Lymphoepithelial Cyst of the Pancreas: A Rare Case Report and Review of Literature

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Abstract Lymphoepithelial cysts are rare pancreatic lesions of undetermined pathogenesis. The literature on this entity is limited to case reports or small series. We describe a case of 66 year male, incidentally diagnosed as lymphoepithelial cyst of pancreas that was managed by enucleation. This is the first case report of lymphoepithelial cyst from India. An extensive Medline search was carried out for lymphoepithelial cyst of pancreas. Till date less than 100 cases were identified in available literature. All these cases (including our case) were analyzed. This entity has uniform and distinctive clinicopathological features. About half of the reported cases were asymptomatic with most of the lesions diagnosed incidentally. Majority of patients presents with non-specific symptoms making preoperative diagnosis difficult. Lymphoepithelial cyst of the pancreas is a rare benign lesion, which is difficult to diagnose preoperatively. High index of suspicion and preoperative fine needle aspiration cytology may help in making diagnosis and avoiding surgery in asymptomatic patients.

Keyword Lymphoepithelial cyst · Cystic lesion · Pancreas · True pancreatic cyst

Introduction

Cystic lesions of the pancreas are relatively rare [1–3]. In adults, 85%–90% of these lesions are pseudocysts [2, 3]. True cysts of the pancreas, characterized by an epithelial lining, are uncommon cystic pancreatic lesions. Although they constitute a challenging differential diagnosis at the clinical, radiological, and pathologic levels, all patients with pancreatic cystic lesions, whether asymptomatic or symptomatic, must be thoroughly investigated to ascertain the underlying nature of the cyst [4]. As more cases of pancreatic cysts are being diagnosed, newer clinicopathological entities are being recognized [5] and the old ones are becoming better characterized [6, 7].

Lymphoepithelial cyst (LEC) of the pancreas is an exceedingly rare nonneoplastic entity of uncertain histogenesis. LEC are true pancreatic cysts lined by squamous epithelium and surrounded by mature lymphoid tissue. The cyst arises typically in middle-aged men, and is usually asymptomatic or causes nonspecific abdominal symptoms. There is no specific serologic marker for this entity. None of its radiological characteristics can help differentiate it from other cystic lesions of the pancreas. Fine-needle aspiration cytology may be able to suggest its benign nature. The outcome after surgical excision is uniformly good with good symptom control and no recurrences.

Successful management of LEC depends on ability to differentiate them from other cystic neoplasm of pancreas. LEC in the pancreas are relatively poorly recognized. They are reported in the literature mostly as individual case

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studies [8–34]. In this article we report a case of lymphoepithelial cyst of pancreas, the first case reported from India and review of the published literature on the condition.

Case Report

A 66-year-old male presented with nonspecific complaints of loss of appetite and loss of weight for 3 months. There was no history of pain in abdomen, vomiting, hematemesis or malena. Patient was non-smoker & occasional drinker. He was non-diabetic and hypertensive on medications. The patient was evaluated and Ultrasonography (USG) abdomen, Contrast enhanced computed tomography (CECT) abdomen (Fig. 1a) and Endoscopic Sonography (EUS) were done, which were suggested of a 4.3 cm round, well-circumscribed, cystic mass in head of pancreas. There was no history of prior episode of pancreatitis, pancreatic insufficiency, trauma or fever. His physical examination

Fig. 1 **a** Preop CECT of patient suggested cystic lesion in head of pancreas. **b** Postop CECT of patient (after 18 months) suggested no evidence of recurrence

Fig. 2 Intraoperative pictures showing the cystic lesion in the head of pancreas before enucleation **a** and during enucleation of the cystic lesion **b**

was unremarkable. His CA19-9 levels were elevated to 687 ng/ml (normal range 1.2–3.9). With the CECT abdomen finding of cystic mass in head region and raised CA19-9 levels, a provisional diagnosis of carcinoma of head of pancreas was made and patient was planned for Whipple's procedure.

