

CASE REPORT

Duodenal Duplication Cyst with Profound Elevation of Intracystic Carbohydrate Antigen (CA 19-9) and Carcinoembryonic Antigen (CEA): A Rare but Important Differential in the Diagnosis of Cystic Tumours of the Pancreas

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ABSTRACT

Context Enteric duplication cysts are rare lesions of uncertain incidence and natural history. Pre-operative confirmation of diagnosis can be difficult. This case reports an adult duodenal duplication cyst presenting with grossly elevated intra-lesional levels of tumour markers.

Case report A 57-year-old female was found to have a complex cystic lesion of the head of the pancreas. Intra-lesional fluid analysis revealed a grossly elevated CA 19-9 and CEA. Resection was undertaken under the assumption that this was a cystic tumour. Macroscopic examination after opening the duodenum revealed a villous, circumferential tumour in the proximal duodenum measuring 4 cm in length. A cystic lesion was present in the medial wall of the tumour and did not communicate with the duodenal lumen. Microscopically, the tumour comprised Brunner's gland hyperplasia with associated mucosal thickening. The wall of the underlying cystic lesion was comprised of muscularis formed by the outer muscle coat of the duodenal wall. The final diagnosis was of a duodenal duplication cyst. There was no evidence of dysplasia or malignancy.

Conclusion This is the first report of a duodenal duplication cyst having elevated intra-cyst fluid levels of amylase, carbohydrate antigen CA 19-9 and carcinoembryonic antigen (CEA). Although rare, this is an important differential diagnosis in the management of cystic tumours of the pancreas.

INTRODUCTION

The diagnosis of cystic tumours of the pancreas can be difficult. The principal effort is directed towards distinguishing benign post-inflammatory pseudocysts from true cystic tumours [1, 2]. Pointers that may help to identify a cystic tumour include the presence of a thick or irregular lining with septae on cross-sectional imaging [2]. Further, endoscopic ultrasound (EUS) with linear EUS-guided aspiration can aid this process of differentiation as cyst fluid can be analysed for tumour markers, amylase and cytology [3, 4]. Elevated levels of intra-cyst tumour markers favour the diagnosis of a true cystic lesion [5]. It is important to make the distinction between post-inflammatory pseudocysts and cystic tumours as the natural history of these conditions is different and this



Figure 1. Oral contrast CT showing contrast in stomach and partially outlining a multi-septate lesion in the head of the pancreas. There is parenchymal calcification in the head of the pancreas.

is reflected in their different optimal management. Cystic lesions carry a varying risk of malignant transformation and most require resection [2]. Further, mistaking a cystic tumour for a pseudocyst can have disastrous consequences and lead to inappropriate drainage surgery [6].

In practice, cystic tumours and pseudocysts are the principal differential diagnoses to be assessed in a patient with a pancreatic cystic lesion; however a third rare possible differential is that of duplication cyst. These are rare congenital abnormalities of the gut characterized by the presence of smooth muscle in the wall and can be lined with gastrointestinal mucosa [7]. Little is known of the natural history and malignant potential of these lesions and as a result of their rarity, knowledge of their presentation accrues principally through single case studies. This paper reports a patient presenting with a pancreatic cystic lesion who underwent resection on the grounds of having a complex cyst with a profoundly elevated intra-cystic carbohydrate antigen (CA 19-9) level together with carcinoembryonic antigen (CEA). Final histology revealed a duodenal duplication cyst without malignancy. To the best of our knowledge, this presentation of a duodenal duplication cyst is unique and highlights both the difficulties in pre-operative diagnosis and

also the dearth of knowledge of this rare condition.

CASE REPORT

A 57-year-old female patient presented with a 12-month history of recurrent severe upper abdominal pain radiating to the back associated with occasional episodes of vomiting. There was no history of jaundice, weight loss or diarrhoea. Her social history was significant for previous heavy alcohol intake some ten years previously but this was not precisely quantifiable. There was a previous medical history of an episode of acute pancreatitis in 1995. On examination, she was not jaundiced and there was no palpable abdominal mass.

Her admission blood tests were normal apart from a minimally elevated serum amylase of 153 U/L (reference range: 40-100 U/L). Trans-abdominal ultrasonography revealed a large complex lesion near the head of the pancreas reported as a pseudocyst causing compression of the first and second parts of the duodenum and extrinsic compression of the common bile duct. In addition, there was dilatation of the main pancreatic duct (MPD) and the common bile duct. Intravenous contrast-enhanced computed tomography (CT) revealed pancreatic parenchymal calcification in an atrophic gland. CT confirmed dilatation of the duct of Wirsung



Figure 2. Venous contrast phase CT showing the relation of the cystic lesion to the head of the pancreas and separation of the main portal vein from the lesion. The lesion is septate and contains fluid which is isodense with bile within the gallbladder.



