

CASE REPORT

An Unusual Mixed Tumor of the Pancreas: Sonographic and MDCT Features

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ABSTRACT

Context Mixed tumors of the pancreas are exceedingly rare. **Case report** We herein report on a 54-year-old female who presented with an enlarging cystic lesion in the head of the pancreas. Right upper quadrant ultrasound and multidetector-row CT scan showed a well-defined unilocular cystic tumor located in the head of the pancreas and surrounded, in part, by a hypervascular solid mass. **Conclusion** Although mixed exocrine/endocrine pancreatic tumors have been described previously, to the best of our knowledge, this is the first case of a pancreatic mixed intraductal papillary mucinous neoplasm/endocrine tumor with illustration of its ultrasound and CT features. Moreover, the importance of preoperative analysis of imaging features in the assessment of pancreatic neoplasms is discussed.

INTRODUCTION

Pancreatic neoplasms typically show either ductal, acinar, or endocrine differentiation. Tumors with mixed (ductal and/or acinar) exocrine and endocrine components are exceedingly rare [1]. Since some exocrine pancreatic neoplasms may contain scattered endocrine cells, it is now commonly accepted that diagnosis of mixed exocrine-endocrine cell tumor of the pancreas requires identification of endocrine cell differentiation in at least 25% of the tumor volume [1]. The histogenesis of mixed exocrine-endocrine tumors is still controversial. However, most authors favor a common multipotent precursor stem cell of endodermal origin from which both endocrine and exocrine cells are derived [2]. Two types of mixed exocrine-endocrine pancreatic tumors can be distinguished. The most common type represents a mixture of two histogenetically distinct tumors, with the two components remaining largely restricted to topographically separate components despite some

areas of intermingling [1, 3]. The other more rare type represents an amphicrine neoplasm, in which individual tumor cells reveal bi-directional differentiation immunohistochemically [1, 3]. Several variations of mixed exocrine-endocrine pancreatic tumors have been described previously. A total of eight collision tumors of intraductal papillary mucinous neoplasm (IPMN) and endocrine tumors have been reported [4, 5]; in addition, 12 cases of mixed ductal-endocrine tumors of the pancreas have been described in the pathological literature [1]. Our case of a mixed IPMN/endocrine tumor, however, is unique because, to the best of our knowledge, no reports have illustrated a pancreatic mixed tumor in the radiological literature previously.

CASE REPORT

A 54-year-old woman was evaluated at our institution with severe abdominal pain similar in nature to a prior episode she experienced three years earlier. At that time, she was diagnosed biochemically and by imaging to have acute interstitial pancreatitis for which she required ten days of hospitalization at an outside institution. A series of CT and MRI scans obtained at that time showed active inflammation, especially around the head of the pancreas, and the presence of a cyst that was located within the pancreatic head. At that time, it was felt that the cyst antedated the episode of pancreatitis. An endoscopic retrograde cholangiopancreatogram obtained during that initial hospitalization was unremarkable.

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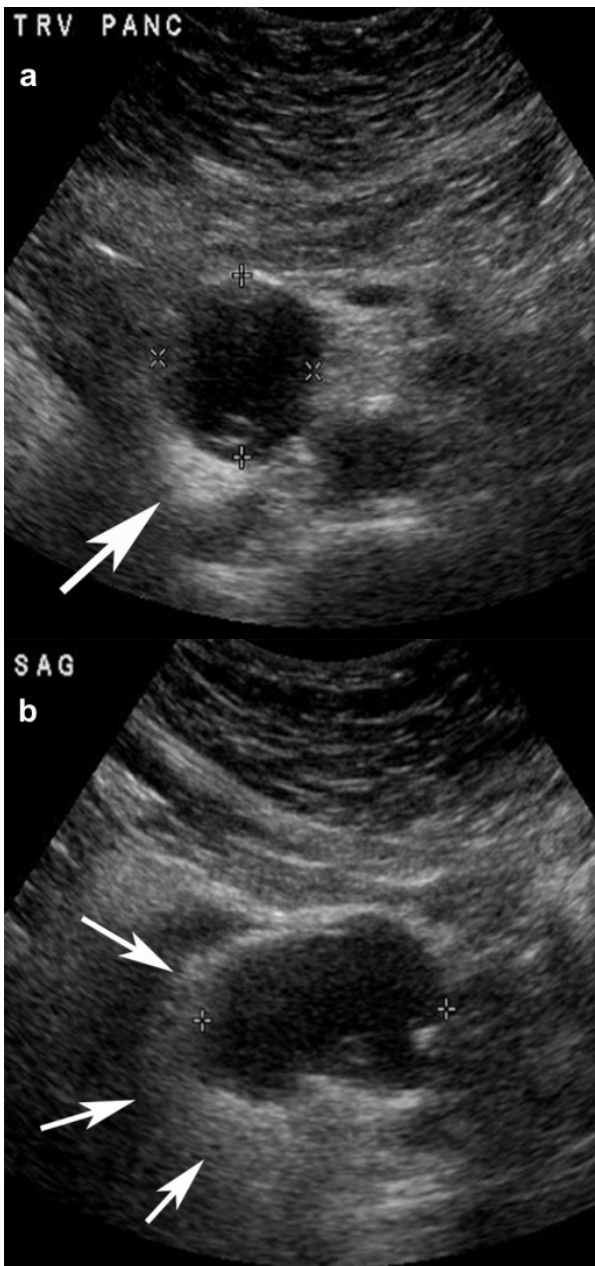


