

# Clinicopathological Study of Cystic Lesions of Pancreas at A Tertiary Care Center

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## ABSTRACT

**Background:** Cystic lesions of pancreas though uncommon are being increasingly identified as a result of developments in imaging techniques. Rapid advances in pancreatic surgeries associated with better patient outcome have led to a variety of pancreatic lesions being increasingly resected and pathologically diagnosed. Newer entities and classification systems have emerged.

**Methods:** This was a hospital based study conducted in the Department of Pathology, Academy of Medical sciences, Pariyaram. In the 91 pancreatic resections done over a period of 3 years from 2013-2016, there were 15 cases of cystic pancreatic lesions which formed the subject of the present study.

**Result:** Cystic pancreatic lesions constituted 16.5% of cases (15 cases) of the 91 pancreatic resections done for various reasons. Of the 15 cases there were 4 non-neoplastic cysts all of which were pancreatic pseudocysts with a M:F ratio of 3:1. There were 11 neoplastic cystic lesions with 4 serous cystadenomas, 3 solid papillary pseudotumors, 2 mucinous cystadenomas and 1 case each of invasive adenocarcinoma in Intraductal Papillary Mucinous Neoplasm (IPMN) and IPMN with low grade dysplasia. Except for the one patient with invasive adenocarcinoma in IPMN all others with neoplastic lesions were females. Age of the patients ranged from 14-67 yrs.

**Conclusion:** Cystic tumors of the pancreas are more common in females with the majority of the tumors being benign when compared to ductal adenocarcinomas which are aggressive tumors with higher incidence in males. The possibility of Solid papillary pseudotumor should always be considered in young females presenting with an encapsulated pancreatic mass especially in the tail of pancreas.

**Keywords:** *cyst, Serous Cystadenoma, Solid Papillary Pseudotumor, Pseudocyst, Whipple's Resection*

## Introduction

Cystic lesions of the pancreas are rare. Pancreatic cysts may be non-neoplastic or neoplastic. Non-neoplastic cysts are classified into retention cysts and pseudocysts.<sup>[1]</sup> Neoplastic cysts may be true cystic neoplasms or secondary cystic change in malignancies like ductal adenocarcinomas.<sup>[2]</sup> The true nature of cystic lesions of pancreas, now being increasingly detected due to advanced imaging modalities can only be made by a thorough histopathological evaluation. When compared to the most common ductal adenocarcinoma of pancreas, Pancreatic Cystic Neoplasms (PCNs) have a favourable prognosis and many a lesions can be cured by surgical resection alone.<sup>[3]</sup> There are a few cystic tumors of the pancreas which are classified under tumors of low malignant potential. Of these solid pseudopapillary tumor is a rare tumor reported mostly in young females. The histogenesis of this tumor is unknown. There are occasional case reports of recurrence of this tumor after surgical resection.<sup>[1,4]</sup>

The incidence of pancreatic resections for cystic lesions of pancreas is on rise. Studies on the distribution of pancreatic cystic lesions and its pathological features are

few. Histopathology is the gold standard for categorizing non-neoplastic and neoplastic cystic lesions and to further grade the neoplastic lesions. Studies on cystic pancreatic lesions have not been conducted in North Kerala. Aim of the study is to categorize various cystic lesions in pancreatic resection specimens and to study the clinicopathological features of pancreatic cystic lesions.

## Materials and Methods

During the period from January 2013 to December 2016, 91 patients had undergone pancreatic resection in Academy of Medical sciences, Pariyaram. There were 15 cases of cystic lesions of pancreas in the 91 pancreatic resections which formed the subject of the present study.

All resected cases were received in 10% buffered formalin. Partial sectioning after inking of resected margin was done to aid fixation. After fixation, specimens were sliced, grossly examined and relevant areas sectioned for tissue processing. All paraffin embedded blocks obtained after processing were sectioned and stained with hematoxylin and eosin (H&E) for histopathological examination.

Statistical analysis used: Descriptive statistics like frequency, percentage, mean and median.

