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CASE REPORT | PANCREAS

Acinar Cystic Transformation of the Pancreas With Main Pancreatic Duct Dilation and Distal Pancreatic Atrophy

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ABSTRACT

We report a rare case of a large, slowly progressive acinar cystic transformation (ACT) of the pancreas with main duct dilation and atrophy of the upstream pancreas. The diagnosis was made through endoscopic ultrasound-guided through-the-needle biopsy and histological identification of cuboidal acinar epithelium and characteristic immunohistochemistry findings. Distal pancreatectomy and splenectomy were performed because of elevated carcinoembryonic antigen levels, atypical cells on biopsy, and an increase in cyst size. Owing to the benign nature of this case, postresection surveillance was not necessary.

KEYWORDS: acinar cystic transformation; duct dilation; endoscopic ultrasound

INTRODUCTION

Acinar cystic transformation (ACT) is a rare pancreatic cystic lesion (PCL) that was described in the early 21st century.[1] The literature reports approximately 75 cases. ACT has distinct clinical, pathologic, molecular features and neoplastic risk from the variety of other PCLs that exist (Table 1).[2,3] The current understanding is that ACT represents a benign, non-neoplastic cystic lesion. The etiology is unclear, but some cases may occur because of ductal obstruction.[4] ACT is more common in adult women between 20 and 50 years of age and is typically located in the head of the pancreas, although it can involve any portion.[5–12] Multicentricity is common.[5,8,9,11,13–15] Abdominal pain is the most common presentation, although it is often incidentally discovered.[6,8–12,14,15] Highly sensitive imaging features include 5 or more cysts, clustered peripheral small cysts, the presence of cyst calcifications, and the absence of communication with the main pancreatic duct.[3,8,9,14,16] Main duct obstruction or displacement is rare, although this can occur.[6–8,11,14,15,17] The mean size is approximately 4 cm, although they can reach 15 cm.[3,5–8,11–14] Generally, no discrete solid lesion is identifiable. The typical appearance is localized unilocular or multilocular cysts, although diffuse pancreatic involvement has been noted.[3,5,7–12,14,15]

Microscopically, cysts are lined by cuboidal or columnar acinar epithelium that stain periodic acid–Schiff-positive and often have intracellular apical eosinophilic zymogen granules.[5–8,11–15] Interspersed ductal-like epithelium is noted in just under half of the cases.[5] Cellular atypia or mitoses, necrosis, infiltrative growth, or other evidence of malignancy is absent.[5,11–14] Immunohistochemistry is diffusely positive for β-catenin, trypsin, chymotrypsin, and cytokeratin 7 and patchy for cytokeratin 19.[6,9,12,14] ACT is also p53-negative and lack proliferative activity (Ki67 index of $< 1\%$).[6,11,12,14,17,18] Next-generation sequencing (NGS) has identified 2 likely pathogenic mutations affecting the *KRAS* (c.34G>C, p.G12R) and *SMO* (c.1685G>A, p.R562Q) genes.[13]

We report the case of an atypical, benign, slowly progressive 10-cm PCL with main pancreatic duct dilation and upstream atrophy that was found to be an ACT of the pancreas.

CASE REPORT

A 45-year-old woman was diagnosed with an incidental 6.3 × 6.9 cm PCL on an MRI of the lumbar spine (February 6, 2019). Two days later, a follow-up computed tomography scan revealed a 10 × 5.5 cm cystic lesion in the proximal body with upstream atrophic

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Table 1. Comparison of key characteristics of various pancreatic cystic lesions

