Lymphoepithelial Cyst of the Pancreas: Can Common Imaging Features Help to Avoid Resesction?

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Abstract

Background: Differentiation of cystic pancreatic neoplasms remains a challenging task for radiologists with main aim of characterizing malignant and premalignant conditions.

Purpose: The study aimed to compare radiological features of lymphoepithelial cysts (LEC) with other cystic pancreatic lesions, which could help to differentiate them in order to avoid unnecessary resection and optimize surveillance.

Material and Methods: We retrospectively reviewed 12 cases of resected and histopathological confirmed LECs in last 12 years, for 10 patients imaging studies were available. 20 patients with mucinous cystic neoplasms (MCN) and 20 patients with branch-duct intraductal papillary mucinous neoplasms (BD-IPMN) were selected consecutively to serve as control groups. Imaging findings as well as clinical data were analyzed.

Results: Three imaging subtypes of LEC were identified: simple cystic morphology (20%) and mixed cystic-solid lesions (80%) with either diffuse subsolid component (30%) or mural nodule (50%). All lesions revealed exophytic location with strong male predominance (9:1). MCNs were presented exclusively in middle-aged woman and IPMN in both sexes showing slight male predominance (13:7). Mean patient age in IPMN (70.5$\pm$7.7 years) was significantly higher compared to other groups ($p<0.001$ for LEC, $p=0.005$ for MCN). Unenhanced CT-attenuation of LEC was higher than MCNs ($p=0.025$) and IPMNs ($p=0.021$).

Conclusion: The present study provides three imaging subtypes of LEC with key features for the differentiation from other cystic pancreatic lesions such as increased native attenuation, absence of connection to main pancreatic duct (MPD) and exophytic location. Clinical data, such as male predominance in LEC, is crucial in differentiating cystic pancreatic lesions.

Introduction

Cystic pancreatic lesions are divided in neoplastic and non-neoplastic lesions, with the bigger part being neoplastic lesions. Most common include intraductal papillary mucinous neoplasms (IPMN), mucinous cystic neoplasms, serous cystic neoplasms (SCN), and solid pseudopapillary tumor, which account approximately 70% of cystic pancreatic lesions. Non-neoplastic lesions are divided in the epithelial and nonepithelial lesions, with most common epithelial lesions being congenital cysts, alimentary duplication cysts, endometrial cysts, and lymphoepithelial cysts, and most common nonepithelial lesions being pseudocysts or walled-off necrosis (1).

LEC of the pancreas are rare benign cystic lesions. They were first described in 1985 by Luchtrat (2) and the majority of available data on radiological features of LECs are case reports. Over the past 30 years, since the first description, over 100 cases were reported (3). As they are rare, their clinical and pathologic features have not yet been fully characterized, especially regarding the differentiation from other cystic lesions (4, 5). In the clinicopathologic analysis of 12 patients, LECs were reported to constitute approximately 0.5% of pancreatic cysts. They were seen in middle-aged patients, predominantly, but not exclusively in men (M/F =

4/1) (6). Recent reviews documenting the demographic features of LECs indicate a strong male preponderance as well (7).

LECs are true pancreatic cysts that are lined by squamous, non-dysplastic epithelium, and surrounded by mature lymphoid tissue (8). Etiological theories include formation from squamous metaplasia of pancreatic ducts, derivation from epithelial remnants in lymph nodes, and displacement of ultimo-branchial remnants that go on to fuse with the pancreas during embryogenesis. There is also a possibility that LECs are a form of teratoma (6).

Because the imaging features of the LECs vary and sometimes are very similar to other pancreatic lesions, it is difficult to differentiate LECs from other pancreatic lesions, however, a correct differentiation and classification is crucial for the clinical decision making and treatment planning. LECs are benign and do not possess malignant potential and, thus, an accurate identification of these lesions is important to avoid unnecessary intervention (8). A correct preoperative diagnosis of a LEC could help prevent surgical interventions, though, today fine-needle aspiration is the only tool that can achieve a diagnosis without resection (3, 9–11).

Both MCNs and IPMNs are characterized by a neoplastic mucin-producing epithelial cell lining with the potential to malignant transformation. Since the rare data about imaging features of LEC, that are available from case series, show an overlapping with MCNs and IPMNs, differentiation of LEC from these potentially malignant pancreatic lesions remains difficult and an important radiological problem. The present study aimed to compare LECs with other cystic lesions of the pancreas and to identify common radiological features which could help to differentiate them from other cystic neoplasms in order to avoid unnecessary resections.

Results

Surgical procedure and histopathology

The patients were considered symptomatic if they had a left upper quadrant (LUQ) or epigastric pain, post-prandial complaints (i.e. cramps) and did not have other specific cause for these symptoms. Clinically, abdominal pain was the most common clinical feature in all three groups. Clinical symptoms served as the main indication for surgical treatment, all 50 patients in the present study underwent a surgical resection.

LEC-patients underwent cyst resection or left (distal) pancreatic resection with or without splenectomy. After surgery, 60% of the patients had minor local complications: four had fluid collections that had to be drained, one had a pancreatic fistula, and one developed a pseudocyst. All complications were treated with radiological interventions without the need of the additional surgical procedures (Fig. 1).

Histopathological reports confirmed LECs of the pancreas in all 10 patients without evidence of malignant transformation. An example of histopathological image is shown in Fig. 2.

Among MCN there were 14 lesions with low grade MCN, 4 lesions with high grade MCN and 2 lesions with invasive carcinoma associated with MCN. Among IPMN there were 18 BD-IPMN and 2 mixed-type IPMN with 13 low grade IPMN, 6 IPMN with carcinoma in situ and 1 IPMN with associated invasive carcinoma.

Baseline results

LECs were more common in middle-aged males (nine males, one female), ranging between 43 to 63 years (mean age: 50.9 ± 6.4 years). Summary of patient demographics, initial LEC findings and surgical procedures are presented in Table 1.

Table 1
Summary of patient demographics, initial LEC findings and surgical procedures.

	Gender	Age	Modality	Location	Size (cm)	Size of mural nodule (cm)	Preoperative diagnosis	Surgical procedure
Pat.1	Male	59	CT	Tail	2.7		Side branch IPMN	Cyst enucleation with lymphadenectomy
Pat. 2	Male	53	CT	Tail	5.0	1.1	MCN	Left resection with splenectomy
Pat. 3	Male	47	CT	Tail	4.4.		SCN	Left resection with splenectomy
Pat. 4	Male	63	MRI	Body	5.8		MCN	Left resection with splenectomy
Pat. 5	Male	49	MRI	Tail	4.4.	2.4	MCN	Left resection with splenectomy
Pat. 6	Male	44	MRI	Tail	3.6	0.8	Side branch IPMN	Cyst enucleation
Pat.7	Male	55	MRI	Body	3.6		Side branch IPMN	Left resection with splenectomy
Pat. 8	Male	48	CT/MRI	Body	4.5		SCN	Cyst enucleation
Pat. 9	Male	44	CT/MRI	Tail	5.3	0.7	Side branch IPMN	Left resection
Pat. 10	Female	47	CT/MRI	Tail	22	5.6	MCN	Left resection with splenectomy

[1] LEC – lymphoepithelial cyst

[2] CT – computed tomography

[3] IPMN - intraductal papillary mucinous neoplasm

[4] MCN - mucinous cystic neoplasm

[5] SCN - serous cystic neoplasm

[6] MRI - magnetic resonance imaging

In contrast, MCNs were presented exclusively in the middle-aged woman with the age range of 37 to 67 years (mean age 51 ± 13 years). There was no statistically significant difference in age between LEC-group and MCN-group (p = 0,983).

