Review

Solid serous adenoma of the pancreas: An uncommon but important entity

M.C. Machado, M.A. Machado*

Department of Gastroenterology, University of São Paulo, São Paulo, Brazil

Accepted 20 March 2008
Available online 25 April 2008

Abstract

Serous cystic neoplasms of the pancreas have currently five recognized subtypes: serous microcystic adenoma, serous oligocystic ill-demarcated adenoma, solid serous adenoma, von Hippel–Lindau-associated cystic neoplasm, and serous cystadenocarcinoma. Although these neoplasms are histologically similar they may differ in location, gross appearance and biology. Solid serous adenoma of the pancreas is by far the rarest subtype with only nine cases published thus far.

In this review, we will discuss clinical features, imaging characteristics and histopathological findings, considering in particular (1) difficulties in preoperative diagnosis; and (2) relevant immunohistochemical analysis.

After analyzing the literature, including one case from our Department, we can conclude that there is enough evidence to support that solid serous adenomas of the pancreas is a solid variant of serous cystadenomas. To date no malignant transformation is reported so far and therefore, to our knowledge, all patients are alive and without recurrence. Incidence is generally around seventh decade of life with no gender preference. Preoperative diagnosis is difficult to establish but magnetic resonance cholangiopancreatography may be useful. Given benign nature of this solid variant conservative surgery is recommended. It is definitively a rare entity but oncologic surgeons should be aware of this neoplasm in order to make a correct preoperative diagnosis that will ultimately result in more conservative surgeries.

© 2008 Elsevier Ltd. All rights reserved.

Keywords: Pancreas; Cystadenoma; Serous; Solid; Neoplasms

Introduction

The majorities of pancreatic tumors are highly malignant and have a poor prognosis with few patients been cured after surgical treatment. Unfortunately much less common and frequently curable tumors are cystic neoplasms of the pancreas which includes serous and mucinous cystadenomas.1 These neoplasms comprise about only 1–2% of pancreatic exocrine tumors but form an important group because of their special clinical presentation and biology.2

Serous cystic neoplasms of the pancreas have currently five recognized subtypes: serous microcystic adenoma, serous oligocystic ill-demarcated adenoma, solid serous adenoma, von Hippel–Lindau-associated cystic neoplasm, and serous cystadenocarcinoma.2 Although these neoplasms are histologically similar they may differ in location, gross appearance and biology.

Solid serous adenoma of the pancreas is by far the rarest subtype with only nine cases published thus far. However, this is probably due to misdiagnosis and underreported cases car this entity was only recognized in 1996 with the description and publication of the first known case by Perez-Ordonez et al. Greater knowledge of this entity will certainly increase the number of reported cases leading to more appropriate management as recently occurred with other pancreatic “rare” neoplasms.11

In this review, we will discuss clinical features, imaging characteristics and histopathological findings, considering in particular:

1. difficulties in preoperative diagnosis
2. relevant immunohistochemical analysis

A literature review was performed based on a Medline search in order to identify articles on solid serous adenoma...
of the pancreas. Keywords included solid serous adenoma, pancreas, cystic tumors, cystadenomas. A total number of nine patients have been reported in nine publications from 1996 to 2007. After the first reported cases there were no further descriptions until 2004 whereas six cases, including one case from our Department, were diagnosed on the last 2 years.

Clinical features

There were six men and four women with mean age of 60.3 years (range: 39–74 years). In three patients, the tumor was an incidental finding. Five patients were symptomatic with uncharacteristic abdominal pain as the main complain. Five neoplasms were located on the body and tail whereas the remaining patients were distributed along head, neck and uncinated process of the pancreas. Mean tumor size was 3.0 cm (range: 1.9–4.5 cm).

Tseng et al. reported the largest single-center experience with pancreatic serous cystadenoma and observed the preponderance in women in the seventh decade of life. Moreover, tumor greater than 4 cm was more likely to be symptomatic. Different from this experience, collective review of published cases of solid serous adenoma of the pancreas did not show prevalence of women (40% of cases). However, the mean age was within the seventh decade of life and all three patients with neoplasms larger than 4 cm were symptomatic at presentation. Collective review also have shown that the mean age of men with solid serous adenoma is more than 6 years older than that of women (62.8 vs. 56.5 years; p > 0.05). Larger size of neoplasms in men (3.1 vs. 2.8 cm; p > 0.05), although not statistically significant, may suggest a delay in diagnosis. Similar findings regarding serous cystadenoma are reported by Tseng et al.12

Imaging findings and preoperative diagnosis

Majority of patients underwent computed tomography scan that showed in most cases an enhanced well-defined solid mass on the pancreas.