	ACT	IPMN	MCN	SCA	cNET	SPN	Pseudocyst	LEC
Mean age (yr)	20–50	65	45	62	—	25–30	—	56
Sex	W > M	M > F	F >> M	F > M	—	F >> M	—	M > F
Mean size	4 cm	Variable	6 cm	4 cm	Variable	8 cm	Variable	5 cm
Most common location	Head	Head	Tail/body	Body/tail	Variable	Tail	Tail	Variable
Ductal communication	No	Yes	No	No	No	No	No	No
Macroscopic features	Unilocular or multilocular cysts	Variable wall thickness, smooth papillary lining epithelium	Thick wall ≥3 mm, unilocular or multilocular with few septae	Thin wall <3 mm, smooth cyst lining, microcystic (honeycomb) > macro/oligocystic > solid	Unilocular, sanguineous or serous fluid	Solid with cystic spaces, sanguineous fluid, necrosis	Unilocular, thick fibrous wall without lining epithelium, dark fluid	Unilocular or multilocular, keratinaceous cheesy debris
Cyst fluid	Low CEA	High CEA, high amylase	High CEA	Low CEA	Low CEA	—	High amylase	Variable viscosity and CEA
Microscopic features	Cuboidal or columnar acinar epithelium	Papillary mucinous epithelium	Mucinous epithelium and ovarian-type stroma	Flat serous epithelium, clear cytoplasm, subepithelial capillary network	Nests/trabeculae of cells separated by fibrous bands	Solid nested areas and pseudopapillary structures	No cyst epithelium, inflammatory/ fibrotic wall	Stratified squamous epithelium surrounded by dense lymphoid tissue with lymphoid follicles
EUS-nCLE	Structures suggestive of acinar units	Papillary projections with outer epithelium and inner vascular core	Epithelial bands without papillae conformation	Intricate fern pattern of capillary networks	Dark clusters (trabeculae) of cells in cords or nests separated by stroma	Dark clusters (trabeculae) of cells in cords or nests separated by stroma	Clumps of inflammatory cells. Dark background because of the absence of epithelium and associated vascular interstitium	Cluster of bright particles (keratin debris) on bland background (squamous epithelium)
Neoplastic risk	Benign; may have neoplastic transformation if mural nodules, driver mutations, or PanIN are present	Risk of malignant transformation	Risk of malignant transformation	Risk of malignant transformation	Risk of malignant transformation	Risk of malignant transformation	Benign	Benign
IHC	B-catenin +, trypsin +, chymotrypsin +, cytokeratin 7 +, cytokeratin 19 patchy +	Gastric-type: MUC5AC+; intestinal-type: MUC2+/CDX2+; pancreatobiliary type: MUC1/ MUC6+	PR > ER+, inhibin+	Inhibin +	Synaptophysin+, chromogranin+	Beta-catenin (nuclear), SOX11+, TFE3+	—	—
Molecular alteration	*KRAS*, *SMO*	*MAPK/GNAS*, *RNF43*. Advanced neoplasia: *TP53*, *SMAD*, *CDKN2A*, *mTOR*	*MAPK*, *RNF43*. Advanced neoplasia: *TP53*, *SMAD*, *CDKN2A*, *mTOR*	*VHL*	*MEN1*, LOH	*CTNNB1*	—	—

Data sources: References 2, 3, 5–8, 11–17, 20.
ACT, acinar cystic transformation; CEA, carcinoembryonic antigen; cNET, cystic neuroendocrine tumor; CT, computed tomography; EUS, endoscopic ultrasound; EUS-nCLE, EUS-guided needle-based confocal endomicroscopy; High CEA, >192 ng/mL; IHC, immunohistochemistry; IPMN, intraductal papillary mucinous neoplasm; LEC, lymphoepithelial cyst; LOH, loss of heterozygosity; Low CEA, <192 ng/mL; MCN, mucinous cystic neoplasm; PanIN, pancreatic intraepithelial neoplasia; SCA, serous cystadenoma; SPT, solid pseudopapillary neoplasm.

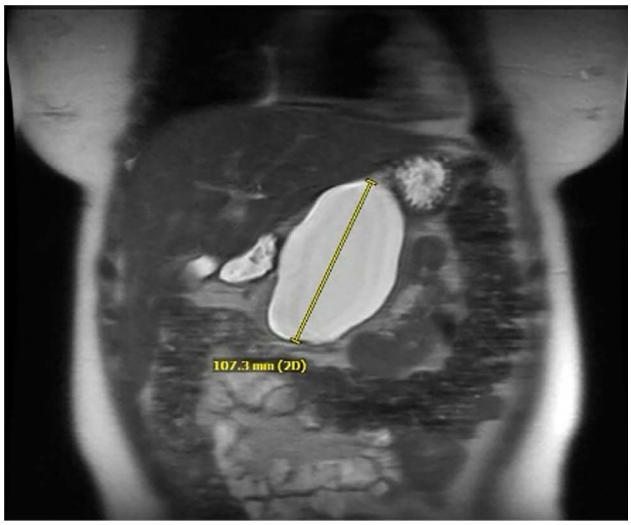

Figure 1. Frontal view from contrasted magnetic resonance imaging of the pancreatic cystic lesion measuring 7.4 × 6.4 × 10.7 cm.

