

World Journal of *Gastrointestinal Surgery*

Monthly Volume 18 Number 7 July 27, 2026



World Journal of *Gastrointestinal Surgery*

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2026-2029

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
<https://www.wjgnet.com>

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ORIGINAL ARTICLE

Retrospective Cohort Study

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ABOUT COVER

Peer Review of *World Journal of Gastrointestinal Surgery*, Priya Hazrah, Professor, Department of Surgery, Lady Hardinge Medical College, New Delhi 110001, Delhi, India. priyahazrah@gmail.com

AIMS AND SCOPE

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INDEXING/ABSTRACTING

The *WJGS* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, PubMed Central, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2026 Edition of Journal Citation Reports® cites the 2025 journal impact factor (JIF) for *WJGS* as 2.1; JIF without journal self cites: 2.0; 5-year JIF: 2.2; JIF Rank: 128/321 in surgery; JIF Quartile: Q2; and 5-year JIF Quartile: Q2.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Si Zhao*; Production Department Director: *Xiang Li*; Cover Editor: *Jia-Ru Fan*.

NAME OF JOURNAL

World Journal of Gastrointestinal Surgery

ISSN

ISSN 1948-9366 (online)

LAUNCH DATE

November 30, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Eva Lieto

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1948-9366/editorialboard.htm>

PUBLICATION DATE

July 27, 2026

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GUIDELINES FOR AUTHORS

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<https://www.wjgnet.com/bpg/gerinfo/241>

ETHICS STATEMENTS OF HUMAN

<https://www.wjgnet.com/bpg/gerinfo/238>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/gerinfo/288>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

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Published by **Baishideng Publishing Group Inc**, 7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568 E-mail: office@baishideng.com <https://www.wjgnet.com>



Pancreatic lymphoepithelial cyst with sebaceous differentiation-encountering and management of these rare tumours: A case report and review of literature

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Peer review: Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific quality: Grade B, Grade C

Novelty: Grade B, Grade C

Creativity or innovation: Grade C, Grade C

Scientific significance: Grade B, Grade B

P-Reviewer: Sun PT, MD, PhD, Chief Physician, China

Received: January 21, 2026

Revised: February 17, 2026

Accepted: April 13, 2026

Published online: July 27, 2026

Processing time: 187 Days and 13.9 Hours

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Abstract

BACKGROUND

Lymphoepithelial cysts (LECs) of the pancreas are rare, benign cystic lesions with unclear pathogenesis, and their diagnostic workup is often challenging. LECs with sebaceous differentiation are even more uncommon. They are typically solitary and asymptomatic, found in men and diagnosed incidentally. While imaging modalities and endoscopic ultrasound (EUS) may help identify cystic lesions of the pancreas, LECs can resemble other entities, making accurate pre-operative diagnosis difficult. Final diagnosis is usually confirmed only after resection.

CASE SUMMARY

A 74-year-old male was incidentally diagnosed with an asymptomatic cystic lesion of the pancreas tail. While there were no deviations in laboratory workup or clinical examination, magnetic resonance imaging and EUS identified a cystic lesion 37 mm in diameter and filled with concentric nodules within fluid. Mucin was found within the cyst at biopsy, and mucinous cystic neoplasm was suspected. Laparoscopic distal pancreatectomy with splenectomy was performed, and pathological examination of the specimen identified an LEC with sebaceous glands.

CONCLUSION

This article emphasizes the importance of recognizing the distinct characteristics

of pancreatic LECs to help clinicians make more informed decisions and avoid unnecessary interventions. Continued reporting of similar cases is vital to improve our understanding and refine diagnostic strategies for these rare pancreatic lesions.

Key Words: Lymphoepithelial cyst; Cystic lesions of the pancreas; Sebaceous glands; Diagnostic workup; Surgical resection; Overtreatment; Case report

Core Tip: This article provides a review of the available literature on extremely rare lymphoepithelial cysts (LECs) of the pancreas, accompanied by reporting management of a patient with such a lesion with sebaceous glands. Pancreatic LECs with sebaceous differentiation are benign and lack malignant potential, but they mimic mucinous cystic lesions radiologically and cytologically, often leading to unnecessary surgery. Thorough pathological examination of the resected specimen is important, as the mechanism of pancreatic LECs is not fully understood. Thus, every reported case may contribute to a better understanding of this rare disease.