Radiologically, solid serous adenoma of the pancreas is hypoechoic on ultrasound and shows contrast enhancement on dynamic CT, MR imaging and arteriography. The correct preoperative diagnosis was made in only one case report. In all other cases, the preoperative diagnosis was a benign or malignant islet cell neoplasm or undefined diagnosis. Most cases (90%) were misdiagnosed as benign or malignant islet cell neoplasm. In three cases, there was a dilated pancreatic duct that aroused suspicion of malignity. However, although rare, this finding can also been noted in some cases of serous cystadenoma.

In spite of location and size of the tumor no patient developed jaundice. This may have two possible explanations: soft texture of the tumor which confers inability to compromise bile duct or complete lack of invasiveness.

According to some authors, solid serous adenoma of the pancreas can be correctly diagnosed by magnetic resonance cholangiopancreatography using heavily T2-weighted MR imaging. Another important characteristic that helps to distinguish this neoplasm from other common pancreatic tumors such as ductal adenocarcinoma or IPMN is its well-defined borders and intense contrast enhancement on dynamic CT and/or MR imaging. However, preoperative diagnosis of this entity remains a challenge and in many cases it will be treated as a potential malignant lesion.

Surgical treatment

Due to benign nature of this neoplasm, conservative procedure can be performed whenever possible. However, enucleation was only performed in three cases out of seven presumed benign cases. In three patients pancreatic resection was performed for malignant suspicion. Hospital stay was not frequently mentioned but varied according to the type of surgical procedure. All patients from collective review were alive at the moment of their description with no recurrence, with mean follow-up of 16.5 months.

Pathological findings

Perez-Ordonez et al. postulated that the cells of solid serous adenoma are serous cystadenoma cells that lack secretory capability that confers the characteristic cystic architecture of serous cystadenoma. Individual cells of this neoplasm strongly resemble those of serous cystadenoma sharing the same microscopic appearance and similar or identical immunoprofile.

Solid serous adenoma of the pancreas is an extremely rare benign neoplasm of the pancreas. It was first described a few years ago and has been increasingly recognized since then with 10 diagnosed cases so far, including one case from our Department. It was initially been described as a solid pancreatic neoplasm composed of cells morphologically and histochemically indistinguishable from those of serous cystadenomas and distinct from other known solid neoplasms of the pancreas supporting solid serous adenoma as a separate disease entity.

In gross examination of the resected specimen usually shows a well-demarcated solid mass. The cut surface of the tumor is composed of thick fibrous bands without signs of necrosis or hemorrhage. Generally, there is no invasion of adjacent structures and non-tumoral pancreas is macroscopic normal.

At microscopic examination neoplasm is solid and composed of small acini with glandular spaces. Light-microscopically the tumor can exhibit a well-demarcated margin with adjacent normal pancreas and surrounded by thick bands of hypocellular fibrous tissue. The stroma separating solid nests of tumor cells are usually...
composed by vascular-rich fibrocollagenous tissue forming trabeculae (Figure 1C). Tumor cells are polygonal with clear or pale eosinophilic cytoplasm with well-defined cell border (Figure 1D).

Immunohistochemical study

Immunohistochemical study was performed in eight cases. Antibodies used for immunostaining of solid serous adenoma of the pancreas varied according the author. Table 1 summarizes main findings. Histochemical profile of solid serous adenoma of the pancreas usually shows positivity for Cam 5.2, CK7, neuronspecific enolase, alpha-inhibin, periodic acid-Schiff, epithelial membrane antigen, MUC6 and calponin. Other antibodies studied in individual cases were also positive such as: Lu5, MUC1, AE1/AE3, CA19-9 and MA902. Negative staining was observed for synaptophysin, chromogranin A, alpha-1-antitrypsin,

