Original Research Article

Solid pseudopapillary neoplasms-experience from a tertiary care centre

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Abstract

Introduction: Solid pseudopapillary neoplasms (SPN/FRANTZ TUMOUR) of the pancreas are rare neoplasms of low grade malignant potential which were first described in 1959 by Frantz. These account for 0.13–2.7% of pancreatic neoplasms and approximately 13% of surgically resected cystic lesions of the pancreas. We present our experience with these rare tumors. **Methods:** Total 406 patients with pancreatic tumours were admitted in our department during the 10 year period (Between 2007 and 2017) were reviewed, only 18 were diagnosed as having SPN (4.4%). Clinico-pathological details, intervention done and follow up of all the cases were studied and reported here. **Results:** 17 patients were woman and1was Man with median age of 23 years (range 11 to 54 years). The tumor size ranged from 3.8 to17cm (average 6.4 cm). 12 patients presented with pain in the abdomen, 4 presented with a painless mass, 1 was detected incidentally and1presented with Malena. In 7 patients the tumor was in the pancreatic head, in 3 it was in the neck, and in the remaining 8 it is in the body and tail. CECT was done in all cases. 8 patients underwent Distal pancreatectomy with splenectomy, 1 underwent a PPPD, 6 patients required classical Whipple operation. 3 underwent central pancreatectomy. Immuno histochemistry showed positivity for beta catenin, vimentin, PR receptor and chromogranin negativity. All 18 patients were free of disease in a median follow- up period of 32 months (range 6 – 84) months. **Conclusion:** SPNs are rare neoplasms, typically affecting young women without notable symptoms, with a low malignant potential but excellent prognosis. Radical surgical resection with clear margins is the treatment of choice.

Key words: Female, Pancreas, Solid pseudopapillary neoplasm of pancreas, Solid-cystic Tumour.

Introduction

Solid pseudopapillary neoplasms (SPN/FRANTZ TUMOUR) of the pancreas are rare neoplasms of low grade malignant potential which were first described in 1959 by Frantz. These account for 0.13–2.7% of all pancreatic tumors and predominantly affects young women occurs in the second or third decades of life [1,2].

Earlier this tumor was called by various names including 'solid cystic tumor', 'papillary cystic tumor', 'papillary epithelial neoplasia', 'solid and papillary epithelial neoplasia', 'papillary epithelial tumor' and 'Frantz's tumor', 'solid and papillary tumor', 'solid-cysticpapillary epithelial neoplasm', 'benign or malignant papillary tumor of the pancreas'[3]. In 1996 WHO coined its current terminology Solid pseudo-papillary tumor in the International classification of the tumours of exocrine pancreas [3]. These tumours have a long asymptomatic period and are usually detected when they have grown to a large size [4-8].

Abdominal mass is the most common presenting symptom, with dyspepsia, early satiety, nausea, or vomiting being less common presenting symptoms. Up to 20% of patients are asymptomatic with tumors identified either incidentally on imaging or at operation for unrelated pathology [9.10]. Grossly, SPTs are identified as well demarcated, encapsulated tumors with extra pancreatic growth. Mixed solid and cystic components are evident with internal necrotic or hemorrhagic debris and lobulated, solid tissue at the

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periphery. Characteristic radiographic features include the presence of an encapsulated mass with solid and cystic components on either CT scan or MRI, with MRI notably better for identification of certain tumor characteristics such as the presence of a capsule, hemorrhage or cystic degeneration [10]. SPT should be added to the differential diagnosis in any patient with a solid and partly cystic mass of the pancreas especially in females under 35 years of age. Surgical resection is the treatment of choice for affected patients and is associated with an overall good prognosis [11].

Radiological and pathological studies have revealed that the tumor is quite different from other pancreatic tumors. But the cell origin of SPT and tumorigenesis are still enigmatic Due to the paucity of the number of cases seen, the natural history of the disease is not fully understood. This study was undertaken to examine the clinico-pathological characteristics of the disease and to evaluate the outcome of surgical intervention in a tertiary referral cancer center.

