



## **A Rare Large Cystic Tumour of Pancreas – A Case Report and Literature Review**

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### **Authors' contributions**

*This work was carried out in collaboration between both authors. Author MP is the primary consultant who performed the surgery and responsible for patient care. Author SB helped during surgery and patient care. Author MP is responsible for the manuscript preparation and submission. Both authors reviewed the manuscript and approved the final manuscript.*

### **Article Information**

#### Editor(s):

(1) Dr. Luis Ricardo Martinhao Souto, Universidade de Marília (UNIMAR), Sao Paulo State, Brazil.

#### Reviewers:

(1) Mahrukh Kamran, Dow University of Health and Sciences, Pakistan.

(2) Shigeki Matsubara, Jichi Medical University, Japan.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/56508>

**Case Report**

**Received 16 February 2020**

**Accepted 21 April 2020**

**Published 27 April 2020**

### **ABSTRACT**

Pancreatic Neuroendocrine tumours usually manifest as solid tumours. Cystic Pancreatic Neuroendocrine tumours are rare entities, which pose diagnostic challenges. Their clinical and pathological features are not well characterized. Here, we report a cystic Pancreatic Neuroendocrine tumours case, together with literature review, highlighting the features of this tumour. A 62-year-old female presented with vague abdominal symptoms and was subsequently found to have large cystic lesion arising from the head of pancreas, compressing the portal and superior mesenteric vein. She underwent pylorus preserving pancreaticoduodenectomy. Histology confirmed grade III Pancreatic Neuroendocrine tumours. No postoperative complications were observed. It is not yet confirmed whether cystic Pancreatic Neuroendocrine tumours are due to necrosis/degeneration of solid Pancreatic Neuroendocrine tumours or a distinct clinical entity with different characteristics. Irrespective of this discussion, cystic Pancreatic Neuroendocrine tumours shows clinically and pathologically distinct features. Awareness and proper recognition will help in their diagnosis. Resection is the treatment of choice. Further genetic/molecular studies will much more characterize this tumour, thereby broadening the treatment options.

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**Keywords:** Cystic pancreatic neuroendocrine tumours; mucinous cystic neoplasm; intraductal papillary mucinous neoplasm.

## ABBREVIATION

MCN	: Mucinous cystic neoplasm
IPMN	: Intraductal papillary mucinous neoplasm
CBD	: Common bile duct
MPD	: Main pancreatic duct
SMA/SMV	: Superior mesenteric artery/vein
PV	: Portal vein
SV	: Splenic vein
EUS	: Endoscopic ultrasound scan

## 1. INTRODUCTION

Pancreatic neuroendocrine tumours (PanNETs) are typically solid neoplasms but in rare instances may present as cystic lesions [1]. This unusual cystic appearance make radiologic differentiation from other cystic pancreatic neoplasms difficult and can make clinical diagnosis challenging [2]. Similar to solid PanNETs, cystic PanNETs develop with an equal sex distribution and over a wide age range (23 to 91 y; mean, 52 y) [3,4]. In addition, the clinical

and histopathologic characteristics of cystic PanNETs are poorly defined [1]. Here with we present a case of successfully treated large cystic neuroendocrine tumour of the pancreas.

## 2. CASE REPORT

62 years old pleasant lady presented to us with colicky abdominal pain over a period of 2 months. She has no significant past medical history apart from peurperal sterilisation. She consulted a GP outside and was treated as dyspepsia. Since her symptoms did not improve after few weeks she had an ultrasound scan. The ultrasound scan showed a large cystic lesion in the abdomen, probably arising from the pancreas. Hence she was referred to our tertiary care HPB unit.

On clinical examination, she was obese with stable vitals. There was no pallor, jaundice, generalised lymphadenopathy. Abdominal examination showed palpable mass in the right hypochondrium. We organized a CT scan of chest, abdomen and pelvis.