Branch duct-IPMNs were found in both sexes showing a slight male predominance (13 male and 7 female). The mean patient age was higher compared to the other two groups, with mean value of 70.5 ± 7.7 years (rage 55 to 78 years), the difference was statistically significant (LEC compared to IPMN p < 0.001 and MCN compared to IPMN p = 0.005).

Imaging findings:

All patients with LEC revealed a well-defined exophytic lesion within the tail (70%) or body (30%) of the pancreatic parenchyma, without communication with the main pancreatic duct. The mean size was 6.1 cm (2.7–22 cm). There were no calcifications within the pancreatic parenchyma or within the cystic lesions. On unenhanced CT scans nine LECs had high attenuating fluid or material, which strongly indicated the presence of keratinous material with unenhanced CT attenuation mean value of 22 HU (ranged 16 to 34 HU). Cystic liver lesions were incidentally found in one patient, another incidental finding was cholecystolithiasis in another patient.

MCN lesions had a solitary / macrocystic appearance in the distal pancreas with a mean size of 5.9 cm. In all cases a pancreatic tail was involved, with 5 out of 20 occupying both the body and the tail of the pancreas. There was also no connection to the pancreatic duct.

In 13 out of 20 cases patients with IPMN the head of the pancreas was affected (with one lesion involving the entire pancreas and the other – the pancreatic head and tail), seven were found in the pancreatic tail. The mean size was significantly smaller than in previous two groups with the mean size of 1.8 cm (p < 0.001). The key differential feature was evidence of communication to the main pancreatic duct, which was easily confirmed using MRCP images (when available).

When comparing LEC with other cystic lesions there was no statistically significant difference in size between LEC and MCN (p = 0.912). On the contrary, branch duct IPMNs were significantly smaller that LEC (p < 0.001). Unenhanced CT attenuation of LEC was significantly higher than MCN (p = 0.025) and IPMNs (p = 0.021). Summary of comparison between three groups is presented in Table 2.

Table 2
Results of the comparison between LEC, MCN and IPMN.

	LEC[1]	MCN[2]	Branch duct IPMN[3]
Number of patients	10	20	20
Mean age (years)	50.9 (p < 0.001)	50.7 (p = 0.005)	70.5
Gender (m:f)	9 : 1	1 : 19	13 : 7
Size (cm)	6.1	5.9	1.8 (p < 0.001)
Mean attenuation values in native phase, HU	20.8 (16 to 34 HU) (p = 0.025)	13.4 (10 to 21 HU)	12.4 (8 to 20) (p = 0.021)
Mural nodules (n)	50% (5/10)	0	0
Duct dilation 3-5mm (n)	0 (< 3mm)	0 (< 3mm)	50% (10/20), mean 4 mm

[1] LEC – lymphoepithelial cyst

[2] MCN - mucinous cystic neoplasm

[3] IPMN - intraductal papillary mucinous neoplasm

[4] HU – Hounsfield unit

Taken the imaging features together, we were able to identify three imaging subtypes of LECs. In 20% the LECs where **simple cystic lesions**. In 80% LECs where **mixed solid-cystic lesions** with different morphology: first group (30%) had **diffuse subsolid component** (Fig. 3) and the second group (50%) had **mural nodules** (Fig. 1 **and** Fig. 4).

Subsolid component was defined as homogeneous or heterogenous area of higher attenuation than simple fluid on noncontrast CT, with unchanged attenuation on arterial/venous phase. The mean size of the mural nodule was 2.1 cm, ranged from 0.8 to 5.6 cm. Four LECs were unilocular, six multilocular (≥ 4) and five had septations. Both septations and solid components showed contrast enhancement in the multiphase studies. One LEC had areas of sponge-like appearance due to septations with some degree of enhancement, similar to those in serous cystic neoplasms.

None of the lesions caused pancreatic duct or bile duct dilation and no atrophy of the pancreatic parenchyma. We found this feature beneficial in differentiating LECs to IPMNs, with IPMNs showing a slight dilatation of MPD in 50% of cases with the mean diameter of 4 mm (ranged 3 to 6 mm).

Overlapping imaging features of LEC and branch-duct IPMN are shown in Fig. 5.

The most likely differential diagnosis in the provided case of a small cystic lesion in the pancreatic tail is IPMN due to lesion morphology. Nevertheless, there was no clear connection with the main pancreatic duct on the MRCP images, so the diagnosis was not certain. Due to the presence of a second bigger lesion both lesions were resected.

Overlapping imaging features of LEC and MCN are shown in Fig. 6. Due to the lesion morphology, similar to MCN and lesion size so it was resected.

Discussion

In the present study, which is one of the largest monocentric radiological studies on LEC, we identified three imaging subtypes of LEC. The first one includes lesions with a simple cystic morphology and the other two are complex cystic lesions with either a diffuse subsolid component or with a mural nodule. In our case series, the majority of LEC (80%) were visualized as mixed solid-cystic lesions. Our findings correspond to data by Borhani et al. (15), where the authors investigated imaging features of pathologically proved LEC in 10 patients with 80% being classified as complex cystic lesions. These three imaging subtypes can be applied to the diagnostical routine in daily clinical practice. They can potentially help to avoid the imaging misdiagnosis of LEC, which are uncommon pancreatic tumors and show a significant overlap of clinical and imaging features.

First typical clinical feature of LEC is a clear male predominance with a ratio of 9 to 1 (M to F). This finding was the main differential feature to MCNs and is in concordance with two LEC-cohorts assembling a male to female ratio of 4 to 1 (6) and 7 to 1 (11). It is reported that the majority of patients with LECs were middle aged men with an average age of 54 years (range 26–82 years in different studies), which corresponds with our results with the mean age of LEC patients being 50 years. This finding served as the main differential feature to IPMN.

