CASE REPORT

Lymphoepithelial Cyst of the Pancreas: A Case Report

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ABSTRACT

Lymphoepithelial cysts are relatively common lesions in the lateral neck region, but a lesion with identical morphology and clinical behavior may sometimes occur in the pancreas (although rare). Lymphoepithelial cysts are characterized histologically according to the presence of a stratified squamous epithelium lining and lymphoid tissue with germinal centers in the cyst wall. In this article, we report a case of seventy-four-year-old women who underwent a pancreatectomy due to the incidental finding of a slow-growing cystic mass in the pancreatic tail. Histopathological examination revealed the rare diagnosis of a pancreatic lymphoepithelial cyst. Pancreatic lymphoepithelial cyst is often diagnosed microscopically in a resected specimen, after a partial pancreatectomy performed on suspicion of a neoplastic cyst. The most clinically important differential diagnosis of lymphoepithelial cysts are mucinous neoplastic cysts of the pancreas: mucinous cystic neoplasia and intraductal papillary mucinous neoplasia demanding surgical treatment, whereas in case of asymptomatic lymphoepithelial cyst, the "watch and wait" approach should be preferred. Preoperative diagnosis of lymphoepithelial cyst remains a challenge. Reviewed is literature pertaining to clinical, cytological and histological examination.

INTRODUCTION

Lymphoepithelial cysts (LECs) are relatively common lesions in the lateral neck region, most often derived from remnants of the second branchial apparatus [1]. Patients usually present with painless swelling. On gross examination, the cysts are unilocular and contain clear to grumous material. Sizes are variable and can reach 10cm. Cytological examination usually demonstrate neutrophils, lymphocytes and debris admixed with mature squamous cells. On the light microscopy, LECs are lined mostly with stratified squamous epithelium and the lumen is usually filled with keratin debris. Lymphoid tissue with germinal centers is present in the wall [1, 2]. In rare cases, LEC can appear in the pancreas. In this paper, we present an unusual case of a LEC in the pancreatic tail and include a review of the relevant literature along with the differential diagnosis and clinical implications.

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Abbreviations IPMN intraductal papillary mucinous neoplasia; LECs lymphoepithelial cysts; MCN mucinous cystic neoplasia
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CLINICAL COURSE

A seventy-four-year-old female patient with a clinical history of arterial hypertension, osteoporosis and smoking, was referred to the Gastroenterology Department of the 2nd Clinic of Internal Medicine at the 3rd Faculty of Medicine & Faculty Hospital Kralovske Vinohrady, because of the incidental finding of a 25×17×16 mm cystic formation in the pancreatic tail described using computed tomography (CT). The CT was originally performed to investigate cysts in the kidneys that were recently identified on ultrasound by urologist. Further endosonographic examination of the pancreas revealed a hypoechogenic multi-cystic lesion on the border of the pancreatic body and tail **(Figure 1)**, with septa, sediment and central nodule. The clinical diagnosis of intraductal papillary mucinous neoplasia (IPMN) or mucinous cystic neoplasia (MCN) was discussed; fine needle aspiration biopsy was performed establishing invaluable cytological findings: a purely erythrocytic background and particles of mucus without nucleated cells on the cytological slide. Oncomarkers in the serum (CEA, CA 19-9, CA 125, CA 72-4) were negative. The patient was recommended to go through with an additional biopsy, but she refused. As a result, she maintained regular follow-ups at the gastroenterology department and the cystic lesion was closely monitored using ultrasonography. However, over the next 10 months the size of the cyst increased for approx. 10 mm. At this point, the patient agreed to undergo a second biopsy. During the endosonograhic examination, approx. 8 mL of a dense, brownish fluid was aspirated and sent for analysis. Biochemical analysis of the cystic