## Result

Of the 91 pancreatic resections there were 66 Whipple's resections, 23 distal pancreatectomy with splenectomy, 1 total pancreatectomy and 1 cystectomy. M:F ratio was 1.46 :1 with age range of 14-85 years. Of these there were 24 non-neoplastic lesions, 9 benign neoplasms, 3 neoplasms of low malignant and 55 malignant neoplasms. Benign and borderline neoplasms showed female preponderance while malignant lesions showed male predominance with majority of the patients being above 60 years of age. (Table: -1)

In the 15 cystic pancreatic lesions there were 4 non-neoplastic cysts and 11 neoplastic cysts. M:F ratio was 1:2.75 with age range of 14-67 years. For non-neoplastic cysts the M:F ratio was 3:1 and for neoplastic cysts the M:F ratio was 1:10. (Table: -2)

In the neoplastic cyst category serous cystadenomas predominated with 3 microcystic types and 1 macrocystic type. All the 4 patients were females with age range of 42-62 years. The tumor was located in the head of pancreas in a case of microcystic serous tumor. In all other cases it was in the tail of pancreas. Microcystic types showed multiple small cysts with sponge like cut surface and central scar, size ranged from 6-10cms. (Figure: -1a) Microscopy showed small cystic spaces lined by bland cuboidal cells with clear cytoplasm and sparse stroma in between the cysts (Figure: - 1b, c, d). Macrocystic type had uniloculated cyst which measured 6 cms and microscopy showed lining by bland cuboidal epithelium.

The next frequent cystic neoplasm was solid papillary pseudotumor. All the 3 patients were females with tumors located in the tail of pancreas and age ranged from 14-40 years. All the lesions were encapsulated with solid and cystic areas, tumor size ranged from 4-10 cms. (Figure:-2a) Microscopy showed solid areas with small cells showing bland nuclei, nuclear grooves, moderate amount of eosinophilic to clear cytoplasm and dyshesive tumor

cells forming pseudopapillae. Foci with sheets of foamy macrophages and cholesterol clefts were identified in 2 cases. (Figure: -2b, c, d)

There were 2 mucinous cystadenomas both in females aged 43 years and 58 years and the tumors were located in the tail of pancreas. The first patient had a 13x11cms multiloculated cyst filled with jelly like material and the second patient had a 4x3cms biloculated cyst. Both the cases showed cyst wall lined by mucinous epithelium without atypia and subepithelial ovarian like stroma. (Figure: -3)

The single case of intestinal type main duct intraductal papillary mucinous neoplasm (MD-IPMN) with invasive adenocarcinoma was seen in a 67 year old male. Total pancreatectomy done showed marked dilatation involving the whole length of main pancreatic duct with mucinous material and multiple gray white solid papillary lesions filling the dilated duct. (Figure:-4a,b) Microscopy showed a tumor with intraductal complex papillary architecture lined by intestinal type columnar epithelium with severe dysplasia and focal areas of invasive malignancy. (Figure:-4c,d)

Branch duct IPMN with low grade dysplasia was identified in Whipple's resection specimen in a 60 year old female. Gross examination showed 2.5x2cms mucin filled cyst in the head of pancreas and mildly dilated pancreatic ducts. Microscopy showed gastric type mucinous epithelium with focal papillary pattern and minimal atypia.

There were 4 non-neoplastic cysts all of which were pseudocysts of pancreas. M:F ratio was 3:1 and the age range was 30-45 years. Gross examination showed thick walled cyst with intraluminal brownish fluid and ragged inner surface in all the cases. Size ranged from 3-10cms. Microscopy showed fibrous cyst wall and granulation tissue without any lining epithelium. Associated chronic pancreatitis was seen in 2 cases. (Figure: - 5)