changes. She was asymptomatic with no history of acute pancreatitis. She had a 30 pack-year smoking history but denied excess alcohol use. A dedicated follow-up magnetic resonance imaging 2 years later (September 28, 2022) revealed a 7.4 × 6.4 × 10.7 cm smoothly marginated cystic mass centered within the pancreatic body lacking wall thickening, mural nodules, or enhancing solid components (Figure 1). There was anterior deviation of the stomach and deformity of the second portion of the duodenum and portal vein. No pancreatic duct connection was visualized, but the upstream pancreatic duct was dilated to 6 mm. CA 19-9 was normal. Endoscopic ultrasound (EUS) (October 11, 2022) noted extrinsic compression of the posterior stomach wall and a pancreatic body cyst measuring 128 × 97 mm with a thin wall revealing a single compartment without septae, associated mass, or internal debris (Figure 2). Cyst fluid analysis (obtained by fine-needle aspiration using a 19-gauge Expect Slimline needle [Boston Scientific, Marlborough, MA]) included carcinoembryonic antigen 240 ng/mL, amylase 3743 U/L, and glucose 75 mg/dL. NGS did not reveal any mutations on a 50-gene panel. EUS-needle-based confocal endomicroscopy demonstrated a flat noncharacteristic background without the presence of known features of mucinous PCLs, neuroendocrine tumor, pseudocyst, or serous cystadenoma (Figure 3). EUS-guided through-the-needle biopsy sampling demonstrated fibrous tissue with mild chronic inflammation and focal reactive lymphoid aggregate and scant atypical cells. The differential included mucinous cystic neoplasm (MCN) because of its atrophic nature and lack of diagnostic features on biopsy vs a lymphoepithelial cyst. Pseudocyst was deemed unlikely because of the lack of inflammatory markers. A decision for surgical resection was made by the multidisciplinary tumor board because of upstream dilation of the main pancreatic duct, pancreatic atrophy, and concern for MCN. The patient underwent near-total robotic distal pancreatectomy, revealing a benign, unilocular, thin-walled epithelial cyst measuring 12.5 × 7.2 × 6.5 cm with features consistent with ACT (Figure 4). On hematoxylin and eosin stain, the cyst was predominately denuded with some sections of cuboidal epithelial lining with focal squamous metaplasia and dual ductal and acinar phenotype (Figure 4). The epithelial lining was positive for CK7, trypsin, CAIX, carcinoembryonic antigen (focal luminal), and p63 (patchy) and negative for chromogranin, inhibin, D2-40, WT-1, PAX8, CD10, and calretinin (Figure 4). P53 showed patchy increased staining. MCN was deemed unlikely because of the lack of definitive mucinous epithelium or ovarian-type stroma.

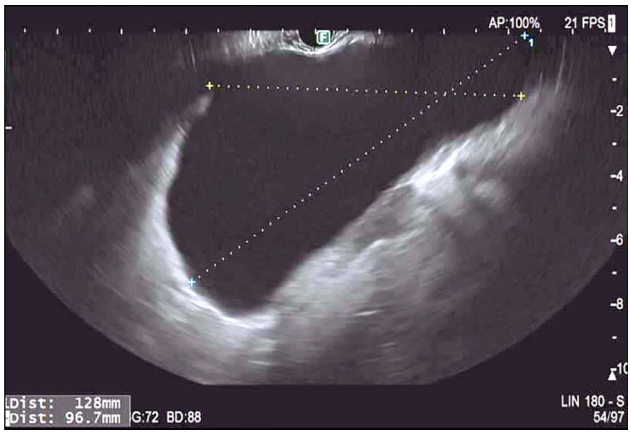

Figure 2. EUS image of 128 × 97 mm cyst located in the pancreatic body. EUS, endoscopic ultrasound.