The patient underwent exploratory laparotomy and on exploration, a 5.2 cm cystic lesion was found in the head of the pancreas (Fig. 2a). The mass was found to be firm and smooth. The cyst content and the wall of the cyst were sent for frozen section examination, which were suggestive of lymphoepithelial cyst of pancreas. Complete enucleation of the cyst from the head of pancreas was performed (Fig. 2b). Postoperative course was uneventful; he was started on oral feed after 48 hours and was discharged on 7th postoperative day. At 18 months after surgery the patient is asymptomatic on regular follow-up with CECT and CA19-9 levels after 6 months & after 18 months and there is no evidence of recurrence on CECT (Fig. 1b). His postoperative CA 19-9 level is normal.

Microscopic evaluation from resected specimen of peripancreatic lymphnode and cyst wall shows multiple cysts lined by squamous epithelium. The subepithelium showed abundant lymphocytes with germinal centre formation. Keratinization was also noted (Fig. 3a & b). Diagnosis of LEC was confirmed.

Discussion

LEC of the pancreas is rare true pancreatic cyst, lined by stratified squamous epithelium. In this review, we searched all the cases of lymphoepithelial cyst of the pancreas published in the literature, from the first case reported by Luchtrath et al [8] in 1985 until the last case reported in 2009. We reviewed 94 cases of LECs of the pancreas including our case [8–34].

A large case series of 12 patients was published and literature was extensively reviewed with the finding of all the relevant cases presented in tabulated form [9]. This landmark paper reviewed 64 cases reported till 2002.

Fig. 3 **a** Micrograph shows cyst wall lined by stratified squamous epithelium. The subepithelium shows abundant lymphocytes with germinal centre formation. (H&E $\times$ 40x) **b** Representative section of the cyst wall, exhibiting a mature squamous lining with surface keratin. The lining is surrounded by lymphoid follicles with germinal centres. (H&E $\times$ 400x)

When the data reported in the literature along with the Adsay series are combined (64 cases reviewed by Adsay et al before 2002 and another 28 cases in this paper after 2002), some general characteristics of LEC become apparent (Table 1, After Adsay et al, 2002). They are seen in middle-aged patients (mean age, 56 y; range, 20–82 y) predominantly in men (M/F, 4/1). The most common symptom at presentation is abdominal pain. Other complaints at presentation include anorexia, weight loss, vomiting, back pain, fever, and chills. Many cases were diagnosed during work-up for other diseases. LEC are often rounded and have a well-defined wall that sharply demarcates it from the pancreas and surrounding adipose tissue. The average size of LEC is 4.5 cm (range, 1–12 cm). They can be multilocular or unilocular (in 50%). These lesions seem to be equally distributed in head, body and tail region of the pancreas.

Pathogenesis of LEC

The histogenesis of LEC is unknown. A proposed mechanism of pathogenesis for LEC is the development from epithelial remnants in lymph nodes [10]. The histological characteristics of LEC are unique, and were first described by Luchtrath and Schiefers [8], who noted the microscopic similarity of the cyst to the branchial cleft cysts of the lateral neck. Microscopically, the LEC are characterized by cysts lined by stratified squamous epithelium and immediately adjacent dense subepithelial lymphoid tissue that contains lymphoid follicles. The lesion is separated from the pancreatic parenchyma by a capsule of thin fibrotic tissue.

Differential Diagnosis

The clinical differentiation of LEC from other cystic lesions of the pancreas can be challenging. LEC have a macrocystic appearance and are thus clearly distinguished from microcystic lesions such as serous microcystic adenoma. Their distinction from macrocystic lesions at clinical level could be problematic. (Algorithm 1)

Chemical analysis of aspirated cyst fluid has proved to be useful in the differential diagnosis of pancreatic cysts in general, the aspirated fluid from LEC has squamous epithelial lining (to differ from pseudocyst) which is rich in lymphoid cells (to differ from mucinous & malignant cystic lesions) & sometimes it may also contain “cheesy” or “caseous” appearance characteristic of keratinaceous debris (like our case) [35–41].