Materials and Methods

Place of study and type of study: A retrospective analysis of all patients diagnosed and treated for SPN in Osmania General Hospital/ College, Hyderabad over the past 10 years (2007 to 2017) was carried out. The clinico-pathological, radiological, operative and survival data were obtained and analysed.

A Contrast enhanced CT scan (CECT) of the abdomen was performed in all the patients and Immuno histochemistry was performed in 6/18 patients. All the patients who underwent resection were followed up every 6 months. The investigations performed included routine blood investigations, chest X-ray, CA-19-9 level and either an ultrasound or a CT scan of the abdomen.

Inclusion criteria: Diagnosed, resected and histopathological confirmed cases of Solidpseudo papillary neoplasms of pancreas were included in this study. In all, 18 patients were identified.

Exclusion criteria: if Histopathology report doesn't show SPN were excluded from the study.

Statistical methods: Continuous data were expressed as median/range and analysed by Kruskal–Wallis test, and categorical variables were expressed as number/ percentage and analysed by chi-square test.

Results

Total 406 patients with pancreatic tumours were admitted in our department during the 10year period was reviewed, only 18 were diagnosed as having SPN (4.4%).17 patients were woman and 1patient was Man. The patients had median age of

Table-1: showing demographic status, clinical presentation, site of lesion, size and Type of surgery.

S.No.	Age/sex	Symptoms	Site of lesion	Maximum Size (cm)	Type of surgery
1	F/11	Pain abdomen	Head	4	Whipples procedure
2	F/19	Pain abdomen	Neck	4.6	Central pancreatectomy
3	F/21	Lump abdomen	Body and tail	10.8	Distal pancreatectomy
4	F/20	Pain abdomen	Body and tail	13.5	Distal pancreatectomy
5	F/26	Pain abdomen	Body and tail	6.8	Distal pancreatectomy
6	M/48	Lump abdomen	Body and tail	11.4	Distal pancreatectomy
7	F/20	Pain abdomen	Head	6.1	Whipples procedure
8	F/29	Pain abdomen	Head	8.6	Whipples procedure
9	F/35	Pain abdomen	Neck	3.8	Central pancreatectomy
10	F/36	Pain abdomen	Body and tail	6.7	Distal pancreatectomy
11	F/21	Incidental detection	Neck	7.6	Central pancreatectomy
12	F/25	Pain abdomen	Body and tail	9	Distal pancreatectomy
13	F/16	lump abdomen	Head	17	Whipples procedure
14	F/15	Lump abdomen	Head	10	PPPD
15	F/20	Pain abdomen	Head	5	Whipples procedure
16	F/34	Anaemia, malena	Head	6	Whipples procedure
17	F/42	Pain abdomen	Body and tail	6	Distal pancreatectomy
18	F/54	Pain abdomen	Body and tail	6	Distal pancreatectomy

23 years (range 11 to 54 years). The tumour size ranged from 3.8 to 17 cm (average 6.4 cm). Twelve patients presented with a dull aching pain in the abdomen. Four presented with a painless abdominal mass in the upper abdominal region. One patient was detected incidentally. One patient presented with Malena. In 7 patients the tumour was located in the pancreatic head, in 3 it was located in the neck, and in the remaining 8 patients it occurred in the body and tail [Table1].

CECT was done in all cases.13 patients showed a well-defined mass with heterogeneous attenuation with solid and cystic components with displacement of adjacent structures [Figure 1]. Of the 18 patients, five had heterogeneous enhancement with large non-enhancing central areas. Predominantly solid tumour in 2 cases is represented by hypodensity on CT scan. There was no biliary or pancreatic ductal upstream dilatation despite large size except in one case where tumour was 17cm size with central haemorrhage.

