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Case report

Lymphoepithelial cyst of the pancreas with sebaceous differentiation

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Abstract: We recently encountered a patient with a lymphoepithelial cyst of the pancreas with sebaceous differentiation. We sought to compare the characteristics of this patient with those previously reported in order to foster a keener understanding of this rare clinical entity. After reviewing the present patient's case in detail, we conducted a comprehensive review of the English-language literature and analyzed the clinical characteristics of reported cases of lymphoepithelial cysts. Our patient was an asymptomatic 60-year-old man who presented with an incidental finding of a cystic lesion in the tail of the pancreas documented by computed tomography. The cyst was enucleated, and was found to contain keratinized material. It was lined by squamous epithelium with small sebaceous glands, and surrounded by lymphoid tissue with germinal centers. Of 33 reported cases, only 6 (18%) contained sebaceous glands. In all patients who underwent operation, the cysts were easily resected, and the outcome was favorable. Lymphoepithelial cyst of the pancreas is rare, and may be difficult to differentiate from cystic neoplasms preoperatively. Therefore resection is indicated. The diagnosis, however, can be confirmed by careful histologic review, and the prognosis is excellent.

Key words: pancreatic true cyst, lymphoepithelial cyst, sebaceous gland

Introduction

Cystic lesions of the pancreas can be classified histologically as pseudocysts, congenital true cysts, acquired true cysts, and cystic neoplasms. True cysts, characterized by an epithelial lining, are rare and display a broad histologic spectrum. Lymphoepithelial cyst (LEC) is defined by the Armed Forces Institute of Pathology (AFIP) classification[1] as a cystic lesion lined by mature keratinizing squamous epithelium supported by distinct lymphoid tissue. According to the World Health Organization (WHO) international histological classification of salivary gland tumors, a benign lymphoepithelial lesion is one of the tumor-like lesions that often occur in the neck.[2] LEC of the pancreas is a rare lesion of unknown etiology. We encountered a case of LEC of the pancreas, which was lined by mature squamous epithelium with small sebaceous glands. The lesion resembled a dermoid cyst, but could be distinguished by the presence of a prominent lymphoid component. We present this case in detail, and discuss its importance in the context of a comprehensive review of the literature.

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Case report

A 60-year-old man was referred to Hyogo Medical Center for further evaluation of a cystic mass in the pancreatic tail that was detected by computed tomography (CT) of the upper abdomen. The patient had a 2-year history of liver dysfunction due to alcoholism. He had no history of abdominal surgery or trauma. Physical examination revealed no abdominal tenderness, organomegaly, or abdominal masses.

Laboratory examination of the serum yielded the following values: amylase, 219 IU/l (normal range [NR], 65 to 235 IU/l); fasting blood sugar, 97 mg/dl (NR, 70 to 105 mg/dl); elastase 1 activity, 262 ng/dl (NR, less than 400 ng/dl); and carcinoembryonic antigen (CEA), 4.9 ng/ml (NR, less than 5.0 ng/ml). The carbohydrate antigen 19-9 (CA19-9) level was elevated to 98 U/ml (NR, less than 37.0 U/ml).

CT of the abdomen showed a round mass, measuring 3 cm in diameter, protruding eccentrically from the tail