**Table 1: Clinicopathological spectrum in pancreatic resections.**

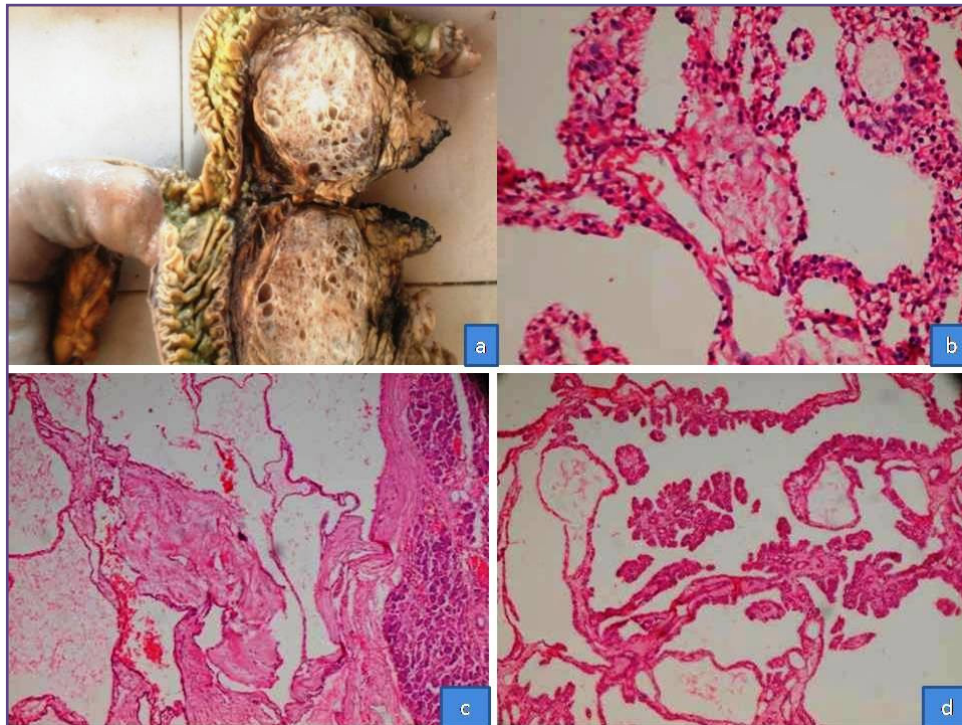
	Diagnosis	No. of cases	Sex		Age group (in years)				% of cases
			M	F	10-20	21-40	41-60	>60	
<b>I</b>	<b>Non-neoplastic lesions</b>	<b>24</b>	<b>19</b>	<b>5</b>	<b>-</b>	<b>7</b>	<b>15</b>	<b>2</b>	<b>26.4</b>
<b>a</b>	Chronic pancreatitis	20	16	4	-	3	15	2	
<b>b</b>	Chronic pancreatitis with pseudocyst	2	1	1	-	2	-	-	
<b>c</b>	Pseudocyst	2	2	-		2	-	-	
<b>II</b>	<b>Neoplastic lesions</b>	<b>67</b>							<b>73.6</b>
<b>1.</b>	<b>Benign</b>	<b>9</b>	<b>1</b>	<b>8</b>	<b>-</b>	<b>-</b>	<b>7</b>	<b>2</b>	<b>9.9</b>

	Diagnosis	No. of cases	Sex		Age group(in years)				% of cases
			M	F	10-20	21-40	41-60	>60	
a	Serous cystadenoma	4	-	4	-	-	2	2	
b	Tubulovillous adenoma-ampulla	2	1	1	-	-	2	-	
c	Mucinous cystadenoma	2	-	2	-	-	2	-	
d	IPMN with low grade dysplasia	1	-	1	-	-	1	-	
<b>2.</b>	<b>Low malignant potential</b>	<b>3</b>	<b>-</b>	<b>3</b>	<b>1</b>	<b>2</b>	<b>-</b>	<b>-</b>	<b>3.3</b>
a	Solid pseudopapillary tumor	3	-	3	1	2			
<b>3.</b>	<b>Malignant</b>	<b>55</b>	<b>34</b>	<b>21</b>	<b>-</b>	<b>2</b>	<b>21</b>	<b>32</b>	<b>60.4</b>
a	Ductal adenocarcinoma	39	26	13	-	2	16	21	
b	Neuroendocrine carcinoma	2	1	1	-	-	1	1	
c	Mixed adeno-neuroendocrine carcinoma	4	2	2	-	-	3	1	
d	Adenosquamous carcinoma	2	-	2	-	-	-	2	
e	Ampullary carcinoma	3	1	2	-	-	-	3	
f	IPMN with adenocarcinoma	1	1	-	-	-	-	1	
g	Metastatic disease/infiltration	4	3	1	-	-	1	3	

