CASE REPORT

Mature Cystic Teratoma of the Pancreas. Case Report and Review of the Literature of a Rare Pancreatic Cystic Lesion

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ABSTRACT

Context Pancreatic cystic lesions are increasingly recognized and comprise different pathological entities. The management of these lesions is challenging, because of inadequate preoperative histological diagnosis. Among this family of lesions, mature cystic teratomas are an extremely rare finding. **Case report** We present the case of a 61-year-old man with a mature cystic teratoma of the pancreas' uncinate process, incidentally discovered at diagnostic imaging. **Conclusions** This case highlights the difficulty to obtain a preoperative diagnosis of this pathological entity and the need of increased awareness about mature cystic teratoma when examining a pancreatic cystic lesion.

INTRODUCTION

Cystic lesions of the pancreas constitute a broad spectrum of entities ranging from non-neoplastic to malignant neoplastic cysts. With the routine use of improved cross-sectional imaging, there has been a dramatic increase in the detection of pancreatic cysts, mainly incidentally discovered. It has been estimated that approximately 1.2% of general medical patients have a pancreatic cyst requiring follow-up [1]. Among this family of pancreatic lesions, mature cystic teratomas are an extremely rare finding. The management of these lesions is challenging, because of inadequate preoperative radiological and histological diagnosis. We report the 33rd case of mature cystic teratoma of the pancreas, reviewing the world literature and reinforcing the need for increased awareness in the clinical management of pancreatic cystic lesions.

CASE REPORT

A 61-year-old man came to our attention for a hypoechoic lesion of the pancreatic head incidentally discovered on abdominal US, that was performed to study the urinary tract due to a slight elevation of PSA levels. The patient was healthy and did not complain any symptom. His past medical history included haemorrhoidectomy and endoscopic removal of colon adenomas. On physical examination, the abdomen was tender and no abdominal masses were palpable.

Workup firstly comprised laboratory analyses (including serum CEA, CA 19-9, alphafetoprotein and chromogranin-A) that were found normal and abdominal CT that showed the presence of a hypodense homogeneous lesion in the uncinate process of the pancreas. The lesion was well-defined, with oval shape and dimensions of 32x19x36 mm (Figure 1). We decided to continue the investigations with abdominal MRI that confirmed the presence of the pancreatic lesion appearing with clear-cut margins, moderately T2

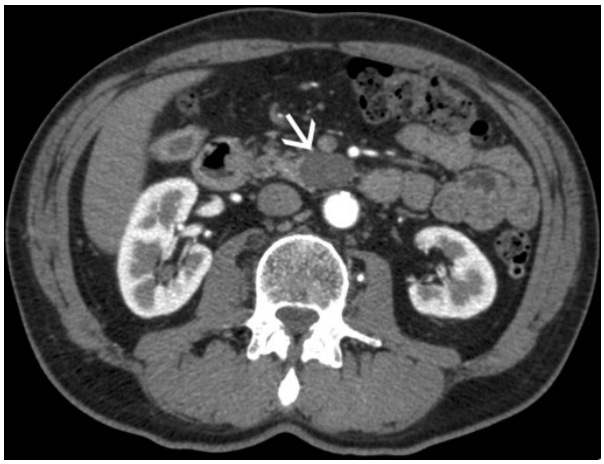

Figure 1. Computed tomography scan of the abdomen showing the presence of a 32x19x36 mm lesion in the uncinate process of the pancreas (white arrow).

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Key words Dermoid Cyst; Pancreatic Cyst; Pancreatico-duodenectomy