Figure 3. Photograph of the operative resection specimen (unmagnified) taken after cross-sectioning of the duodenum. The circumferential, thick-walled, villous tumour is clearly seen. The green dye marks the medial border of the duodenum with the pancreas.

and a complex septate cystic mass closely related to the head of the pancreas measuring 4 cm in maximal transverse diameter (Figures 1 and 2). The lesion was reported as being “almost certainly a pancreatic pseudocyst”. There were no gallstones and the main portal vein was patent. Endoscopic retrograde cholangiopancreatography (ERCP) showed extrinsic compression at the junction of the first and second parts of the duodenum. The MPD was dilated with a 1.5 cm cystic area filling in the head. At ERCP, injection of contrast into the MPD showed no filling of the large cyst seen on CT. She underwent EUS with cyst drainage using the linear probe. EUS showed a multi-loculated cyst and 27 mL of pink fluid was aspirated. Post-aspiration EUS confirmed that the cyst was completely decompressed. Cytological examination of the cyst fluid showed polymorphonuclear leukocytes in an inflammatory exudate. There were no mucosal or epithelial cells nor evidence of malignancy. Cyst fluid biochemistry revealed an amylase of 66,681 U/L (reference range: 0-100 U/L), CEA of 275 µg/L (reference range: 0-7 µg/L) and CA 19-9 greater than 24,000 U/mL (reference range: 0-22 U/mL).

The evidence of raised intra-cystic tumour markers in conjunction with CT-evidence of a complex cyst was considered an indication for surgical resection and after discussion the patient underwent laparotomy. At operation

she was found to have an irregular cystic lesion measuring about 5 cm in transverse diameter arising from the substance of the head of the pancreas and also involving the uncinate process. The appearances were not typical of a pseudocyst and thought to be more in keeping with cystadenoma or cystadenocarcinoma. No cyst aspiration or frozen section biopsy was undertaken as it was considered that there was a risk of tumour dissemination and the patient underwent Whipple pancreaticoduodenectomy. Apart from a period of prolonged post-operative gastric stasis her recovery was uncomplicated and she is asymptomatic at early follow-up some 4 months after surgery. Macroscopic examination after opening the duodenum revealed a villous, circumferential tumour in the proximal duodenum measuring 4 cm in length. Cross-sectioning revealed a cystic lesion in the medial wall of the tumour that did not communicate with the duodenal lumen (Figure 3). Microscopically, the tumour comprised Brunner’s gland hyperplasia with associated mucosal and muscular thickening (Figure 4). The wall of the underlying cystic lesion was comprised of muscularis formed by the outer muscle coat of the duodenal wall. The inner surface was largely denuded and there was dense active inflammation. There were focal areas of gastric epithelium and ectopic pancreatic

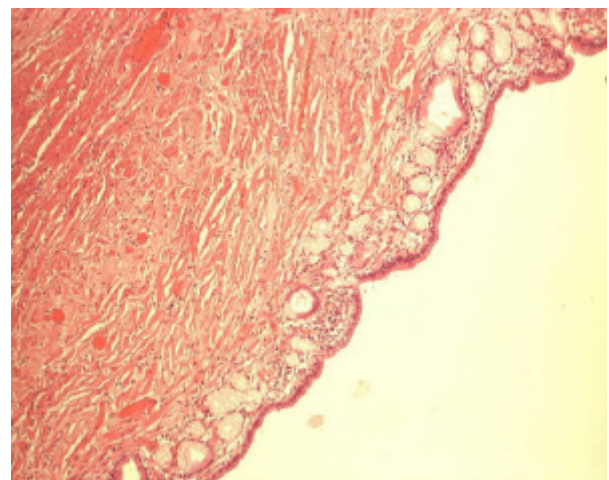


Figure 4. Haematoxylin and eosin preparation (x40) showing the wall of the cyst lined focally by gastric epithelium and containing smooth muscle in the deeper layers.

tissue on some sections. Metaplastic epithelial changes were noted in some pancreatic ducts. The final diagnosis was of a duodenal duplication cyst. There was no evidence of dysplasia or malignancy.

DISCUSSION

Duodenal duplication cysts are rare and their infrequency is such that there is little information on their incidence and natural history. Most present in childhood and can be treated endoscopically or by surgery [8]. Presentation in adults is yet more uncommon and this entity would not normally be considered in the differential diagnosis of cystic lesions of the pancreas [9].

In practice, the accurate diagnosis of cystic lesions of the pancreas is not always discernible by imaging modalities and endoscopic ultrasound with aspiration of cyst fluid for biochemical and cytological analysis may be of some value [2]. A finding of raised cyst-fluid tumour markers in the presence of radiological suspicion of malignancy is an indication for surgical resection [10] and other investigations such as biopsy are relatively contra-indicated. In the case reported here, a correct diagnosis was not made either pre-operatively or intra-operatively and the patient underwent pancreaticoduodenectomy for what was thought to be a cystic tumour.

According to our literature search, this is the first report of a duodenal duplication cyst presenting as a pancreatic cystic lesion having elevated intra-cyst fluid levels of amylase, carbohydrate antigen CA 19-9 and carcinoembryonic antigen (CEA). The information provided here may be added to that contained in two similar reports describing duplication cysts elsewhere in the gastro-intestinal tract (one gastric [11] and the other ileal [12]) having elevated levels of both CA 19-9 and CEA. In addition, there have been two other reports of an increase in intra-cyst fluid levels of CA 19-9 (but not CEA) in a gastric [13] and a colonic duplication cyst [14].