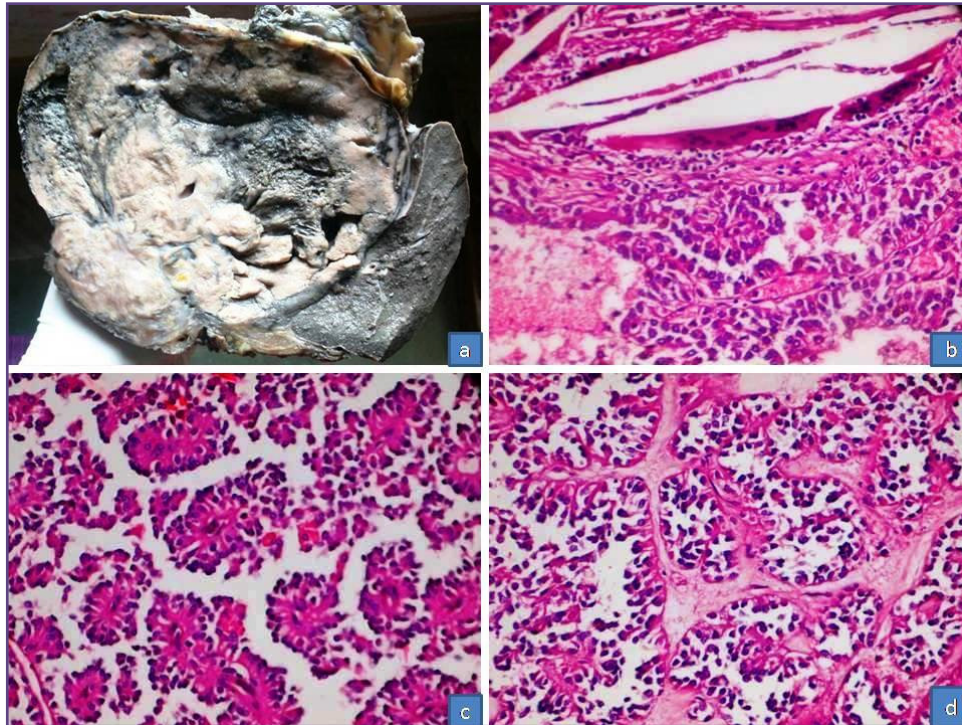
**Table 2: Clinicopathological spectrum of pancreatic cystic lesions.**

	Age/Sex	Type of resection	Diagnosis
1	40/F	Distal pancreatectomy & splenectomy	Solid papillary pseudotumor
2	30/M	Distal pancreatectomy & splenectomy	Pseudocyst with chronic pancreatitis
3	14/F	Distal pancreatectomy & splenectomy	Solid papillary pseudotumor
4	43/F	Distal pancreatectomy & splenectomy	Mucinous cystadenoma
5	67/M	Total pancreatectomy	Intestinal type MD-IPMN with invasive adenocarcinoma
6	36/F	Distal pancreatectomy & splenectomy	Solid papillary pseudotumor
7	62/F	Distal pancreatectomy & splenectomy	Microcystic serous cystadenoma
8	42/F	Whipple's resection	Microcystic serous cystadenoma
9	62/F	Distal pancreatectomy & splenectomy	Microcystic serous cystadenoma
10	48/F	Distal pancreatectomy & splenectomy	Macrocystic serous cystadenoma
11	39/M	Cystectomy	Pseudocyst
12	36/M	Whipple's resection	Pseudocyst with chronic pancreatitis
13	45/F	Distal pancreatectomy & splenectomy	Pseudocyst
14	60/F	Whipple's resection	IPMN with low grade dysplasia
15	58/F	Distal pancreatectomy & splenectomy	Mucinous cystadenoma

MD-IPMN : Moderately differentiated intraductal papillary mucinous neoplasm; F-female; M-Male.



