancreaticoduodenectomy

Postoperative course, short- and long-term outcomes (Table 3)

The median time to drain removal was on postoperative day 5, while the median length of hospital stay was 6 days. Minor complications (CD grade <III) were seen in 7 (24.1%) patients, while only 1 patient had a major complication (CD grade ≥III). Clinically relevant POPF occurred in 3 (10.3%) patients (1 central pancreatectomy, 2 WPD), all of which were grade B and closed spontaneously within 4 weeks. PPH occurred in 3 (10.3%) patients (1 grade A, 1 Grade B, 1 Grade C), 1 of whom had to be re-operated on postoperative day 6. Two patients were readmitted within 90 days, while there was no 90-day mortality. At median follow up of 37 months, 28 (96.6%) patients were alive, while 1 patient died 22 months after surgery due to COIVD-19 pneumonitis during the pandemic. Recurrence was noted in 1 patient (3.4%) nearly 4 years after they underwent enucleation, and the patient is currently under follow up.

Discussion

Often described alongside cystic neoplasms of the pancreas, SPEN is a rare tumor of very low malignant potential, believed to arise from an exocrine component of the organ. Table 4 summarizes the experience of some authors who have managed these cases. The tumor has a female preponderance, affecting those in their 2nd-4th decade of life. Less than 10% of tumors are seen in men [19]. In our series, the female: male ratio was ~9:1, while it was 6:1 in a study by Kumar *et al* [11]. Much higher proportions of male patients (23.8% and 25.5%) were reported in 2 Chinese studies [9,20]. The clinical presentation is very

Table 3 Short-term and long-term outcomes

Outcome	Number of events (percentages)
Postoperative complications	8 (27.6%)
CD grade I-II	7 (24.1%)
CD grade ≥III	1 (3.4%)
Clinically relevant POPF	3 (10.3%) (all grade B)
PPH	3 (10.3%) (1 grade A, 1 Grade B, 1 Grade C)
Median drain removal day	5
Reoperation	1 (3.4%) (Grade C PPH)
Median hospital stay (days)	6
Readmission within 90 days	2 (6.9%)
90-day mortality	0
Median follow up (months)	37 months (range 15 months to 9 years)
Recurrence	1 (3.4%)
Survival	28/29 (96.6%)

CD grade, Clavien-Dindo Grade, POPF, postoperative pancreatic fistula, PPH, post-pancreatectomy hemorrhage

Table 4 Review of the literature

Author [ref.]	Country	Study period	Number of cases	M:F	Median size (cm)	Surgery	Morbidity	Follow up	Survival
Kumar [11]	India	2007-2018	50	7:43	7.7	46 PR, 2 En	Clavein–Dindo grade II 7(14.6%), IIIa 8(17%), IIIb 1(02%)	29 months	49/50
Liu M [9]	China	2008-2018	243	62:181	4.83	229 PR, 10 En	-	46 months	239/243. 98.4% 5yr OS
Liu Q [16]	China	2001-2021	454	84:370	5.38±3.70	135 En, 316 PR	17.0%	66 months	361/454
Tjaden [17]	Germany	2001-2018	52	8:44	4.4	4 En, 48 PR	50%	54 months	52/52
Cho [18]	South Korea	1992-2018	66	10:56	6.1±3.3	15 En, 51 PR	63.6%	511.2	66/66

En, enucleation; M:F, male:female ratio; PR, pancreatic resection

non-specific, and patients may be asymptomatic for several months. Vague abdominal pain, bloating and abdominal fullness are the usual symptoms. A few patients may present with a large upper abdominal mass. Jaundice/cholangitis, gastric outlet obstruction and weight loss are uncommon, although not unheard of [21]. Some cases may be diagnosed incidentally on imaging performed for an unrelated indication. Spontaneous tumor rupture with life-threatening bleeding is extremely rare [22]. With a mean tumor size of 6.1±1.9 cm, we found that pain was the commonest symptom (86.2%), while 31% presented with a palpable abdominal lump. In another Indian series, median tumor size was 7.7 cm, pain was present in 60% of cases, while the diagnosis was incidental in 22% of patients [11]. Liu M *et al* reported a mean tumor size of 4.83 cm, with 63.4% of their patients being asymptomatic at presentation, and only 19% having pain [9]. Mean tumor size in a systematic review by Law *et al* was 8.6 cm [23].