Figure 1. Ultrasound images obtained in the axial (a.) and sagittal (b.) planes demonstrate a 4.0x3.1x2.9 cm cystic lesion (calipers) in the inferior part of the pancreatic head with irregular borders, and the presence of a hyperechoic soft tissue mass (arrows) encircling the cystic lesion posteriorly and inferiorly.

During the current evaluation at our hospital, a right upper quadrant ultrasound examination demonstrated a 4.0x3.1x2.9 cm unilocular cyst in the inferior portion of the pancreatic head, with irregular hyperechoic borders inferiorly (Figure 1). The cyst was increased in size compared to the prior imaging study. A subsequent multiplanar contrast-enhanced multidetector-row CT scan, obtained to further characterize and stage the presumed neoplasm, confirmed the presence of a cystic pancreatic head lesion measuring 2.7x2.6 cm. A hypervascular well defined rim measuring 8 mm was bordering the cystic mass inferiorly (Figure 2). Due to a high degree of suspicion for a mucin-producing

neoplasm, the patient was referred for CT-guided fine needle aspiration biopsy of the cystic pancreatic lesion. A total of four 22-gauge 15 cm long needles were percutaneously advanced within the mass using fluoro-

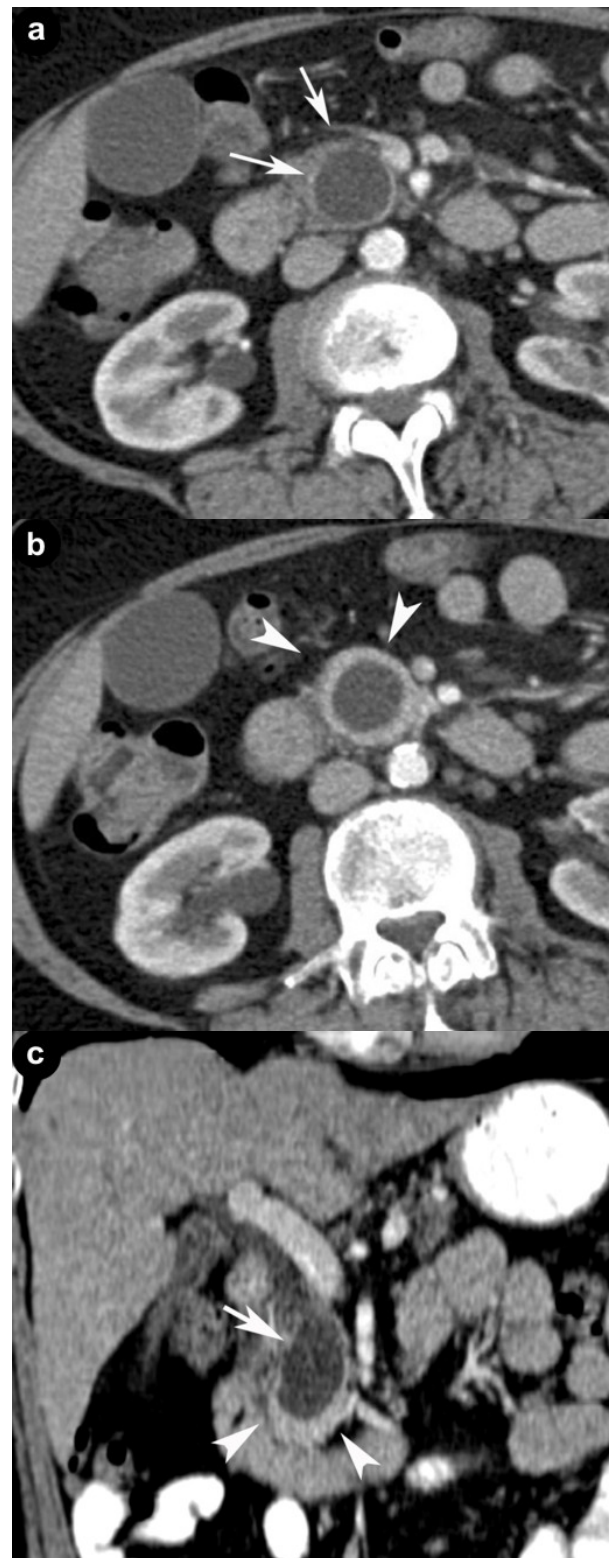


Figure 2. Axial (a., b.) and coronal (c.) late arterial phase contrast-enhanced CT images of the pancreas show the presence of a cystic pancreatic head lesion (arrows) measuring 2.7x2.6 cm. A hypervascular well defined rim (arrowheads) measuring 1.5 cm was bordering the cystic mass inferiorly.