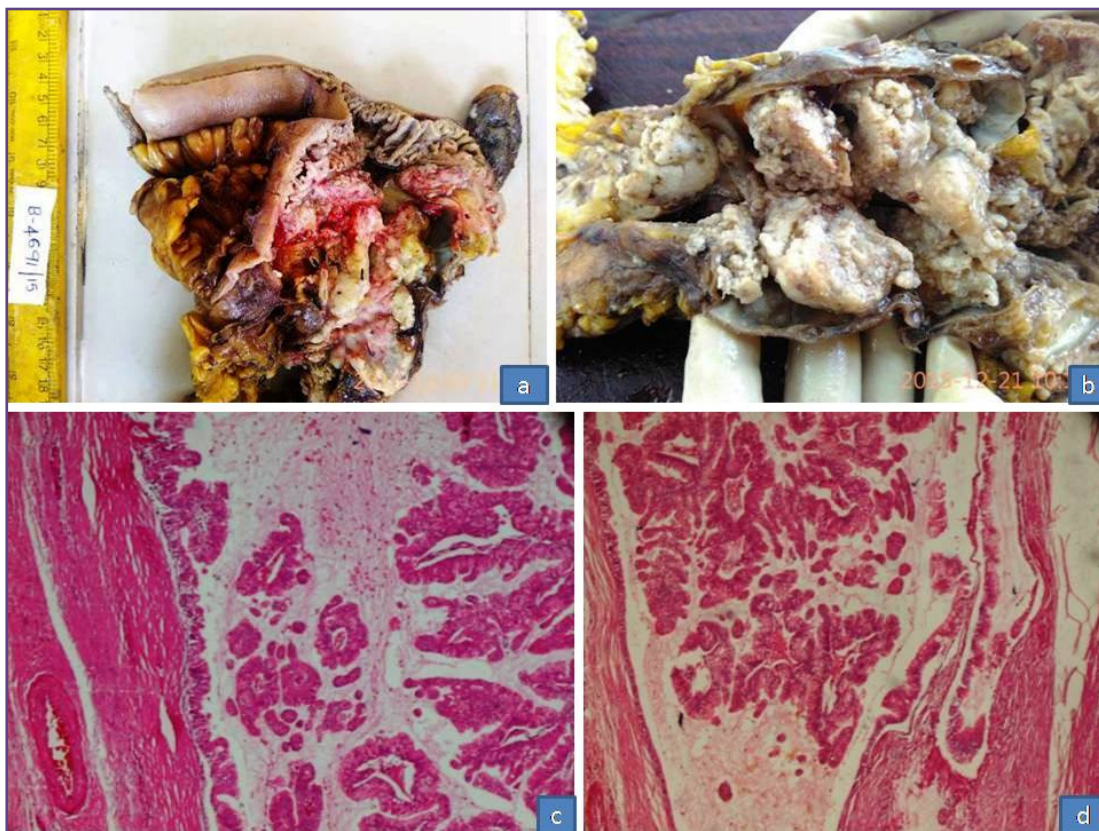
**Fig. 1: Microcystic serous cystadenoma :a-Whipple's resection specimen with a circumscribed tumor of sponge like consistency with microcysts in head of pancreas; b,c&d- Photomicrograph showing small cystic spaces lined by bland cuboidal cells with clear cytoplasm (H&E-10x).**



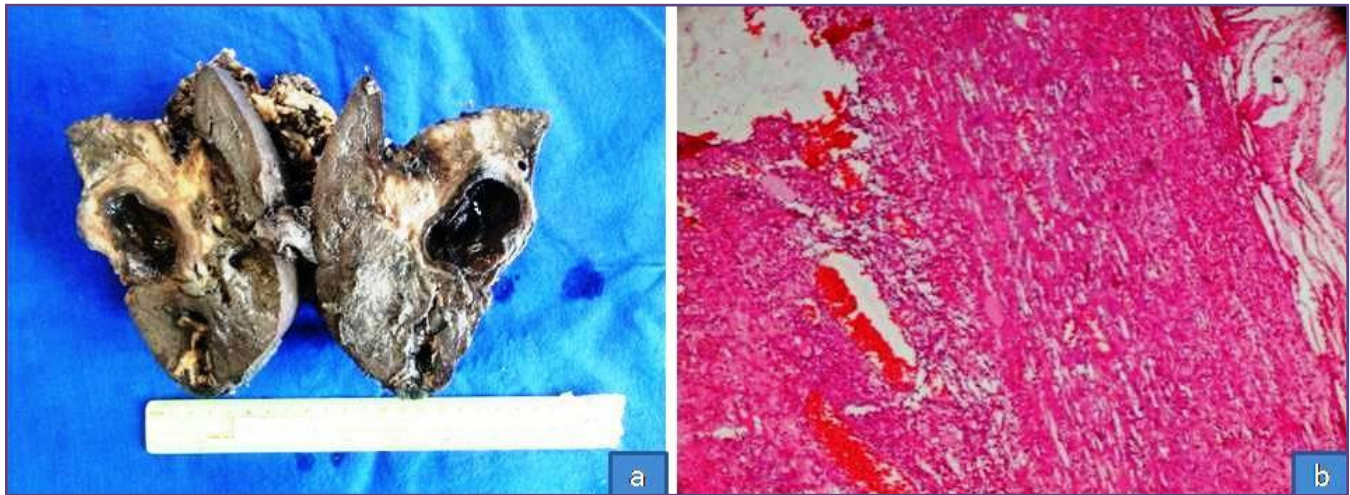
**Fig. 2: Solid Pseudopapillary Tumor- a)Distal pancreatectomy with splenectomy,encapsulated tumor with solid and cystic areas in tail of pancreas;b,c & d)Photomicrograph showing bland,dyshesive cells forming pseudopapillae.Cholesterol clefts and collections of foam cells noted in b(H&E-40x).**