Kim et al. (16) as well as Adsay et al. (6) reported that the most characteristic morphological and imaging finding of LEC is its exophytic location with contour deformation; we were able to verify this finding. This feature can be a result of development of LEC from epithelial remnants in the lymphatic node that normally has an extrapancreatic location. Adsay (6) und Sewkani (7) reported that LEC could be found in any location of the pancreas including head, body, and tail. In the following studies (17–21), the LECs were localized in the body and tail, which is in line with our findings with distribution ratio of tail to body of 7:3.

LECs also showed a higher HU attenuation on the native CT scans when compared to both MCNs and branch duct IPMNs. This feature can be a result of the granular keratinized material in the cyst fluid intraluminal, one of the pathologic characteristics of the LECs. We found it beneficial in differentiation LECs to MCNs and IPMNs. Kudo et al. (22) reported slight signal reduction in out-of-phase MRI compared to that of in-phase, indicating co-existence of fat and water. Fukukura et al. (23) stated that LECs could have a lipid component which has negative CT attenuation values. We were not able to verify these finding in our patient collective.

A malignant transformation of LEC has not been reported, epithelial changes are often reactive due to secondary inflammation of the cyst. The elevation of tumor markers is not a distinctive clinical feature of malignancy as around 30–40% of LEC showed elevated CEA and CA 19 – 9 levels being benign lesions (24).

With imaging it is possible to differentiate pseudocyst when a clinical history of acute pancreatitis and follow-up imaging are given. Pseudocysts are most commonly a result of pancreatic inflammation with a rupture of the pancreatic duct due to acute pancreatitis. They can also form as a result of pancreatic trauma with parenchymal rupture. They have no malignant potential and normally are followed-up or treated with minimal invasive intervention, therefor we didn't include these patients as a control group in our study.

CT and MRI remain the main radiological modalities for the differentiation of cystic pancreatic lesions; however, radiological features of LEC could be indistinguishable from other cystic pancreatic neoplasms. The first diagnostical challenge in the present study was similar appearance to the branch-duct IPMN. Many authors reported that LECs were not associated with pancreatic duct dilation and were associated with a normal pancreatic duct and pancreatic parenchyma. We have similar findings and found this feature helpful in differentiating the LEC from IPMNs, with IPMNs showing a slight dilation of MPD with the mean value of 4 mm (ranged from 6 to 3 mm). This imaging feature is likely due to the peripheral location of LEC as well.

Secondly, we found radiological appearance indistinguishable to SCNs in some cases, especially to the SCNs that have a subsolid imaging character, which could be found in up to 20% of cases. In such cases small cystic components are indistinguishable on CT images showing a sponge-like appearance. Similar features were found in one LECs in our group. In such cases, precise attention should be put on the clinical data of the patient such as sex and age, as the most SCNs are found in the older women. Otherwise, both SCNs and LECs are benign lesions and do not require surgery, thus making differentiation between them not clinically relevant. Nevertheless, SCN could be potentially differentiated as they have strong female predominance and occur in elderly patients.

Thirdly, LEC can have similar appearance to a mucinous cystic neoplasm with oligocystic morphology. The examples above show that preoperative diagnosis of lymphoepithelial cysts from other cystic neoplastic pancreatic lesions, which require surgical intervention, is difficult based solely on radiological criteria. LECs still remains a diagnostic dilemma and surgical resection is frequently offered because a malignant or premalignant cystic pancreatic lesion cannot be excluded.

The major limitation of our study its limited number of patients, explanation to this is the rarity of the LECs. Secondly, there was no standardized imaging protocol of CT and MRI within 12 years because of the retrospective study design; some patients already had imaging studies, performed outside our institution and were referred to our European pancreatic center for treatment. Although some imaging differences between patients were present, the image quality and provided diagnostic information was sufficient for decision making. Such imaging heterogeneity also reflects realistic clinical workflow.

Conclusion

In conclusion, clinical data is crucial in the differential diagnosis of the cystic lesions of the pancreas. The present study showed a strong male predominance of LEC, which is beneficial in the differential diagnosis with MCN.

Our study provides key radiological features, such as connection to MPD, dilatation of MPD, and location, for the imaging differentiation of LEC and other cystic pancreatic lesions. Firstly, compared to branch-duct IPMN, LEC showed no communication and no dilatation of the main pancreatic duct. Secondly, the location can also serve as a differential feature with lesions located in the pancreatic head unlikely to be LEC with most typical location in pancreatic tail. However, under some circumstances LECs are indistinguishable from other pancreatic neoplasms and a correct preoperative diagnosis cannot be done using imaging only. In such cases, a multidisciplinary approach should be strongly considered in order to correlate the imaging finding with clinical data and the possibility of watch and wait approach.

Methods

Ethics approval and consent

This study was performed according to the Declaration of Helsinki. Our study was approved by the Institutional Review Board (IRB) of Heidelberg University Hospital (Number S 011/15). Due to its retrospective design the informed consent for the patients was waived by the IRB.

Patient selection and data collection

We reviewed 12 cases of resected and histopathological confirmed LECs of the pancreas in our institution (Department of Diagnostical and Interventional Radiology of Heidelberg University Hospital) in the last 12 years; a total of 10 patients with available clinical and imaging data were found. 20 patients with MCNs and 20 patients with branch duct IPMNs, who underwent resection during the same time period, were selected consecutively out of the institutional study collective and served as control groups. Therefore, the study included 50 patients with cystic pancreatic lesions, among them 10 patients with LECs, 20 patients with MCNs and 20 patients with branch duct IPMNs. Patients with SCN and pancreatic pseudocysts were not included in the study as these lesions are begin and could be better differentiated with clinical data, such as episodes of acute pancreatitis and patient age / gender. Data such symptoms, laboratory tests, histopathological findings, follow-up, and imaging findings were retrospectively analyzed for all patients.

Diagnostical Imaging

Due to the retrospective design of the present study, imaging was not standardized. In the LEC-group three patients underwent both preoperative CT and MRI, four underwent MRI, and three underwent CT only.

CT examinations were performed on scanners from Siemens Healthcare, Philips Healthcare and GE Healthcare with either 16 or 64 rows. Kernels for image reconstruction were soft. All CTs included unenhanced images and two-phase contrast-enhanced-images after intravenous injection of nonionic

contrast medium. Coronal reconstructions in the venous (n = 6) and both arterial and venous (n = 4) phases were available.

MRI with magnetic resonance cholangiopancreatography (MRCP) was available for 7 patients. MR imaging was performed on scanners from Siemens Healthcare (Forchheim, Germany), Philips Healthcare (Best, Netherlands) and GE Healthcare (New York, USA) with field strengths ranging from 1 to 1,5 Tesla. All MRI studies included following imaging sequences: T2-weighted axial images without fat suppression (fs) and coronal T2-weighted images with or without fat suppression (fs). T1-weighted images before and after contrast injection were obtained with dynamic protocol after injection of extracellular contrast agent as a bolus injection of 0.2 ml/kg gadolinium chelate. Arterial phase was defined as full enhancement of hepatic arteries and absence of enhancement of hepatic veins, portal venous phase, defined as full enhancement of portal veins and antegrade enhancement of hepatic veins, and late phase, defined as similar enhancement of portal veins and hepatic veins and enhancement of liver parenchyma to lesser degree than in portal venous phase. Diffusion-weighted images were available for 4 patients and included b-values of 0, 50, and 800 s/mm^2.

