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Case Report

Macrocystic serous cystadenoma of the pancreas: Report of 4 cases

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ABSTRACT

Background: Macrocystic serous cystadenomas (MaSCA) are rare benign tumor of the pancreas which represent an atypical macroscopic morphologic variant of serous cystadenomas (SCA). They are characterized by a limited number of cysts with a diameter of >2 cm and share imaging features overlapping those of mucinous cystic neoplasm (MCN) and branch-duct intraductal papillary mucinous neoplasm (BD-IPMN), thus frequently making the pre-operative radiologic diagnosis difficult.
Materials and methods: Four cases of MaSCA, which were surgically treated in our structure, are reported.
Results: Two women (62 and 39 year-old) presented with upper abdominal pain and palpable mass underwent CT with evidence of a lobulated cystic neoformation (98 × 70 and 94 × 75 mm respectively) originating from the body and the tail of the pancreas respectively. They underwent distal pancreatectomy for suspected MCN. A 38 year-old woman underwent laparoscopic distal pancreatectomy because of the incidental finding of an unilocular cystic lesion in the pancreatic tail (23 mm) of indeterminate origin (MCN, SCA or metastasis). In a 40 year-old woman, admitted for acalculous acute pancreatitis, an unilocular cystic lesion in the body of the pancreas (62 mm) was detected and confirmed after 2 months at CT, therefore she underwent distal pancreatectomy for suspected pseudocyst or SCA. In all of the 4 patients the histological examination of the specimens revealed a MaSCA.
Conclusion: Imaging techniques have a low diagnostic power in terms of differentiation of MaSCA from malignant lesions (as MCNs and BD-IPMN). In the clinical practise of MaSCA, surgery appears to gain indications that are wider than those correlated to the pathologic outcome, because of the necessity of a correct differential diagnosis from potentially malignant cystic tumors and the frequent symptoms requiring treatment.

1. Introduction

Serous cystadenoma (SCA) represents a form of pancreatic cystic neoplasm which accounts for 10–15% of pancreatic tumors and is characterized by benign behavior and heterogeneous macroscopic features [1–3].

Although the microscopic structure of pancreatic SCA is uniform, the macroscopic feature shows a wide heterogeneity. The typical appearance is microcystic with a sponge-like or honeycomb texture, but solid or macrocystic variants are reported with increasing frequency. The macrocystic serous cystadenomas (MaSCA) is characterized by a limited number of cysts, usually less than 6, showing a diameter >2 cm [4–6].

Abbreviations: SCA, Serous Cystadenoma; MaSCA, Macrocystic Serous Cystadenoma; MCN, Mucinous Cystic Neoplasm; BD-IPMN, Branch Duct - Papillary Mucinous Neoplasm; CT, Computed Tomography; HU, Hounsfield Units; BMI, Body Mass Index; MRI, Magnetic Resonance Imaging; EUS, Endoscopic Ultrasonography; FNA, Fine Needle Aspiration; MRCP, Magnetic Resonance Cholangiopancreatography; MCA, Mucinous Cistoadenoma.

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Although many classifications have been reported a consensus has not been established and still a confounding terminology persists [3,6,7]. MaSCAs are variably reported also as oligocystic, multicystic, oligolocular, unilocular [2,3,5–10]. Some authors consider macrocystic even cysts with a diameter of 1–2 cm, if unilocular [11,12]. The overall estimated incidence of MaSCA is 10% of all cases of SCA [1,8].

A correct pre-operative diagnosis can be difficult since the radiologic features of MaSCA are frequently undistinguishable from those of mucinous cystic neoplasm (MCN) and branch-duct intraductal papillary mucinous neoplasm (BD-IPMN) which both have a malignant potential [4,5,8,10–13]. Moreover, if in the patient's past medical history episodes of acute pancreatitis are reported, pseudocyst enters the differential diagnosis [13].

2. Material and methods

Between January 2009 and March 2014 a total of 48 cases of cystic pancreatic neoplasms were surgically treated in the general surgery and transplantation unit of the University Hospital of Udine. Among these, 4 turned out to be MaSCAs. Demographic, clinical and histopathologic data of these patients were retrospectively reviewed.