Citation: Badovinac D, Luzar B. Pancreatic lymphoepithelial cyst with sebaceous differentiation-encountering and management of these rare tumours: A case report and review of literature. *World J Gastrointest Surg* 2026; 18(7): 119186

URL: <https://www.wjgnet.com/1948-9366/full/v18/i7/119186.htm>

DOI: <https://dx.doi.org/10.4240/wjgs.v18.i7.119186>

INTRODUCTION

The pancreas presents a potential site for several different cystic lesions for which diagnostic methods are often inconclusive or dubious. Lymphoepithelial cysts (LEC) are rarely encountered in the pancreas. These are benign, squamous-lined cystic tumors with no potential for malignant alteration[1,2]. The mechanism of LEC histogenesis is not fully understood, and there are several theories on the mechanism of lesion formation: (1) An enlarged or obstructed pancreatic duct is transformed with squamous metaplasia; (2) Inclusion of ectopic pancreatic tissue or epithelium into peripancreatic lymph nodes; (3) Misplacement of branchial cysts during fetal development; and (4) that LEC is a type of teratoma[2-4].

Pancreatic LEC was first described in 1985 by Lühtrath and Schriefers[3] and since then, less than 250 cases have been described in the literature[5]. LECs with sebaceous differentiation are even more rare; to date, only sporadic cases have been reported[6-17]. Outside of the skin, sebaceous glands are often found in other organs of ectodermal origin. However, they are extremely rare in endodermal organs like the pancreas[11]. This article reports a case of pancreatic LEC with sebaceous differentiation and reviews other reports in the literature.

CASE PRESENTATION

Chief complaints

The patient was asymptomatic.

History of present illness

A 74-year-old male without any abdominal symptoms or weight loss was referred to the university hospital for further diagnostic workup in December 2023.

History of past illness

The patient had arterial hypertension, dyslipidemia, chronic atrial fibrillation and peripheral arterial disease with lower extremity claudication. He had no medical history suggestive of past acute pancreatitis episodes.

Personal and family history

The patient ceased smoking years earlier and was an occasional consumer of small quantities of alcohol.

Physical examination

There were no specific deviations that suggested abdominal or gastrointestinal pathology, nor were laboratory tests abnormal, including serum amylase and lipase levels and tumor markers.

Laboratory examinations

As mentioned above, all laboratory tests were normal, including serum tumor markers.

Imaging examinations

The lesion was first discovered incidentally on a chest computed tomography (CT) scan in November 2018. Abdominal CT was indicated, which was performed in August 2019, as the patient did not make an appointment for the scan earlier. An irregular lobulated formation near the pancreatic tail measuring 40 mm × 20 mm was described, with wall thickness up to 1.6 mm. The cyst component had negative Hounsfield Units, with no density alteration after contrast application. Pseudocyst was proposed as the most probable diagnosis (Figure 1). Follow-up imaging was delayed, likely due to the coronavirus disease 2019 pandemic, and the patient forgot about the lesion; subsequently he was lost to follow-up in the years to follow.

Several years later, in July 2023, the pancreatic lesion, now measuring 42 mm × 23 mm, was incidentally rediscovered upon CT urography at a regional hospital for acute urinary retention and hematuria. Magnetic resonance (MR) with MR cholangiopancreatography (MRCP) was performed, describing a well-defined 37 mm × 25 mm large formation at the anterior part of the pancreas tail, consisting of a small amount of fluid and at least five nodular lesions 10 mm in diameter (Figure 2), demonstrating heterogenic hypointensity on T2 sequence and slight hyperintensity on the periphery and hypointensity centrally on T1 sequence, with no postcontrast enhancement. The contents of the cystic lesion demonstrated complete restriction of diffusion. No septations were described. The pancreatic duct was not dilated and did not share communication with the lesion, and the gland parenchyma appeared morphologically normal. Working diagnosis of a pancreatic pseudocyst or walled-off necrosis was made, although there was no other radiological evidence of current or past pancreatitis.