CT scan guidance; three samples were obtained from the wall of the lesion and all were sent for cytologic evaluation (Figure 3). Following this, the final needle was used to aspirate the fluid from the cystic lesion. The samples were sent for cytologic and biochemistry evaluation. Cyst fluid chemistries were reported as follows: CEA 261.1 ng/mL; amylase 31,840 U/L, and lipase 102,500 U/L. On cytology, atypical epithelioid cells were identified. These cells were arranged singly and in loose clusters, but without pseudorosettes. The nuclei revealed finely stippled chromatin with occasional binucleation. In addition, scant strips of columnar, mucinous epithelium were noted. The mucinous epithelium was composed of tall mucin-containing cells with slightly oval shaped hypochromatic pale nuclei with small peripheral nucleoli and mild nucleus folding. No psammoma bodies, papillary clusters or ductules were noted. The background also revealed a mild degree of cellular debris, mucin, and a few histiocytes. Finally, a rare fragment of necrotic tissue with an acinar architecture was identified on the cellblock section. A specific cytologic diagnosis could not be rendered.

Due to a presumptive diagnosis of a complex side-branch IPMN based on the CT features, elevated cyst fluid CEA and amylase/lipase levels, and because the patient's symptoms had improved substantially following the fluid aspiration, the patient then underwent an elective Whipple procedure. Histopathological analysis of the resection specimen revealed a single smooth-walled cyst (2.5x2.5x2.2 cm) with a focal area of white papillary excrescences (1.0x0.8 cm) lining the lumen of the cyst. The cyst was filled with white clear fluid; no communication with the main pancreatic duct was noted (Figure 4). Microscopically, the cyst wall was lined with a single layer of columnar mucinous epithelium with minimal



Figure 3. Axial unenhanced CT images of the pancreas obtained during the fine needle aspiration biopsy show the presence of 22G needles in the wall and lumen of the cystic pancreatic mass.