For the control groups imaging studies were performed with a standard imaging protocol used in our hospital. For all of them both CT (unenhanced and contrast enhanced imaging) and MR imaging was available. CT examinations were performed on scanner from Siemens Healthcare with 64 rows. MR imaging was performed on scanners from Siemens Healthcare (Forchheim, Germany) with field strength 1,5 Tesla.

Radiological evaluation

Two radiologists (EK, 10 years of experience in abdominal imaging and EEG with 2,5 years of experience), blinded to the histopathological reports, analyzed the images independently, using a Picture Archiving and Communication System (PACS) workstation. Imaging analysis included the following parameters: location (head, body, tail), lesion appearance (cystic, subsolid), septation (present, absent), enhancing mural nodules (present, absent), and dilatation of main pancreatic duct (MPD) > 3 mm and common bile duct (CBD) > 8 mm upstream of the lesion (present, absent; for lesions without proximity to the MPD or CBD and for lesions located at the tip of the pancreatic tail the latter two parameters were classified as not applicable). Size of lesions (mm) and attenuation values (Hounsfield units, HU) on unenhanced images, as well as in the arterial and venous phases were measured. To assess the attenuation on unenhanced, arterial and venous CT scans, HU were measured using circular regions of interest (ROI) located in the most homogeneous part of the lesion. Afterwards, discrepancies in image interpretation were resolved by consensus between the two radiologists.

The following parameters were assessed for CT images only: calcification (present, absent) and CT density on unenhanced phase (hypodense, isodense, hyperdense).

The following parameters were assessed for MR images only: signal intensity (hypointense, isointense, hyperintense) and signal uniformity (homogeneous, heterogeneous) of the lesion on unenhanced T1- and T2-weighted imaging with and without fat saturation, presence of T1-hyperintense spots with

corresponding T2-hypointensity as evidence for haemorrhage (present, absent), signal intensity on DWI with b ≥ 500 s/mm2 compared to the surrounding pancreas (hypointense, isointense, hyperintense).

Statistical analysis

Data management was carried out by SAS software release 9.4 (SAS Institute, Cary, North Carolina, USA) and statistical analysis was made using IMB SPSS software, version 24 (IBM Corp.). Data is reported as mean ± SD. Agreement between radiologists was quantitated using Cohen's kappa for nominal categorical variables (12) and weighted kappa (linear weights) for ordinal categorical variables (13). As proposed by Landis and Koch (14), kappa values were interpreted as poor (< 0.00), slight (0.00–0.20), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80), and almost perfect agreement (0.81–1.00). Mann–Whitney U test was performed to compare continuous parameters between groups. For categorial parameters absolute numbers are shown. Two-sided p-values were computed, the differences were considered statistically significant at P-value of 0.05 or less.

Declarations

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Autor contribution statement

EK Conceptualization, Methodology, Formal analysis, Investigation, Validation, Writing – original draft, Writing – review and editing

EEG Formal analysis, Investigation, Validation, Writing – review and editing

MG Methodology, Formal analysis, Investigation, Histology

TH Conceptualization, Investigation, Validation, Writing – original draft, Project administration, Supervision, Surgery

PM Methodology, Formal analysis, Investigation, Supervision, Writing – review and editing

HUK Writing – review and editing, Supervision, Project administration, Resources

MK Writing – review and editing, Supervision, Project administration, Resources

Declaration of Competing Interest

The authors declare no conflict of interest.

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References

1. Karoumpalis, I. & Christodoulou, D. K. Cystic lesions of the pancreas. *Ann Gastroenterol.* **29** (2), 155–161 (2016).
2. Lüchtrath, H. & Schriefers, K. H. Pankreaszyste unter dem Bild einer sogenannten branchiogenen Zyste [A pancreatic cyst with features of a so-called branchiogenic cyst]. *Pathologe.* **6** (4), 217–219 (1985).
3. Kavuturu, S. *et al.* Lymphoepithelial cysts of the pancreas. Can preoperative imaging distinguish this benign lesion from malignant or pre-malignant cystic pancreatic lesions? *JOP.* **14** (3), 250–255 (2013).
4. Domen, H. *et al.* Lymphoepithelial cyst of the pancreas. *Case Rep Gastroenterol.* **6** (3), 604–611 (2012).
5. Iacono, C. *et al.* Lymphoepithelial cyst of the pancreas. Report of two cases and review of the literature. *Int J Pancreatol.* **19** (1), 71–76 (1996).
6. Adsay, N. V. *et al.* Lymphoepithelial cysts of the pancreas: a report of 12 cases and a review of the literature. *Mod Pathol.* **15** (5), 492–501 (2002).
7. Sewkani, A. *et al.* Lymphoepithelial cyst of the pancreas: a rare case report and review of literature. *Indian J Surg.* **72**, 427–432 (2010).
8. Arumugam, P. *et al.* Lymphoepithelial Cyst of the Pancreas. *Case Rep Gastroenterol.* **10** (1), 181–192 (2016).
9. Mege, D. *et al.* Lymphoepithelial cyst of the pancreas: an analysis of 117 patients. *Pancreas.* **43** (7), 987–995 (2014).
10. Terakawa, H. *et al.* Clinical and radiological feature of lymphoepithelial cyst of the pancreas. *World J Gastroenterol.* **20(45**, 17247–17253 (2014).
11. Osiro, S. *et al.* Is preoperative diagnosis possible? A clinical and radiological review of lymphoepithelial cysts of the pancreas. *JOP.* **14** (1), 15–20 (2013).
12. Cohen, J. A Coefficient of Agreement for Nominal Scales. *Educ Psychol Meas.* **20**, 37–46 (1960).
13. Cohen, J. Weighted kappa: Nominal scale agreement provision for scaled disagreement or partial credit. *Psychol Bull.* **70**, 213–220 (1968).
14. Landis, J. R. & Koch, G. G. The Measurement of Observer Agreement for Categorical Data. *Biometrics.* **33**, 159 (1977).
15. Borhani, A. A. *et al.* Lymphoepithelial cyst of pancreas: spectrum of radiological findings with pathologic correlation. *Abdom Radiol.* **42** (3), 877–883 (2017).
16. Kim, W. H. *et al.* Lymphoepithelial cyst of the pancreas: comparison of CT findings with other pancreatic cystic lesions. *Abdom Imaging.* **38** (2), 324–330 (2013).
17. Jian, B. *et al.* Lymphoepithelial cysts of the pancreas: endosonography-guided fine needle aspiration. *Diagn Cytopathol.* **36**, 662–665 (2008).
18. Ali, S. *et al.* EUS-guided Trucut biopsies may enable the diagnosis of lymphoepithelial cysts of the pancreas. Report of two cases. *JOP.* **10**, 409–412 (2009).
19. Alcalde Quirós, M. J. *et al.* Lymphoepithelial cyst of the pancreas mimicking a cystic neoplasm. *Rev Esp Enferm Dig.* **102** (1), 63–65 (2010).