Endoscopic ultrasound (EUS) in December 2023 described a well-defined cystic lesion in the distal part of the pancreas, 30 mm in diameter, which was filled with concentric nodules flowing freely in fluid (Figure 3). Fine-needle aspiration (FNA) of these nodules was performed and a slightly hemorrhagic fluid was collected for cytology. Unfortunately, for unknown reasons, the fluid was not sent for evaluation of tumor marker levels (CA19-9 and CEA). An attempt to take samples of nodular lesions within the cyst was also made, but the nodules were mobile within the fluid (not mural) and presented as necrotic debris. The remaining pancreas parenchyma was homogenous with an appropriate main pancreatic duct. Cytopathological examination identified mucin in the specimen, suggesting diagnosis of mucinous cystic neoplasm (MCN). No malignant cells were found in the specimen.

MULTIDISCIPLINARY EXPERT CONSULTATION

In January 2024, the patient's case was presented to a multidisciplinary team and due to suspicion of a large MCN (more than 40 mm on CT), excellent clinical performance and normal nutritional status of the patient, surgical resection was indicated.

FINAL DIAGNOSIS

A large MCN of the pancreas tail was the primary differential diagnosis.

TREATMENT

Laparoscopic distal pancreatectomy with splenectomy (due to proximity of the splenic hilum and severe post-punction inflammatory adhesions) was performed in early March 2024. The postoperative clinical course was uneventful. A mild biochemical pancreatic leak was present; however, no clinical interventions were needed, and the patient was discharged 7 days after surgery.

OUTCOME AND FOLLOW-UP

Gross examination of the resected pancreatic specimen revealed the presence of a unilocular cystic cavity within the pancreatic tail measuring 30 mm × 20 mm in largest dimensions. The content of the cyst was whitish/yellowish and soft. Histological examination revealed that the cyst was lined by stratified squamous epithelium lacking atypia (Figure 4A and B). Multiple lobules composed of mature sebocytes were present within the stratified squamous epithelium (Figure 4C). In addition, duct-like structures suggestive of sebaceous differentiation were observed (Figure 4D). No hair follicles were identified. The cyst lumen contained limited amounts of laminated keratin, possibly mimicking septations and nodules seen by preoperative imaging modalities. Dense lymphatic tissue was present in the wall of the cyst with focal formation of germinal centers (Figure 4B). The histomorphological features were consistent with a LEC showing areas of sebaceous differentiation. On his last visit to the outpatient clinic in December 2025, the patient was in good clinical condition with no surgical sequelae.

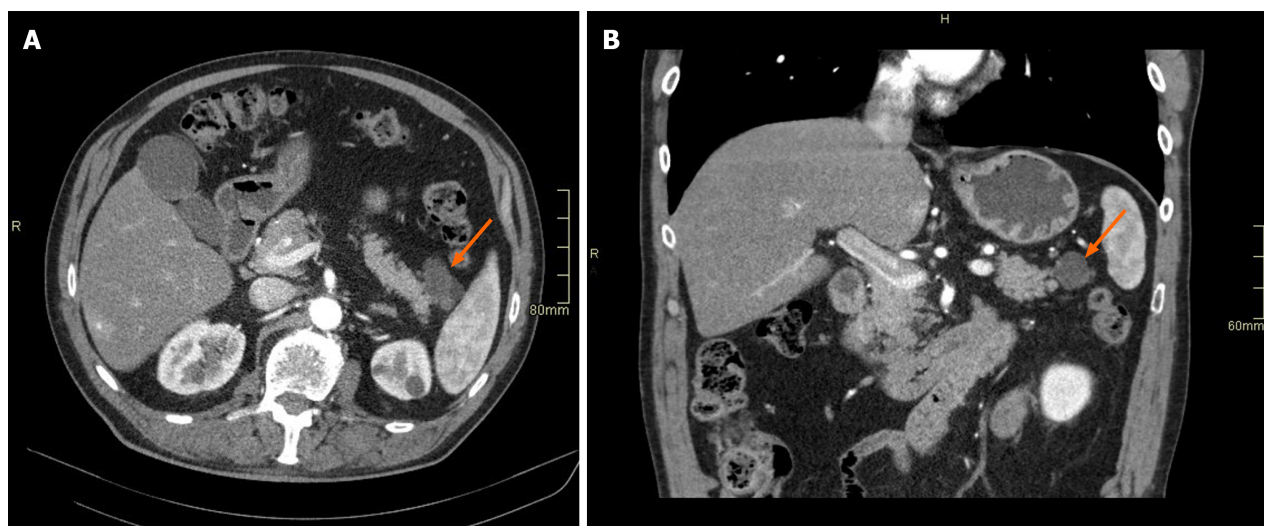


Figure 1 A lobulated lesion visualized by abdominal computed tomography scan in August 2019 (orange arrows). A: Axial view; B: Coronal view.

