

Cystic neoplasms of the pancreas

Dr Beate Haugk MD FRCPath
Royal Victoria Infirmary, Newcastle upon Tyne

Pancreatic cystic neoplasms are rare; they account for only 5% of primary pancreatic neoplasms.¹ They are a heterogeneous group which includes mainly cystic neoplasms of the exocrine pancreas, rare cystic pancreatic endocrine and cystic mesenchymal tumours. The most important four types of cystic neoplasms of the exocrine pancreas are serous cystic neoplasms, mucinous cystic neoplasms, intraductal papillary mucinous neoplasms and solid pseudopapillary neoplasms. In addition, there are less common cystic variants of pancreatic ductal adenocarcinoma² and pancreatic acinar cell carcinoma. These different types of cystic neoplasms vary significantly in their malignant potential. Serous cystic tumours have virtually no malignant potential. Solid pseudopapillary tumours have a low malignant potential. The mucinous neoplasms present as a spectrum of pre-malignant and malignant lesions mirrored in a low malignant potential for non-invasive lesions and a high malignant potential for invasive tumours.³ Cystic variants of pancreatic ductal and acinar cell carcinomas exhibit the same high malignant potential as their solid counter parts. Mucinous tumours and solid pseudopapillary tumours require surgery as curative treatment.

The pre-operative identification of a pancreatic cystic neoplasm requiring surgery presents a great challenge to the diagnostician. Due to advanced imaging techniques cystic lesions of the pancreas are being detected with increased frequency and an aggressive surgical approach to cystic lesions is becoming less practical.⁴ Pancreatic cystic neoplasms are thought to account for approximately 10-15% of all pancreatic cystic lesions.¹ 75-85% of pancreatic cystic lesions are pseudocysts which can be treated conservatively. The pre-operative distinction of pancreatic cystic neoplasms from non-neoplastic cysts of the pancreas warrants a multimodal approach. In addition to vital clinical information, this, in the ideal setting, incorporates cross sectional imaging and endoscopic ultrasound, cyst fluid analysis and ultrasound guided FNA cytology. Clinical information such as history of pancreatitis, symptoms, gender and age may present valuable clues to the diagnosis. Location within the pancreas, microcystic or macrocystic appearance and relationship to the pancreatic duct system on imaging will provide important information. Appearance of the cyst fluid and fluid markers such as CEA and amylase may further aid the diagnostic process.⁵ Endoscopic ultrasound guided FNA cytology may allow assessing presence and absence of mucin but most importantly will be able to detect cytological features of malignancy.⁶ A multimodal and multidisciplinary diagnostic approach is vital and a combination of endoscopic ultrasound appearance, FNA cytology, fluid CEA and fluid appearance has been shown to significantly improve sensitivity and accuracy of malignant lesions/lesions with malignant potential. Subsequent histological assessment of the resection specimens will confirm or determine the diagnosis. It will give an indication of malignant potential and allow sub-typing. The tumour can be graded and staged and local excision can be assessed to plan further treatment and follow-up.

Serous cystic neoplasms can present as one of five subtypes. Serous microcystic adenoma is the commonest (1-2% of all pancreatic tumours) and its prognosis following complete resection is excellent.³ In the presence of multiple serous cysts

Von Hippel-Lindau syndrome should always be considered. Serous cystadenocarcinoma appears exceptionally rare and its existence has even been disputed.³ Solid pseudopapillary tumours account for only a small proportion of pancreatic cystic tumours⁷ and their cystic appearance is due to pseudocystic degeneration which may not be present in smaller lesions. 5% of tumours show recurrence or metastases but there are currently no histological criteria to predict malignant behaviour. Intraductal papillary mucinous neoplasms have become the most common pancreatic cystic neoplasm accounting for 24%.^{7,8} They can be distinguished from mucinous cystic neoplasms by their communication with the main pancreatic duct or a branch duct. They can be extensive and involve the entire duct system. The neoplastic epithelium can show changes ranging from minor epithelial atypia to moderate dysplasia to high grade dysplasia/intraepithelial carcinoma. The prognosis is excellent for lesions with atypia confined to the lining epithelium but becomes poor for tumours with stromal invasion. Four different histological types of IPMNs can be distinguished: gastric, intestinal, pancreatobiliary and oncocytic. The intestinal and pancreatobiliary type appear to have a higher malignant potential.⁸ The mucinous cystic tumours are similar to the ovarian counterpart and the specialised ovarian stroma is characteristic.⁹ The intraepithelial changes also range from no atypia to intraepithelial carcinoma. The prognosis for non-invasive mucinous cystic neoplasms is excellent. In one series of mucinous cystic neoplasms 17.5% were malignant and the prognosis poor¹⁰ but this may depend on the extent of invasion into tumour wall and adjacent tissues. Both types of mucinous tumours should be sampled extensively and, if possible, embedded in their entirety, to exclude small foci of invasion.

Pancreatic cystic neoplasms are a small, but diagnostically important subgroup of pancreatic neoplasms, as a significant proportion of them, in particular pre-invasive mucinous tumours, have a low malignant potential and can be cured by appropriate and timely surgical intervention.

References:

1. Visser BC, Muthusamy VR, Yeh BM, Coakley FV, Way LW. Diagnostic evaluation of cystic pancreatic lesions. *HPB (Oxford)* 2008;10 (1):63-69.
2. Kosmahl M, Pauser U, Anlauf M, Klöppel G. Pancreatic ductal adenocarcinomas with cystic features: neither rare nor uniform. *Mod Pathol.* 2005;18 (9):1157-64.
3. Campbell F, Azadeh B. Cystic neoplasms of the exocrine pancreas. *Histopathology* 2008; 52 (5): 539-51.
4. Spinelli KS, Fromwiller TE, Daniel RA, Kiely JM, Nakeeb A, Komorowski RA, Wilson SD, Pitt HA. Cystic pancreatic neoplasms: observe or operate. *Ann Surg* 2004;239 (5): 651-7.
5. Linder JD, Geenen JE, Catalano MF. Cyst fluid analysis obtained by EUS-guided FNA in the evaluation of discrete cystic neoplasms of the pancreas: a prospective single-center experience. *Gastrointest Endosc* 2006;64(5):697-702.

6. Attasaranya S, Pais S, LeBlanc J, McHenry L, Sherman S, DeWitt JM. Endoscopic ultrasound-guided fine needle aspiration and cyst fluid analysis for pancreatic cysts. *JOP* 2007;8(5):553-63.
7. Kosmahl M, Pauser U, Peters K, Sipos B, Lüttges J, Kremer B, Klöppel G. Cystic neoplasms of the pancreas and tumor-like lesions with cystic features: a review of 418 cases and a classification proposal. *Virchows Arch.* 2004;445(2):168-78.
8. Andrejevic-Blant S, Kosmahl M, Sipos B, Kloppel G. Pancreatic intraductal papillary mucinous neoplasms: a new and evolving entity. *Virchows Arch* 2007 451 (5): 863-9.
9. Goh BK, Tan YM, Chung YF, Chow PK, Cheow PC, Wong WK, Ooi LL. A review of mucinous cystic neoplasms of the pancreas defined by ovarian-type stroma: clinicopathological features of 344 patients. *Surgery.* 2007;141(6):834-5.
10. Crippa S, Salvia R, Warshaw AL, Domínguez I, Bassi C, Falconi M, Thayer SP, Zamboni G, Lauwers GY, Mino-Kenudson M, Capelli P, Pederzoli P, Castillo CF. Mucinous cystic neoplasm of the pancreas is not an aggressive entity: lessons from 163 resected patients. *Ann Surg* 2008;247(4):571-9.