

LETTER

Lymphoepithelial Cyst of Pancreas. Role of Endoscopic Ultrasound Guided Fine Needle Aspiration

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Summary

Lymphoepithelial cysts of the pancreas are extremely rare, benign, nonneoplastic cysts that may simulate pseudocysts or cystic neoplasm of the pancreas. Endosonographic and cytologic features of pancreatic lymphoepithelial cysts are poorly characterized because of their rarity. However, appropriate prospective diagnosis of pancreatic lymphoepithelial cysts using endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) cytology may permit conservative management because of their benign nature. We conducted a MEDLINE search using the MeSH terms “pancreas”, “cyst” and identified 16 patients who were diagnosed with endosonography or computerized tomography (CT) guided fine needle aspiration. Usefulness and pitfalls of EUS- or CT-guided cyst fluid analysis in the pre-operative diagnosis of pancreatic lymphoepithelial cysts are discussed.

Dear Sir:

endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) of pancreatic lesions is now well accepted in clinical practice since it allows for a definitive diagnosis of most pancreatic lesions. EUS-FNA is used increasingly for patients with pancreatic cystic lesions to distinguish lesions that must be resected from lesions that can be managed

expectantly. Lymphoepithelial cysts (LECs) of the pancreas are extremely rare, benign, nonneoplastic cysts that can simulate cystic neoplasms clinically and radiographically. Endosonographic as well as cytologic features of LECs are poorly defined because of their rarity. We conducted a systematic review of MEDLINE/PubMed to identify patients with LEC reported in the English language literature that were diagnosed with a CT- or EUS-guided FNA to study the role of EUS-FNA in differentiating pancreatic LECs from other cystic lesions of the pancreas.

The systematic search of MEDLINE/PubMed database from 1950 to 2007 was conducted using the MeSH terms “pancreas” and “cyst”. The search was limited to “Humans” and “English” language. The search revealed a total of 1,988 articles, each article was reviewed. The bibliography of the relevant articles was also searched to identify additional studies. A total of 16 patients with lymphoepithelial cyst diagnosed by a CT or EUS guided FNA were identified and are summarized in Table 1.

The term “LEC of the pancreas” was proposed by Truong *et al.* in 1987 [1]. The morphologic findings are distinctive and were first described by Luchtrath and Schriefers, who noted the histologic similarity to brachial cleft cyst of the lateral neck [2]. The etiopathogenesis as well as histogenesis of LECs remain unclear; however, the lesions are not believed to be neoplastic and to date

no metastatic behavior has been reported. The largest series in the literature was reported by Adsay *et al.* [3], which included a total of 12 patients. LECs occur in both genders at any age, but more commonly in the middle-age man. The lesion may appear either intrapancreatic or peripancreatic and may be either uniloculated or multiloculated containing keratinous debris.

The first description of cytologic findings of LECs was published by Mitchell in 1990 [4]. However, the definite criteria for cytologic diagnosis of LECs are not available likely because of rarity of this clinical condition. To our knowledge, 16 patients with LECs have been reported who were diagnosed by CT- or EUS-guided FNA (Table 1). The FNA specimens typically showed abundant

anucleated squamous cells with few benign appearing nucleated squamous cells; keratinous and amorphous debris; occasional multinucleated giant cells; and plate-like cholesterol crystals. The presence of lymphocytes was variable in FNA specimens likely because of sampling error, aspiration of cyst content as opposed to cyst wall aspiration. The occasional presence of mucinous epithelium suggests contamination with duodenal or gastric epithelium.

LECs appears hypoechoic, uniloculated (Figure 1) or multiloculated on EUS. Occasionally, fine or coarse sludge like hyperechoic echo architecture is also seen likely due to the debris within the cyst (Figure 1). Differential diagnosis of LEC may include pseudocyst or cystic neoplasm of the pancreas

Table 1. Clinical and cytology findings of computed tomography- or endoscopic ultrasound-guided fine needle aspiration of pancreatic lymphoepithelial cysts.