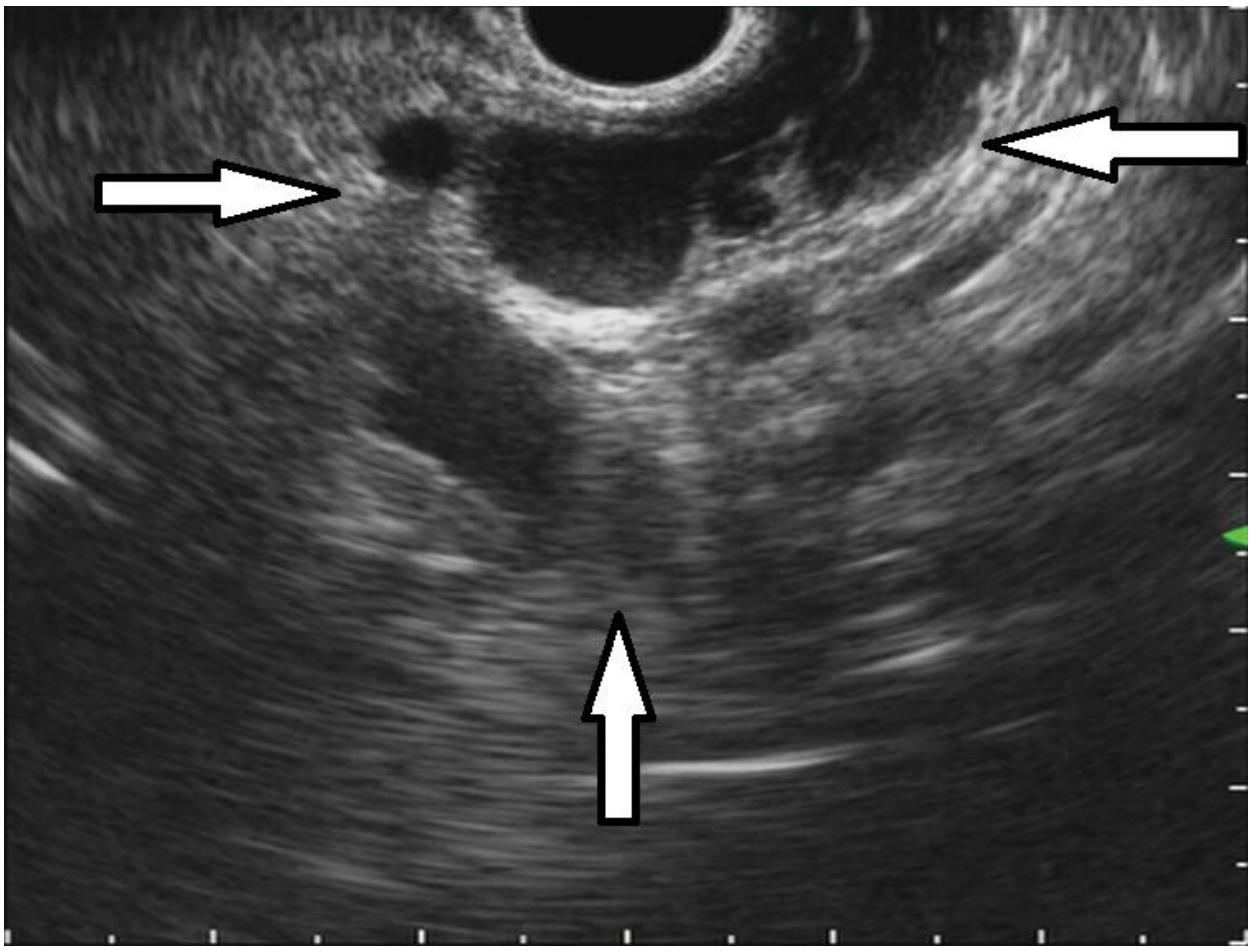

Figure 1. Endosonography showing a hypoechogenic multicystic lesion with septa and central nodule in pancreatic tail.