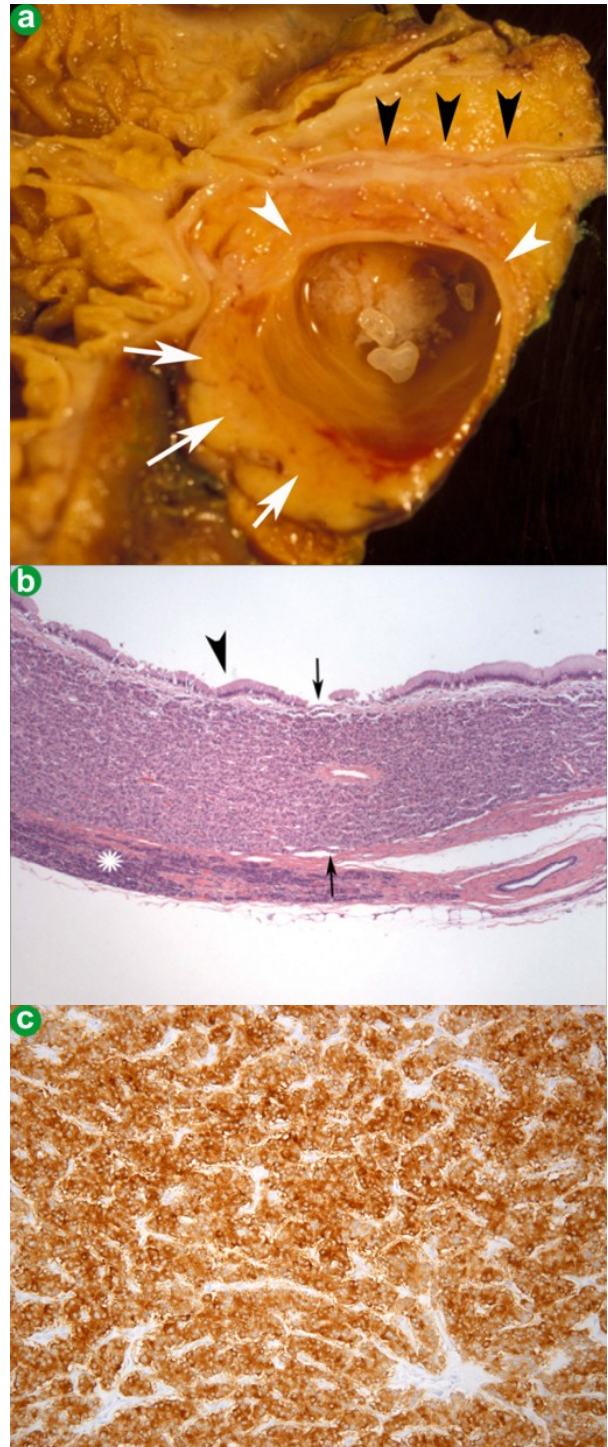


Figure 4. Histopathologic evaluation. **a.** Gross specimen photograph shows a thick walled cyst (white arrowheads) with a focal area of white irregular papillary excrescences lining the luminal surface. On the lower left side, the wall of the cyst is thickened and irregular (white arrowheads). Note relationship to the main pancreatic duct (black arrowheads). **b.** Low power microscopic image of the wall of the cyst. The luminal side of the cyst shows a single layer of mucinous columnar cells with minimal cytologic atypia (black arrowhead). Beneath the epithelium is a band of epithelioid cells arranged in elongated trabeculae, and cords, composed of cells with regular round oval nuclei, eosinophilic cytoplasm and stippled chromatin (black arrows). Note surrounding normal pancreatic parenchyma (*). **c.** Immunohistochemistry stain for synaptophysin confirms diffuse strong positivity in the tumor cells for this endocrine marker.

atypia. An underlying ovarian-like stroma was not identified. Surrounding the cyst was a dense, uniform population of epithelioid cells containing round to oval nuclei with stippled chromatin and slightly eosinophilic cytoplasm. These cells were arranged in elongated trabeculae and cords. No necrosis or hemorrhage was present. Immunohistochemistry analysis demonstrated the following staining profile in the epithelioid cells: positive for synaptophysin and negative for alpha-1-antitrypsin, alpha-1-chymotrypsin, chromogranin, and trypsin. MUC-2 (mucin 2, oligomeric mucus/gel-forming) was positive in the mucinous columnar cells. A final diagnosis of a pancreatic mixed tumor composed of an endocrine tumor and a benign IPMN was rendered.

The patient recovered well from the pancreatic surgery and is alive and well, without any evidence of local or distant recurrent disease.