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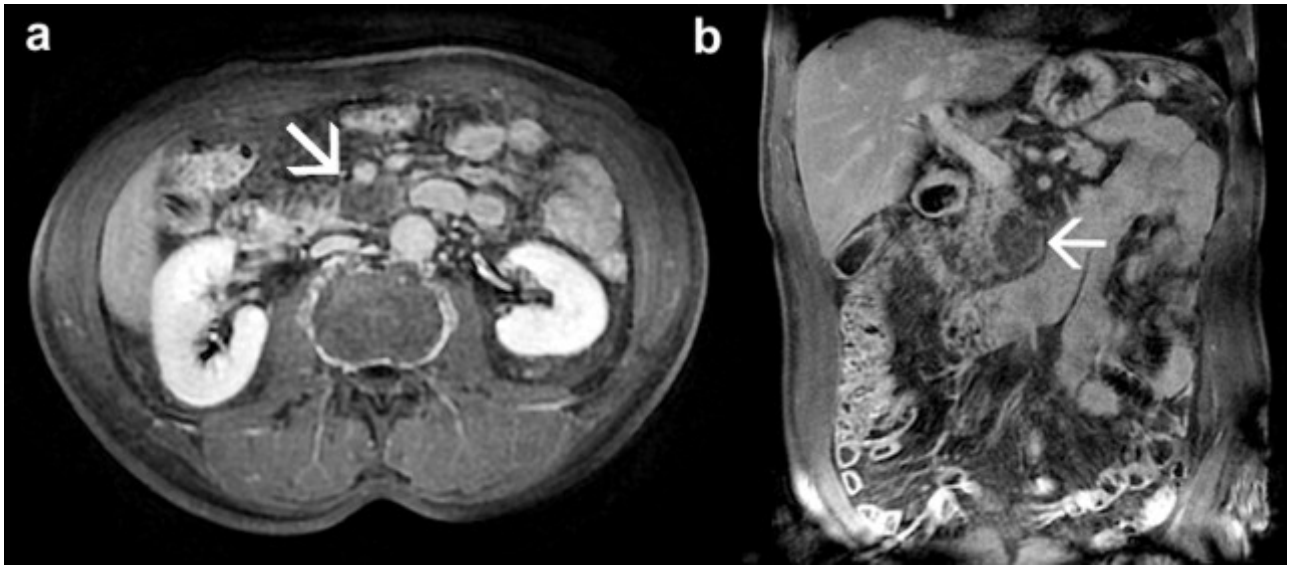

Figure 2. Axial (**a.**) and coronal (**b.**) magnetic resonance imaging scans of the abdomen showing the presence of a clear-cut margins lesion in the pancreatic head (white arrows).

hyperintense and without enhancement after paramagnetic contrast agent (Figure 2).

In addition, we performed EUS: the lesion appeared hypoechoic, without septations or signs of vascular infiltration; fine needle aspiration (FNA) of the lesion was performed for cytological examination, but it resulted unspecific.

Considering the non conclusive results of the performed examinations we planned an explorative laparotomy with possible duodenopancreatectomy. Intraoperatively, the manual exploration of the pancreas revealed a 3 cm diameter soft lesion, localized in the uncinate process, with well defined borders and without alterations of the pancreatic surface. There was no evidence of other lesions in the peripancreatic lymph nodes nor in the liver; no free fluid in the abdomen was found. The puncture of the lesion leaded to white mucoid material that was found to be acellular at intraoperative cytological examination. Considering the dimensions of the lesion, the age of the patient, the location in the pancreatic parenchyma, the presence of intracystic mucoid material and the impossibility to have a definitive histological diagnosis of the lesion, we decided to perform a pylorus preserving pancreaticoduodenectomy.

Macroscopic examination of the surgical specimen showed a 3.5 cm cystic lesion localized in the uncinate process, containing white thick material (Figure 3). Microscopic analysis revealed intrapancreatic cystic neoplasm with stratified squamous epithelium and skin appendages, surrounded by a wall of lymphoid tissue (Figure 4). The differential diagnosis was questioned between lymphoepithelial cyst and benign mature cystic teratoma, but the presence of sebaceous focal areas, immunoreactive for epithelial membrane antigen (EMA), supported the second diagnosis (Figure 4).

The postoperative course was uneventful and the patient was discharged 12 days after surgery.

At 12-month follow-up the patient was asymptomatic, without any evidence of recurrent disease.