**Fig. 3:** mucinous cystadenoma. Gross- Distal pancreatectomy with splenectomy, multiloculated cyst with jelly like material in tail of pancreas .Photomicrograph- cyst lined by mucinous epithelium without atypia and subepithelial ovarian like stroma.(H&E-40x).



**Fig. 4:** Invasive adenocarcinoma in IPMN .a&b)Total pancreatectomy - markedly dilated main duct, mucinous material and multiple gray white solid papillary lesions filling the dilated duct;c&d)photomicrograph showing intraductal complex papillary architecture lined by intestinal type columnar epithelium with severe dysplasia and areas of invasive malignancy. (H&E-40x).



**Fig. 5: Pancreatic pseudocyst.a(gross)- Distal pancreatectomy with splenectomy ,thick walled cyst in tail of pancreas. b(photomicrograph) - fibrous cyst wall and granulation tissue without any lining epithelium.(H&E-40x).**

### Discussion

A variety of non- neoplastic, benign and malignant cystic lesions can occur in the pancreas. Pathologically, pancreatic cystic lesions are classified into simple retention cysts, pseudocysts and cystic neoplasms. The non-neoplastic cysts are further divided into epithelial cysts and non-epithelial or pseudocysts. Non-neoplastic pancreatic cysts may mimic neoplastic cysts on radiology.<sup>[1]</sup> So such cysts may be encountered in pathological practice, the non-neoplastic nature of which is confirmed by histopathology. Pseudocysts are the most common non-neoplastic cysts of the pancreas and have a strong association with chronic pancreatitis. Other less frequently encountered non-neoplastic cysts include lymphoepithelial cysts, epidermoid cysts and infectious cysts.<sup>[6]</sup>

In contrast with solid tumors of pancreas, most of which are ductal adenocarcinomas with grave outcomes, the vast majority of cystic neoplasias are either benign tumors or low-grade malignancies with indolent behaviour.<sup>[7]</sup> Cystic tumors constitute 5-10% of all pancreatic neoplasms. Most common true cystic neoplasms of the pancreas are serous cystic neoplasms. Mucinous cystic neoplasms (MCN) are the second commonest and is seen almost exclusively in perimenopausal females. Invasive carcinoma may develop in MCNs.<sup>[8]</sup> So extensive sampling is warranted. Other rare true cystic neoplasms are intraductal papillary mucinous neoplasms and solid papillary pseudotumors.

Cystic change can rarely be seen in ductal adenocarcinoma which is the commonest pancreatic tumor. It may be due to central necrosis, cystic dilatation of distally located obstructed ducts or due to cystic dilatation of infiltrating tubular units.<sup>[2]</sup>

Serous cystadenomas are benign tumors. Because of the presence of abundant intracytoplasmic glycogen rendering clear cell morphology to the lining cells they are also known as glycogen rich cystadenomas.<sup>[9]</sup> Patients may present with abdominal pain or with incidentally detected lesion on radiological evaluation. Tumors can occur anywhere in the pancreas with a predilection for body and tail. Grossly the tumors are well circumscribed with central scar and spongy cut surface. Microscopy show multiple cystic spaces lined by cuboidal cells with clear cytoplasm.<sup>[9,10,11]</sup>

Serous cystadenocarcinomas are extremely rare tumors with less than 20 cases reported so far. The gross features and cytoarchitecture of this tumor is indistinguishable from serous cystadenomas. In the one case reported by Van Dyke et al patient had liver metastasis at the time of resection. The resected tumor was well circumscribed, measured 15.5x12cms and on microscopy demonstrated the typical cytoarchitecture of serous cystadenoma except for rare foci of perineural invasion. There is no definite histopathological criteria to diagnose cystadenocarcinoma though vascular and perineural invasion and direct invasion into adjacent structures indicates a locally aggressive disease and malignant potential. The diagnosis of malignancy can only be established by the clinical behaviour of the neoplasm (metastatic disease). All cystadenocarcinomas reported are >4cms in diameter. So serous cystic tumors more than 4cms should be considered for resection.<sup>[12]</sup>