3. Cases report

A 62 year-old woman in overall good clinical conditions and without a significant past medical history presented with recurrent dull epigastric discomfort and a palpable abdominal mass. A multiphasic contrast-enhanced CT scan showed a unilocular, lobulated without septation, cystic neoformation originating from the body of the pancreas with extrinsic growth and occupying the hepatogastric space. No mural nodules, satellite cysts or calcifications were associated with the cystic wall, which was thin. The cystic content showed homogeneous fluid attenuation of about 15 HU without evidence of septations. The largest diameters on the transverse plane were 98 × 70 mm. No other lesions were identified. CA 19.9, CEA and CA 125 serum level were within the normal range. The patient's general practitioner planned a conservative management and three months after the diagnosis a control CT scan was repeated showing a significant increasing in the dimensions of pancreatic neoformation (120 × 100 mm), thus causing a marked compression on the splenic and the inferior mesenteric veins. Cystic content persisted homogeneously fluid (about 20 UH). Repeated dosage of serum tumor markers showed no level variation. Based on radiological features, a mucinous cystadenoma was suspected. Thus, the patient was referred to us and consequently underwent laparotomic distal splenopancreatectomy. The post-operative course was uneventful. The level of CA 125, CEA, CA 19-9 and CA 15-3 in the cystic content were 14560 UI/ml (n.v. <30), 8.8 ng/mL (n.v. <3), 45356.7 UI/ml (n.v. <31) and 65.2 UI/ml (n.v. <32) respectively. The histological examination of the specimen revealed a MaSCA.

A 39 year-old woman in overall good clinical condition presented with recurrent upper abdominal pain. A palpable mass was evident in the left hypocondrium upon physical examination. Routine blood tests and tumor markers levels were within the normal range. The patient was investigated with a multiphasic contrast-enhanced CT scan and MRI which showed a lobulated cystic lesion of the pancreatic tail with septation and lobulated margins. The largest diameters on the transverse plane were 94 × 75 mm and it compressed the stomach, the spleen and the splenic vein. The pre-operative diagnosis was MCN. The patient underwent laparotomic distal pancreatectomy with splenectomy. No complication occurred during the post-operative course. The histological examination of the specimen revealed a MaSCA.

A 38 year-old obese (BMI 37) woman, who had previously undergone total thyroidectomy and adjuvant radiometabolic therapy because of a multicentric papillary carcinoma of the thyroid (pT3N1M0), was referred because of the incidental finding of a cystic lesion in the pancreatic tail of unknown origin. Tumor markers serum levels were within the normal range; thyreoglobulin serum level was negative. Contrast-enhancement MRI showed a single unilocular ovoid cyst with lobulated margins and simple fluid content in the pancreatic tail, delimitated by a thin wall showing moderate contrast-enhancement. A thin internal septum was observed, showing no contrast enhancement. No mural nodules were visible. Neither an increase in size (23 mm) nor changes in radiological features were observed compared to a CT performed 3 months before. It was difficult to establish whether a communication with the main pancreatic duct was present because of the compression by the cyst. EUS identified an area in the lesion suspicious for a wall nodule or a mucin deposit; while FNA examination was not conclusive. The pre-operative diagnostic suspects were MCN, SCA, or a distant metastasis of thyroid carcinoma. The patient underwent laparoscopic distal pancreatectomy without splenectomy. The post-operative course was uneventful. The histological examination of the specimen revealed a MaSCA.

A 40 year-old obese woman in overall good clinical conditions and without a relevant past medical history was admitted for acalculous acute pancreatitis. She underwent a multiphasic contrast-enhanced CT scan 72 h after the onset of symptoms which showed a cystic lesion in the body of the pancreas; it measured 62 mm in diameter and was unilocular with lobulated margins but without septation. The pancreatic parenchyma, which was distal to the lesion, was edematous with a dilatation of the main pancreatic duct and of the branch ducts. The patient was managed conservatively and the episode resolved rapidly within a few days. After 2 months the CT scan showed the persistence of the cystic lesion, therefore MRI and EUS were performed confirming the dimension (without growth) and the morphology of the lesion and the persistence of the pancreatic ducts dilatation. FNA was performed showing normal CEA and amylase levels, increased CA-19.9 level (15499 UI/ml); the cytologic examination resulted not diagnostic. Serum tumor markers levels were within the normal range. Preoperative differential diagnosis included pseudocyst and SCA. The patient underwent laparotomic distal pancreatectomy with splenectomy. The post-operative course was uneventful. The histological examination of the specimen revealed a MaSCA.