The traditional markers such as CEA, CA19-9, CA-125, and fluid viscosity would be expected to be significantly lower in LEC than in mucinous neoplasms [25, 26]. Only few cases presented with elevated serum levels of CA 19-9 [17, 26, 32]. This is an interesting finding considering that

Table 1 Published cases of Lymphoepithelial cyst in world literature (After Adsay et al, 2002)

S.No	Author/Year	Case	Presentation/Symptoms	Location	Procedure	Followup
1.	Chatelain et al [11], 2002	50/M	Asymptomatic	–	–	–
2.	Chatelain et al [11], 2002	61/M	Asymptomatic	–	–	–
3.	Imamura H et al [12], 2002	–	–	–	–	46 months followup
4.	Zou XP et al [13], 2004	43/F	Epigastric pain, vomiting	Head, Tail	Conservative	–
5.	Capitanich P et al [14], 2004	53/M	Asymptomatic	Tail	DP+Splenectomy (DPS)	No recurrence
6.	Jouini et al [15], 2004	20/F	Abdominal pain, vomiting	Tail	DPS	No recurrence
7.	Au-Young IT et al [16], 2004	48/M	Abdominal pain	Tail	Lap DP	Minor pancreatic fistula
8.	Barbaros et al [17], 2004	55/M	Asymptomatic, ↑CA 19-9	–	–	–
9.	Ciprian corby S et al [18], 2005	44/M	Low chest pain	Tail	DPS	No recurrence
10.	Neyman EG et al [19], 2005	–	–	–	–	Role of MDCT in evaluation
11.	Kanno A et al [20], 2005	–	–	–	–	–
12.	Kanno A et al [20], 2005	–	–	–	–	–
13.	Castaldo et al [21], 2006	–	–	–	–	–
14.	Shinmura et al [22], 2006	–	–	–	Resection	No recurrence
15.	Colovic et al [23], 2006	49/M	Abdominal pain	Tail	Resection	No recurrence
16.	Ivicic J et al [24], 2007	59/M	Acute pancreatitis	–	Resection	No recurrence
17.	Younus S et al [25], 2007	–	–	–	–	–
18.	Idetsu A et al [26], 2008	77/ M	Asymptomatic, ↑CA 19-9	Body	DPS	No recurrence
19.	Frezza EE et al [27], 2008	56/M	Recurrent abdominal pain	Tail	DPS	No recurrence
20.	Roger N et al [28], 2008	54/M	Asymptomatic	Neck	Whipple's	No recurrence
21.	Matsukawa H et al [29], 2008	59/M	Asymptomatic	Body, tail	Enucleation	No recurrence
22.	Kobayashi T et al [30], 2008	55/M	Asymptomatic	Body	Enucleation	No recurrence
23.	Zielinska Pajak E et al [31], 2008	47/M	Presented with primary gastric lymphoma	Head	Resection	No recurrence after 24 months
24.	Zielinska Pajak E et al [31], 2008	50/m	Asymptomatic	Body	Resection	No recurrence after 42 months
25.	Yamaguchi T et al [32], 2008	72/M	Asymptomatic, ↑CA 19-9	Uncinate	Resection	–
26.	Alvarez Catro AM et al [33], 2008	–	–	–	–	–
27.	Langam R et al [34], 2009	–	–	–	–	–
28.	Sewkani et al, 2009 (Present case)	66/M	Loss of appetite, loss of weight, ↑Ca 19-9	Head	Enucleation	No recurrence 18 months later

squamous metaplasia in pancreatic ductal epithelium is often immunohistochemically negative for these markers.

Role of EUS +/-FNAC in Lymphoepithelial Cyst of Pancreas

The most important differential diagnosis of LEC is with the primary cystic neoplasm of the pancreas (Algorithm 2). Cystic pancreatic neoplasms rarely have a lymphoid reaction. Such changes, if present, are limited in degree and do not form a sub-epithelial band as seen in LEC. The definitive diagnosis of LEC of the pancreas is generally

established postoperatively after histological evaluation of the completely excised lesion.