DISCUSSION

The management of ACT can be complex. Initial workup includes noninvasive measures such as tumor markers and surveillance imaging with computed tomography or magnetic resonance imaging. EUS with fine-needle aspiration or needle-based confocal endomicroscopy with biopsy are generally reserved for when malignancy is suspected or definitive diagnosis is necessary.[19,20]

While initially hypothesized to be the benign precursor of acinar cystadenocarcinoma, ACT is now considered to have no malignant potential.[4,5,11,13] Exceptions may include cases with mural nodules, driver mutations, or pancreatic intraepithelial neoplasia.[9,10,13] These may benefit from long-term surveillance with eventual surgical intervention and intermittent post-resection imaging surveillance because of the theoretical concern for malignant transformation.

The management of uncomplicated cases favors imaging surveillance and potential biopsy for histologic diagnosis rather than outright surgical intervention, especially for young or asymptomatic patients.[12] Reasons to consider surgery include local expansion, development of symptoms, and desire to exclude PCLs associated with malignancy.[6,9,12–14] Most surgical cases require extensive pancreatic resections.

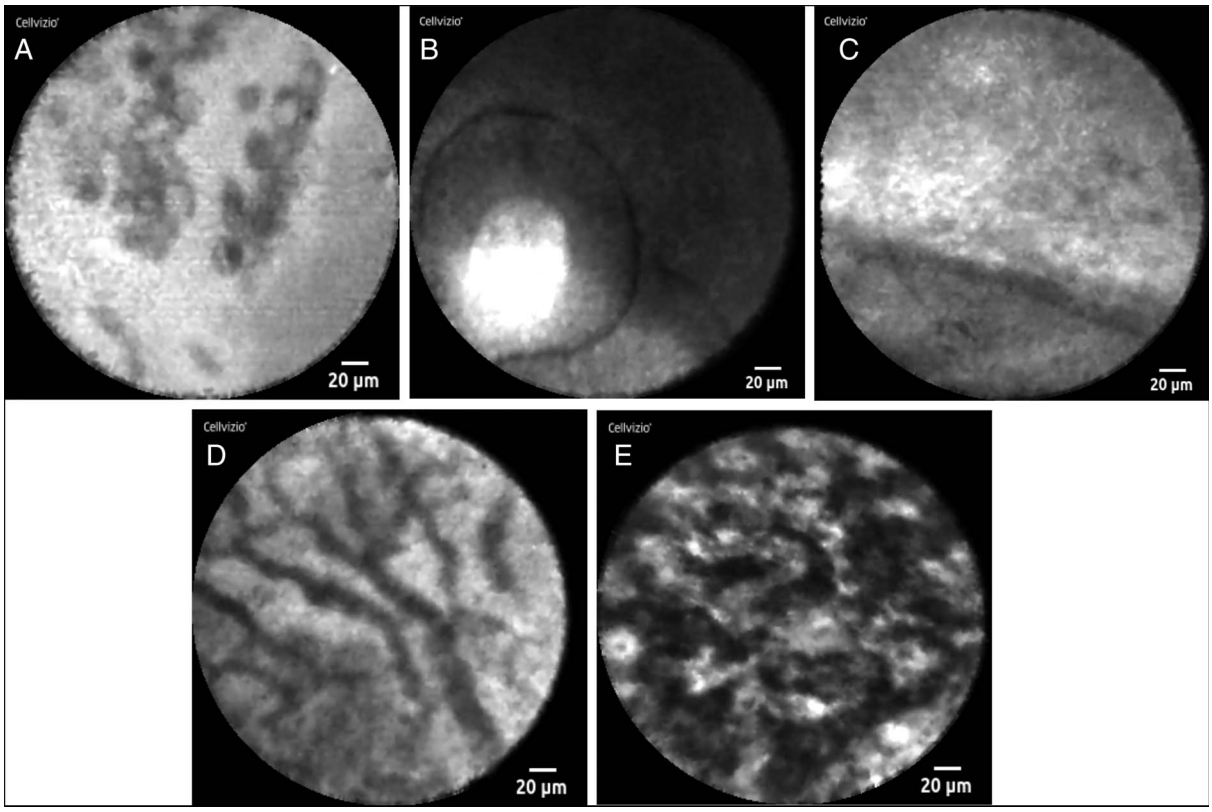

Figure 3. (A) EUS-nCLE of acinar cystic transformation of the pancreas showing flat noncharacteristic background without the presence of known features of (B) IPMN with papillae, (C) mucinous cystic neoplastic with flat epithelium, (D) serous cystadenoma with a fern pattern of vascularity, or (E) cystic neuroendocrine tumor—trabecular nests of cells. EUS-nCLE, endoscopic ultrasound-guided needle-based confocal endomicroscopy; IPMN, intraductal papillary mucinous neoplasia.