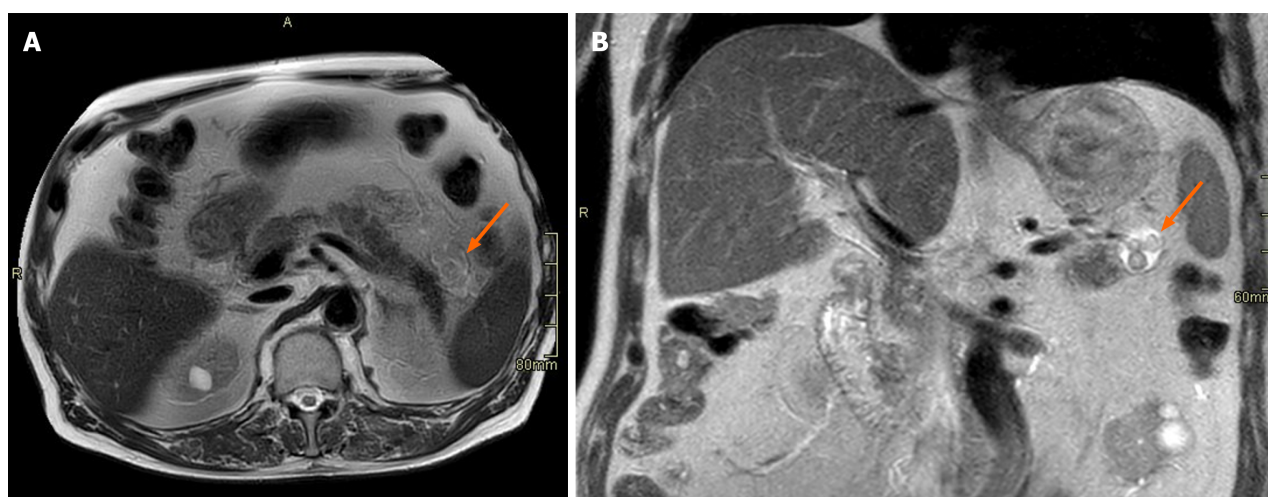


Figure 2 Magnetic resonance of the upper abdomen demonstrating the lesion (orange arrows). A: T2 sequence, axial view; B: Post-contrast T2 sequence, coronal view.

DISCUSSION

Cystic tumors of the pancreas are a heterogeneous group of lesions that often pose a diagnostic challenge. Using highly sensitive imaging modalities, pancreatic cystic lesions can be found in 13%-18% of people in the general population[18]. Using combinations of abdominal CT scan, MRCP and EUS with FNA, the diagnosis can be made between intraductal papillary mucinous neoplasm, serous cystic neoplasm or MCN. However, LEC often proves difficult to diagnose.