4. Discussion

The clinical series by Lewandrosky in 1992 was the first report who identified the macrocystic form as a specific and distinct variant of the SCA of the pancreas [14]. Thereafter, the WHO in 1996 subclassified the serous cystadenoma in microcystic adenoma, macrocystic/oligocystic adenoma and cystadenocarcinoma [10].

Several descriptions for a typical radiologic feature of macrocystic variant have been proposed with the aim to maximize the possibility of making a correct pre-operative diagnosis, thus distinguishing this benign lesion from potentially aggressive tumors as MCN, BD-IPMN and cystadenocarcinoma which share the same macrocystic structure [4,5,8,10–13]. The malignant progression from SCA to serous cystadenocarcinoma is an extremely rare event with a reported incidence of 1–5% [15,16]. The diagnosis can be established just in presence of locoregional direct invasion or distant metastasis, since the histological feature of these malignant lesions is usually indistinguishable from their benign counterparts. Several parameters have been investigated to identify any predictive factor for aggressive behavior. Those with the highest evidence

are tumor diameter >6 cm and tumor location in the head of the pancreas [14,17].

Procacci in 1997 was one of the firsts to advise a systematic classification of SCA according to the radiologic feature in microlacunar, macrolacunar and mixed structure (formed by a microlacunar core surrounded by cysts of over 2 cm in diameter) [7]. According to this study the macrolacunar/macrocystic structure was characterized by round or ovoid morphology, regular contours due to an existing capsule, and either an unilocular pattern or central sparse septa enclosing large cystic spaces.

Khurana identified multiple septations, wall enhancement, presence of mural nodules or papillary projection as negative predictive elements for a diagnosis of MaSCA [6]. According to Cohen-Scali the location in the pancreatic head, lobulated contour, thin wall/capsule and absence of wall enhancement were independently specific radiologic findings for MaSCA [13]. Lobulation was defined as the presence of rounded contours that could not be described as the borders of the same circle. Septation, liquid content of the cyst, wall thickness, wall calcification were also evaluated but no difference was evident among MaSCA, MCN and pseudocyst [13].

According to the morphologic classification of macrocystic neoplasm of the pancreas proposed by Kim, the typical imaging features of MaSCA are either multicystic or lobulated cystic with or without internal septation [3]. Multicystic shape was described as a conglomeration of two or more round cysts where cyst was defined as a simple closed curve without concavity to differentiate it from an internal locule in septated shape, as reported by Kim and Sun [3,11]. No difference was found among MaSCA, MCN and BD-IPMN in terms of location, greatest dimension, presence of calcification or mural nodules.

Since unilocular MaSCA and MCA show largely overlapping imaging features, the differential diagnosis of unilocular cysts of the pancreas is still challenging, frequently involving a multi-step diagnostic approach including CT, MRI and EUS [1,16]. Not surprisingly however, the final diagnosis is frequently achieved just by histological examination after surgery, showing that the imaging cannot have a conclusive role.

CT and MRI provide images with high spatial and temporal resolution in order to assess subtle anatomic details and patterns of contrast enhancement, respectively [3,6,11–13,18–23]. Both CT and MRI can assess the type of cystic lesion. Due to a higher contrast resolution, MRI with MRCP is better suited to show thin septa, small papillary projections and the communication (or not) with the main pancreatic duct, which is a major criterion to differentiate between SCA and MCA (in absence of communication) from BD-IPMN (in presence of communication) [6,12,20,21]. It should be pointed out that communication may be difficult to be observed in larger cysts compressing the main pancreatic duct, as occurred in our cases. Moreover, MRI enables to increase the detection of possible additional smaller cysts (<1 cm in diameter) and to characterize the cystic content (e.g., fluid versus hemorrhagic) [12,22,23]. On the other hand, MRI cannot directly describe parietal calcifications, which are a frequent finding in MCA when using CT.