The molecular biological basis of the elevation of intra-lesional tumour markers in duodenal (and other gastrointestinal) duplication cysts is unknown but it may be speculated that oncofetal antigens such as CEA may be produced by immature epithelium. The presence of pancreatic acinar tissue within the cyst wall may be related to the production of amylase and glycoprotein markers such as CA 19-9.

The clinical significance of elevated tumour markers within duodenal duplication cysts is also unknown. Although there is a solitary case report of adenocarcinoma arising in a duodenal duplication cyst [15] and other reports of cancerous change in other gastrointestinal duplication cysts [16] the relative risk of malignant transformation is unknown. However, in the clinical setting (such as in this case), this lack of specific information on the risk of cancer is unlikely to influence management: a complex septate lesion in the pancreas with elevated intra-cyst tumour markers will require resection in its own right.

In summary, this is the first report of an adult duodenal duplication cyst presenting with high intra-cyst CA 19-9, CEA and amylase levels. Although rare, this is an important differential diagnosis in the management of cystic tumours of the pancreas.

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Keywords Cyst Fluid; Pancreatic Cyst; Tumor Markers, Biological

Abbreviations CA 19-9: carbohydrate antigen 19-9; MPD: main pancreatic duct

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References

1. Siriwardena AK. Contemporary Management of Pancreatic Pseudocysts. *Pancreatology* 2005; 5:507-9. [PMID 16103739]
 2. Brugge WR, Lauwers GY, Sahani D, Fernandez-del Castillo C, Warshaw AL. Cystic neoplasms of the pancreas. *N Engl J Med* 2004; 351:1218-26. [PMID 15371579]
 3. Visser BC, Muthusamay VR, Mulvihill SJ, Coakley F. Diagnostic imaging of cystic pancreatic neoplasms. *Surg Oncol* 2004; 13:27-39. [PMID 15145031]
 4. Levy MJ, Clain JE. Evaluation and management of cystic pancreatic tumors: emphasis on the role of EUS FNA. *Clin Gastroenterol Hepatol* 2004; 2:639-53. [PMID 15290655]
 5. Ryu JK, Woo SM, Hwang JH, Jeong JB, Yoon YB, Park IA, et al. Cyst fluid analysis for the differential diagnosis of pancreatic cysts. *Diagn Cytopathol* 2004; 31:100-5. [PMID 15282721]
 6. Martin I, Hammond P, Scott J, Redhead D, Carter DC, Garden OJ. Cystic tumours of the pancreas. *Br J Surg* 1998; 85:1484-6. [PMID 9823906]
 7. Frering V, Velecela E, Fouque P, Champetier P, Partensky C. Upper digestive duplications in adults. *Ann Chir* 1995; 49:928-35. [PMID 8787320]
 8. Siddiqui AM, Shamberger RC, Filler RM, Perez-Atayde AR, Lillehei CW. Enteric duplications of the pancreatic head: definitive management by local resection. *J Pediatr Surg* 1998; 33:1117-20. [PMID 9694106]
 9. Holcomb GW 3rd, Gheissari A, O'Neill JA Jr, Shorter NA, Bishop HC. Surgical management of alimentary tract duplications. *Ann Surg* 1989; 209:167-74. [PMID 2916861]
 10. Allen PJ, Jaques DP, D'Angelica M, Bowne WB, Conlon KC, Brennan MF. Cystic lesions of the pancreas: selection criteria for operative and nonoperative management in 209 patients. *J Gastrointest Surg* 2003; 7:970-7. [PMID 14675706]
 11. D'Journo XB, Moutardier V, Turrini O, Guiramand J, Lelong B, Pesenti C, et al. Gastric duplication in an adult mimicking mucinous cystadenoma of the pancreas. *J Clin Pathol* 2004; 57:1215-8. [PMID 15509688]
 12. Nomura T, Shirai Y, Hatakeyama K, Nikkuni K. An adult ileal duplication cyst containing markedly elevated concentrations of carcinoembryonic antigen and carbohydrate antigen 19-9. *Am J Gastroenterol* 2002; 97:208-9. [PMID 11808956]
 13. Ikehata A, Sakuma T. Gastric duplication cyst with markedly elevated concentration of carbohydrate antigen 19-9. *Am J Gastroenterol* 2000; 95:842-3. [PMID 10710108]
 14. Legros JR, Duclaut I, Michot F, Teniere P, Scotte M. Cystic mass of the pancreatic region associated with elevated CA 19-9 serum levels revealing a colonic duplication in an adult. *Gastroenterol Clin Biol* 2004; 28:1291-3. [PMID 15671942]
 15. Falk GL, Young CJ, Parer J. Adenocarcinoma arising in a duodenal duplication cyst: a case report. *Aust N Z J Surg* 1991; 61:551-3. [PMID 1859319]
 16. Shivnani AT, Small W Jr, Benson A IIIrd, Rao S, Talamonti MS. Adenocarcinoma arising in rectal duplication cyst: case report and review of the literature. *Am Surg* 2004; 70:1007-9. [PMID 15586516]
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