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Case Report

Pancreatic mass is not always a killer

Pancreatic cystic lymphangioma: A case report

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ABSTRAT

Pancreatic cystic lymphangioma is a rare benign pancreatic tumor, accounting for less than 0.2% of all pancreatic lesions. Due to the lack of specificity on imaging findings, most of case reports' diagnosis were made after aggressive treatment. We herein report a case of a pancreatic lymphangioma located in the uncinate and diagnosed post-operatively in a 52 years-old woman who was presented with intense intermittent epigastric pain. To avoid a non-necessary intervention, an accurate preoperative diagnosis is essential. Therefore, pancreatic cystic lymphangioma should be considered in the differential diagnosis of pancreatic tumors. Nowadays, EUS-FNA seems to have the potential to provide a final diagnosis of this benign tumor. The best way to take this diagnosis into consideration and perform the EUS-FNA is to establish a score that would integrate different risk factors and epidemiological findings of pancreatic cystic lymphangioma. Here, we established a road map for the management of the pancreatic lymphangioma based on predefined score.

Keywords

lymphangioma,
pancreatic cyst,
rare tumor,
endoscopic ultrasound,
fine needle aspiration

INTRODUCTION

Cystic lymphangioma is a benign tumor that results from the obstruction of lymphatic flow leading to the development of lymphangiectasis (1). This obstruction may be related to congenital malformation, and abdominal traumatism; it may also be a resultant of surgery, radiation therapy, or infection, mostly in adult forms (2). Cystic Lymphangioma is more seen in children (3). It occurs frequently in the head and neck region (in 75% of the cases), in the axilla (in 20% of the cases), and rarely in the mediastinum (4). Lymphangioma of the pancreas is extremely rare accounting for less than 1% of all lymphangiomas, and 0.2% of pancreatic lesions (5). This rare type of lymphangioma is generally encountered in females (4) with unspecific symptoms like abdominal pain, nausea, vomiting and palpable abdominal mass depending on the cyst size. The majority are localized in pancreatic body or tail, although they can arise from other parts of the pancreas (6).

Pancreatic lymphangioma appears as cystic lesions on imaging studies.

The differential diagnosis of pancreatic cystic lesions, other than pancreatic lymphangioma, may include pseudo cyst, simple cyst, mucinous cyst neoplasms, serous cyst adenoma and intraductal papillary mucinous neoplasms; consequently, conventional imaging examinations like abdominal US, CT scan or MRI could not distinguish it from other malignant tumors. Therefore, preoperative non-interventional diagnosis has been very difficult (7) and thus treatment of the mass is usually aggressive. However, since this is a benign mass with favorable prognosis (3), it is possible to take a conservative approach (8), or remove it by simple surgical excision (9).

We herein report a case of an adult woman with cystic lymphangioma located in the uncinate process of the pancreas

that was diagnosed post-operatively. After describing this rare case, we will discuss the possible differential diagnoses of this entity and establish a road map for the management of this tumor based on pre-defined score.

CASE

A 52-year-old woman, previously healthy, presented to the ER with intense intermittent epigastric pain, radiating to the back and shoulders. These symptoms were accompanied by nausea and vomiting; however, she did not suffer from fever and chills. She has a past medical history of recurrent kidney stones complicated by a right pyelonephritis in 2015. It was treated with a double J catheter. She denied history of any abdominal trauma or surgery. She does not consume alcohol and tobacco. She had no personal or family medical history that would predispose her to pancreatic lesions (no familial pancreatitis syndromes). She had a normal physical examination.

Laboratory studies showed cholestasis with slightly elevated alkaline phosphatase (AP) and gamma-glutamyl transferase (GGT) (two folds above normal) with normal bilirubin amylase lipase and transaminase values and negative tumor markers (Ca 19-9 and CEA). Abdominal ultrasound was performed showing a paramedian, retroperitoneal cystic septated mass of 65*42 mm. Additionally, a gallbladder full of gallstones with no signs of complication was detected. No dilation of bile ducts was found. The investigations were completed by abdominal magnetic resonance imaging showing a well-defined multilocular microcystic mass of the uncinate process of the pancreas just below the pancreatico-biliary confluence, measuring 5.4*4.5 cm, with parietal posterior contrast enhancing nodule of 4 mm. There was no dilation of Wirsung or biliary ducts. No lymphadenopathy was perceived, and no vascular (mesenteric portal or hepatic) invasion was detected. No hepatic metastasis or lesion were found (Figure 1).