Both MCN and IPMN have higher propensity toward aggressive biologic behavior upon detection and toward later transformation, which implies the necessity for more restrictive clinical indications to surgery and more aggressive approach for surgical resection [4,7,24]. The International consensus in 2012 and the European consensus in 2013 stated the guidelines for the clinical management of the cystic tumors of the pancreas [16,25]. The presence of symptoms represents an indication for surgery in all cases, regardless of the pre-operative diagnosis. With regards to side-branch IPMNs, the presence of mural nodules and main duct involvement or dilatation (>6 mm) are considered important risk factors for an aggressive behavior as well as a growth rate over 2 mm/year and increased serum levels of CA 19-9. Dimensions correlate with the risk of malignancy but there is no safe lower size limit that completely excludes malignancy, thus initial observation without immediate resection is suggested even for BD-IPMN >3 cm without any other risk factor, particularly in elderly patients [26]. On the other hand, <65 year-old patients with a cyst >2 cm may be candidates for resection owing to the cumulative risk of malignancy. According to the European consensus a diameter >4 cm must still be considered an absolute indication for surgery. With regards to MCN, surgical resection is recommended for all surgically fit patients. Moreover, a lesion >4 cm, presence of mural nodules, mass forming lesions or peripheral “egg shell” calcifications are suggestive of invasive malignancy. In the management of asymptomatic SCA surgery is indicated just in case of inability to definitely exclude a pre-malignant or malignant tumor, for which a macrocystic pattern represents a clear risk factor [5].

The detection of the radiologic features specific for aggressive behavior is also important in order to choose the surgical approach, discerning between an oncological radical resection and a pancreas- and/or spleen-preserving procedure. Pancreatectomy with lymph node dissection remains the standard treatment for invasive and non-invasive MCNs and IPMNs [25]. However, in patients without high risk factors for malignancy (diameter >4 cm, increased serum levels of CA 19-9, mural nodules, main duct involvement or dilatation, “egg shell” calcifications) a segmental resection or an enucleation may be performed, even with the laparoscopic approach.

5. Conclusion

MaSCA are benign lesions which would not require surgical resection themselves but clinical follow up, having given for granted that the radiologic diagnosis is sure and symptoms are absent. Their overall incidence is lower than that of MCNs and BD-IPMN which share the same macrocystic feature.

On the one hand, multiphasic contrast enhanced CT scan and MRI show a low diagnostic power in terms of differentiation of MaSCA from MCNs and BD-IPMN, although they can detect the presence of radiologic risk factors of aggressive biologic behavior in some cases. FNA cytology, EUS and ERCP do not seem to add any relevant element to the diagnostic workup. On the other hand, the majority of patients presents with large lesions most frequently causing abdominal pain.

From a retrospective pathological point of view, the surgical management of MaSCA is an over-treatment since the benign behavior of the lesion, but the presence of symptoms and the impossibility during the pre-operative diagnosis to exclude a lesion with an aggressive behavior justified it. Thus, considering all the aforementioned factors in the clinical practise of MaSCAs, surgery seems to play an essential role which is greater than those required by the natural course of the pathology, but justified by the necessity of a correct diagnosis.

Ethical approval

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Author contribution

Riccardo Pravisani: Participated substantially in conception, design, and execution of the study and in the analysis of data; also

participated substantially in the drafting of the manuscript.

Sergio Giuseppe Intini: Participated substantially in conception, design, and execution of the study and in the analysis and interpretation of data.

Rossano Girometti: Participated substantially in execution of the study and in the analysis and interpretation of data.

Claudio Avellini: Participated substantially in execution of the study and in the analysis and interpretation of data.

Cosimo Alex Leo: Participated substantially in the drafting and editing of the manuscript.

Walter Bugiantella: Participated substantially in the drafting and editing of the manuscript.

Andrea Risaliti: Participated substantially in conception of the study; also participated substantially in the editing of the manuscript.

Conflict of interests

The authors declare no conflict of interest.

The paper is not based on a previous communication to a society or meeting.

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