20. Karim, Z., Walker, B. & Lam, E. Lymphoepithelial cysts of the pancreas: the use of endoscopic ultrasound-guided fine-needle aspiration in diagnosis. *Can J Gastroenterol.* **24**, 348–350 (2010).
21. Raval, J. S. *et al.* Pancreatic lymphoepithelial cysts express CEA and can contain mucous cells: potential pitfalls in the preoperative diagnosis. *Mod Pathol.* **23**, 1467–1476 (2010).
22. Kudo, D. *et al.* Usefulness of in-phase and out-of-phase magnetic resonance imaging for the detection of pancreatic lymphoepithelial cyst. *Hepatogastroenterology.* **58** (109), 1403–1405 (2011).
23. Fukukura, Y. *et al.* Lymphoepithelial cysts of the pancreas: demonstration of lipid component using CT and MRI. *J Comput Assist Tomogr.* **22** (2), 311–313 (1998).
24. Takamatsu, S. *et al.* Lymphoepithelial cyst of the pancreas. *Journal of Hepato-Biliary- Pancreatic Surgery.* **3** (4), 485–490 (1996).

Figures

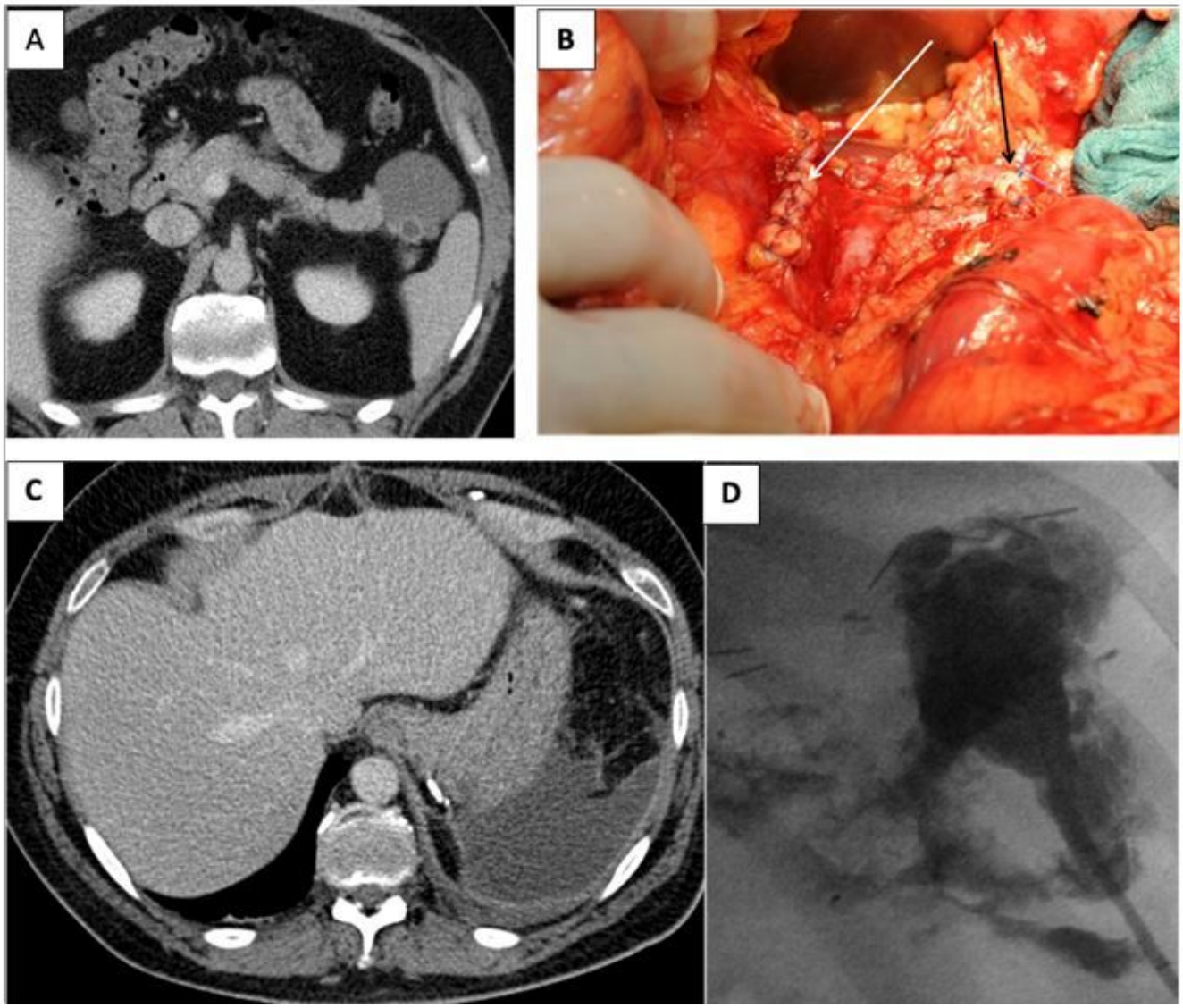

Figure 1

a-d. 53-year old male patient with LEC in the distal part of pancreatic tail with a mural nodule, size of the lesion 5,4 cm, size of the mural nodule 1,1 cm. Axial CT image in the venous phase (a) shows cystic lesion in the distal pancreatic tail with solid component (HU values of the solid component 38 HU in native phase, 103 HU in the arterial phase and 90 HU in venous phase). Intraoperative view (b) after a pancreatic left resection with splenectomy, cut margin pancreas (white arrow), splenic artery stump (black arrow). Axial CT image in venous phase (c) within first postoperative follow-up shows a fluid collection with membranisation in the periphery, as a local post-OP complication. Fluoroscopy image (d) after draining under the CT guidance shows big left sided subphrenic collection.