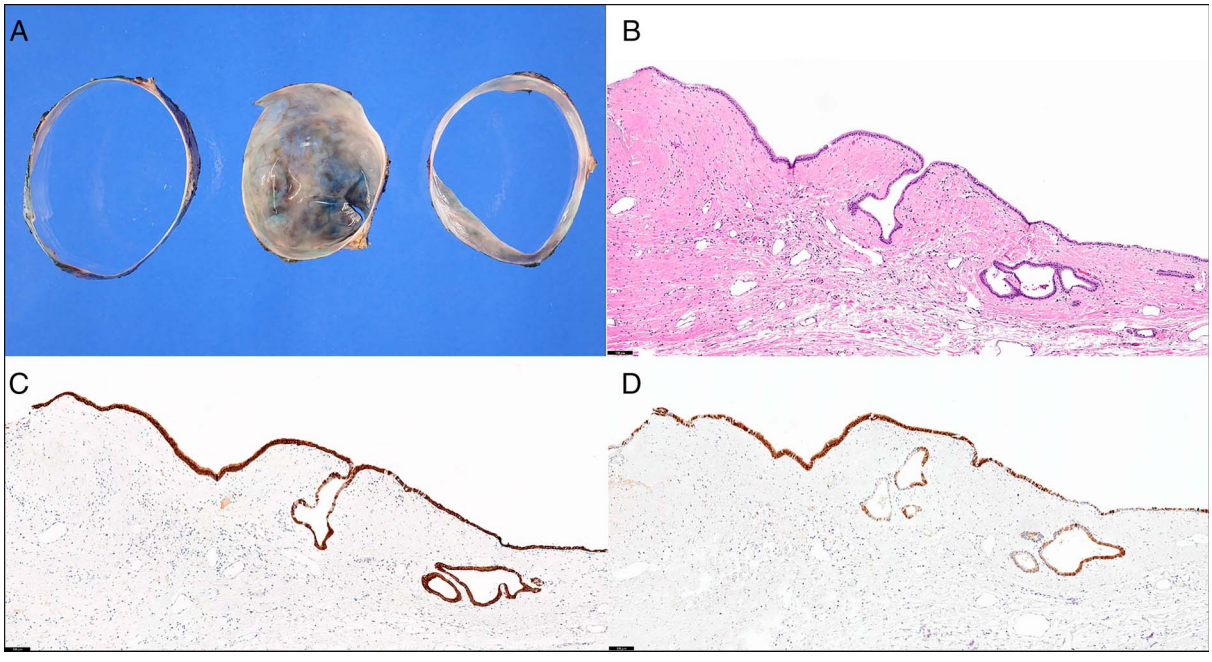

Figure 4. (A) Gross photograph demonstrates unilocular, smooth, and thin-walled cyst. (B) Cyst epithelium is composed of nonmucinous, cuboidal epithelium. By immunohistochemistry, the cyst epithelium is positive for CK7 (C) and trypsin (D), supporting both ductal and acinar differentiation.

Common features of this case are that the original cyst was incidentally discovered and was initially believed to be a pseudocyst or MCN, leading to surgical intervention. However, unique features of this ACT include the rare findings of main PD dilation with distal pancreatic atrophy and benign pathology despite its large size (10 cm). The lack of concerning findings, such as mural nodules, pancreatic intraepithelial neoplasia, or mutations on NGS support the decision to defer postresection follow-up.

DISCLOSURES

Author contributions: A. Nehaal performed the majority of the literature search and writing. C. Troy provided input in writing the text. SG Krishna performed the procedure, provided input in the writing process, edited the text, and reviewed the final manuscript, and is the article guarantor. W. Chen provided figures and edited the final manuscript.

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