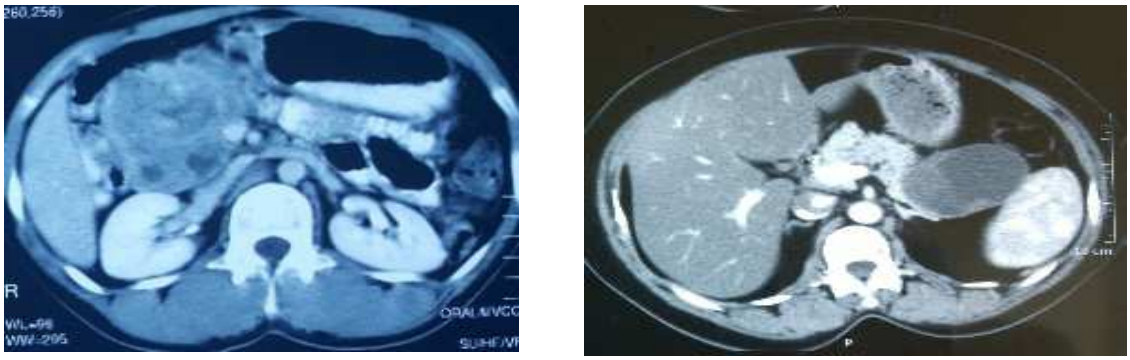

Figure-1: CECT Abdomen: well-defined mass with heterogeneous attenuation with solid and cystic components with displacement of adjacent structures in Head (A) and Tail (B).

In one case, the mass was significantly compressing Inferior Vena Cava (IVC) however there was no IVC invasion or thrombosis. In 4 cases, portal vein was compressed and displaced, and in one case the portal vein was partially encased for less than 180º circumference. six patients had undergone a preoperative FNAC: in 4 patients the FNAC correctly diagnosed SPN.

Eight patients underwent distal pancreatectomy with splenectomy, one underwent a pylorus-preserving pancreatoduodenectomy, six patients required classical Whipple operation. 3 underwent central pancreatectomy. None of these patients had distant metastasis.

3 patients had biochemical (Grade A) Pancreatic leak, one had delayed gastric emptying and I patient had haemorrhage.

There was no postoperative mortality. All 18 patients were free of disease in a median follow- up period of 32 months (range 6 – 84) months. One patient developed diabetes and one patient had pancreatic exocrine deficiency.

The tumour was well encapsulated in all the cases [Figure 2 (A)]. Tumours on cut section were predominantly solid, pale to deep brown or yellow, heterogenous cut-surface with haemorrhage and necrosis, and soft to firm in consistency [Figure 2(B)].

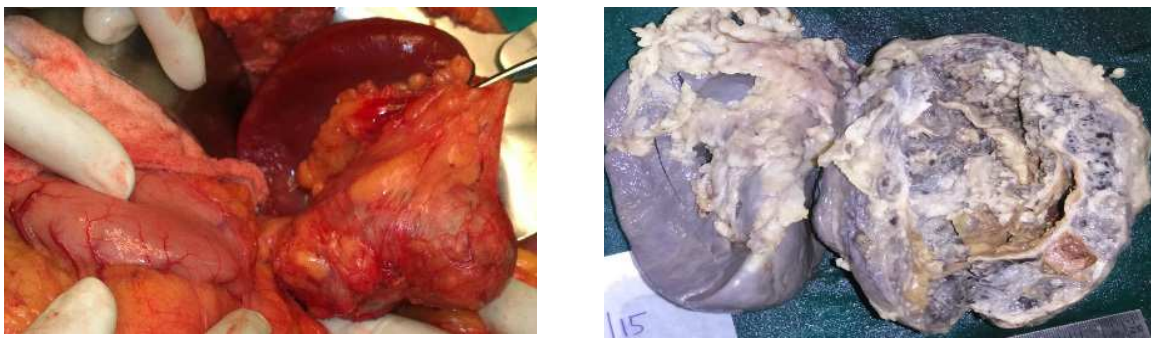

Figure-2:(A)well encapsulated tumour at Tail of pancreas. (B) Heterogenous cut-surface with haemorrhage and necrosis.