Case Reference	Age (years)	Gender	Symptoms	Size (cm)	Location	Chemistry
Patients diagnosed by a CT-guided FNA						
#1 Mitchell 1990 [4]	42	Male	Abdominal pain	6	Head	None
#2 Cappellari 1993 [5]	44	Male	Abdominal pain	6	Head	Amylase: 120 U/L
#3 Rino 1995 [6]	58	Male	Asymptomatic	6.1	Head	None
#4 Bolis 1998 [7]	64	Male	Abdominal pain	5.5	Head, body	None
#5 Centeno 1999 [8]	47	Male	Abdominal pain	2	Tail	CEA: 26,880 ng/mL CA 125: 11 U/L CA 19-9: >5x10 ⁶ U/mL Amylase: 256 U/L
#6 Liu 1999 [9]	56	Male	Abdominal pain	5	Tail	None
Patients diagnosed by an EUS-guided FNA						
#7 Liu 1999 [9]	49	Male	Abdominal pain	6	Tail	None
#8 Mandavilli 1999 [10]	49	Female	Abdominal pain	6	Neck, body	None
#9 Zou 2004 [11]	43	Female	Abdominal pain	4.4	Body, tail	None
#10 Capitanich 2004 [12]	53	Male	Abdominal pain	5	Tail	None
#11 Policarpio-Nicolas 2006 [13]	63	Male	Abdominal pain	6	Neck, body	CEA: 35,028 ng/mL Amylase: 480 U/L Lipase: 20 U/L
#12 Policarpio-Nicolas 2006 [13]	33	Male	Abdominal pain	2.7	Head	None
#13 Policarpio-Nicolas 2006 [13]	58	Female	Abdominal pain	1.8	Tail	None
#14 Policarpio-Nicolas 2006 [13]	48	Male	Shortness of breath	4	Body	None
#15 Renou 2007 [14]	45	Female	Incidental	3	Head	CEA: 413 ng/mL CA 19-9: 39,612 U/mL Amylase/Lipase: normal
#16 Hebert-Magee 2007 [15]	48	Male	Abdominal pain	4.4	Body	None

CA: carbohydrate antigen; CEA: carcinoembryonic antigen; CT: computed tomography; EUS: endoscopic ultrasound; FNA: fine needle aspiration

Table 1. (Continues).

Case	CT/EUS morphology	FNA findings	Cell block	Final
Patients diagnosed by a CT-guided FNA				
#1	Low density mass	Anucleated squamous cells and benign nucleated cells	None	LEC
#2	Cystic mass	Numerous anucleated squamous cells, few superficial squamous cells, histiocytes, rare lymphocytes, and plate-like cholesterol crystals	None	LEC
#3	Cystic mass	Anucleated and nucleated squamous cells	None	LEC
#4	Homogenous mass	None	Stratified squamous epithelium with subepithelial lymphocytic infiltrates and keratinous material	None
#5	Unilocular cystic lesion	None	Keratinous debris, mature keratinized squamous epithelium, and wall with dense lymphoid infiltrate	LEC
#6	Cystic mass	Predominantly anucleated cells, rare benign nucleated cells, background of keratinous and amorphous debris, and plate-like cholesterol crystals	Keratinized squamous epithelium with distinct granular cell layer and lymphoid aggregate	LEC
Patients diagnosed by an EUS-guided FNA				
#7	Not described	Predominantly anucleated squamous cells, rare benign nucleated cells, background of keratinous and amorphous debris, and plate-like cholesterol crystals	None	LEC
#8	Not described	Mixture of benign squamous epithelial cells, anucleated squames, and lymphocytes in the background of keratinaceous debris	Fragments of benign squamous epithelium, lymphoid tissue, foreign body type giant cells, numerous cholesterol clefts	LEC
#9	Not described	Keratinizing squamous epithelial cells some which showed no nucleus and a few lymphocytes	None	None
#10	Isoechoic with fine granular tissue	None	None	LEC
#11	Hypoechoic, multilocular	Numerous anucleated squamous cells with keratinous mucoid-appearing debris, rare benign nucleated squamous cells, mucinous epithelium (contaminant) and plate-like cholesterol crystals	Anucleated keratinous debris, cholesterol crystals, stromal tissue with mucinous epithelium	LEC
#12	Hypoechoic, multilocular	Numerous anucleated squamous cells and amorphous keratinous debris, few benign parakeratotic squamous cells, and fragments of squamous cells	None	LEC
#13	Hypoechoic, unilocular	Numerous anucleated squamous cells, foreign body giant cells, and amorphous keratinous debris	None	LEC
#14	Hypoechoic, unilocular	Numerous anucleated squamous cells, amorphous keratinous debris, rare benign nucleated squamous cells, and plate-like cholesterol crystals	None	None
#15	Hypoechoic, unilocular, fine sludge like hyperechoic material ("starry sky")	Inflammatory cells consisting mainly of histiocytes and some columnar epithelial cells	None	LEC
#16	Hypoechoic, unilocular, coarse sludge like hyperechoic material	Mixture of anucleated squamous epithelial cells, cholesterol crystals, histiocytes, lymphocytes, background of keratinous and amorphous debris	None	LEC