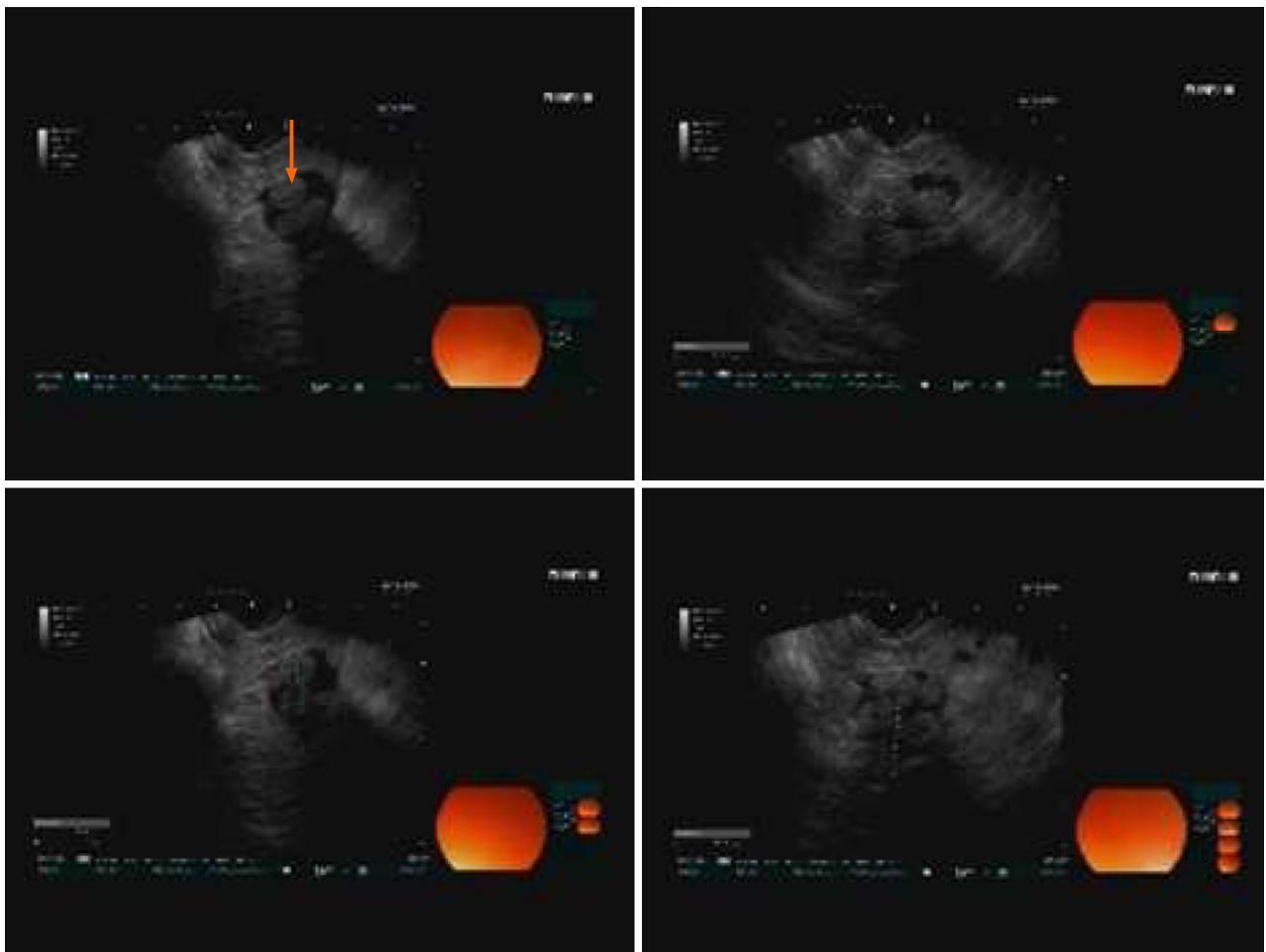
LEC of the pancreas is a very rare benign cystic lesion accounting for about 0.5% of all pancreatic cysts[8]. They are four times more common in males than in females, with the mean age at diagnosis of 55. They are almost exclusively solitary tumors, and in more than 70% of cases, they are in the body or tail of the pancreas. At the time of diagnosis, the mean LEC size is 47 mm, and only approximately half of the cases are symptomatic, mainly due to mass effect, causing abdominal pain, nausea, weight loss and rarely jaundice or fever[5]. CA19-9 serum levels may be elevated in as much as half of the patients[19].

LECs with sebaceous differentiation are even a rarer subgroup of LECs. Sebaceous glands are generally abundant in the skin. Ectopic sebaceous glands are also often found in non-skin organs of ectodermal origin. However, they are very rare in endodermal organs such as the thymus, larynx or esophagus, even within neoplastic lesions[20]. The pancreas is also of endodermal origin. After a thorough review of literature in the English language, we found only sporadic cases of pancreatic LEC with sebaceous differentiation described thus far (Table 1).