**Fig. 1.** Large cystic lesion at the head with atrophic pancreas and dilated duct



**Fig. 2. Large cystic lesion of pancreas compressing portal and superior mesenteric vein (bold arrows)**

CT scan of the abdomen showed - There is well-defined hypodense lesion with irregular enhancing wall (upto 1.3 cm thick) is seen in the head and uncinate process of the pancreas, measuring 10 x 10.3 x 12 cm (Fig. 1). No calcification / enhancing septa / scar. In the medial aspect the lesion causes significant narrowing of PV/SMV (approximately 9cm) with loss of fat plane (Fig. 2). SMA is seen separately. The lesion causing mass effect over the proximal CBD causing upstream dilation of CBD (diameter

1.5 cm) and central intrahepatic biliary radicals. CT chest – did not reveal any distant metastases. All her labs including CA19-9 level, were within normal limits. With the provisional diagnosis of mucinous cystic neoplasm – she was counseled for whipple's procedure.

### **3. PROCEDURE**

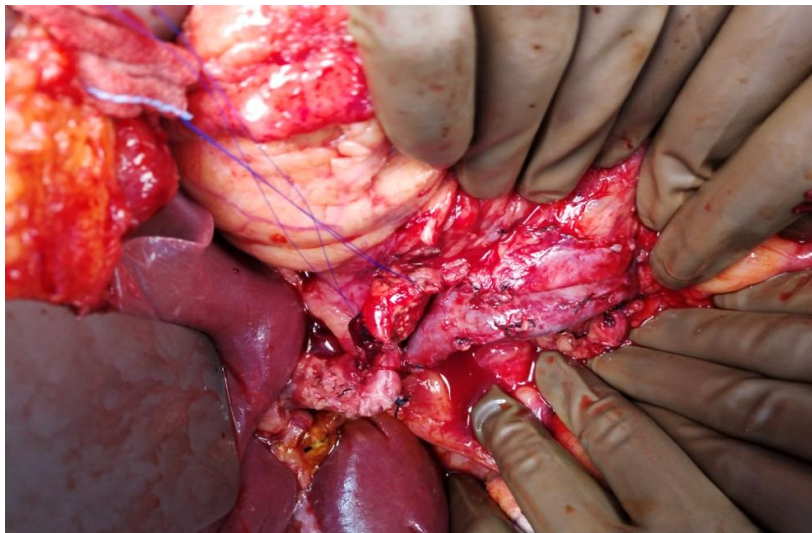
She had initial laparoscopy – to rule out peritoneal disease. Then her abdomen was

opened with roof top incision. Intraoperative findings as follows:

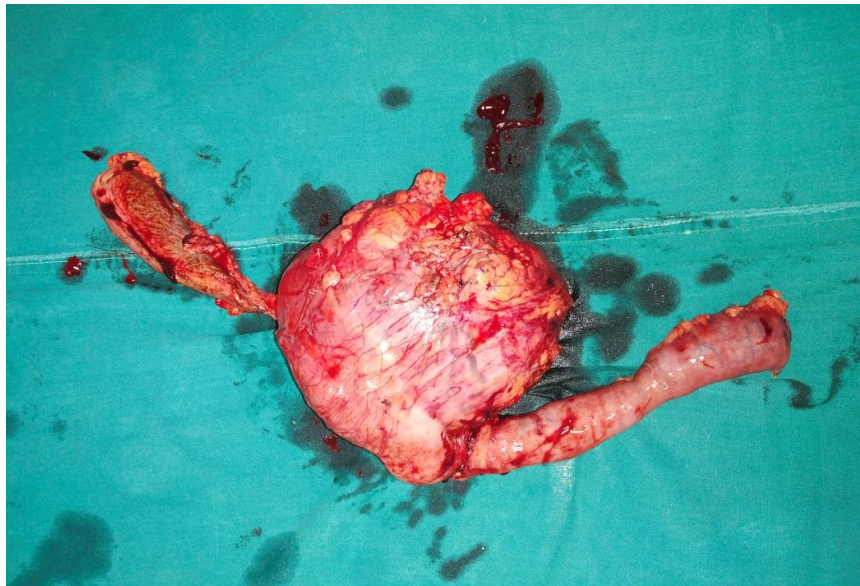
- Large cystic lesion arising from the head of the pancreas compressing PV and SMV.
- Large branch from SMV supplying the lesion – required resection and suturing the defect in SMV.
- Mesocolon adherent to the cystic lesion – middle colic vessels ligated.
- Thin walled gall bladder with multiple stones and dilated CBD.
- Firm pancreas with dilated MPD (4-5 mm).