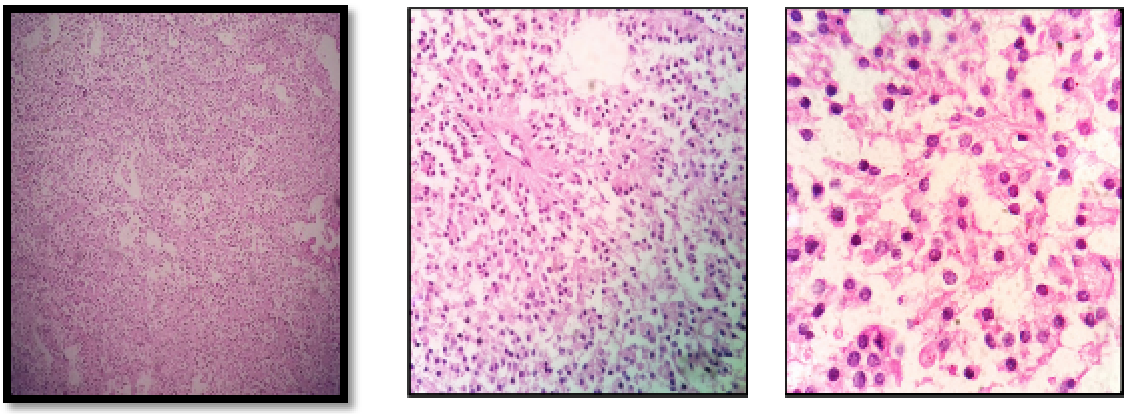

Figure-3: Histopathological examination: [Fig3 (A)] the tumour was composed of poorly cohesive uniform, cuboidal cells arranged in papillary pattern with thin fibrovascular core. [Fig 3(B)] The tumour cells had round to oval nuclei, fine chromatin and moderate amount of eosinophilic cytoplasm. [Fig 3(C)] The characteristic features like nuclear grooves were seen in all the cases.

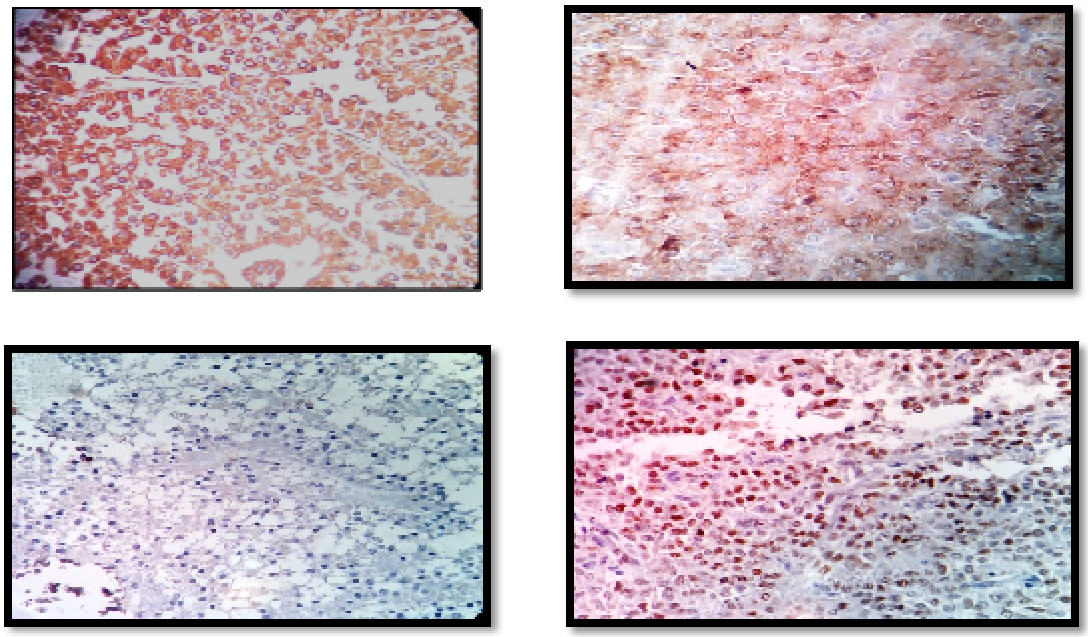

Figure-4: Immuno histochemistry: Tumour showed positivity for (A) Beta catenin, (B) vimentin, (C) PR receptor and (D) chromogranin negativity

