CASE REPORT

Diffuse Pancreatic Mucinous Cystic Neoplasm Treated by Total Pancreatectomy

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ABSTRACT

Context Multifocal or diffuse mucinous cystic neoplasm are uncommon and may be difficult to distinguish from multifocal intra-ductal mucinous neoplasm or diffuse serous cystadenoma. Case report A forty-seven-year old lady with vague abdominal pain was noted to have cystic lesions ranging from 5 to 20 mm throughout her pancreas. The cysts had enlarged over several years of observation. There was no evidence of pancreatic duct dilatation or communication with the pancreatic duct on magnetic resonance imaging. Cyst fluid analysis for carcinoembryonic antigen and amylase were non-diagnostic. A total pancreatectomy was performed, with histology confirming numerous cysts lined by mucus producing cells, without obvious ovarian-like stroma. The stroma did however demonstrate positive staining for oestrogen receptor and smooth muscle actin. These findings were most consistent with a mucinous cystic neoplasm, despite the apparent absence of typical ovarian like stroma. Conclusion Multifocal or diffuse pancreatic mucinous cystic neoplasm are uncommon and may be suspected when imaging demonstrates multiple pancreatic cysts without communication with the pancreatic duct or pancreatic duct dilatation. Surgical resection is indicated due to the increased risk of malignancy.

INTRODUCTION

Mucinous cystic neoplasm (MCN) of the pancreas constitute approximately 2% to 5% of all pancreatic tumours and 10% of all pancreatic cystic neoplasm [1]. They are typically seen in females 40 to 50 years of age. The lesions are most often present in the body or tail of the pancreas and are rarely multifocal [2]. They are considered pre-malignant tumours, with the risk of malignancy correlating with increasing age, size and presence of solid nodules [3]. The risk of invasive cancer is considered to be less than 15%, with virtually no malignancy in MCNs less than 4 cm without mural nodules [4, 5]. It is unclear whether the risk of malignancy is greater in the setting of multifocal MCNs. Multifocal cystic lesions involving the pancreas are most commonly noted in the setting of side-branch intraductal papillary mucinous neoplasms (IPMN) [2]. Magnetic resonance imaging of the pancreas usually demonstrates communication between the main pancreatic duct and the cysts, which can be diagnostic. Multifocal or diffuse pancreatic cystic lesions may occur in patients with serous cystadenomas (SCA). Diffuse involvement of the pancreas by SCA is recognized in association with von Hippel-Lindau (VHL) syndrome [6]. Diffuse involvement of the pancreas by MCN, to our knowledge, has not been described. Therefore, we describe a case of multifocal pancreatic cysts involving the entire pancreas. This patient was treated by surgical resection, and histology showed features most in keeping with diffuse MCN.

CASE REPORT

A forty-seven-year old female with intermittent abdominal pain and recently diagnosed diabetes underwent computed tomography (CT) that revealed diffuse cystic involvement of the pancreas. She had no history of definitive pancreatitis and blood tests including full blood examination, liver function tests, and urea and electrolytes were within normal levels. Serum calcium and lipase levels were also normal. Serum tumour markers including carcinoembryonic antigen (CEA), carbohydrate antigen (CA-19.9), and chromogranin A were within normal limits. The cysts involved the entire pancreas, with the pancreatic body measuring 37 mm in maximum thickness on abdominal CT imaging. The cyst had enlarged when compared to a maximum pancreatic body thickness of 28mm on CT imaging performed 2 years earlier for a similar complaint. She had been lost to follow-up after the initial diagnosis of pancreatic cysts.

Her medical history included diet controlled diabetes of 12 months duration, without obvious risk factors. She had hyperthyroidism related to a non-specific thyroiditis, treated several months earlier by total thyroidectomy. She was investigated for possible pheochromocytoma given a history of intermittent tachycardia and hypertension, with
the finding of normal serums and urinary catecholamines. With the finding of diffuse cystic involvement of the pancreas, the possibility of VHL was considered. Genetic testing however excluded VHL Syndrome. There was also no clear history suggestive of pancreatic exocrine insufficiency.

Magnetic resonance cholangiopancreatography (MRCP) was performed with no evidence of cyst communication with the pancreatic duct and no evidence of solid nodules (Figure 1). Endoscopic ultrasound performed showed similar findings with a zero CEA level on aspiration and an amylase level of 365 IU/L. Mucin could not be demonstrated in the aspirate. Given the findings of enlarging cysts, recent diagnoses of diabetes, with the risk of concurrent pancreatic malignancy the patient was offered a total pancreatectomy.

Macroscopically the pancreas measured 150x48x20mm. Multiple cysts five to 20mm diameter was present throughout. The pancreatic duct was not dilated measuring 2 to 3mm diameter. No communication between the cysts and the pancreatic duct was demonstrated (Figure 2).

On histology dilated cystic spaces predominantly lined by pancreaticobiliary type epithelium were demonstrated, with focal mucinous Di-PAS positive epithelium (Figure 3). The cysts were surrounded by a densely fibrous and hyalinised stroma. The typical ovarian type stroma that consists of spindle cells with little cytoplasm and round to slightly elongated nuclei was not seen. The stromal tissue was positive for oestrogen receptor and smooth muscle actin (SMA) (Figure 3 cd). The findings were consistent with multifocal MCN involving entire pancreas. The patient had an uncomplicated post-operative course and was discharged home at day 13. The patient remains well, now 3 years post total pancreatectomy.