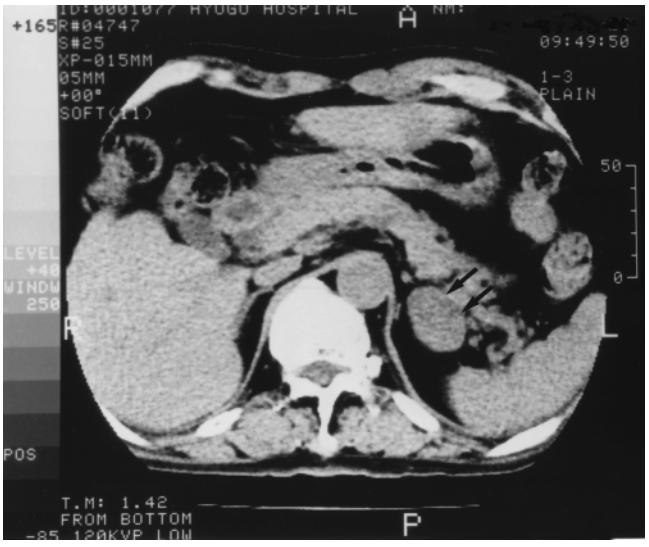

Fig. 1. Computed tomography scan of the abdomen reveals a round mass, measuring 3 cm in diameter, protruding eccentrically from the tail of the pancreas (*arrows*)

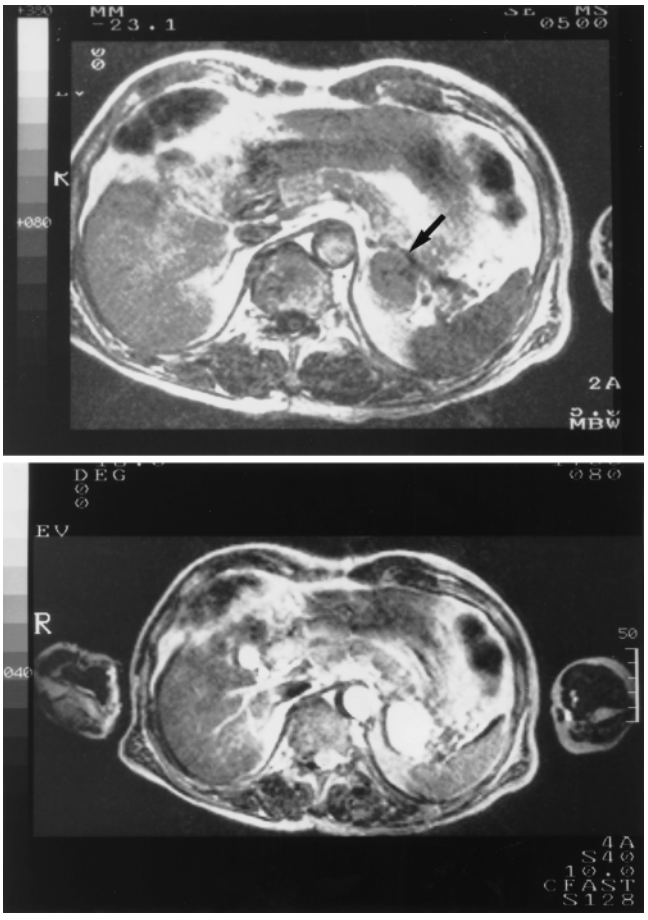

Fig. 2a,b. Magnetic resonance imaging of lymphoepithelial cyst of the pancreas. **a** T1-Weighted image of the abdomen, revealing a hypointense mass with low signal structures (*arrow*). **b** T2-Weighted image of the abdomen, revealing a hyperintense mass consistent with a cystic lesion

of the pancreas (Fig. 1). The density of the mass was identical to that of the pancreatic parenchyma. Radiologic studies with contrast medium showed that the lesion was a spherical low-attenuation mass with an enhancing rim; it was thus considered to be of cystic density. Ultrasonography (US) demonstrated a hypoechoic mass with posterior echo enhancement and lateral shadowing despite a solid internal echo. T1-Weighted magnetic resonance imaging (MRI) revealed a hypointense mass with low signal structures which was hyperintense on T2-weighted images, consistent with the presence of a cystic lesion (Fig. 2a,b). Abdominal angiography showed the splenic artery to be externally compressed by the mass in the pancreas. Endoscopic retrograde cholangiopancreatography (ERCP) showed no abnormalities in either the pancreatic duct or the extrahepatic biliary tract. These findings, in particular, the T1-weighted MRI, were felt to be consistent with a diagnosis of mucinous cystic neoplasm. At laparotomy, a smooth, well circumscribed mass was found in the tail of the pancreas. No gross evidence of pancreatitis or lymph node enlargement was noted. The splenic artery was compressed but did not appear to be infiltrated by the mass.