fluid revealed elevated levels of carcinoembryonic antigen (CEA) = 882 μg/l (ref. <2.5 μg/l) and cancer antigen 19-9 (CA19-9) = 187 kU/l (ref. <30.9 kU/l). Morevover, additional CT examination elucidated a slightly lobulated formation without calcifications in the body of the pancreas bending cranially to the wall of stomach, while the rest of the pancreas was structurally normal without expansion of the main duct **(Figure 2)**. Owing to the aforementioned enlargement of the cyst, as well as the clinical suspicion of a mucinous tumor (elevation of CEA over 800 μg/l in cyst fluid, uncertain communication with Wirsung duct), a distal pancreatectomy was recommended by the multidisciplinary team at the hospital. Prior to surgery, a short pancreatic stent was introduced via ERCP to prevent the postoperative pancreatic leak. Concurrent exploration for a communication with ductus Wirsungi excluded the clinical diagnosis of IPMN. Resection of the body and the tail of the pancreas was subsequently performed together with splenectomy and cholecystectomy in the General Surgery Clinic at the 3rd Faculty of Medicine & Faculty Hospital Kralovske Vinohrady. One month later, the pancreatic stent was endoscopically removed.

Histopathological Examination

A gross specimen measuring 92×33×20 mm, consisting of the pancreatic tail and spleen (weight 60 g) was delivered to the Department of Pathology for dissection. An encapsulated mass measuring 40×30×23 mm was identified in the upper pancreatic margin. On the cut section, multiple cysts containing viscous grumous material were observed, with dirty yellowish areas in the surrounding peripancreatic fat tissue. Microscopically, the cysts were lined with keratinizing stratified squamous epithelium without cellular atypia and focally with admixed mucinous PAS-positive goblet cells **(Figure 3)**. The cystic content was comprised of desquamated keratin, cellular debris and foamy macrophages. Abundant lymphoid tissue with germinal centers was found within the cyst wall, in hematoxylin-eosin stain **(Figures 4, 5)**. Older fat necrosis with cholesterol crystals, giant multinuclear macrophages and scarring were present in the surrounding adipose tissue. These findings were compatible with the diagnosis of a pancreatic LEC, with post-inflammatory changes in peripancreatic fat tissue. Examination of the spleen and gall bladder demonstrated no significant pathological changes.

DISCUSSION

Pancreatic LEC was first described by Lüchtrath and Schriefers in 1985 [3]. In contrast to the head and neck region, LEC is a rare diagnosis in the pancreas. Single case reports or small groups of patients, including recent references, have appeared in the literature [3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35]. LECs are seen in middle-aged patients, predominantly but not exclusively