DISCUSSION

Teratomas are neoplasms of germ cell origin that are able to generate tissues from the three germinal layers:

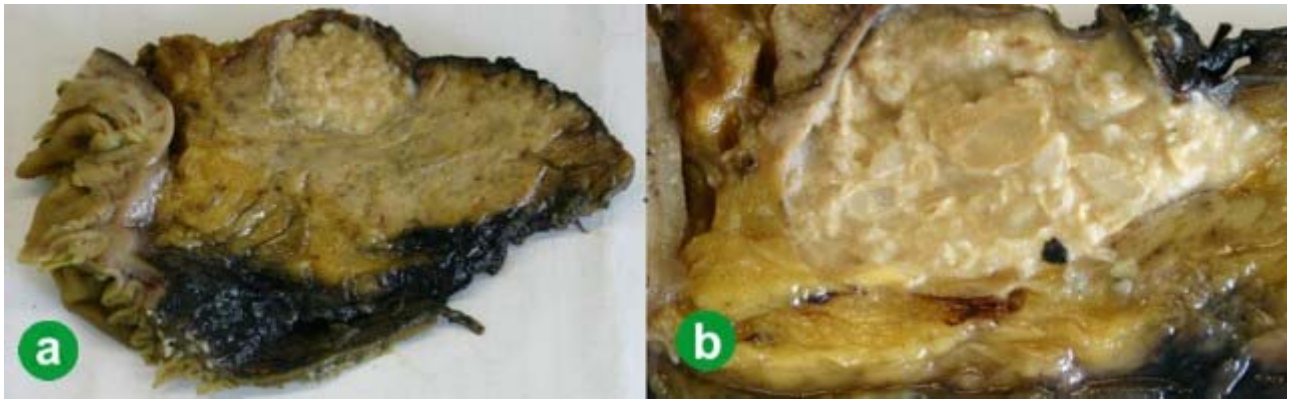

Figure 3. a. Macroscopic view of the cut surface of the surgical specimen that shows a 3.5 cm cystic lesion with clear-cut margins, containing yellowish thick material. The posterior edge is inked. **b.** Detail of the cystic lesion.

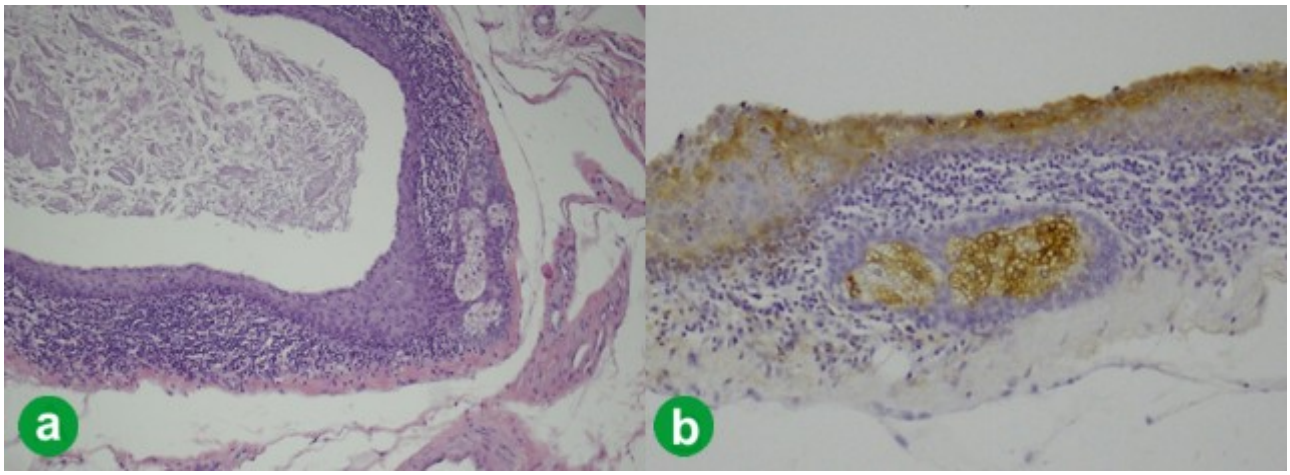

Figure 4. a. Microscopic analysis revealing an intrapancreatic cystic neoplasm with stratified keratinized squamous epithelium and sebaceous glands, surrounded by a wall of lymphoid tissue (hematoxylin and eosin staining 10x). **b.** Immunohistochemical analysis of epithelial membrane antigen (EMA) expression in the resected pancreatic tissue, showing the staining of sebaceous glands (anti-human EMA, E29 clone, DakoCytomation, Glostrup, Denmark; 10x).