The mass was enucleated, revealing a smooth, brownish cyst measuring 4 × 3 × 3 cm and composed exclusively of semisolid, tan-white, atheromatous material. The cyst wall, which was easily separated from the cyst contents, ranged from 0.2 to 0.3 cm in thickness.

On microscopic examination, the cyst was lined by keratinizing stratified squamous epithelium several cell layers thick. The cyst wall was surrounded by a dense lymphocytic infiltrate with scattered germinal centers (Fig. 3a). The lesion was well circumscribed by a thin, fibrous capsule. There was no hair, but sebaceous glands were present in the squamous epithelium (Fig. 3b). Nuclear pleomorphism and mitotic figures were absent. The histopathologic diagnosis was a benign lymphoepithelial cyst of the pancreas. The patient recovered uneventfully and was well at last follow-up 1 year after surgery. His CA 19-9 level remained slightly elevated, at 90 U/ml.

Discussion

Cystic lesions of the pancreas can be classified as pseudocysts and true cysts. The distinguishing characteristic of true cysts is the presence of an epithelial lining, while the wall of a pseudocyst is completely fibrous. True cysts, lined by stratified squamous epithe-

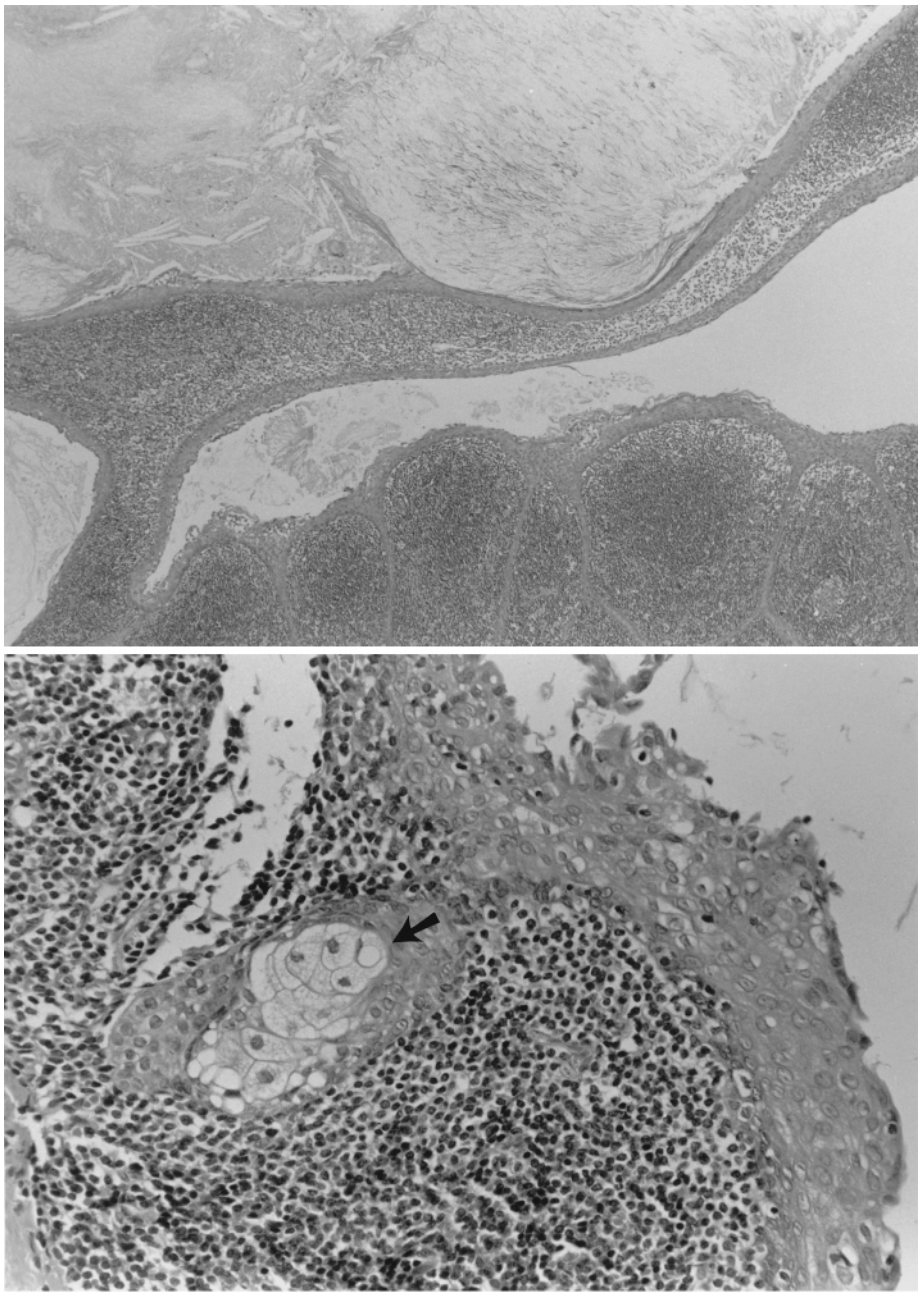

Fig. 3a,b. Photomicrograph of the cyst. **a** The cyst is lined by squamous epithelium and is surrounded by lymphoid tissue with germinal centers. **b** Sebaceous glands are seen beneath the squamous epithelium of the cyst (*arrow*). **a** H&E, ×100; **b** H&E, ×200