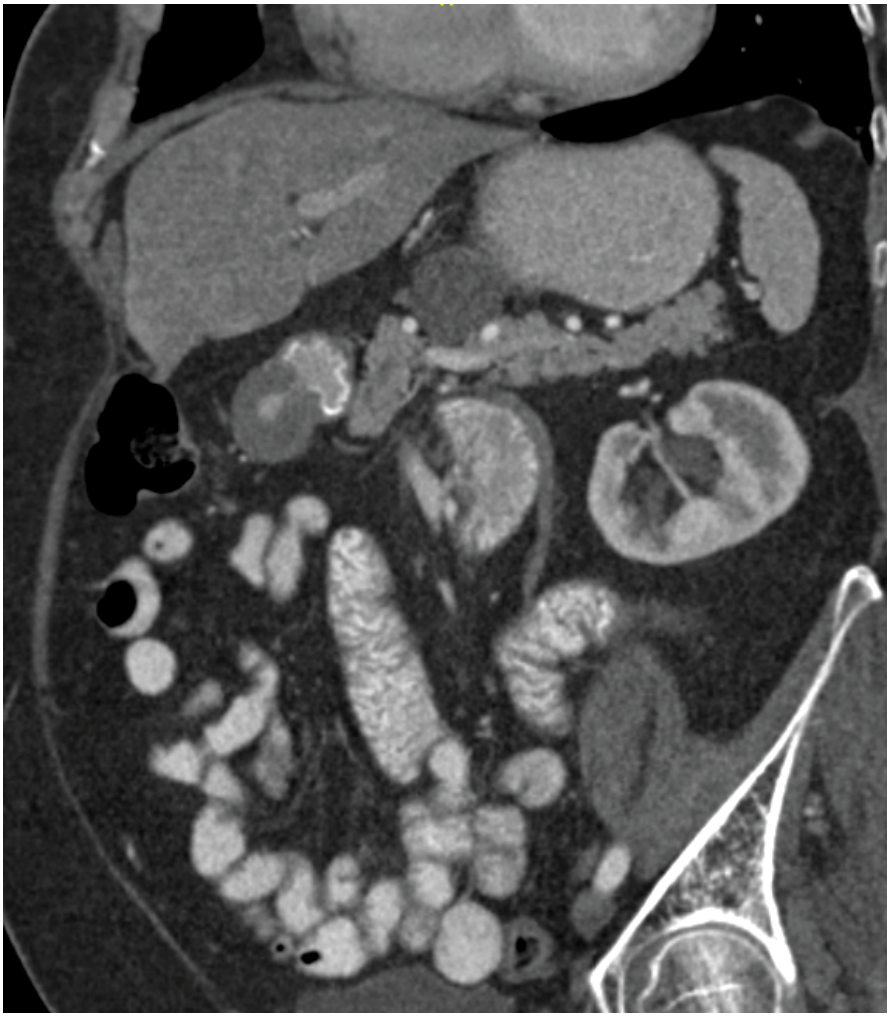

Figure 2. CT scan after intravenous contrast media administration showing exophytic cystic lesion arising from the superior contour of the pancreatic body. It has unilocular appearance with slightly lobulated contours, the content is low density with fine septum, without solid portions or calcifications. The main pancreatic duct is not dilated.