- Few hepato-dudoenal lymphnodes.
- Paraumbilical hernia – omentum as content.
- No evidence of liver/peritoneal metastases or free fluid in the abdomen.

Patient underwent successful pylorus preserving pancreatico duodenectomy (PPPD). Even though, the portal vein and SMV were adherent to the tumour, they were released completely without any oncological compromise (Fig. 3) and the whole tumour was removed (Fig. 4). Standard reconstruction was performed.



**Fig. 3. Intraoperative picture showing released PV/SMV/SV**



**Fig. 4. Resected specimen**

#### 4. HISTOLOGY

Pathological examination shows a tumour in the head of pancreas. The tumour is encapsulated with a thick capsule and focal capsular dehiscence involved by tumour. The tumour is composed of sheets, trabeculae and acinar pattern of arrangement with delicate rich vascular network. The cells are relatively uniform and show finely granular amphophilic to eosinophilic cytoplasm, centrally located round to oval coarsely clumped nucleus with distinct nucleolus. Mitosis upto 3/2 mm<sup>2</sup> is seen. Tumour necrosis, haemorrhagic areas are seen and central areas show cystic degeneration with cystic and hemosiderin laden macrophages. All margins clear of tumour. 21 lymphnodes found and were free of tumour.

##### 4.1 Immuno Histo Chemistry Markers

Synaptophysin	: Immunoreactive in tumour cells (3+)
Chromogranin	: Immunoreactive in tumour cells (3+)
NSE	: Immunoreactive in tumour cells (3+)
CD-56	: Immunoreactive in tumour cells (3+)
Pan CK	: Immunoreactive in tumour cells (2+)
Ki-67	: 24 %

Immunohistochemistry confirmed this lesion as pancreatic neuroendocrine tumour (Pan NET, G3)

Her postoperative period was uneventful and she was successfully discharged on Day 6. Her case was discussed in tumour board and decided for adjuvant therapy. She received adjuvant chemotherapy. On 18 months follow up with PET-CT imaging – she is doing well with no evidence of recurrence.

#### 5. DISCUSSION

Pancreatic neuroendocrine tumours (PanNETs) are rare neoplasms that comprise up to 5% of pancreatic malignancies. These neoplasms have an estimated incidence of 4 to 5 individuals per 100,000 per year in the United States [5]. However, their incidence is increasing, likely due to advancements and increased use of radiographic and endoscopic imaging [6]. The classification of PanNETs is complex and

generally subdivided into either functional (hormone secreting) or nonfunctional. In addition, tumour size and histologic grade, as defined by the proliferation rate, are prognostically important. The majority of PanNETs are nonfunctional and, as a result, frequently go undiagnosed until late in their clinical course. Although PanNETs are typically solid, in rare instances these tumours present as cystic lesions. Grossly the size varies from 1cm to 18 cm. It is generally assumed that cystic PanNETs are the result of tumour necrosis within solid PanNETs. Thus, they are thought to be similar in biological behaviour and malignant potential to their solid counterparts. But conflicting reports suggest that cystic PanNETs represent a distinct entity rather than a morphologic variant. In fact, several studies have found cystic PanNETs to be more frequently associated with multiple endocrine neoplasia type 1 (MEN-1) and less aggressive than their solid counterparts [7-9].