Table 1
Main histochemical findings in reported cases of solid serous adenoma of the pancreas

<table>
<thead>
<tr>
<th>Marker</th>
<th>Reference</th>
<th>2</th>
<th>3</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Present</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periodic acid-Schiff (PAS)</td>
<td></td>
<td>n</td>
<td>n</td>
<td>1/1</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>1/1</td>
<td>1/1</td>
<td>3/3</td>
</tr>
<tr>
<td>Lu5 (pan-cytokeratin)</td>
<td></td>
<td>1/1</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>Cam 5.2</td>
<td></td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>n</td>
<td>1/1</td>
<td>1/1</td>
<td>7/7</td>
</tr>
<tr>
<td>Alpha-inhibin</td>
<td></td>
<td>1/1</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>1/1</td>
<td>n</td>
<td>1/1</td>
<td>3/3</td>
</tr>
<tr>
<td>Neuronspecific enolase (NSE)</td>
<td></td>
<td>1/1</td>
<td>1/1</td>
<td>n</td>
<td>1/1</td>
<td>n</td>
<td>1/1</td>
<td>n</td>
<td>n</td>
<td>4/4</td>
</tr>
<tr>
<td>Synaptophysin</td>
<td></td>
<td>0/1</td>
<td>0/1</td>
<td>n</td>
<td>0/1</td>
<td>n</td>
<td>0/1</td>
<td>0/1</td>
<td>0/1</td>
<td>0/6</td>
</tr>
<tr>
<td>Chromogranin A</td>
<td></td>
<td>0/1</td>
<td>0/1</td>
<td>0/1</td>
<td>0/1</td>
<td>n</td>
<td>n</td>
<td>0/1</td>
<td>0/1</td>
<td>0/6</td>
</tr>
<tr>
<td>MUC1</td>
<td></td>
<td>1/1</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>MUC6</td>
<td></td>
<td>1/1</td>
<td>n</td>
<td>n</td>
<td>1/1</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>2/2</td>
</tr>
<tr>
<td>Vimentin</td>
<td></td>
<td>0/1</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>0/1</td>
<td>n</td>
<td>0/1</td>
<td>0/3</td>
</tr>
<tr>
<td>Epithelial membrane antigen (EMA)</td>
<td></td>
<td>n</td>
<td>1/1</td>
<td>1/1</td>
<td>n</td>
<td>1/1</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>3/3</td>
</tr>
<tr>
<td>AE1/AE3</td>
<td></td>
<td>n</td>
<td>n</td>
<td>1/1</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>1/1</td>
</tr>
<tr>
<td>CK7</td>
<td></td>
<td>n</td>
<td>n</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
<td>n</td>
<td>1/1</td>
<td>5/5</td>
</tr>
</tbody>
</table>

n — not performed.
insulin, glucagons, gastrin, somatostatin, VIP, serotonin, bombesin, calcitonin, lipase, chymotrypsin, trypsin, MUC5, HMB-45, CD-10, S-100 protein, calretinin, tyrosine hydroxylase, estrogen receptor, progesterone receptor, CK5/6, CK10, CK14, CK20, CEA, MA903, renal cell carcinoma, CD34, smooth muscle actin and WT-1.

**Conclusion**

Solid neoplasms of the pancreas are typically associated with malignancy, whereas cystic tumors more often tend to be benign. Solid serous adenoma of the pancreas, however, is more related to the cystic tumors than to solid ones. Clinically, this is true as the collective review shows no evidence of metastases or recurrence. Therefore, surgical excision may represent definitive treatment and cure.

In conclusion, there is enough evidence to support that solid serous adenomas of the pancreas is a solid variant of serous cystadenomas. To date no malignant transformation is reported so far and therefore, to our knowledge, all patients are alive and without recurrence. Incidence is generally around seventh decade of life with no gender preference. Preoperative diagnosis is difficult to establish but magnetic resonance cholangiopancreatography may be useful. Given benign nature of this solid variant conservative surgery is recommended. It is definitively a rare entity but surgeons should be aware of this neoplasm in order to make a correct preoperative diagnosis that will ultimately result in more conservative surgeries.

**Conflict of interest**

The authors have no conflict of interest.

**References**