The reported cases of pancreatic LEC with sebaceous differentiation have all been in male patients with a mean age of 63.6 years. At 74 years of age, our patient is the second oldest reported. The reason for the male predominance of pancreatic LECs is currently unknown. In contrast, there is no male predominance in LECs of the parotid, which suggests that sex distribution is not related to a universal mechanism but is perhaps organ-specific[21]. As in our case, five patients

Table 1 Features of all the reported cases of pancreatic lymphoepithelial cysts with sebaceous differentiation

Ref.	Year reported	Sex	Age (years)	Location in the pancreas	Size	Loculation	Clinical picture
Fitko <i>et al</i> [6]	1994	Male	60	Body	45 mm × 22 mm × 20 mm	Unilocular	Pain
Rino <i>et al</i> [10]	1995	Male	58	Head	50 mm × 50 mm × 50 mm	Multilocular	Asymptomatic
Koga <i>et al</i> [8]	1995	Male	62	Head	52 mm × 52 mm	Multilocular	Asymptomatic
Fukukura <i>et al</i> [12]	1998	Male	70	Tail	100 mm × 70 mm	Unilocular	Diarrhoea
Fujiwara <i>et al</i> [13]	2000	Male	60	Tail	40 mm × 30 mm × 30 mm	Unilocular	Asymptomatic
Hébert-Magee <i>et al</i> [9]	2009	Male	48	Body	52 mm × 40 mm × 30 mm	Unilocular	Asymptomatic
England and Allen [16]	2011	Male	67	Head	100 mm × 65 mm × 60 mm	Multilocular	No data
Nakamura <i>et al</i> [7]	2013	Male	67	Body	42 mm × 24 mm × 22 mm	Multilocular	Asymptomatic
Maehira <i>et al</i> [11]	2016	Male	66	Head	20 mm	Unilocular	Asymptomatic
Arumugam <i>et al</i> [17]	2016	Male	79	Tail	86 mm × 62 mm	Multilocular	Pain
Samuel <i>et al</i> [14]	2017	Male	67	Tail	37 mm × 19 mm	Unilocular	Pain
Namba <i>et al</i> [15]	2019	Male	49	Tail	No data	Multilocular	Weight loss, diarrhea
Our case	2024	Male	74	Tail	30 mm × 20 mm	Unilocular	Asymptomatic