Because cancer was suspected, the patient underwent a pylorus -preserving pancreaticoduodenectomy, a cholecystectomy and hilar lymphadenectomy with good outcomes. She was discharged five days after surgery. The postoperative course went well, without complaint in the follow-up period. The pathology result reported a pancreatic cystic lymphangioma (Figure 2).

DISCUSSION

The differential diagnosis of pancreatic lesions includes a variety of inflammatory, non-neoplastic, and neoplastic lesion, which may be symptomatic or not. Among the least known pancreatic lesions are the lymphangiomas. Pancreatic cystic lymphangioma is a rare benign cystic lesion, accounting for less than 100 cases reported since its first report by Koch in 1913 (3). It is more frequent in females, and affects all age groups (4). It is found most of the time in pancreatic body or tail but can eventually be found in other parts of the pancreas. In this

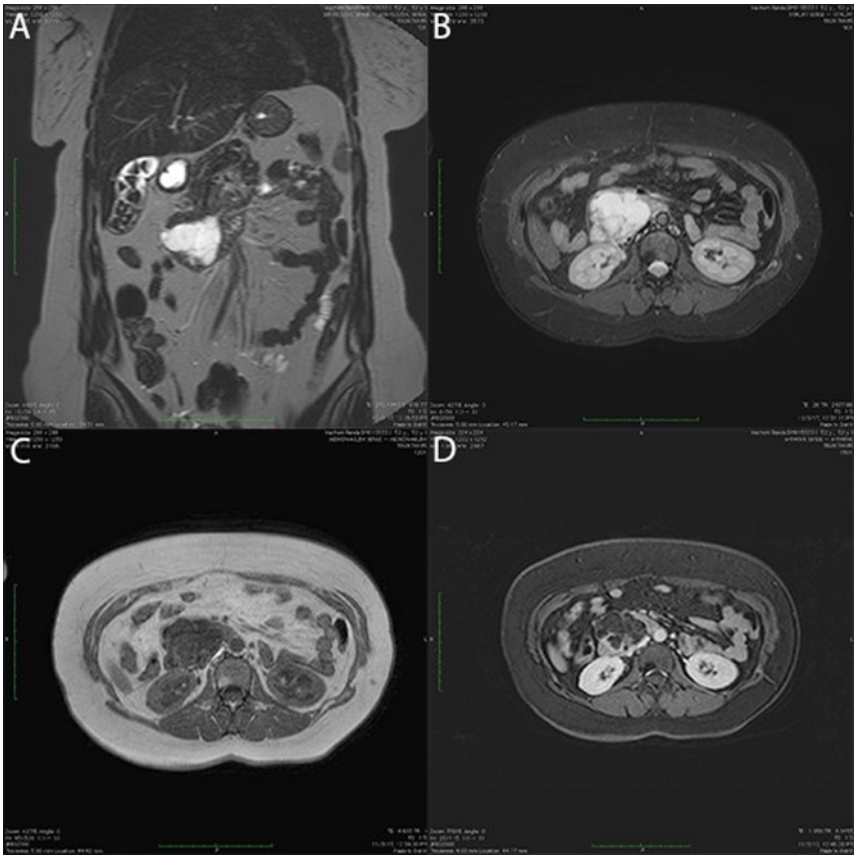

Figure 1. Abdominal Magnetic Resonance Imaging Cuts. **A** Coronal T2, **B** Axial T2 with Fat signal saturation and Axial T1 **C** Before and after **D** gadolinium intra venous injection cuts showing a well-defined multilocular microcystic mass of the uncinate process of the pancreas