lium, include epidermoid cysts and LEC. LEC of the pancreas is characterized by the presence of mature, keratinizing squamous epithelium surrounded by lymphoid tissue. The histogenesis of LEC has not been established. LEC is a tumor-like lesion that often occurs in the neck.[1–3] Although pancreatic LECs are always attached to the pancreas, whether they actually arise from the pancreas is not known. To the best of the authors' knowledge, only 34 cases of LEC of the pancreas, including the present case, have been reported in the English-language literature.[3–26] The clinical features of these patients are summarized in Table 1. Of the 33 previously reported patients 29 were men and 4, women, with a mean age of 55.7 ± 12.0 years (range, 26 to 74 years). Thirteen of the 34 cysts (44.2%) were located only in the head of the pancreas, 12 (35.3%) only in the body, and 7 (20.6%) only in the tail. Nineteen of the 34 cysts (55.9%) were multilocular, 1 (2.9%) was oligolocular, 1 (2.9%) was bilocular, and 13 (38.2%) were unilocular.

LEC usually occurs as an asymptomatic abdominal tumor incidentally detected by CT or US, although some LECs cause clinical symptoms, such as diarrhea or abdominal pain, by extrinsic compression of the

Table 1. Clinical features of 33 lymphoepithelial cysts of the pancreas reported in the literature, plus features of our patient