**Figure 3** Series of images of the cystic lesion with nodular inclusions (orange arrow) seen by endoscopic ultrasound.

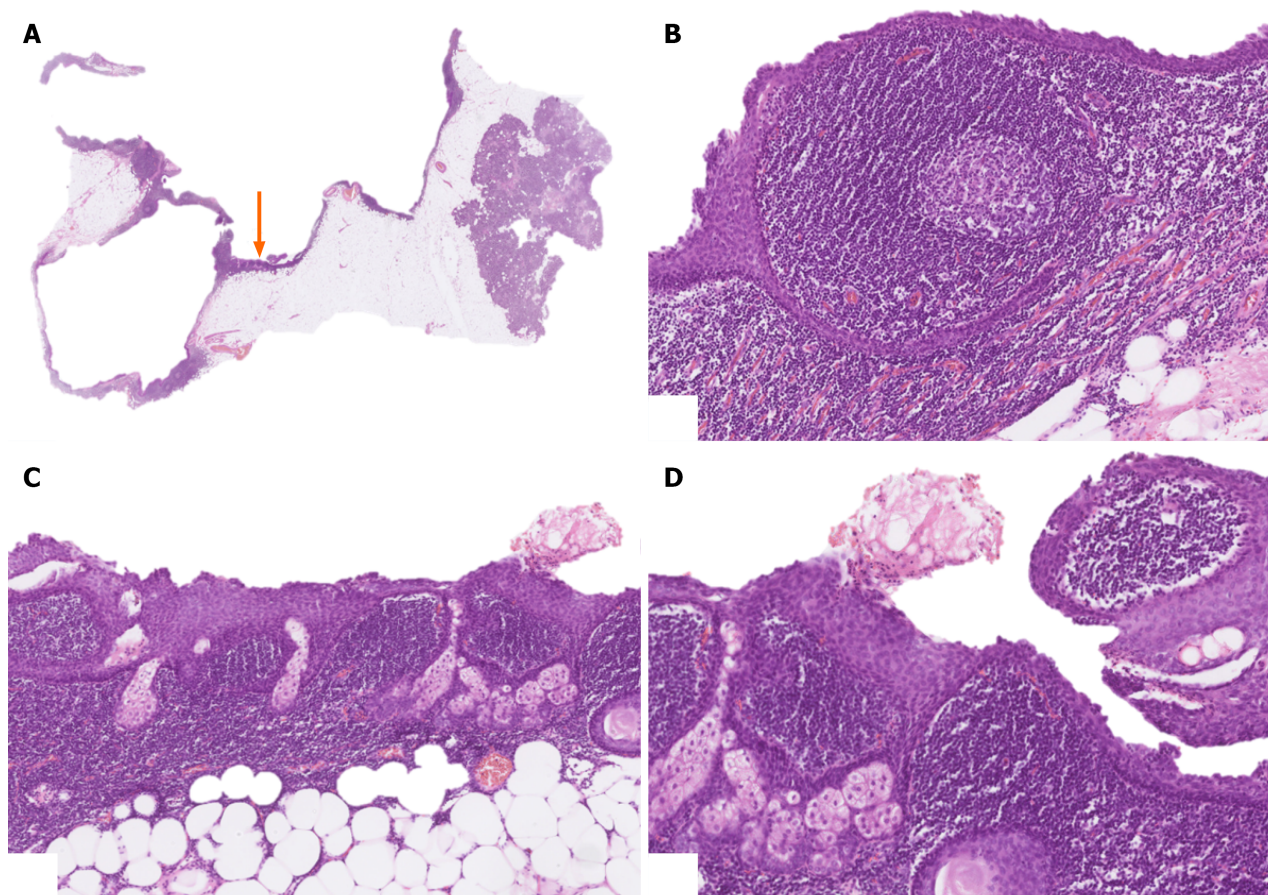


Figure 4 Lymphoepithelial cyst of the pancreas with sebaceous differentiation. A: The cyst was localized in the pancreatic tail. The arrow depicts the area with sebaceous differentiation (5 × magnification); B: The cyst was lined by stratified squamous epithelium. Note the dense lymphatic tissue with formation of germinal centers in the cyst wall (80 × magnification); C: Numerous mature sebaceous lobules were present within the stratified squamous epithelium (40 × magnification); D: In addition to mature sebaceous glands, focal formation of sebaceous ducts was also present (80 × magnification).

presented with the tumor in the pancreas tail, four in the pancreatic head, and three in the pancreas body. The average reported size was 53 mm, and seven out of 13 presented as a unilocular cystic lesion. Five of the reported tumors had caused abdominal symptoms, while the rest were asymptomatic. Most cases were reported to be identified incidentally.

Of all 13 patients, only one had a conclusive and accurate preoperative diagnosis with the help of FNA. In other patients, even with FNA, the preoperative diagnosis was either inconclusive or highly variable, ranging from epidermoid cyst and MCN to cystadenocarcinoma. EUS, CT-guided biopsy, or FNA is not sensitive enough for accurate diagnosis because of their poor ability to detect fluid or acellular material. Furthermore, cyst-specific sensitivity of cytological samples is modest. Thus, while such an approach may provide cytologic material suggestive of LEC, its overall diagnostic yield varies from 21% to 63% [19,22-24]. Macroscopically, the aspirate sometimes presents as clear yellow fluid, but it is more often a whitish, caseous, greasy material with fat and keratin detritus. Microscopic examination reveals a stratified squamous epithelium with a subepithelial layer of lymphoid tissue containing lymphoid follicles [2,17,25]. Amylase levels are typically low in LEC, yet CA19-9 levels are often elevated [26]. FNA should be primarily used to exclude malignancy or MCN rather than specifically diagnose rare benign lesions of the pancreas [22,24]. In our patient, FNA could not specifically diagnose LEC, although EUS detected floating, likely keratin nodules within the cyst. However, considering that cytopathology suggested MCN and the large size of the lesion, even early identification of keratin nodules suggestive of LEC could not change the decision for surgical treatment. Thus, FNA should not be routinely utilized in the diagnosis of pancreatic LECs but may be considered in the presence of suspicious features or when the diagnosis is uncertain.