endoderm, mesoderm and ectoderm. They can be classified as mature or immature on the basis of the presence of immature neuroectodermal elements within the tumor [2]. The mature types can be further classified as solid or cystic. Mature cystic teratomas (also called dermoid cysts) are congenital well-differentiated cystic lesions, thought to arise from the inclusion of skin at the embryonic time of neural groove closure [3]. They are typically located in the ovaries, but they may also occur in the pathway of ectodermal cell migration along the midline of the body, such as testes, cranium, brain, mediastinum, omentum, retroperitoneum, sacrococcygeal region, neck and abdominal viscera. The rarest site of presentation is the pancreas [2, 4, 5].

To our knowledge, the world literature reports 33 cases [2, 6,7 ,8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 17, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, n31, 32, 33, 34, 35] (including the present one) of pancreatic mature cystic teratomas with complete data (therefore, we excluded from the present review the case presented by Lushpai [36] for incomplete presentation of clinical information). The first case was described in 1918 by Kerr [6] and it was not until the case published by Judd [7] in 1922 that dermoid cysts were included in the classification of pancreatic cystic lesions by Primrose [37].

The clinical presentation of mature cystic teratomas is not specific. Most of patients complained abdominal pain and presented a palpable mass in the upper abdominal quadrants (Table 1). Only 6 cases of 33 (18.2%) were asymptomatic. The median age at diagnosis was 40 years (range 0.3-74 years), without gender preference (15 females, 18 males). The location of mature cystic teratoma was the pancreatic head in 13 patients (39.4%), the body in 12 (36.4%), the tail in 5 (15.2%) and unknown in 3 patients (9.1%). The median dimension of the lesion was 7.5 cm, ranging from 2.2 to 20 cm.

From the analysis of the reported radiological findings, the appearance of these lesions depends on the proportions of the various tissues of which they are composed [27]. The lesion would appear hyperechoic at US, with distinct margins and presence of calcified tissues (while in our case it was hypoechoic, without calcifications). At CT and MRI techniques, the characteristics suggesting the diagnosis of dermoid cyst are clear boundary of the uni- or multi-locular cystic mass, with solid components in varying proportions and areas of fat-like density or gross calcifications within the solid components [23, 27, 30].

At histological examination, dermoid cysts present a wall composed of stratified squamous epithelium and underlying connective tissue. The cyst cavity contains a combination of both cystic and solid elements, including hair, teeth, calcium, cartilage, and dermal appendages such as hair follicles, sweat glands, and sebaceous material [5]. Dermoid cysts are benign neoplasms, although a small percentage of mature teratomas may develop into malignant forms: therefore, a complete sampling of the lesion is necessary to exclude the presence of immature foci [23, 29]. Up to now all pancreatic teratomas reported correspond to mature type, whose behavior is benign.

Differential diagnosis and management of cystic lesions of the pancreas is challenging, mainly because of the hard distinction between the more common benign cystic lesions from their malignant counterparts [38]. As a matter of fact, pancreatic mature cystic teratomas should be differentiated from many different cystic lesions such as serous cystadenoma, mucinous cystic neoplasms, intraductal papillary mucinous neoplasms (IPMNs), solid pseudopapillary tumors, lymphoepithelial cysts, secondarily cystic solid neoplasms and non neoplastic cysts (as retention cysts, pseudocysts, etcetera) [1].

Among this wide spectrum of pathologies, it is imperative to rule out alarming lesions such as mucinous cystic neoplasms or IPMNs, that are associated with a high risk of malignant degeneration, that has been estimated to be 10-50% for mucinous cystic neoplasms and 35-45% for IPMNs [39, 40].

Table 1. Reports of pancreatic mature cystic teratomas in the world literature.