CT: computed tomography; EUS: endoscopic ultrasound; FNA: fine needle aspiration; LEC: lymphoepithelial cyst

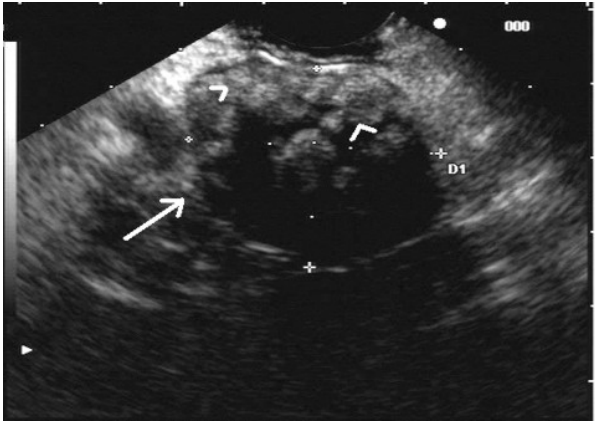


Figure 1. Endosonographic view showing the hypoechoic lesion (arrow) with hyperechoic sludge like material likely representing debris (arrowheads); the lesion was resected and confirmed to be a lymphoepithelial cyst on histopathology.

such as mucinous cystic neoplasm and intraductal papillary mucinous neoplasm. Squamous epithelium should not be seen in aspirates from pseudocyst and amylase levels are usually elevated markedly, whereas CEA levels are usually lower [8]. Aspirates from mucinous cysts usually show background extracellular mucus with or without mucinous epithelium. However, the degenerated squamous material of LEC may be misinterpreted as mucoid material [10, 13]. Chemical analysis of pancreatic LECs fluid has been reported rarely (Table 1). Normal or slightly increased amylase levels and high CEA and CA 19-9 have been reported [8, 13, 14]. Significant increase in CEA and CA 19-9 can be misinterpreted leading to a false diagnosis of mucinous neoplasm especially because EUS-guided FNA samples may show both squamous and glandular contaminant. However, the presence of abundant anucleated squamous epithelium should favor a diagnosis of pancreatic LEC.

If the patient is asymptomatic and EUS-FNA firmly establishes the diagnosis of LEC based on cytological examination of the cyst fluid, surgery can be avoided and then patient may be followed with serial cross-sectional imaging of the upper abdomen [16]. However, the absence of LEC cytological proof does not definitely rule out LEC diagnosis, even if high CEA and CA 19-9 levels are recorded in the cyst fluid [8, 13,

14]. Several types of surgical treatment options are available in patients who are symptomatic and these include simple enucleation or pancreatectomy (distal or pancreaticoduodenectomy).

In conclusion, LECs of pancreas are extremely rare, nonneoplastic cysts of the pancreas. Definite pre-operative diagnosis may be possible based on clinical and cytologic features and thus allowing conservative management. However, clinician should be aware of certain pitfalls of cyst fluid analysis (elevated CEA and CA 19-9 in some patients) that may prevent a correct pre-operative diagnosis. In such patients surgery is a reasonable option for definitive diagnosis.