LEC of the pancreas has both solid and liquid elements visible by diagnostic imaging, making it difficult to rule out malignancy or distinguish it from other pathologies, especially MCN. Certain radiological features on imaging modalities may help with preoperative diagnosis, yet they are not specific to any single disease. Complex cystic appearance or a mixture of cystic and solid components is among the most reported findings, as is exophytic location of the lesion usually arising from the pancreas body or tail. Floating ball-like components within the cyst, as seen by EUS in our patient, are another very important feature suggestive of LEC. These are typically comprised of keratin, which can form a solid or sludge [27]. LECs have no communication with the main pancreatic duct, and a lipid component of the tumor is sometimes observed. They demonstrate higher attenuation on unenhanced CT compared with intraductal papillary mucinous neoplasm or MCN, but not relative to serous cystic neoplasms. On MR imaging, lesions may show mild T1 hyperintensity and marked T2 hyperintensity [12,26,28]. However, these features overlap with those of other cystic pancreatic tumors [23].

Pancreatic LECs have no malignant potential[1,2]. As demonstrated in our case, no significant tumor growth, morphological changes or clinical symptom development were observed over the 5 years from initial incidental detection to surgical resection. In this regard, our case represents the longest reported follow-up of a patient with pancreatic LEC. Unfortunately, most of these cystic tumors are definitively diagnosed only after surgical resection. Given the benign nature of LECs, surgery may expose asymptomatic patients to overtreatment and potentially severe postoperative complications. Therefore, accurate preoperative diagnosis requires a combination of clinical, radiological and cytological data, allowing asymptomatic patients to potentially avoid surgical resection.

On pathological examination of the surgically resected tissue, reported cases of LECs with sebaceous differentiation show cysts with thin, transparent walls filled with soft yellow or caseous material. The cyst walls are lined by squamous epithelium, sometimes with keratinization, and are underlain by dense lymphoid tissue, occasionally containing germinal centers. No hair follicles have been identified in any reported specimens.

Sebaceous glands are typically embedded within the epithelium[8-10,13], although two cases described glands located beneath the epithelial layer within the lymphoid tissue[6,11]. Aside from our case, a review of the literature did not identify other examples of sebaceous ducts within lymphoepithelial pancreatic cysts. However, in the absence of immunohistochemical staining, identification of sebaceous ducts relies on morphology alone. Some authors have also noted pancreatic tissue adherent to the cyst wall, and none of the reported cases demonstrated dysplasia or malignancy.

The pathogenesis of LECs remains unclear. In addition to previously proposed theories, a correlation between LECs of the parotid gland and human immunodeficiency virus (HIV) infection has been reported[29]. However, only a single case of pancreatic LEC has been associated with HIV infection[30], making a meaningful association between these entities unlikely.

Given the limited number of reported cases, the mechanism underlying sebaceous differentiation at various sites is also not well understood, but it may reflect the multipotentiality of germinative cells within the squamous epithelium[6]. Further detailed case reports are needed to better elucidate the pathogenesis of pancreatic LECs, with or without sebaceous differentiation.

This study is limited by the reporting of a single case of pancreatic LEC with sebaceous differentiation, with few comparable cases available in the literature. Additionally, only English-language publications were reviewed, so relevant non-English reports may have been overlooked. Furthermore, the absence of CA19-9 and CEA measurements from cyst fluid obtained during EUS represents a missed opportunity to inform preoperative diagnosis and better define the role of tumor markers in pancreatic LECs.

CONCLUSION

Pancreatic LECs are a rare group of benign tumors, and those with sebaceous differentiation are even rarer, with only sporadic cases reported. These lesions are typically clinically silent and carry no malignant potential; therefore, specific treatment is generally not indicated. However, despite advances in imaging and the use of FNA, the diagnostic workup of these cystic lesions is often misleading or inconclusive. As a result, a definitive diagnosis is usually established only after surgical resection and histopathological evaluation. Detailed reporting of such cases is important to improve recognition and understanding of this entity.

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FOOTNOTES

Specialty type: Gastroenterology and hepatology

Country of origin: Slovenia

Author contributions: Badovinac D and Luzar B were responsible for literature review, manuscript conceptualization and writing; all authors have read and agreed to the published version of the manuscript.

Informed consent statement: Informed consent of the patient for publication of his case was obtained.

Conflict-of-interest statement: The authors declare no conflict of interest.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Corresponding Author's Membership in Professional Societies: Slovenian Society for Gastroenterology and Hepatology.

S-Editor: Qu XL

L-Editor: Filipodia

P-Editor: Xu ZH



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