Specific new mucinous benign pancreatic cysts-a new pathological unit

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INTRODUCTION

Pancreatic cystic lesions consist of a variety of pathological nodules and can generally be classified into neoplastic and non-neoplastic cysts [1]. The following types of cystic neoplasms are predominant: Mucinous Cystic Tumors (MCT), Intrauterine Papillary Mucinous Tumors (IPMTs) and Solid Pseudopapillary Neoplasms (SPPNs) that are both premalignant and malignant [2]. Serous cystic lesions from another large group of cystic neoplasms that are predominantly benign [3]. On the other hand, non-neoplastic cystic tumors consist of congenital cysts, lymphoepithelial cysts, retentive cysts and endometrial cysts [3]. Recently, a new group of non-neoplastic cystic lesions, called Mucinous Non-neoplastic Cysts (MNC), has been described. We present of pancreatic cystic tumors with signs which increased possibility of this diagnosis [4, 5].

MATERIALS AND DESCRIPTION

Eleven patients aged from 49-73 years old (6 women and 5 men) were scanned by US, computer-tomographically (CT), ERCP and MRI. Cystic lesions of the pancreas ranged from 26 to 33 mm was detected. The major pancreatic canal is not dilated (Figure 1).

At a control US study 6 months later in five of the patients the finding was presented with an increase of the cystic lesion up to 38 mm (Figure 2).

An MRI study was conducted of the same patients to better characterize the cystic lesions. The finding is a 38 mm cyst in the pancreas, seemingly communicating with the pancreas canal (Figure 3).

Fig. 1. CT image representing a cystic lesion in the pancreatic body (Non dilated pancreatic duct)
The main pancreatic canal and its lateral branches are not dilated in all of our patients. Laboratory tests for liver function tests, serum carcinoembryonic antigen and carbohydrate antigen C 19-9 are within the normal range. Whipple's resection were performed in 6 patients. Due to an unspecified diagnosis of cystic neoplasm of the pancreas in three patients were performed distal pancreatectomy and in two cases central pancreatectomy. The histological preparation showed a simple cyst with a mucosal epithelium (Figure 4).

There is no abnormal presence of atypia and dysplasia of the epithelium as well as communication with the pancreatic duct. The pancreatic tissue was not histologically presented with significant changes. Within 2 year follow-up with US and CT investigation, no signs of tumor recurrence were found.

RESULT AND DISCUSSION

Kosmahl et al., describe a new cystic pancreatic change in five patients for whom the term Mucinous Non-neoplastic Cyst (MNC) is introduced [1]. The same group subsequently reported 4 cases (of 9 patients) presented this new group of cystic pancreatic changes in a retrospective review of 418 cases of cystic tumors [2].

The pancreatic cysts of our study demonstrate histological features susceptible to MNCs, including single-cell cyst-plated cytoplasmic cell cytoplasmic mucin cells, lack of cell proliferation or atypia without pathologically demonstrated communication with the pancreatic duct and fine sciatric support stroma. An argument against this diagnosis is the presence of communication with the major pancreatic duct presented on preoperative MRI, which makes retention cyst and IPMT difficult.

MNCs are characterized pathologically with mutant epithelial differentiation, lack of cellular atypia or increased proliferation, a fine layer of acellular stroma, and lack of communication with the pancreatic channel [1]. These cysts by definition do not exhibit any neoplastic features such as dysplasia, proliferative activity, signs of invasive growth or metastasis. The origin and development of this pathology is not known and can only be supposed [5, 6]. Clinical and pathological features are presented in Table 1.

Abnormal MNCs should be differentiated from other cystic neoplasms of the pancreas, which are covered with mucosal epithelium, such as Mucinous Cystic Tumours (MCTs), Intrauterine Papillary Mucinous Tumours (IPMTs) and retention cysts.

The images of MNCs upon MRI may be indistinguishable from that of MCNs, especially if the cysts are large and have thick walls. FNA cytology of the epithelium of MNCs shares that of retention cysts. Retention cysts can be excluded based on the absence of potential causes or evidence of ductal obstructions; however, this is not always possible. Nevertheless, although EUS-FNA could not distinguish MNCs from retention cysts, treatment and prognosis will not be affected owing to the benign nature of both diseases (Figure 5).

MCTs are large, well-differentiated cystic pancreatic tumours that are usually presented as single or multifocal pancreatic cysts in middle-aged women [7, 8-11]. These tumors, like MNCs, are covered with a mucosal epithelium, demonstrating a periodic positive acid-Schiff and Alcian blue reaction as well as positivity of cytokeratins 7, 8, 18, 19 and 20, 7, 8.