Case number	Year	Author	Age (years)	Sex	Symptoms	Location	Size (cm)	Loculation	Diagnostic studies	Serum CA 19-9 (U/ml)	Appendages present
1	1985	Luchtrath[19,21]	36	M	Weight loss, leukocytosis	Body, tail	9 × 5 × 2	Multilocular	CT, US		
2	1987	Truong[4]	35	M	Diarrhea, abdominal pain	Body	6 × 6 × 4	Unilocular	CT		
3	1987	Carr[5]	50	F	Asymptomatic	Body	3	Multilocular	Surgery		
4	1990	Mockli[6]	72	M	Dyspnea	Tail	4	Multilocular	Autopsy		
5	1990	Yamamoto[7]	64	M	Asymptomatic	Body	4 × 3 × 3	Multilocular	CT, US, EUS, MRI	70	
6	1990	Mitchell[8]	42	M	Abdominal pain, fever	Head	6	Multilocular	CT, ERCP, FNAB		
7	1991	Hisaoka[9]	65	M	Asymptomatic	Body	5 × 3 × 2.5	Multilocular	CT, US, EUS	Elevated	
8	1991	Ramsden[10]	73	M	Asymptomatic	Body	2	Unilocular	Autopsy		
9	1991	Kaiserling[11]	53	M	Fatigue	Tail	8	Multilocular	CT, US, ERCP, FNAB	125	
10	1992	DiCorato[3]	43	M	Asymptomatic	Tail	3 × 3 × 1.5	Multilocular	CT		
11	1992	Bastens[19,21]	66	F	Abdominal pain, weight loss	Head	4	Unilocular	CT, US, ERCP		
12	1993	Cappellari[12]	44	M	Abdominal pain, back pain	Head	6	Bilocular	CT, FNAB		
13	1993	Hausegger[19,21]	66	M	Asymptomatic	Tail	5	Unilocular	CT, ERCP		
14	1993	De Lorenzi[19,21]	59	M	Asymptomatic	Head	6.5	Multilocular	CT, US, MRI, ERCP		
15	1994	Goodman[13]	68	M	Abdominal pain, nausea	Body	13	Unilocular	CT, ERCP, UGI		
16	1994	Ueno[14]	69	M	Abdominal pain	Body		Multilocular	CT, US, MRI, ERCP	118	
17	1994	Ueno[14]	58	M	Abdominal pain	Body	4	Multilocular	CT, US, ERCP	2690	
18	1994	Fitko[15]	60	M	Abdominal pain	Body	4.5 × 2.5 × 2	Unilocular	CT, US, FNAB		Sebaceous glands
19	1995	Katz[16]	42	F	Abdominal pain, back pain	Head	5 × 4 × 3.5	Multilocular	CT, ERCP		
20	1995	Koga[17]	62	M	Asymptomatic	Head	5.2 × 5.2	Multilocular	CT, US, MRI, ERCP		Sebaceous glands
21	1995	Koga[17]	56	M	Asymptomatic	Head	3.5 × 2 × 2	Multilocular	CT, US, MRI, ERCP		Sebaceous glands
22	1995	Rino[18]	58	M	Asymptomatic	Head	5 × 5 × 5	Multilocular	CT, US, ERCP, FNAB	39	Sebaceous glands
23	1996	Iacono[19]	56	M	Epigastralgia	Head, body	3.5	Unilocular	CT, US		
24	1996	Iacono[19]	47	M	Asymptomatic	Body, Tail	7	Unilocular	CT, US		
25	1996	Schinke-Nickl[20]	59	—	Diarrhea, abdominal cramps	Head	6 × 3 × 2	Oligolocular	CT, MRI, ERCP	Elevated	
26	1997	Kazumori[26]	48	M	General fatigue	Tail	2.5 × 2.3 × 1.3	Multilocular	CT, US, MRI	79	
27	1997	Gafa[23]	57	M	Abdominal pain	Head	2.5	Unilocular	US		
28	1998	Strapko[21]	42	F	Abdominal pain, fever	Body	4	Multilocular	CT, US, ERCP	63	
29	1998	Fukukura[22]	70	M	Diarrhea	Tail	10 × 7	Unilocular	CT, US, MRI		Sebaceous glands
30	1998	Fukukura[22]	74	M	Asymptomatic	Head	4 × 3	Multilocular	CT, US, MRI		
31	1998	Bolis[24]	64	M	Gastrointestinal complaints	Head	5.5 × 3	Unilocular	CT, EUS, FNAB		
32	1998	Kim[25]	26	M	Abdominal pain	Head	4 × 4 × 4	Unilocular	CT, US	169	
33	1998	Kim[25]	50	M	Epigastralgia	Body	9 × 6 × 4	Multilocular	CT, US		
34		Present patient	60	M	Asymptomatic	Tail	4 × 3 × 3	Unilocular	CT, US, MRI	98	Sebaceous glands