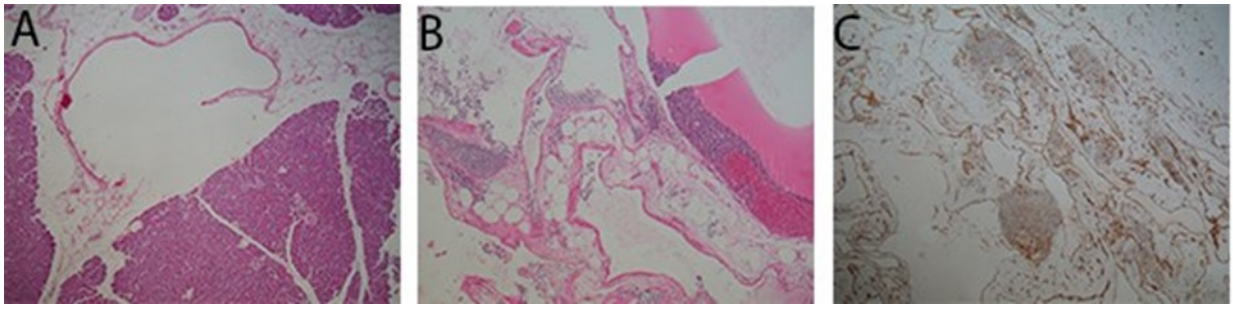

Figure 2. Hematoxylin and eosin staining shows dilated lymphatic channels of varying sizes, separated by thin septa. The cystic spaces are lined with flattened or cuboidal endothelial cells. No cell atypia found. **A** The tumor is surrounded by normal pancreatic tissue. **B** Lymphoid has aggregated around the lymphatic channels. **C** Immunostaining results indicated that the cyst wall lining cells were CD34-positive

case, the lesion arises in the uncinate process of the pancreas. Tumor size varies from 3 to 20 cm, with an average around 12 cm in diameter (10). Pancreatic lymphangioma is composed of dilated cysts lined by flat endothelium, with abundant lymphoid aggregates and smooth muscle in the inner wall of the cyst (11). Pancreatic lymphangioma is usually asymptomatic and discovered incidentally. Conservative management with good follow-up of patients who are asymptomatic remains the best approach (8). Depending on its size, or when complicated, pancreatic lymphangioma becomes symptomatic (12). Abdominal pain and palpable abdominal mass are the most common symptoms (13), along with nausea and vomiting. Acute abdomen pain can rarely occur due to complications such as cyst rupture, infection or hemorrhage (12). Our patient presented with radiating back pain. If these symptoms require therapeutic intervention, surgical excision is the treatment of choice, since incomplete resection may lead to recurrence (9).

However, pancreatic lymphangioma is a benign tumor, and no malignant transformation have been reported yet (3). This explains why lymphangiomas generally require only cystectomy; pancreatic neoplasms, on the other hand, usually require pancreatectomy, which is a far more aggressive operation. Therefore, the issue of morbidity and mortality of exercising an excessively aggressive surgery in pancreatic lymphangioma must be considered. Hence a confident preoperative diagnosis is important to avoid unnecessary excessive interventions. Yet, most of the pancreatic lymphangiomas have been diagnosed after surgical resection, mistaken for malignant lesion (14). In fact, on one hand, signs and symptoms of pancreatic lymphangioma are not specific, and can mimic other malignant pancreatic lesions. On the other hand, there are no specific features on CT, US and MRI which may confidently differentiate a lymphangioma from other pancreatic cysts or tumors. CT scan and MRI show well circumscribed and encapsulated polycystic water-dense tumor divided by septa. They are useful to determine the size and location of the cyst, but cannot distinguish this lesion from other cystic neoplasms (2). US typically shows a polycystic tumor (10). Therefore, differential diagnosis includes pseudocysts, simple cysts, echinococcal cysts and neoplastic cystic tumors such as serous cystadenomas, mucinous cystic neoplasm (MCN) and intraductal papillary mucinous neoplasm (IPMN) (3). Furthermore, carbohydrate antigen 19-9 (CA19-9) and carcinoembryonic antigen (CEA) have insufficient sensitivity (15) to rely on to differentiate between malignant and non-malignant tumors. Thus, the final diagnosis is mostly histological in post-operative stages. Histology reveals interconnecting lymphatic channels, lined by endothelial cells. These channels are divided by thin septa composed of smooth muscle cells, mature lymphocytes and some histiocytes (16). These channels contain serous, serosanguineous or chylous fluid (5). Immunohistochemical reactivity is positive for CD 31 and factor VIII-R, which are markers for endothelial cells (10). We also were unable to diagnose the present case preoperatively, and the diagnosis of lymphangioma was made post-operatively.