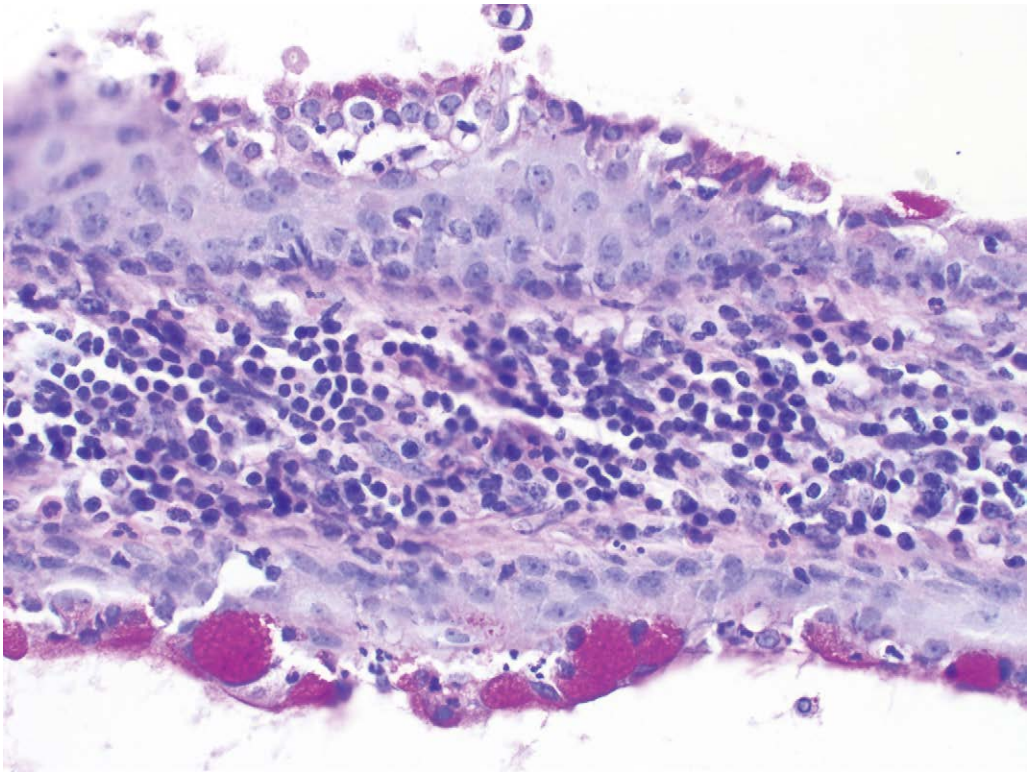

Figure 3. Histopathological image showing focal presence of goblet cells in the otherwise squamous cyst lining. PAS, 40X.

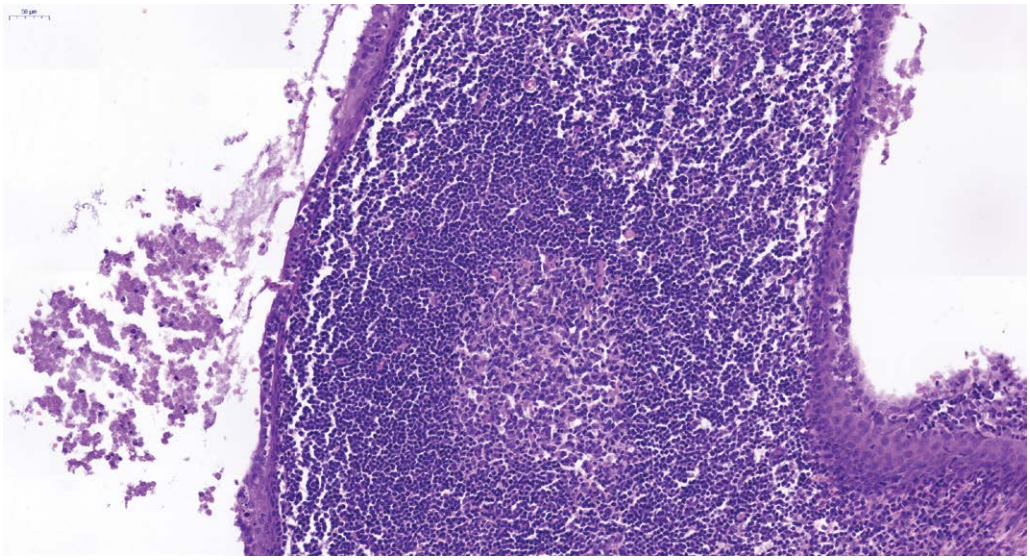

Figure 4. Histopathological scan showing stratified squamous epithelium and lymphatic germinal center within the cyst wall. HE, 20X.