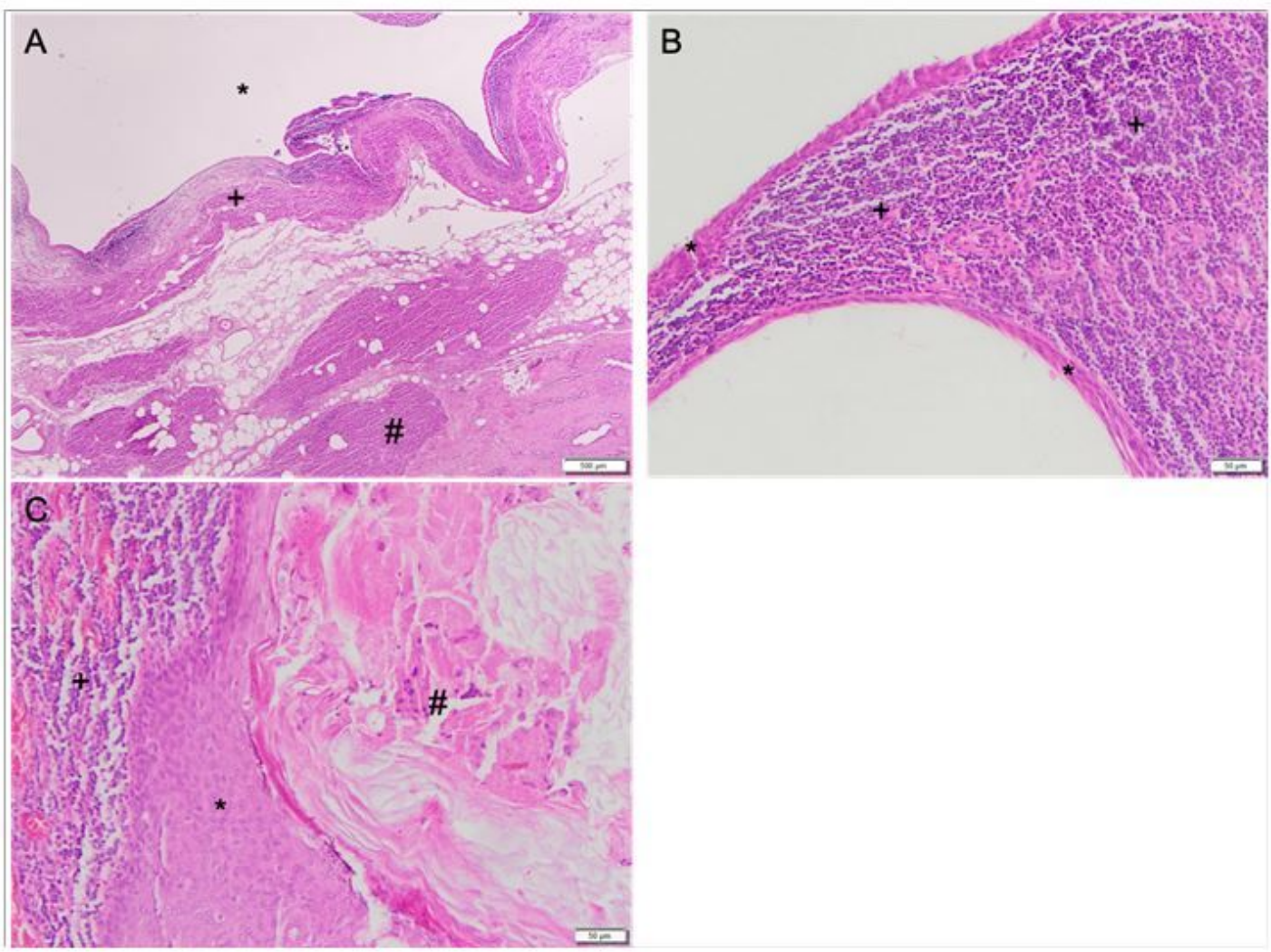

Figure 2

a-c. Pathological analysis of LEC. Overview on a lymphoepithelial cyst in low magnification (a) shows cyst lumen (*), cyst wall (+), adjacent pancreas tissue (#). View with the higher magnification (b) shows that the cyst is layered by squamous epithelium (*) with underlying dense „band-like“ infiltrates of lymphocytes. No epithelial dysplasia. Second view with the higher magnification (c) shows typical squamous epithelium (*) with keratinization (#), and underlying „band-like“ lymphocyte aggregations. No epithelial dysplasia.