Abdominal imaging in the form of CECT, the preferred noninvasive modality, will reveal a well-encapsulated, heterogeneously enhancing solid mass lesion containing multiple cystic components [24,25]. The extent of cystic degeneration is higher in larger tumors, while smaller tumors may appear entirely solid. The periphery of the lesion may show foci of calcification (Fig. 1). A large lesion may show a mass effect on surrounding structures, in the form of biliary obstruction, gastric outlet obstruction or splenic congestion. Very rarely, aggressive tumors may show infiltrative features. MRI or magnetic resonance cholangiopancreatography may be used selectively in doubtful cases, or when other cystic neoplasms with ductal communication are suspected [26]. The role of EUS is uncertain, although it offers the advantage of targeting the lesion for a tissue diagnosis [27]. However, tissue diagnosis is recommended only in uncertain cases when the differential includes other diagnoses [28,29]. We arrived at a diagnosis with CECT alone in 82.7% cases, while 20.7% and 17.2% of our cases additionally underwent MRI and EUS, respectively. Some patients underwent multiple investigations to arrive at a pre-operative diagnosis with reasonable certainty. EUS was resorted to only in doubtful cases, where other differential diagnoses were being considered that would alter the definitive management (e.g., anti-helminthic therapy for pancreatic hydatid cyst, neoadjuvant therapy for pancreatic ductal adenocarcinoma). Tumor markers, such as CEA, CA 125 and CA 19-9, are usually not elevated [9].

In terms of location, 34.5% tumors were in the head, while 65.5% were in the body and tail—similar to the distribution described in a systematic review involving 2744 patients, where 59.3% of tumors were in the body/tail, while 36% were in the head/uncinate process. In contrast, a series by Kumar *et al* had 66% of tumors confined to the head of the pancreas. Ectopic pancreatic tissue in the omentum or mesocolon may harbor the tumor in extremely rare cases [30].

Since the tumor has very low aggressiveness and malignant potential, parenchyma-preserving surgical approaches are preferred when feasible, especially when there is no risk of injury to the pancreatic duct [9]. Papavramidis *et al* reported involvement of adjacent organs, such as the spleen, colon and duodenum in 9% of their cases [3]. Large lesions infiltrating into adjacent viscera should indicate *en bloc* resection to achieve cure [31]. Wang *et al* showed that enucleation of SPEN was associated with a shorter operative time, less blood loss, and a lower rate of exocrine insufficiency when compared to pancreatic resection, with comparable morbidity and no greater risk of tumor recurrence [32]. We resorted to enucleation in 37.9% of cases, while 62.1% underwent pancreatic resection. Resection in 16 patients (55.2%) was attempted laparoscopically, and successfully completed in 12 patients (41.1%). Two patients required segmental colonic resection, because of dense adhesions with the mesocolon, while 4 required splenectomy, as it was not possible to preserve the splenic vasculature. Liu *et al* performed enucleation in only 3.7% cases, while the remaining patients underwent pancreatic resection, which was accomplished laparoscopically in 11.4% (n=30) [9]. Frost *et al* performed pancreatic resection in 18 patients, while only 3 underwent local excision [22]. In a Chinese study comprising 63 patients, enucleation was performed in only 7.9%, while the remainder underwent pancreatic resection. A subset of patients may require vascular resection to attain R0 status [33]. We had no such patients. Kumar *et al* performed enucleation in only 4% of cases and pancreatectomy in 92%, with 20% requiring