On histopathological examination, the tumour was composed of poorly cohesive uniform, cuboidal cells arranged in papillary pattern with thin fibrovascular core [Fig3(A)]. The tumour cells had round to oval nuclei, fine chromatin and moderate amount of eosinophilic cytoplasm [Fig 3(B)]. The characteristic features like nuclear grooves were seen in all the cases (Fig 3(C)]. Stromal changes such as hyalinization and myxoid change in the core of the pseudo papillae. Few foci of haemorrhage and necrosis were also presentImmuno histochemistry was done 6cases. Tumour showed positivity for beta catenin, vimentin,PR receptor and chromogranin negativity[Figure 4].

Histology did not reveal any feature of parenchymal, perineurial or angioinvasion and lymph node involvement

Discussion

Solid pseudopapillary neoplasms are slow growing exocrine pancreatic tumours. This tumour was first described by Frantz VK in 1959 [1] as a “papillary tumour of the pancreas, benign or malignant” has a strong predilection for adult females with a male: female ratio of 1:10 [2]. seventeen cases in this study were female patients and similar exclusivity in females was reported by Patil TB et al., [12], and other studies have also consistently reported female preponderance [13,14,15]. It is more common in young non-Caucasian

women, usually Asian and African-American women, between the second and third decades of life [16]. The median age of 23 years in the present study was concordant with the studies of Patil TB et al., and Mao C et al., [12,14].

Though, SPN can occur in any part of the pancreas, but tail of the pancreas appears to be the most common location. In this study, in 44.4% cases the tumour was located in tail of pancreas, as were 50% and 71% cases reported by Patil TB et al., and Huang HL et al., respectively [12,13]. The average size of 6.4 cm in the present study was close to the mean size of 5.8 cm reported by Wang DB et al., [13]. In the series by Paruchuri RK et al., all nine tumours were encapsulated, and calcification was seen in two out of nine cases, similar to our experience [15].

CECT scan, ultrasonography (US) and Endosonography (EUS) have been used with variable success in diagnosing SPN. CT scan and EUS are more sensitive and specific and have shown more accuracy in diagnosing SPN [14,15].

Ultrasound shows a well-defined mass with solid and cystic components and increased vascularity. Contrast enhanced CT shows an encapsulated lesion with enhancing solid and non-enhancing cystic areas with some showing calcific foci. Haemorrhagic density may be seen within the lesion. On MDCT the SPN are encapsulated tumours, which are round to oval in shape and exhibit heterogeneous attenuation with peripheral iso- to hyperdense areas [15], similar to our study. Magnetic resonance imaging (MRI) can be diagnostic. Typically, a large, well-defined, encapsulated lesion with heterogeneous high or low signal intensity on T1-weighted, heterogeneous high signal intensity on T2-weighted, and early peripheral heterogeneous enhancement with progressive fill-in is found on gadolinium-enhanced dynamic MRI. These features help differentiate this rare tumour from other pancreatic neoplasms [16]. In our series, we relied on CT imaging for the pre- operative work-up.

Differential diagnosis for SPN would include pancreatic cancer and pancreatic Neuroendocrine Tumours (NET) [6]. Hyper attenuation of SPN compared to the surrounding pancreatic parenchyma on contrast-enhanced triphasic CT images is due to SPN's rich blood supply, which helps to differentiate it from pancreatic neuroendocrine tumour. Also, unlike adenocarcinomas, secondary changes in the pancreas, such as dilatation of the upstream pancreatic duct or pancreatic parenchymal atrophy are usually not seen in SPN. MRI also helps in differentiate SPNs from islet cell tumours, in whom cystic components have moderately increased signal intensity on T1-weighted and increased signal intensity on T2-weighted images [6].