However, some authors uphold the **usefulness of Endoscopic ultrasound guided fine-needle aspiration (EUS-FNA) in the preoperative diagnosis** of pancreatic lymphangioma (14). EUS seems to be the optimal procedure of pancreatic lesions, with the advantage of allowing FNA of the cyst fluid for cytology. Pancreatic lymphangioma appears on EUS as a well-defined, uni- or multicystic cavity with thin septae. The content is anechoic, in general without solid components. These features are not exclusive for lymphangioma but its ability to safely obtain cyst fluid for analysis during EUS improve the diagnostic yield. On the FNA, the cyst fluid appears to be chylous and milky-white. The biological exam shows high triglycerides level, and the cytological exam shows a large population of small, mature lymphocytes (17). These aspirated fluid characteristics allow more confident diagnosis. Thus, the performance characteristics of EUS-FNA are very impressive: the literature reported a specificity of 100% and an accuracy of 86% (5). This technique has also a smaller risk of intraperitoneal dissemination compared with the percutaneous route (15). According to the literature, 8 cases of pancreatic lymphangiomas have been diagnosed

only with EUS-FNA, avoiding unnecessary interventions (14). In our case, we did not perform EUS-FNA since we did not suspect lymphangioma due to suspicion of MCN and IPMN.

Subsequently, it would be interesting to do a score test, based on the risk factors and epidemiology of these different differential diagnoses, that would be able to differentiate from the beginning between pancreatic lymphangioma and pancreatic cancers. For instance, one should be more tempted to proceed with EUS-FNA if a patient had no personal or family medical history that would predispose him to pancreatic lesions. Among the risk factors and epidemiology of the pancreatic cancers (15), we find history of cigarette smoking, diabetes, obesity, chronic pancreatitis, first-degree relatives' history of pancreatic cancer, higher prevalence among US and western Europe population, and patients in their 6th decade (Table 1). Among the risk factors and epidemiology of pancreatic lymphangioma, we find history of abdominal trauma, infection, surgery, exposure to radiotherapy, and a higher prevalence in female (Ratio 2:1) (Table 1.).

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To conclude, lymphangioma should be considered in the differential diagnosis of pancreatic lesions, and the use of EUS-FNA as diagnostic tool must be considered according to an eventual score that would be estimated from risk factors and personal medical history.

Conflict of interest

The authors do not have any conflict of interest.

References

1. Fahimi H, Faridi M, Molanaee S, Gholamin S, Khors M, i. Cystic Lymphangioma of the Pancreas: Diagnostic and Therapeutic Challenges. JOP J Pancreas. 2010 [cited 2018 Mar 29];11(6).
2. Sohn B-K, Cho C-H, Chae H-D. Cystic lymphangioma of the pancreas. J Korean Surg Soc. 2011 Aug;81(2):141–5.
3. Fujii M, Saito H, Yoshioka M, Shiode J. Rare Case of Pancreatic Cystic Lymphangioma. Intern Med Tokyo Jpn. 2017 Nov 20;
4. Radoje B Colovic, Nikica M Grubor, Marjan T Micev, Henry Dushan E Atkinson, Vitomir I Rankovic, Mihajlo M Jagodic. Cystic lymphangioma of the pancreas. World J Gastroenterol. 2008 Nov 28; 14(44): 6873-6875.
5. Coe AW, Evans J, Conway J. Pancreas cystic lymphangioma diagnosed with EUS-FNA. JOP J Pancreas. 2012 May 10;13(3):282–4.
6. Gureş N, Gurluler E, Alim A, Berber I, Gurkan A. CystiC Pancreatic Lymphangioma. Rare Tumors. 2012 Apr 19;4 (2):85–6.
7. Talaiezadeh A, Ranjbari N, Bakhtiari M. Pancreatic Lymphangioma as a Rare Pancreatic Mass: A Case Report. Iran J Cancer Prev. 2016 Feb;9(1):e3505.
8. Sanaka MR, Kowalski TE. Cystic lymphangioma of the pancreas. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc. 2007 Mar;5(3):e10-11.
9. Kim HH, Park EK, Seoung JS, Hur YH, Koh YS, Kim JC, et al. Cystic lymphangioma of the pancreas mimicking pancreatic pseudocyst. J Korean Surg Soc. 2011 Jun;80 Suppl 1:S55-58.
10. Ghatak S, Ray S, Sanyal S, Sonar PK, Khamrui S, Basu K, et al. An unusual cause of acute abdomen in adults: giant cystic lymphangioma of the pancreatic head. A clinical case and literature review. JOP J Pancreas. 2011 May 6;12 (3):266–70.
11. Goh BKP, Tan Y-M, Ong H-S, Chui C-H, Ooi LLPJ, Chow PKH, et al. Intra-abdominal and retroperitoneal lymphangiomas in pediatric and adult patients. World J Surg. 2005 Jul;29(7):837–40.
12. Paal E, Thompson LD, Heffess CS. A clinicopathologic and immunohistochemical study of ten pancreatic lymphangiomas and a review of the literature. Cancer. 1998 Jun 1;82(11):2150–8.
13. Igarashi A, Maruo Y, Ito T, Ohsawa K, Serizawa A, Yabe M, et al. Huge cystic lymphangioma of the pancreas: report of a case. Surg Today. 2001;31(8):743–6.
14. Hussain I, Ang TL. Cystic pancreatic lymphangioma diagnosed with endoscopic ultrasound-guided fine needle aspiration. Endosc Ultrasound. 2017 Apr;6(2):136–9.
15. Harrison's Principles of Internal Medicine, 19e | AccessMedicine | McGraw-Hill Medical
16. Carvalho D, Costa M, Russo P, Simas L, Baptista T, Ramos G. Cystic Pancreatic Lymphangioma – Diagnostic Role of Endoscopic Ultrasound. GE Port J Gastroenterol. 2016 Mar 29;23(5):254–8.
17. Fonseca R, Pitman MB. Lymphangioma of the pancreas: a multimodal approach to preoperative diagnosis. Cytopathol Off J Br Soc Clin Cytol. 2013 Jun;24(3):172–6.