DISCUSSION

The World Health Organization (WHO) and Armed Forces Institute of Pathology (AFIP) formally divide mucin producing neoplasms of the pancreas into mucinous cystic neoplasms and intraductal papillary mucinous neoplasms (IPMN) [6]. Mucinous cystic neoplasms are uncommon pancreatic tumors that occur predominantly in middle-aged women and are located nearly exclusively in the body and tail of the pancreas [7]. These tumors are lined by mucinous epithelium that can exhibit various grades of dysplasia. By definition, they are surrounded by a characteristic ovarian-like stroma microscopically [7]. In contrast, IPMNs are characterized by intraductal growth, either from the main pancreatic duct or one of its side-branches, and typically have a more pleomorphic shape [8]. IPMN are slightly more common in males and do not have a predilection for the pancreatic body and tail [9].

Mixed tumors of the pancreas are rare. Cubilla and Fitzgerald reported their incidence to be 0.2% in a series of 645 pancreatic neoplasms [10]. Mixed ductal-endocrine pancreatic tumors, the most common among mixed tumors, are most often described in middle-aged patients, with an equal distribution between men and women. They are usually located in the head of the pancreas, are large sized at diagnosis, and only rarely present with an endocrine syndrome [11]. Mixed tumors in the pancreas consisting of a mucin-producing cystic neoplasm and another tumor are even more uncommon. To the best of our knowledge, only three mixed pancreatic tumors have been described that are, at least, partially composed of a mucinous cystic neoplasm. Hakamada *et al.* [12] recently reported an anaplastic carcinoma associated with a mucinous cystic neoplasm in a pregnant patient, and Bloomston *et al.* [13] reported a second case of a carcinosarcoma in a background of a mucinous cystic neoplasm of the pancreas. A total of eight collision tumors of IPMN and endocrine neoplasms have been described so far. Marrache *et al.* [5] postulated that a combination of

endocrine tumors and IPMN was not fortuitous, since the frequency of endocrine tumors in combination with IPMN in their group of patients was higher than the anticipated frequency of this combination in the general population. However, more recently, Stukavec *et al.* [4] suggested, by using double fluorescent immunolabeling and confocal laser scanning microscopy, that a combination of an endocrine neoplasm and an IPMN only represents a fortuitous association of neoplastic duplicity.

Three additional important observations may be derived from this case study. First, it is important to stress that the presence of a pancreatic cystic lesion concurrent with a first episode of pancreatitis, as in this patient, should prompt further evaluation for a cystic neoplasm. This is particularly true if a definite etiology is not found for the episode of pancreatitis. An association between IPMN and concurrent acute pancreatitis has been described in the literature previously [14, 15, 16]. Secondly, the results of the CT-guided fine needle aspiration biopsy were inconclusive. Theoretically, an endoscopic-guided fine needle aspiration biopsy would have revealed a presumptive diagnosis [17]. However, to the best of our knowledge, there are three published studies that directly compare CT-guided and endoscopic sonographically guided fine-needle aspiration biopsies of pancreatic masses [18, 19, 20]. In a retrospective study, Qian and Hecht [18] suggested that CT-guided biopsies may be more sensitive for diagnosing malignancy than endoscopic sonographically guided biopsies. In their study, CT-guided biopsies and endoscopic sonographically guided biopsies had sensitivities of 71% and 42%, respectively. Likewise, in the study of Mallery *et al.* [19], CT- and transabdominal sonographically guided pancreatic biopsies (80%) had a higher sensitivity than endoscopic sonographically guided biopsies (74%); however, the difference was not statistically significant. We also found higher sensitivity for CT guidance (95%) compared with endoscopic sonographic guidance (85%) [20]. However, the difference did not reach statistical significance in our study either. Lastly, this case illustrates the importance of feature analysis when detecting a cystic pancreatic lesion on cross-sectional imaging. Although a specific diagnosis would not likely have been rendered preoperatively in this case, radiological investigations provided several clues that could have prompted consideration of this unusual type of pancreatic neoplasm. The presence of a unilocular oval cyst in the pancreatic head suggests a diagnosis of a sidebranch IPMN, or the rare macrocystic variant of serous pancreatic adenoma [16]. Moreover, the hypervascularity of the soft tissue mass bordering the cystic lesion limits the differential diagnosis to an endocrine tumor, and less likely a hypervascular metastasis, or serous microcystic pancreatic adenoma [21]. Therefore, in retrospect, it is not surprising that the presented mixed tumor was composed of an endocrine tumor and an IPMN.

Conflict of interest The authors have no potential conflicts of interest

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