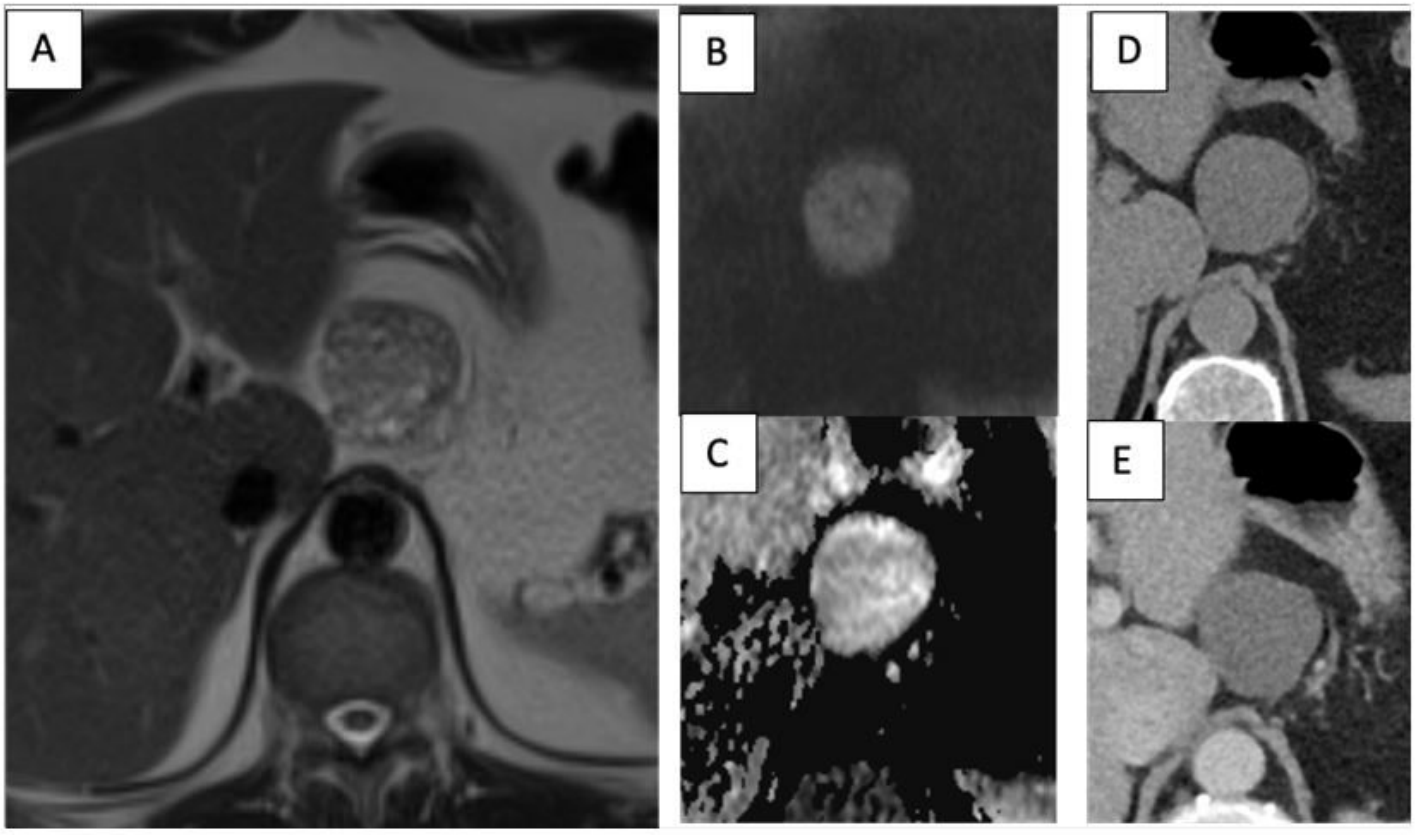

Figure 3

a-e. 48-year old patient with 4,5 cm size LEC in the pancreatic body with exophytic location. Axial T2-weighted MR image (a) shows diffuse subsolid morphology of the lesion. Axial DWI MR image (b) and axial ADC MR image (c) show no restricted diffusion. Axial CT image in native phase (d) shows an isodense CT attenuation of the lesion. Axial CT image in venous phase (e) shows no significant enhancement of the lesion.

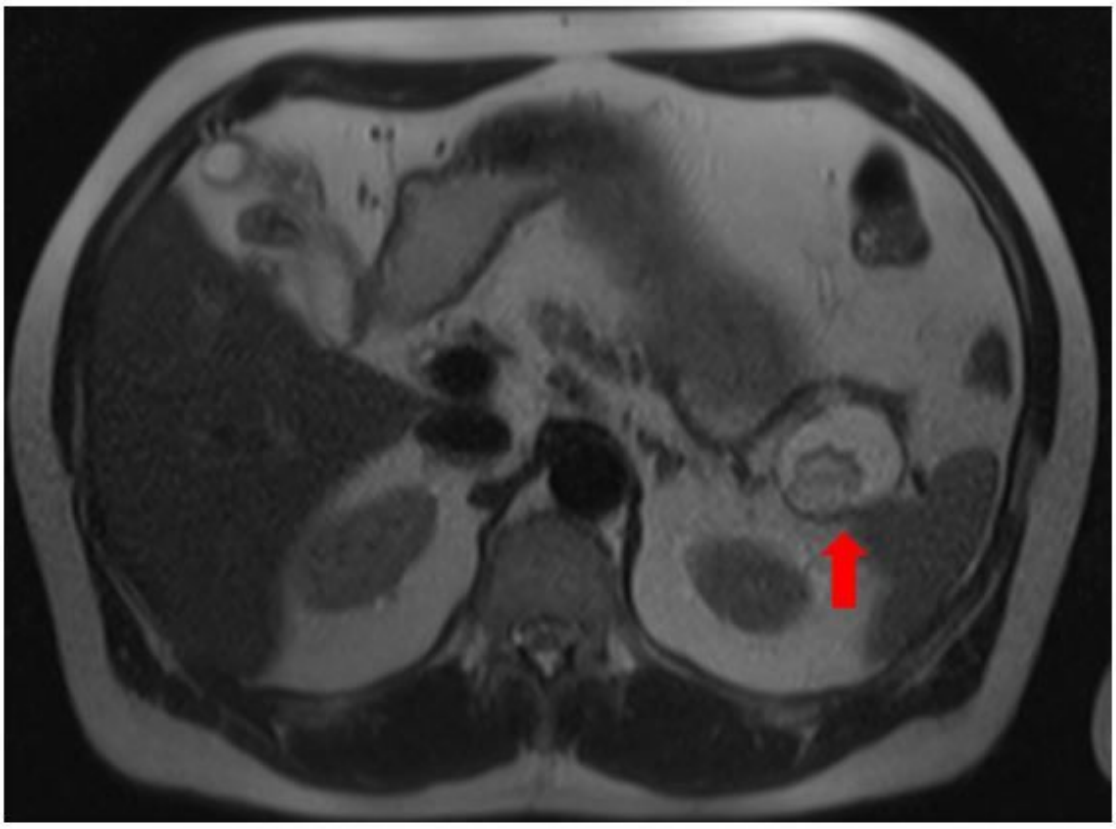

Figure 4

49-year old male patient with LEC in the pancreatic tail with 4,4 cm size. Axial T2-weighted MR image without fat suppression shows a cystic pancreatic lesion in tail of the pancreas with mural nodule in the dorsal part, nodule size 2,4 cm.