Since its original description by Thigpen in 1940, [10] subsequent studies have been conflicting as to whether cystic PanNETs represent a distinct biological entity or are formed by necrosis and degeneration. The etiology of cystic PanNETs remains controversial, and several theories have been put forth. 1) Slow-growing PanNETs develop a fibrous capsule that eventually restricts the blood supply to the tumour, resulting in infarction and necrosis. 2) Cystic change or necrosis correlated with large tumour size 3) Haemorrhage within the tumour is the inciting event in cyst development. 4) Alternatively, cyst development may be related to an FNA. 5) Exomic sequencing has identified a subset of PanNETs with recurring mutations in MEN-1, DAXX/ATRX, and the mTOR pathway. Thus, it is not unreasonable to assume that an underlying genetic etiology may be responsible for cystic PanNETs [1].

Cystic PanNETs were typically sporadic (91%), nonfunctional (91%), solitary (87%), and were discovered incidentally (62%). In comparison with their solid counterparts, cystic PanNETs were more frequently found in the tail (53% vs. 36%). In addition, cystic PanNETs were less likely to demonstrate tumour necrosis, perineural invasion, vascular invasion, regional lymph node metastases, and synchronous distant metastases compared with solid PanNETs. Prognostically, they present at a lower pathologic stage using both the AJCC and ENETS staging systems and decreased Ki-67 proliferation index compared with solid PanNETs.

However, whether these prognostic predictors are valid for cystic PanNETs remains to be proven [1].

Although some studies have reported that a hyper vascular rim could identify cystic Pan NETs preoperatively, accurate preoperative diagnosis of cystic PanNETs was reported to be only 23% [11]. MRI may perform better than CT for detecting ductal communication in pancreatic cysts, that usually is not considered as a cystic pancreatic neuroendocrine tumours feature [2]. The relatively low resolution of cross sectional imaging compared with EUS precludes the ability to separate cystic Pan NETs from other cystic neoplasms [12,13]. Concurrently, the improvement in endoscopic techniques has allowed nonsurgical sampling and evaluation by endoscopic ultrasound-guided fine-needle aspiration biopsy. Due to the high rate of diagnostic accuracy and low rate of complications, EUS has become an integral part of the preoperative assessment of pancreatic cysts. The most important advantage with endoscopic ultrasound is the possibility to obtain tissue and fluid samples from the cysts helpful for the assay of tumour markers such as CEA, enzymes like amylase, molecular markers and cytology. All of these are essential for the achievement of a correct preoperative diagnosis and an appropriate tumour management [2].

The primary difficulty was distinguishing cystic PanNETs from other cystic neoplasms of the pancreas such as IPMN or MCN. As the clinical management for different cystic neoplasms of the pancreas varies, preoperative diagnosis is of utmost importance. Both main duct-IPMNs and MCNs can be associated with an invasive ductal adenocarcinoma [10,14,15]. Recent exomic sequencing of PanNETs has identified a subset of tumours harboring mutations within the mammalian target of rapamycin (mTOR) pathway [16]. The mTOR pathway inhibitor, everolimus, has been shown to increase progression-free survival in a subset of PanNET patients [17]. Hence, in the future, patients with PanNETs may be treated with targeted therapies inappropriate for IPMNs and MCNs.

Since the cystic PanNETs pose diagnostic challenge it is advisable to resect these lesions. Their high resectability rate supports the role of surgical approach and complete resection is actually the treatment of choice for cystic PNETs. Accurate preoperative diagnosis is important for patient management as “watch-and-wait”

approach could be highly risky in patients with pancreatic mass lesions.

## 6. CONCLUSION

In summary, cystic PanNETs are a distinctive subgroup of PanNETs with unique clinical and pathologic features. Because of their cystic nature, these neoplasms often present a diagnostic dilemma to both the experienced radiologist and pathologist. Awareness and proper recognition of these entities including their associated findings can aid in their diagnosis. Resection is the treatment of choice. Future genetic and molecular studies should help shed light on the pathogenesis and expand the treatment strategies for these neoplasms.

## CONSENT

Patient and family has given consent for medical publication of images and other clinical information.

## ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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*Peer-review history:*  
*The peer review history for this paper can be accessed here:*  
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