Case	Author and year of publication	Age (years)	Sex	Symptoms	Signs	Diagnostic procedures
#1	Kerr, 1918 [6]	55	F	Epigastric swelling	Mass, RUQ	Roentgenogram
#2	Judd, 1921 [7]	33	F	Backache, weakness	Mass, LUQ	Unknown
#3	Dennis, 1923 [8]	40	M	Backache	Mass, RUQ and epigastrium	Unknown
#4	DeCourcy, 1943 [9]	2	F	Vomiting	Mass, epigastrium	Roentgenogram, barium enema
#5	Hoang-su, 1956 [10]	18	M	Abdominal mass	Mass, epigastrium	X-ray
#6	Bittner, 1970 [11]	2	F	Liver failure	Mass, epigastrium	Unknown
#7	Iovchev, 1972 [12]	8	M	Abdominal pain, vomiting, fever	Mass, LUQ	Unknown
#8	Pomosov, 1973 [13]	6	M	Abdominal pain, vomiting	Mass, LUQ	Unknown
#9	Komarov, 1973 [14]	4	F	Abdominal pain, vomiting	Mass, epigastrium	Unknown
#10	Tobik, 1974 [15]	34	F	Abdominal pain	Mass, LUQ	Unknown
#11	Assawamatiyanont, 1977 [16]	11	F	Asymptomatic	Mass, LUQ	X-ray, intravenous pyelogram, barium enema, US
#12	Lazaro da Silva, 1984 [17]	21	M	Nausea, constipation	Mass, LUQ	Unknown
#13	Mester, 1990 [18]	25	F	Abdominal pain, vomiting	RUQ tenderness	X-ray, oral cholecystogram, intravenous cholangiography
#14	Vermeulen, 1990 [19]	46	M	Abdominal pain	None	US, CT
#15	Jentschura, 1990 [20]	57	M	Backache, abdominal pain	Mass, LUQ	US, CT
#16	Markovsky, 1993 [21]	53	F	Abdominal pain	Mass, LUQ and epigastrium	CT, CT guided FNA
#17	Jacobs, 1993 [22]	57	F	Abdominal pain, weight loss	None	US, CT
#18	Iacono, 1993 [23]	26	F	Abdominal pain, fever, weight loss	Mass, RUQ	US, CT, arteriography
#19	Kraimps, 1993 [24]	42	M	Weight loss, dyspepsia, nausea	None	US, CT, ERCP
#20	Das, 1996 [25]	0.3	F	Asymptomatic	Mass, epigastrium	Barium study, US, CT
#21	Fernandez-Cebrian, 1998 [26]	74	M	Backache, dysuria	Mass, LUQ	X-ray, US, CT
#22	Strasser, 2002 [27]	44	M	Abdominal pain	None	CT, MRI, CT guided FNA
#23	Chih-Wei, 2003 [28]	2	M	Asymptomatic	Epigastric mass	US, CT
#24	Salimi, 2004 [29]	16	M	Progressive jaundice, weight loss	Hepatosplenomegaly	US, percutaneous transhepatic cholangiography, ERCP, CT
#25	Seki, 2005 [30]	57	M	Asymptomatic	Unknown	US, CT, MRI
#26	Seki, 2005 [30]	60	F	Asymptomatic	Unknown	US, CT, MRI
#27	Koomalsingh, 2006 [31]	52	M	Epigastric pain	Mild epigastric tenderness	X-ray, CT, upper endoscopy, EUS
#28	Tucci, 2007 [2]	64	M	L4-S1 chronic radiculopathy	Unknown	US, CT, MRI, upper endoscopy
#29	Rivkine, 2007 [32]	45	F	Abdominal pain	None	US, CT, MRI, EUS with FNA
#30	Zhang, 2008 [33]	67	M	Chest tightness, shortness of breath	None	CT
#31	Scheele, 2010 [34]	40	M	Upper abdominal pain	None	US, MRI, upper endoscopy, EUS
#32	Casajoana Badia, 2010 [35]	43	F	Epigastric pain, vomiting	Mass, mesogastrium	CT
#33	Present case, 2011	61	M	Asymptomatic	None	US, CT, MRI, EUS with FNA

LUQ: left upper quadrant; RUQ: right upper quadrant

Preoperative EUS-guided FNA, with cytological, biochemical and tumor markers cyst fluid analysis seems to be a safe procedure to investigate pancreatic cystic lesions, but it does not allow an unquestionable diagnosis of nature and malignancy of the lesions [41].