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Abbreviations LEC: lymphoepithelial cyst

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References

1. Truong LD, Rangdaeng S, Jordan PH Jr. Lymphoepithelial cyst of the pancreas. *Am J Surg Pathol* 1987; 11:899-903. [PMID 3674287]
2. Luchtrath H, Schriefers KH. A pancreatic cyst with features of a so-called branchiogenic cyst. *Pathologie* 1985; 6:217-9. [PMID 4048076]
3. Adsay NV, Hasteh F, Cheng JD, Bejarano PA, Lauwers GY, Batts KP, et al. Lymphoepithelial cysts of the pancreas: a report of 12 cases and a review of the

literature. *Mod Pathol* 2002; 15:492-501. [PMID 12011254]

4. Mitchell ML. Fine needle aspiration biopsy of peripancreatic lymphoepithelial cysts. *Acta Cytol* 1990; 34:462-3. [PMID 2343707]

5. Cappellari JO. Fine-needle aspiration cytology of a pancreatic lymphoepithelial cyst. *Diagn Cytopathol* 1993; 9:77-81. [PMID 8458289]

6. Rino Y, Morohoshi T, Funo K, Imada T, Yamamoto Y, Jojima T, et al. Lymphoepithelial cyst of the pancreas: a preoperatively diagnosed case based on an aspiration biopsy. *Surg today* 1995; 25:1043-6. [PMID 8645938]

7. Bolis GB, Farabi R, Liberati F, Macciò T. Lymphoepithelial cyst of the pancreas. Report of a case diagnosed by fine needle aspiration biopsy. *Acta Cytol* 1998; 42: 384-6. [PMID 9568141]

8. Centeno BA, Stockwell JW, Lewandrowski KB. Cyst fluid cytology and chemical features in a case of lymphoepithelial cyst of the pancreas: A rare and difficult preoperative diagnosis. *Diagn Cytopathol* 1999; 21:328-30. [PMID 10527479]

9. Liu J, Shin HJ, Rubenchik I, Lang E, Lahoti S, Staerckel GA. Cytologic features of lymphoepithelial cyst of the pancreas: two preoperatively diagnosed cases based on fine-needle aspiration. *Diagn Cytopathol* 1999; 21:346-50. [PMID 10527483]

10. Mandavilli SR, Port J, Ali SZ. Lymphoepithelial cyst (LEC) of the pancreas: cytomorphology and differential diagnosis on fine-needle aspiration (FNA). *Diagn Cytopathol* 1999; 20:371-4. [PMID 10352910]

11. Zou XP, Li YM, Li ZS, Xu GM. Lymphoepithelial cyst of the pancreas: a case report. *Hepatobiliary Pancreat Dis Int* 2004; 3:155-7. [PMID 14969862]

12. Capitanich P, Iovaldi ML, Medrano M, Malizia P, Herrera J, Celeste F, et al. Lymphoepithelial cysts of the pancreas: case report and review of the literature. *J Gastrointest Surg* 2004; 8:342-5. [PMID 15019932]

13. Policarpio-Nicolas ML, Shami VM, Kahaleh M, Adams RB, Mallery S, Stanley MW, et al. Fine-needle aspiration cytology of pancreatic lymphoepithelial cysts. *Cancer* 2006; 108:501-6. [PMID 17063496]

14. Renou C, Giovannini M, Monges G, Rifflet H, Muller P, Harafa A, et al. Pitfalls of cyst fluid findings obtained by endoscopic ultrasonography fine-needle aspiration on a pancreatic lymphoepithelial cyst. *Am J Gastroenterol* 2007; 102:213-5. [PMID 17278274]

15. Hebert-Magee S, Garvin D, Ahlawat SK, Haddad N, et al. Lymphoepithelial cyst of the pancreas with sebaceous differentiation: Cytomorphology and diagnosis on fine-needle aspiration. *Diagn Cytopathol* 2008 (In press).

16. Anagnostopoulos PV, Pipinos II, Rose WW, Elkus R. Lymphoepithelial cyst in the pancreas: a case report and review of the literature. *Dig Surg* 2000; 17:309-14. [PMID 10867475]