Table 1. Demographic and clinical features of patients with adenocarcinoma and pancreatic lymphangioma

	Pancreatic lymphangioma	Adenocarcinoma
Age of distribution	All age, mainly young	65-84 years
Gender distribution	Females	Males > females
Risk factors	Surgery Radiation therapy Infection	Cigarette smoking Longstanding history of type 1 or - type 2 diabetes - Obesity Chronic pancreatitis ABO blood group status Jewish and African-American Hereditary (16%)
Typical clinical presentation	Abdominal pain Nausea and vomiting Palpable abdominal mass	Jaundice Abdominal discomfort Pruritus Lethargy Weight loss Epigastric pain
		Backache New-onset diabetes Acute pancreatitis Nausea and vomiting
Typical localisation	Body or tail	Head of pancreas
Typical imaging characteristics	CT scan and MRI: well circumscribed and encapsulated polycystic waterdense tumor divided by septa. US: polycystic tumor EUS: well-defined, uni- or multicystic cavity with thin septae. Anechoid content, in general without solid components.	US: hypoechoic mass, double duct sign - CT: poorly defined masses with extensive surrounding desmoplastic reaction. Hypodense on arterial phase scan most of the time. Double duct sign - MRI: T1: hypointense cf. normal pancreas T1 FS: hypointense cf. normal pancreas T1 + C (Gd): slower enhancement than normal pancreas T2/FLAIR: variable, depending on the amount of reactive desmoplastic reaction MRCP: double duct sign ERCP: stenosis (irregular and/or shouldered), obstruction, narrowing and abnormal branching of the main pancreatic duct, acinar defect of the pancreas EUS: heterogeneous hypoechoic solid mass with irregular borders
Typical aspirate characteristic	Chylous and milky-white	-
Typical cytology findings	Large population of small, mature lymphocytes	Anisonucleosis Nuclear membrane irregularity - Nuclear crowding/ overlapping/threedimensionality Nuclear enlargement
Typical carcinoembryonic antigen (CEA) level	Normal	↑ in most cases
Typical DNA analysis	Insufficient data	Somatic mutation: KRAS p53 p16 SMAD4 Germline mutation: STK11 BRCA2 P16/CDKN2A PALB2 -hMLH1 and MSH2
		ATM PRSS1
Relative malignant potential	Non-malignant	Malignant
Prognosis	Excellent	Poor
Treatment	Conservative approach if asymptomatic Excision of the lesion if symptomatic	Head: Duodenopancreatectomy Body and tail: left spleno-pancreatectomy