The cyst fluid analysis of the most common pancreatic cystic lesions reveals different patterns for the above mentioned parameters. The cytological examination of the fluid shows mucine-positive columnar cells with variable atypia in mucinous cystic neoplasms and IPMNs; cuboidal glycogen-rich cells can be found in serous cystadenoma, while macrophages and inflammatory cells can be seen in pseudocysts [42, 43].

Amylase dosage in the cyst fluid reveals very high levels (usually in the thousands) in pseudocysts, while low levels (<250 ng/mL) are found in serous and mucinous cystic neoplasms. High amylase levels would be consistently found in IPMNs, in contrast to mucinous cystic neoplasms, because of the connectivity to the pancreatic ductal system [1].

Among the several cancer antigens that can be evaluated in the cyst fluid, CEA has been shown to be the most accurate to distinguish mucinous from nonmucinous cysts [1]. High concentrations of CEA (>192 ng/mL) within cyst fluid are typical of IPMNs and mucinous cystic neoplasms, while serous

Table 1. Continued.

Case	Pancreas cyst location	Cyst size (cm)	Treatment	Follow-up
#1	Head	Unknown	External drainage, marsupialization	Reoperation: resection, drainage
#2	Body and tail	Unknown	Resection/excision	Cholecystectomy after 2 years
#3	Head	Unknown	External drainage, marsupialization	Persistent fistula after 1 year
#4	Body	Unknown	Resection and drainage	Uneventful
#5	Unknown	Unknown	Resection/excision	Unknown
#6	Head	Unknown	Resection/excision	Well after 6 months
#7	Body	Unknown	External drainage	Well after 7 months
#8	Tail	Unknown	Distal pancreatectomy	Well after 6 months
#9	Unknown	Unknown	External drainage	Unknown
#10	Unknown	Unknown	Cystogastrostomy	Unknown
#11	Body	9x8x6	Excision	Uneventful
#12	Head	Unknown	Superior mesenteric vein ligation, biopsy and drainage	Tumor resection after 3 months
#13	Head	8x8x8	Excision	Well after 14 years
#14	Body	3x3x3	Distal pancreatectomy	Uneventful
#15	Body	10x13.7x8.5	Distal pancreatectomy	Uneventful
#16	Body	20x20x11.5	Excision	Uneventful
#17	Body	6.5x3x2	Excision	Unknown
#18	Head	12x12x12	Pancreaticoduodenectomy	Recurrence free at 6 years
#19	Head	4.5x4.5x4.5	Pancreaticoduodenectomy	Uneventful
#20	Body and tail	9.5x8.5	Resection	Unknown
#21	Body	10x8x9	Distal pancreatectomy, splenectomy	Recurrence free after 2 years
#22	Uncinate process	7x5x7	None (for previous teratoma)	Unknown
#23	Head and body	12x12x12	Excision	Unknown
#24	Head and body	Unknown	Excision, choledochoduodenostomy	Unknown
#25	Body	5.5x3.7x3.3	Excision	Unknown
#26	Body	2.1x2.2x1.5	Middle pancreatectomy	Unknown
#27	Tail	3.5x3	Excision	Recurrence free at 16 months
#28	Tail	8.5x3	Distal pancreatectomy	Unknown
#29	Uncinate process	5.5	Excision	Uneventful
#30	Body	4.6x3x2.2	Distal pancreatectomy, splenectomy	Unknown
#31	Head and body	6.4x4.9x3.8	Pancreaticoduodenectomy	Self-limiting low-output pancreatic fistula
#32	Head and body	15x10x10	Distal pancreatectomy	Pancreatic fistula, splenic infarction, abscess
#33	Uncinate process	3.2x1.9x3.6	Pancreaticoduodenectomy	Recurrence free at 1 year

cystadenoma and pseudocysts are usually associated with very low levels (<5 ng/mL) of this tumor marker [1, 42]. However, considerable overlap exists in cyst fluid CEA concentrations among these pancreatic cystic lesions and, moreover, CEA levels do not allow to distinguish benign from malignant mucinous neoplasms [1, 42].