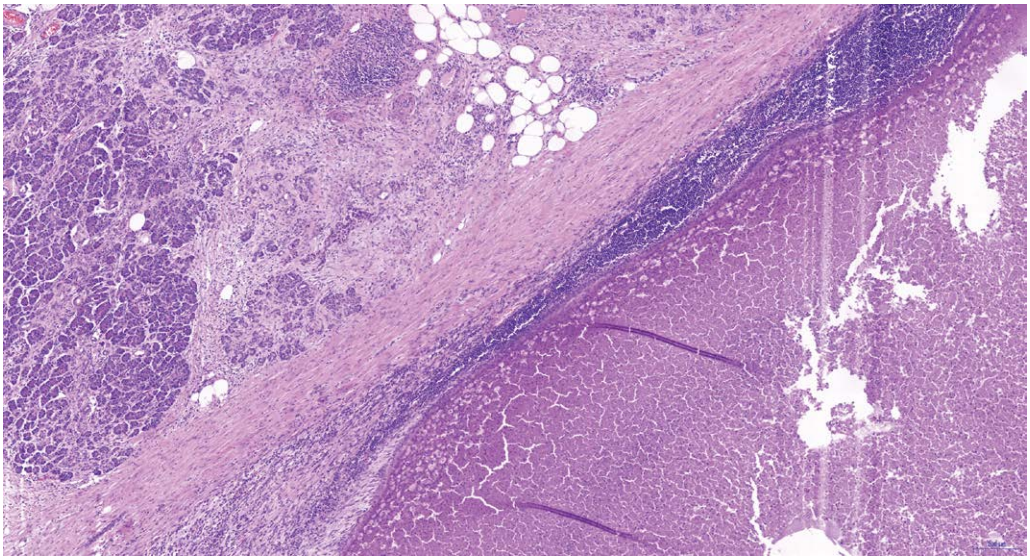

Figure 5. Histopathological scan showing cystic cavity containing tissue debris with foamy macrophages and squamous lining, with surrounding pancreatic tissue with secondary fibrotic changes. HE, 8X.

in men (M/F=4/1). The most common symptom at presentation is abdominal pain. Other complaints include nausea, vomiting, anorexia, weight loss, back pain, fatigue, fever, and chills. Many cases are diagnosed during a work-up for other diseases.

Grossly, LEC presents as a multilocular or unilocular, intrapancreatic or peripancreatic cystic mass with the mean size of 4.8 cm (range 1.2-17 cm) [4]. LECs are usually situated in the tail of the pancreas, the cysts are round and filled with a cheesy, granular, yellow-brown substance. In a few cases, the cysts contained thick serous fluid instead of the keratinaceous debris [4]. The inner surfaces of the cysts are granular, devoid of any prominent projections [4].

Microscopically, LECs have a squamous lining and a dense subepithelial rim of lymphoid tissue [4, 5, 10, 11, 12, 20, 25, 27, 28, 29, 30, 31], the lining may also be focally attenuated. Occasionally, columnar mucinous cells or goblet cells are found [4, 12], at the luminal surface of otherwise squamous epithelium. There are reports of foci with sebaceous differentiation in LECs [7, 8, 9]. The lymphoid tissue of pancreatic LECs is composed of elements ordinarily present in lymph nodes: scattered lymphoid follicles surrounded by a dense infiltrate of small round bland lymphocytes. In some cases, keratin granulomas and microscopic foci of fat necrosis in the lymphoid areas or in the areas immediately adjacent to the pancreas were present [4]. In our case, there was older fat necrosis with cholesterol crystals and giant cell granulomas in the peripancreatic adipose tissue.

The etiopathogenesis of LECs is not known. Conditions that are typically associated with LEC of salivary glands, such as a history of Sjögren disease, HIV infection, or lymphoma have not been reported in cases of pancreatic LECs [4]. There are several proposed mechanisms for the pathogenic background of LEC such as development from epithelial remnants in lymph nodes [5], or cystic transformation of pancreatic ducts that have undergone squamous metaplasia [6]. It has also been speculated that LECs may be a form of teratoma or a branchial cleft cyst

that have been displaced and fused with the pancreas during embryogenesis [3]. The sebaceous glands included in the pancreatic LEC, described in some rare cases [7, 8, 9], may support the hypothesis concerning teratomas.

LECs are benign lesions. Complete surgical removal is curative. No recurrences or progression into lymphoma or carcinoma have been documented, therefore, if the LEC can be diagnosed preoperatively, the option of "watch and wait" may be clinically acceptable [4].