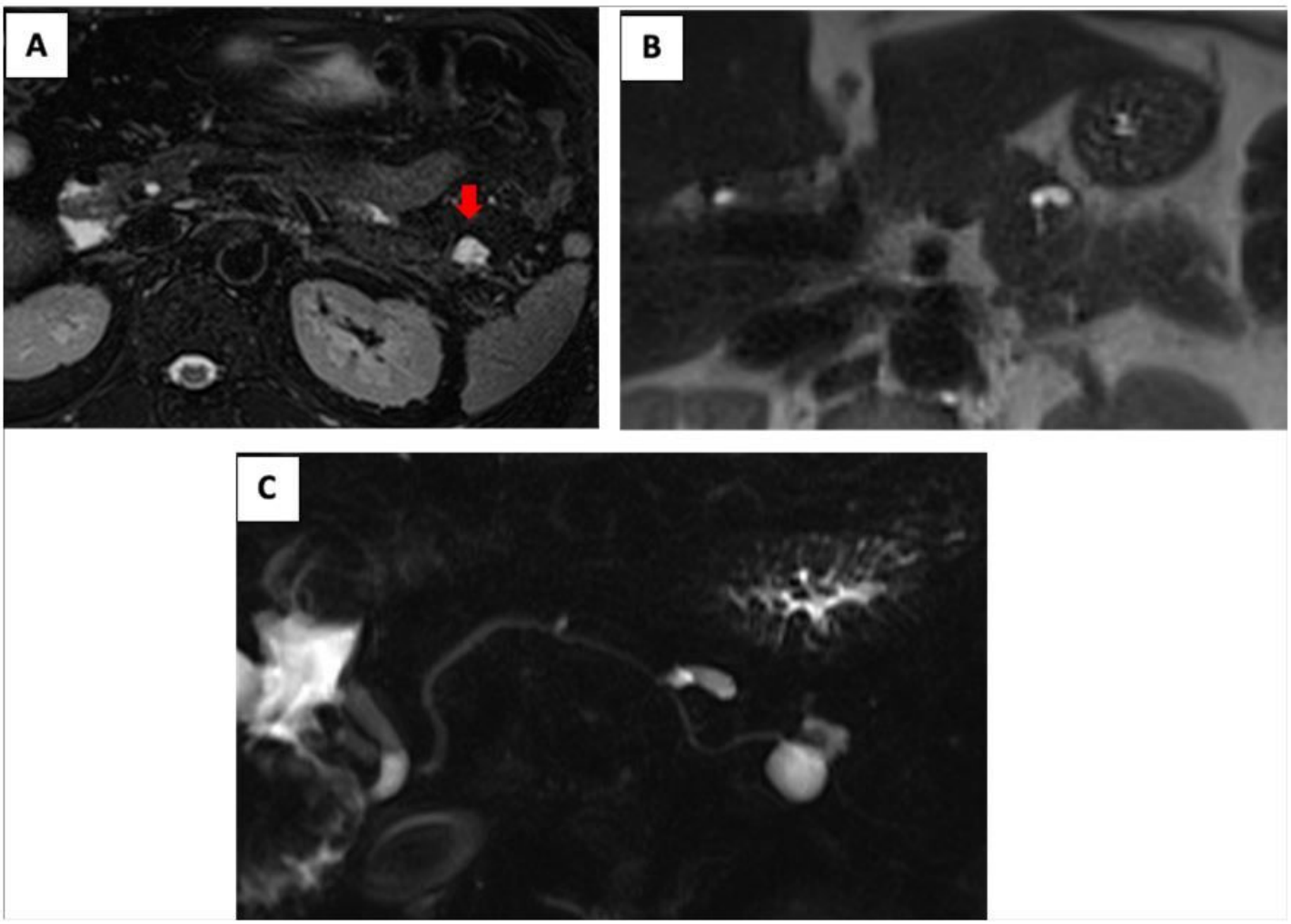

Figure 5

a-c. Comparison of LEC and side branch IPMN. 44-year old male patient with two cystic lesions within the pancreatic tail. Axial T2-weigted MR image with fat suppression (a) shows small LEC in the distal part of pancreatic tail with a similar image to an IPMN. Bigger LEC (not shown) showed enhanced mural nodule, which was an indication for the surgery. 48-year old male patient with IPMN in the pancreatic tail. Axial T2-weighted MR image without fat suppression (b) shows a side branch IPMN in the pancreatic tail. Coronal MRCP MR image (c) shows the communication of the lesion to the main pancreatic duct, which was the key differential feature.

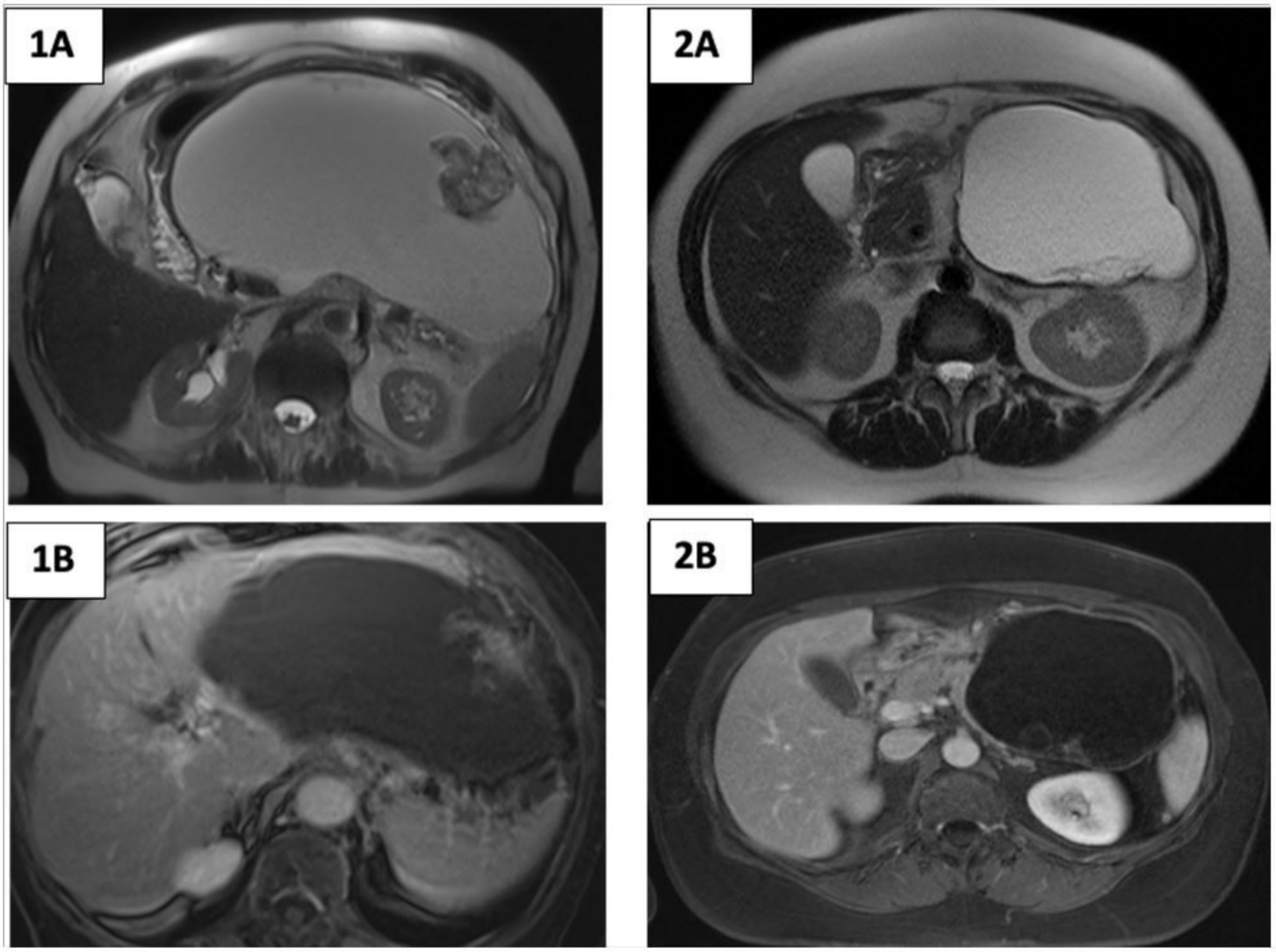

Figure 6

a-d. Comparison of LEC and MCN. a-b. 47-year old female patient with huge LEC in the pancreatic body and tail, lesion size 22 cm. Axial T2 weighted MR image without fat suppression (a) and T1-weighed MR image in the venous phase (b) show a LEC with mural nodules and enhancing solid component in the ventral wall of the lesion (size of the solid component 5,6 cm). c-d. An identical image to a mucinous cystic neoplasm in a different patient. Axial T2 weighted MR image without fat suppression (c) shows a big MCN in the pancreatic body and tail with septations in the dorsal parts. Axial T1-weighted MR image with fat suppression (d) shows an enhancing solid component in the dorsal parts of the cystic lesion.