DISCUSSION

Pancreatic cysts are increasingly detected by abdominal imaging performed for investigation of vague abdominal complaints [1, 7]. In the majority of cases incidental cysts represent side branch IPMN that are not infrequently multifocal [2]. Other causes of multifocal pancreatic cysts are less common and may include multiple developmental cysts in the setting of polycystic liver or kidney disease and serous cystadenomas [2, 6, 8]. The occurrence of multifocal MCN diffusely replacing the entire pancreas, to our knowledge, has not been previously described. This appears to represent a new entity.

In the setting of diffuse mixed side-branch and main duct IPMN, cyst replacement of the majority of the pancreas is described [2]. Communication between side branch cysts and the main duct can be observed on MRCP, and in such cases distinguishes IPMN from MCN and SCA. IPMN tend to have equal male to female occurrence, whereas the male to female ratio is reported to be 1:9 and 1:3 in the case of MCN and SCA respectively [9]. Diffuse SCA involving the entire pancreas is described and occurs most commonly setting of VHL syndrome [6, 10]. In a recent review of 23 patients with VHL, SCA were noted in 47% of patients with diffuse involvement in 73% of these cases [6, 10]. The imaging features noted in our case was initially thought to represent diffuse SCA and our patient was investigated for the possibility of VHL syndrome, which was excluded by genetic testing, with final histology confirming diffuse MCN.

Cyst fluid analysis was undertaken to further determine the nature of the pancreatic cysts in our case. A CEA level of 192 ng/mL as a threshold, in one study was shown to differentiate mucinous from non-mucinous cysts with an accuracy of 80% [11]. CEA was not detected in the fluid aspirated in our case and no mucin was identified. We elected to proceed to surgery after exclusion of VHL syndrome, despite no definite proof that the cysts were mucinous in nature, given documented enlargement of the cysts, continued vague abdominal symptoms, and concerns of possible underlying malignancy. The patient’s recent development of diabetes mellitus, in the absence of clear risk factors raised further concerns of possible occult pancreatic malignancy [12]. Features associated with an increased risk of malignancy such as large tumour size (>4 cm), septal thickening and present of intracystic excrescences on imaging studies were not observed in our patient [13].

Pre-operative suspicion of MCN in this case was low, given that MCN are generally unifocal [2]. Cases of diffuse pancreatic involvement by MCN have not been reported. Occurrence of multifocal MCN is rare with only 5 cases of multiple MCN identified on review of published literature from 1990 to 2014 [14-18]. In four cases, two MCNs were identified. The remaining case identified three separate

![Figure 1](image1.png) Magnetic resonance cholangiopancreatography demonstrating diffuse cystic lesions throughout the pancreas in transverse (a.) and coronal sections (b.). No clear communication with the pancreatic duct or pancreatic duct dilatation is noted.

![Figure 2](image2.png) Excisions pancreas specimen (a.) demonstrating numerous cysts thought the head, body and tail. (b.) Sectioning of the pancreas demonstrates multiple cysts without any clear communication with the pancreatic duct and no evidence of pancreatic duct dilatation.
lesions involving the pancreatic neck, tail and body [18]. MCN are thought to have a development origin from deposits of the left primordial gonad within the dorsal pancreas that are in very close proximity during the fourth and fifth weeks of development, explaining the finding of ovarian like stroma surrounding the cysts in the majority of cases [19]. They are therefore most frequently noted in female patients and usually involve the pancreatic body and tail, with only 5% to 10% of MCNs involving the pancreatic head [19]. Histologically MCN are characterized by a mucinous-type epithelium that is typically flat. Intracellular mucin can be demonstrated in these lesions by periodic acid-Schiff (PAS) staining. The cysts are typically surrounded by tissue that resembles ovarian stroma, characterized by densely packed spindle cells with sparse cytoplasm and uniform, elongated nuclei [20]. The ovarian-type stroma in MCN often stains positively for estrogen and progesterone receptors, actin, desmin, and vimentin[19]. In our case the entire pancreas was replaced with cystic structures surrounded by a dense hyalinised stroma that histologically was not typical for the ovarian-like stroma seen in MCN, however immunohistochemical staining with oestrogen and SMA is in keeping with ovarian-type stroma [19]. PAS positivity, demonstrating mucin in the cyst lining cells was present. No communication with the pancreatic ducts was demonstrated to suggest an IPMN. International guidelines generally require the presence of an ovarian like stroma for a diagnosis of MCN [2]. Our case appears to be an exception to this or else represent a new entity.

Multifocal cysts within the pancreas occur, but very rarely replace the entire pancreas. IPMN and SCA are the most common cysts diffuse pancreatic cysts. IPMN can usually be identified by cyst communication with pancreatic duct and has an equal occurrence in male and females. SCA can produce a similar appearance, but usually show no evidence of cyst communication with the pancreatic duct and are more common in females and usually occur in the setting of VHL syndrome. A case of diffuse MCN involving the entire pancreas is rare and to date has not been reported. The features of positivity for estrogen, actin and PAS staining was most suggestive of MCN in our case despite the absence of an obvious ovarian like stroma.

Conflicting Interest
The authors had no conflicts of interest

References