The most clinically important differential diagnosis of LECs is mucinous neoplastic cysts of the pancreas: mucinous cystic neoplasia (MCN) and intraductal papillary mucinous neoplasia (IPMN) demanding surgical treatment. Another important differential diagnosis can be solid pseudopapillary neoplasia, occurring predominantly in young women. Solid pseudopapillary neoplasia is regarded as low-grade malignant tumor, and requires resection as well. On the other hand, like in case of asymptomatic LEC, the "watch and wait" approach can be preferred in case of serous adenoma, a fully benign pancreatic tumor representing another important differential diagnosis. As in our case, pancreatic LEC is often diagnosed by histopathological examination of a resected specimen following partial pancreatectomy performed on suspicion of a neoplastic cyst.

The clinical differential diagnosis of LEC is challenging. The most common clinical and imaging mimicry of this is a cystic neoplasm of pancreas, either benign or malignant [10]. Preoperative distinction of LECs from neoplastic mucinous cysts by imaging techniques is difficult [11]. There is prevailing male sex and tail-localization in pancreatic LECs [18], with leading preoperative diagnosis of IPMN [19]. Borhani *et al.* described round shape and exophytic location in the pancreatic body and tail as typical, but unspecific preoperative features of LECs [20].

Cyst fluid CEA analysis provides a highly accurate test for the diagnosis of a mucinous cyst [12, 13], but it does not distinguish non-neoplastic from neoplastic cysts [14, 15]. Mucin-producing cells were described in a significant number of LECs [12]. Pancreatic LEC may be associated with increased plasmatic CA 19-9 level as well [16, 17]. Some studies revealed fine needle aspiration and proper cytological assessment as the only tool that can achieve a diagnosis without resection [17, 21, 22, 23]. Cytology classically shows abundant anucleate squamous cells, multinucleated giant cells, mature lymphocytes on a background of keratinaceous debris, and a lack of neoplastic cells [29]. Cytological examination may aid in the correct diagnosis if tissue elements characteristic of a lymphoepithelial cysts, including squamous and lymphoid tissue fragments are found [30]. However, cytologic examination is often unreliable and unspecific.

Some authors do not recommend needle biopsy for cystic lesions of the pancreas because of risk of the dissemination of tumor cells or the development of pseudomyxoma [32].

Despite all difficulties in preoperative diagnostic mentioned above, there are several papers describing some more specific imaging characteristics of LEC. These characteristics include mosaic pattern depending on the degree of keratin amount in ultrasonography, enhancement of the wall and septa of the cyst without pancreatic duct dilatation in CT and cystic fluid with higher intensity than water in T1-weighted MRI and cystic fluid with lower intensity than water in T2-weighted MRI [32]. Terakawa *et al*. present male gender and elevation of serum CA19-9 as clinical attributes of LEC [32], however, these features were not present in our case.

In case of unclear preoperative diagnosis, a frozen biopsy of the cystic mass is recommended by some authors [33, 34]. If the microscopic evaluation verifies the diagnosis of LEC, a simple cyst enucleation should be sufficient treatment rather than full surgical resection, which has been commonly performed in many previous case reports, including our case. However, Arumugam *et al*. state there is no reliable preoperative diagnostic method and surgical excision and pathological analysis remain the gold standard in symptomatic patients and when malignancy cannot be excluded [35].

The histological differential diagnosis of LECs is concerned with distinguishing LECs from dermoid cysts, epidermoid cysts in intrapancreatic accessory spleens, lymphangiomas, and pseudocysts; nevertheless, after surgery, there are usually no difficulties concerning histopathological identification of LEC.

CONCLUSION

Lymphoepithelial cyst (LEC) of the pancreas is a rare fully benign lesion, often treated by partial pancreatectomy performed on suspicion of a neoplastic mucinous cyst, like in our case. The reliability of preoperative diagnostics remains controversial. There are several references favorizing imaging methods or cytological analysis of cystic fluid, some authors recommend intraoperative frozen section histology, in case of LEC leading to simple enucleation of the cyst. However, surgical excision and histopathological analysis remain the gold standard in symptomatic patients and when malignancy cannot be excluded, like in our case.

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CONFLICT OF INTEREST

The authors have no conflicts of interests to declare.

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