CT, Computed tomography; US, ultrasonography; ERCP, endoscopic retrograde cholangiopancreatography; MRI, magnetic resonance imaging; FNAB, fine needle aspiration biopsy; EUS, endoscopic ultrasonography; CA, carbohydrate antigen

pancreatic duct. Of the 33 cases of LEC we reviewed, 30 were detected by CT and 22 were detected by US (some being detected by both modalities). CT uniformly displayed a well circumscribed, round mass of low density protruding from the surface of the pancreas, consistent with a cystic lesion.[27] US was not as consistent in identifying the lesion as cystic. The rest of the pancreas was reported as normal by both CT and US in all patients.[27] The MRI findings of LEC have been described by Koga et al.,[17] who characterized the lesions as hyper-in-hypointense on T1-weighted imaging and hypo-in-hyperintense on T2-weighted imaging. This signal pattern was felt to reflect the keratinized material. However, in the present patient, the lesion was hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging, as has been described by Yamamoto et al.[7]

Patients with LEC do not present with typical laboratory findings. Slight elevations of CA19-9 were present in 11 of the 34 reported patients (including our patient) (32.4%). Elevated CA19-9 levels in cystic fluid, as well as in the serum, had been noted in 2 of the 33 patients reported previously (6.1%).[11,14] As it has been shown that the excretory ducts of the normal pancreatic tissue and some of the epithelial cells lining the cyst were immunoreactive for CA19-9, it can be concluded that CA19-9 in the cyst contents is probably produced by cells derived from the exocrine pancreas.[11] Schinke-Nickl et al.[20] reported a patient in whom the CA19-9 level was elevated only in the serum, and not in the cyst aspirate. Yamamoto et al.[7] concluded that there was no relationship between LEC and elevated CA19-9 levels, because the CA19-9 levels remained elevated after resection. A high serum level of this tumor marker may lead to an erroneous diagnosis of neoplasm, and therefore CA 19-9 serum levels should not be used to diagnose such lesions preoperatively.[21] Excluding the 2 patients in whom the LEC was detected only at autopsy, the cysts were removed easily, with uneventful postoperative recovery periods and favorable outcomes.[27] Fine needle aspiration biopsy (FNAB) is becoming increasingly important in the early diagnosis of pancreatic lesions.[6,18,24] In LEC, FNAB shows threads of tissue composed of stratified squamous epithelium with a small subepithelial, mature lymphocytic infiltrate and keratinous material.[6,24] In the present patient, FNAB could not be performed for technical reasons. Bolis et al.[24] have reported that FNAB is reliable and that its use may prevent unnecessary surgery in patients with LEC of the pancreas.

In the present patient, there were small sebaceous glands beneath the epithelium, and lymphoid tissue containing germinal centers surrounding the epithelium. In five previously reported patients, sebaceous glands were detected beneath the squamous epithelium. The possibility of a dermoid cyst was considered in the present patient. Ishida et al.[28] have reported a dermoid cyst surrounded by lymphoid tissue without germinal centers. However, lack of hair follicles and sweat glands and the presence of dense lymphoid tissue with germinal centers in our patient confirmed the histopathologic diagnosis of LEC of the pancreas. The occurrence of sebaceous glands in various locations unrelated to hair follicles has been well documented.[29] Sebaceous gland differentiation may be due to the pluripotential nature of germinative cells in the squamous epithelium.[15]

In conclusion, LEC of the pancreas should be considered in the differential diagnosis of cystic lesions of the pancreas. Preoperative diagnosis is difficult, and the lesion may be mistaken for a neoplastic process.[21] Serum tumor markers may be misleading. For these reasons, surgical excision is usually performed. However, LEC is a benign tumor-like lesion and surgery can be avoided with a reliable preoperative diagnosis.

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