However, a young female having a well-circumscribed and capsulated tumour in the pancreas with haemorrhage and cystic changes, appearing as heterogeneously cystic central component and solid periphery, is in all likelihood SPN.

FNAC has been used for the preoperative cytological diagnosis of SPN [17,18]. The cytology specimen is usually highly cellular and is characterized by the presence of epithelioid cells that present singly or in aggregates containing fibrovascular cores. No evidence of pleomorphism or mitotic activity is seen in the cells. The most conclusive criterion for identification of SPN is the pseudopapillary arrangement with bland appearing tumour cells. EUS-guided FNAC has been reported, and this can help in correctly diagnosing SPN pre-operatively [19]. In the current series, 4/18 patients had a pre-operative percutaneous US-guided FNAC, and the diagnosis of SPN was made correctly in 3 patients. It is not necessary to have a tissue diagnosis pre-operatively, and surgery can be advised on the basis of radio- logical imaging.

On gross examination, SPN is a well encapsulated tumour. On cut section it shows solid and cystic areas with necrotic and haemorrhagic patches. Grossly SPN may mimic pancreatic pseudocyst or other cystic neoplasms. Yellow or haemorrhagic cut surface of SPN separates it from other cystic pancreatic neoplasms. Microscopically pancreatic pseudocyst lacks epithelial lining [3].

Solid pseudo-papillary neoplasms have specific histological features of SPN, such as pseudopapillae or structures resembling ependymal rosettes, but lacking acinar, cribriform and nested or trabecular pattern, which is seen in Acinar Cell Carcinoma (ACC) and NET, respectively. Nuclear grooving is a characteristic finding in SPN as opposed to salt and pepper chromatin of NET, and nuclear pleomorphism with single, central prominent nucleolus in ACC.

Immunopositivity for CD10, vimentin and β-catenin, and negativity to chromogranin A (characteristic in NET), and trypsin or chymotrypsin (characteristic of ACC), further confirms the diagnosis of SPN [3]. In our

series Immuno histochemistry was done 6 cases. Tumour showed positivity for beta catenin, vimentin, CD10, PR receptor and chromogranin negativity.

Marchegiani G et al., reviewed 131 cases and considered 16 (12.2%) cases as malignant SPN due to the presence of at least two of the three histological features that is invasion of pancreatic parenchyma, perineural and or blood vessels. After a median of 62 months after surgery, only two (1.5%) malignant SPNs had a recurrence [20]. In our series histology did not reveal any feature of parenchymal, perineurial or angioinvasion and lymph node involvement.

No patient had recurrence during 32 moths of median follow-up period.SPN is a tumour of low-grade malignant potential [21]. The logical conclusion is that complete surgical excision is the best option for patients who have SPN. Thus, surgery should always be attempted in a suspected case of SPN even if it implies that major resections (like pancreaticoduodenectomy along with adjacent organ resection) have to be performed. A local recurrence rate of 6.2% is reported in cases treated by radical surgical excision, and hepatic or Krukenberg-type distant metastases develop in 5.6% of cases [22]. In our series, all the patients who underwent resection were disease-free on follow-up.

Conclusions

A high index of clinical suspicion is necessary to suspect and diagnose SPN. This diagnosis should be borne in mind when young female patients present with a well encapsulated pancreatic mass. CT scan and EUS are valuable pointers to the pre-operative diagnosis. Surgical excision offers the best chance for cure and should always be attempted irrespective of the magnitude of resection involved. Patients with SPN have an excellent prognosis after surgical excision. The important observation in this study is the vessel involvement/encasement is not seen, though lesions reaching up to 15cm in size.

Authors Contribution:

1. Prepared the manuscript and performed all surgeries.
2. Helped in data collection and involved in patient care.
3. Helped in data analysis and statistical analysis. Assisted majority of surgeries.
4. Supervised the paper and involved in patient care of these patients.

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