IPMT is a clearly defined clinicopathological unit described and demarcated by MCTs by the World Health Organization
Cytology and cyst fluid CEA analysis

Seven MNCs had an endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) prior to surgical resection. The FNA specimens were analyzed for: background (mucinous or necrotic), cellularity (hypercellular or scant cellular), architecture (honeycombed flat sheets or papillary clusters), nuclear features (membrane, chromatin, pleomorphism, nucleoli) and fibrotic stroma. These features were reported as either present or absent (1 or 0). In addition, cyst fluid Carcinoembryonic Antigen (CEA) concentrations in 5 MNC were measured by a specific immunoassay.

Sometimes the ductal communication is not presented to the US, CT or ERCP, but can be seen on the MRI or pathological study and vice versa [15]. In the seven subjects presented, none of them were tested with MPTs and only one with ERCP, which does not prove communication with the duct [1]. The remaining four patients were studied with CT, which is not particularly reliable in portraying communication. The communications can be demonstrated in some of the patients if MRCP or ERCP is performed.

Multiple cystic fluid pathological parameters can be used to categorize the lesions, including fluid amylase, lipase, Carcinoembryonic Antigen (CEA), cancer antigen (CA)-125, mucin content, cytology, DNA content, and detection of genetic mutations. To date, CEA is the most reliable pathological marker in discriminating between mucinous and non-mucinous PCLs.

Brugge et al. reported that a CEA value ≥ 192 ng/mL indicates a mucinous lesion [16, 17]. CEA showed a sensitivity and specificity of 73% and 84%, respectively, in categorizing PCLs [17]. When combined with CEA, cystic fluid mucin (MUC) content analysis can add to the diagnostic accuracy [18]. Cysts with MUC5A, MUC2, and MUC1 overexpression have the highest risk of being premalignant or malignant [19]. Molecular analysis of the cystic fluid may provide a specific tool for detecting malignant cysts. Winner et al. documented that the presence of the K-ras mutation and >2 loss of heterozygosity was 96.2% specific for malignant cysts [20]. On the other hand, both of these parameters were less sensitive than CEA in discriminating between mucinous and non-mucinous cysts. A combination of these parameters with CEA is better at differentiation [20]. Micro RNA expression is a promising tool for categorization of different PCLs. Micro RNAs-noncoding RNA molecules that control mRNA processing—are expressed differently in various PCLs [21].

![Fig. 5. EUS image showed a small homogeneous hypoechoic lesion in pancreas tail on endoscopic ultrasound](image)

<table>
<thead>
<tr>
<th>Case #</th>
<th>Age/sex</th>
<th>Symptoms</th>
<th>Location</th>
<th>Cyst/Fluid</th>
<th>Size</th>
<th>Cytology</th>
<th>Fluid CEA (ng/ml)</th>
<th>Surgical procedure</th>
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<tbody>
<tr>
<td>1</td>
<td>56F</td>
<td>abdominal pain</td>
<td>head</td>
<td>Unilocular/clear</td>
<td>13 mm</td>
<td>suspicious</td>
<td>N/A</td>
<td>Whipple's resection</td>
</tr>
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<td>2</td>
<td>60M</td>
<td>none</td>
<td>tail</td>
<td>Unilocular/ mucoid</td>
<td>33 mm</td>
<td>N/A</td>
<td>N/A</td>
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<tr>
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<td>head</td>
<td>Multilocular/ mucoid</td>
<td>16 mm</td>
<td>suspicious</td>
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<td>4</td>
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<td>none</td>
<td>Body/ tail</td>
<td>Unilocular/ hemorrgic</td>
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<td>5975</td>
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<td>head</td>
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<td>66F</td>
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<td>head</td>
<td>Multilocular/clear</td>
<td>11 mm</td>
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<td>neck</td>
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<td>Multilocular/ mucoid</td>
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<td>mucinous cystic neoplasm</td>
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</table>
CONCLUSION

Diagnosis of MNC can be significantly hampered by the overlapping of many clinical-pathological signs with retention cyst, MCTs and IPMTs.

We recommend that a patient with a diagnosis of "benign" MNC be closely monitored by US, CT or ERCP investigation, because of the inability to absolutely confirming the benign nature of the lesion-well defined, without penetration in surrounding tissues and no metastasis. Moreover, the existence of the MNC, as a truly unique cystic lesion, remains controversial because the reported cases of this neuralgia may simply represent a variant of an existing pancreatic pathology that overlaps the underlying pathological features of pancreatic cystic tumours plagued with mucosal epithelium. All imaging diagnosticians, surgeons, and pathologists need to share their experience in order to increase diagnostic possibilities for this particular pathology.

REFERENCES