Current guidelines suggest indeed that all mucinous cystic neoplasms, main-duct and mixed variant of IPMNs, branch-duct IPMNs in association with symptoms, or high-risk features of malignancy (such as main pancreatic duct dilation greater than 6 mm, cyst size greater than 30 mm, mural nodules or positive cytology) should be surgically resected after consideration of patient's surgical risk [40, 42]. As patient management algorithms are increasingly evolving to non-surgical options, it is critical to accurately discriminate mucinous from non-mucinous and benign from pre-malignant or malignant mucinous cystic lesions [1]. Considering that radiological findings are often inconclusive, the ongoing diagnostic issue is to differentiate these lesions in a preoperative setting.

In this context, the possibility of a trustworthy preoperative diagnosis of pancreatic mature cystic teratoma seems hard to be achieved. In the literature, three cases of preoperative diagnosis of dermoid cyst by FNA cytology were reported. In one case a CT guided FNA was performed and the cytological preparation of the cyst fluid revealed nucleated and non-nucleated squamous cells, keratin debris and inflammatory cells [21].

A CT-guided fine needle biopsy was also performed in the case reported by Strasser *et al.* [27]: the histology revealed the presence of fatty tissue, but the patient did not undergo surgical operation because of prior history of histologically proven teratoma. Therefore, in this case, the histology of the whole lesion was not

obtained. In the case described by Rivkine *et al*. [32] EUS-guided FNA was performed: the cytological examination revealed the presence of regular cylinder-cubic cells, and the tumor markers analysis of the cyst fluid showed high levels of CEA (7,322 ng/mL) and CA-19.9 (15,755 IU/L). It has to be noted that such elevation of tumor markers in the fluid of pancreatic cystic lesions is associated with the diagnosis of mucinous neoplasms (mucinous cystic neoplasms or IPMNs) [39].

In our case the patient was asymptomatic and the pancreatic lesion was incidentally discovered; diagnostic imaging and EUS-guided FNA were not conclusive for defining the nature of the pancreatic cyst. Considering the impossibility to exclude the mucinous nature of the lesion and its dimensions greater than 3 cm, following the criteria proposed by Allen *et al*. [40], there was not indication for observation of the lesion. Even at laparotomy it has been impossible to obtain a histological diagnosis of the lesion; therefore, a radical resection of the pancreatic head was performed.

The reported surgical therapy for pancreatic mature cystic teratomas has included external drainage of the cyst in four cases [6, 8, 12, 14] with necessity of reintervention for persistent tumor fistula in half of the cases. One patient [15] underwent cystogastrostomy (with unknown long term results), while all the other patients (28 of 33) received excision/resection of the lesion. After surgical resection, the reported postoperative course was uneventful in almost all the cases; only 2 patients had a course complicated by pancreatic fistula [34, 35] and no cases of recurrent disease in the follow-up were reported. Over the years the external drainage procedures have been abandoned because a complete healing (due to retained elements of secretory epithelium) is unlikely and the possibility of recurrence or fistula formation is increased [31]. Conservative treatment has not been described in the literature.

Mature cystic teratomas are strictly benign neoplasms and theoretically they do not require surgery. Nonetheless the application of the current guidelines for pancreatic cystic lesions [40, 41] does not permit to avoid radical surgical resection for these lesions, because of inadequate preoperative diagnostic techniques. Until a reliable method to ensure a definitive preoperative histological diagnosis of benign nature became determined, limited surgery such as lesion's excision should be avoided. Therefore, from an oncological standpoint of view, the recommended surgical therapy for pancreatic mature cystic teratomas is radical pancreatic resection.

The increase in detecting pancreatic cysts at diagnostic imaging will permit more frequent observation of mature cystic teratomas and more frequently in asymptomatic and older patients than in the past years. Since 1990, after the widespread use of CT and MRI techniques, the rate of asymptomatic patients with mature cystic teratoma has increased from 8.3% to 23.8% and the median age has raised from 14.5 to 46 years. Nowadays, these cysts do not appear anymore to occur mainly in childhood or in young age and it has come the time to "think about" mature cystic teratoma when examining a pancreatic cystic lesion.

In conclusion, clinicians should be more aware of mature cystic teratomas in the management of pancreatic cystic lesions. There is still a considerable difficulty in diagnosing these lesions preoperatively, leaving surgical exploration a necessary step through the diagnosis. Radical surgical resection represents the definitive treatment, it achieves a conclusive diagnosis, and it avoids the complications associated with cyst drainage.

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