The main issue in the treatment of this benign lesion is its differentiation from other cystic lesions of the pancreas, most importantly pseudocysts and cystic neoplasm [35]. Since the treatment options and the prognosis of these entities is different. In these situations, fine needle aspiration (FNA) of the lesion may be able to suggest the benign nature of the lesion and as a true cyst of the pancreas [35–41]. Cytological material obtained from LEC reveals nucleated or anucleated squamous epithelial cells, occasional histiocytes and rare lymphocytes, without evidence of neoplastic cells.

Recently few authors have reported the role of endoscopic ultrasound (EUS) and EUS guided FNA in the evaluation of cystic lesions of the pancreas and in diagnosis of LEC preoperatively, and thus avoiding unnecessary surgery in patients [35, 42–48].

The presence of squamous material and lymphocytes on cytologic examination after EUS guided FNAC is diagnostic of LEC. Aspirate CEA level may be elevated and should be considered in conjunction with cytologic results to avoid misdiagnosis as a mucinous cystic neoplasm. Asymptomatic LEC should be managed conservatively. This could avoid unnecessary surgery in selected cases. In radiologically benign appearing lesions, EUS+FNA confirmation of a negative cytology and low fluid CEA can further provide evidence to support a monitoring approach and deferral of surgical intervention [35].

The classical finding of LEC on EUS is hypoechoic uniloculated or multiloculated cystic lesion. Occasionally, fine or coarse sludge like hyperechoic echo architecture is also seen likely due to debris within the cyst [48]. If the patient is asymptomatic and EUS-FNA firmly established the diagnosis of LEC based on cytological examination of the cyst fluid, surgery can be avoided and then patient can be followed with serial imaging of the abdomen.

Management Options

Surgical management of the LEC has been variably described in the literature from conservative and regular follow-up in asymptomatic patients to classical Whipple's procedure (pancreatoduodenectomy) in few patients. No recurrences or progression into lymphoma or carcinoma have been documented in the cases of LEC in which follow-up information was available. Thus, if the tumor can be diagnosed preoperatively, the option of "wait and watch" may be clinically acceptable. However, in most cases, the possibility of another type of pancreatic cystic neoplasm is difficult to rule out with the current investigative methods.

After reviewing the available literature we suggest following recommendations regarding management of lymphoepithelial cyst of the pancreas:

- 1) Preoperative FNA or EUS and FNA should strongly be considered in a high surgical risk and asymptomatic patient.
- 2) If the FNA establishes the diagnosis of a LEC, the operation can be avoided and the patient may be followed with serial imaging.
- 3) In the symptomatic patients with acceptable surgical-risk, an exploration of the upper abdomen should be undertaken.
- 4) A frozen section biopsy of the cystic mass should be obtained during the operation. If the microscopic

evaluation verifies the diagnosis of a LEC, a simple cyst enucleation should be sufficient treatment.

- 5) In symptomatic patients, if lesion is situated in body or tail of pancreas, then simple distal pancreatectomy with splenic preservation should be performed, only if simple enucleation of the cyst is not feasible.
- 6) In the cases where cyst involved the head of the pancreas, and either involving or compressing duodenum or the common bile duct, enucleation or drainage procedure rather than resection procedure (Whipple's or pylorus preserving pancreatoduodenectomy) should be performed.

Conclusion

True pancreatic cysts lined by stratified squamous epithelium are rare. We present a case of lymphoepithelial cyst and review of the present literature. These lesions, despite their rarity, must always be kept in the differential diagnosis of a cystic pancreatic lesion. It requires a high degree of suspicion and fine needle cytology (EUS +/-FNA) in all patients to diagnose this rare entity. All patients with pancreatic cystic lesions, whether asymptomatic or symptomatic, must be thoroughly investigated to ascertain the underlying nature of the cyst. Regular follow-up is all that is required in asymptomatic patients with proven diagnosis. Enucleation of the cyst avoids the unnecessary resection in these patients. However due to uncommon nature and difficulty in radiological diagnosis most cases will continue to be identified on pathological examination after resection.

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