Mucinous cystic neoplasms of the pancreas almost exclusively occur in women predominantly in the body and the tail of pancreas, with peak incidence in fifth decade.<sup>[8]</sup> MCNs are defined by the World Health Organization (WHO) as cystic epithelial neoplasms that

occur almost exclusively in women; do not communicate with the pancreatic ductal system and which are composed of columnar, mucin-producing epithelium, supported by ovarian-type stroma. These tumors are classified into MCN with mild dysplasia (adenoma), with moderate dysplasia (borderline neoplasm), with high grade dysplasia and MCN with invasive carcinoma. The prevalence of invasive cancer in MCN is low. [13] MCN have low biologic aggressiveness and the prognosis is much better than that of ductal carcinoma. [14]

Intraductal Papillary Mucinous Neoplasms (IPMN) are cystic tumors of the pancreas and occur mainly in elderly males. It may involve the main duct (MD) or the branch duct (BD) of the pancreas, produce mucin and show papillary differentiation. [15] According to the site of involvement it is classified into MD, BD and combined types. MD-IPMN show segmental or diffuse dilatation of MPD > 5mm in the absence of other causes of obstruction. [16]

MD-IPMNs when compared to BD-IPMNs have higher malignant potential. WHO classifies IPMN into those with low grade dysplasia, intermediate grade dysplasia and high grade dysplasia. Four histological types have been identified—the gastric, intestinal, pancreaticobiliary and oncocytic type. Intestinal type IPMNs are usually MD type lesions and gastric type IPMNs are usually BD type lesions. [17] Intestinal type lesions have a higher histological grade. As per International consensus guidelines 2012 the type of invasive carcinoma developing in IPMN, colloid versus tubular should be mentioned in reporting as it has prognostic implications. Colloid carcinomas show intestinal differentiation (CDX2 & MUC2 positive) and have better prognosis. The gastric type is low grade (MUC5AC positive, MUC1 negative) and only a small percentage progress to invasive malignancy which is of tubular type. Oncocytic type show complex papillae lined by 1-5 layers of cuboidal cells. One distinctive feature of this histological type is the presence of intraepithelial lumina containing mucin giving the tumor a cribriform architecture. Pancreaticobiliary type is considered to be a high grade version of gastric type and may progress to tubular carcinoma. Tumors may express MUC1 a marker for aggressive behaviour in pancreas. [18]

Differential diagnoses of IPMN include MCN, retention cyst and Pancreatic intraepithelial neoplasia (PanIN). MCNs do not communicate with the pancreatic duct and have subepithelial ovarian like stroma. PanINs are microscopic lesions not visible on gross examination. [19] Schmidt CM et al recommended surgery for all fit patients with MD-IPMN and for BD-IPMN with mural nodularity or positive cytology irrespective of size or location to lower the risk of invasive carcinoma. [20]

Solid papillary pseudotumor (SPPT) is a rare tumor usually seen in young females and frequently in the tail of pancreas though it can occur anywhere in the pancreas. The histogenesis of this tumor is unknown and lack definite endocrine or exocrine differentiation. [4] Tumors are usually encapsulated with solid, cystic and hemorrhagic areas. They are tumors of low grade malignant potential and complete surgical excision is the treatment of choice with excellent prognosis. There are a few case reports of local recurrence and distant metastasis in SPPT. Diagnosis of SPPT should be considered in young females with pancreatic mass. [21,22]

Other rare cystic tumor of pancreas is cystic acinar cell tumor which includes acinar cell cystadenoma and acinar cell cystadenocarcinoma. Prognosis is same as that for regular acinar cell tumor. [23]

## Conclusion

Cystic tumors of the pancreas are significantly less frequent than solid tumors. Though the incidence of non-neoplastic lesions like chronic pancreatitis and malignancies like ductal carcinoma of pancreas show male predominance cystic tumors of pancreas have a very high female preponderance. Majority of PCNs are benign. Solid papillary pseudotumors present at a relatively younger age when compared to other PCNs. In females presenting with cystic pancreatic mass on radiological examination the possibility of cystic tumors of pancreas should always be kept in the differential diagnosis as these tumors have a very favourable outcome and surgical resection is curative in most of the cases.

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