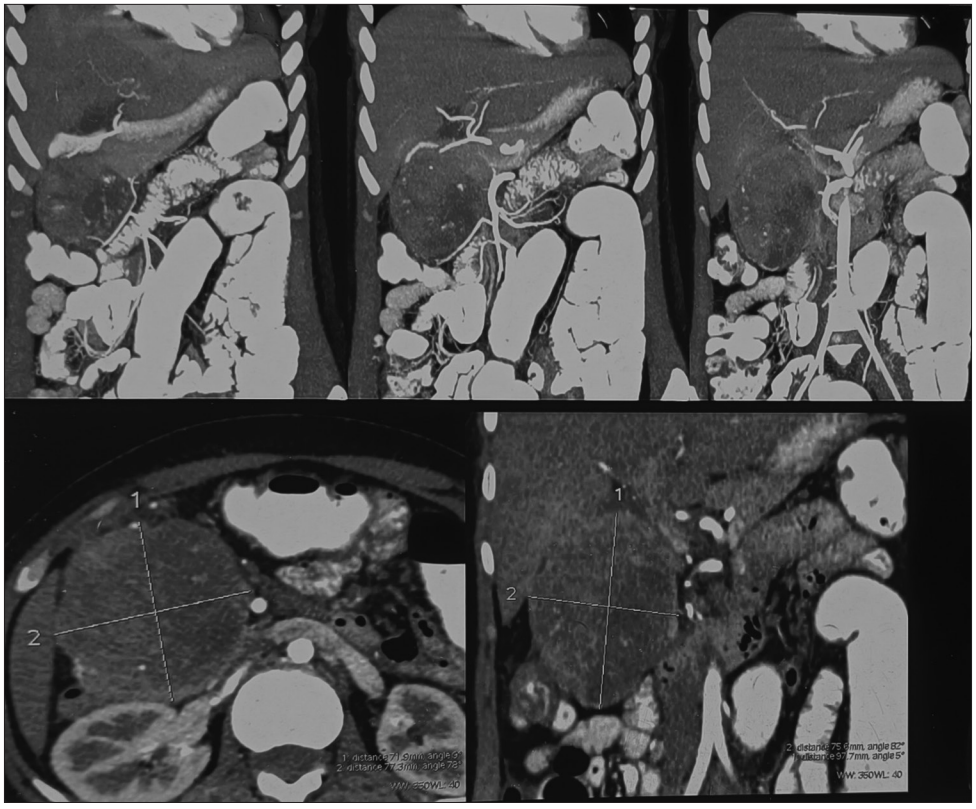

Figure 1 Contrast-enhanced computed tomography image, showing well-encapsulated, heterogeneously-enhancing solid mass lesion containing multiple cystic components, with multiple peripheral foci of calcification

superior mesenteric/portal vein resection [11]. Cheng *et al* undertook venous resection in 8 cases [33]. Lymphatic spread is rare, although the role of formal lymphadenectomy is uncertain [10,27]. Fig. 2 shows an enucleated intact specimen and its cut-section.

SPEN may metastasize to distant sites in 10-15% patients [34]. Some series have prompted surgical resection of synchronous or metachronous lesions to achieve long-term survival [31, 34,35]. Malignancy with metastasis was seen in 1 patient. The series by Frost *et al* also had 1 patient in whom distal pancreatosplenectomy with wedge resection of liver metastasis was performed, while Kumar *et al* had 2 patients with liver metastasis, treated by non-anatomical liver resection. Interestingly, Lubezky *et al* reported histological features of malignancy in 40.6% of their patients [27]. Perioperative morbidity is mainly attributed to pancreatectomy-specific complications, which can be as high as 64% [5]. Our morbidity rate was 27.6%, with only 1 patient developing CD > grade III complication. Wang *et al* reported a morbidity rate of 20.6% [20], similar to the 19% major morbidity reported by Kumar *et al* [11].

Reported rates of recurrence after surgical resection are usually less than 10% [36,37,]. In a review of 718 patients, recurrence was seen in 6.6%. In our series, 1 patient had recurrence (3.4%), while Liu M *et al* reported recurrence in 1.4% cases. Frost *et al* had no case of recurrence in their series. The role of adjuvant therapy is not clearly defined.

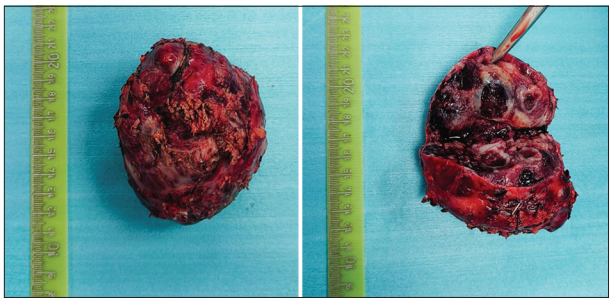

Figure 2 Enucleated specimen (right) and its cut-section (left) showing predominantly solid tumor with multiple areas of cystic degeneration

Patients with recurrence, or metastatic or unresectable disease may be offered chemotherapy and radiation, but the experience with these strategies is confined to small case series only [38,39]. Cisplatin, gemcitabine and 5-fluorouracil are the chemotherapeutic drugs most commonly used [40]. Overall 5-year survival with surgical management can be achieved in more than 95% of cases [3]. In a series of 553 patients with SPEN, Yu *et al* reported 1-, 3- and 5-year survival rates of 99.4%, 97.5% and 96.9%, respectively [11]. Twenty-eight out of 29 patients (96.6%) in our series were alive at the time of submission of this study and doing well.

In conclusion, SPEN represents an indolent, low-grade malignant tumor with a female preponderance, presenting in a younger age group with vague abdominal pain, or a palpable

lump, and can be reasonably diagnosed preoperatively by cross-sectional imaging. Surgical resection is curative, and many patients can benefit from minimally invasive techniques, as in our study. The extent of resection is dictated by the location of the tumor and its relation to surrounding structures. Excellent outcomes in both the short and long term can be achieved. However, patients are advised to remain under periodic follow up as very late recurrences are not unheard of.

Summary Box

What is already known:

- Solid pseudopapillary epithelial neoplasm of the pancreas represents an indolent, low-grade malignant tumor, most commonly affects females in a younger age group (20-30s)
- Diagnosis can be reasonably established preoperatively by cross-sectional imaging

What the new findings are:

- Enucleation is a suitable surgical option in some cases
- Patients can benefit from minimally invasive techniques
- Excellent outcomes, both short- and long-term, can be achieved

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