

Management of Serous Cystadenoma of the Pancreas

Jennifer F. Tseng

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Abstract Serous cystadenoma of the pancreas is a diagnosis being entertained with increasing frequency. The histopathologic findings, diagnostic strategy, differential diagnosis, and treatment strategy of these generally benign but sometimes symptomatic lesions are discussed. Based on the available case series, surgical resection should be considered in good-risk patients with symptomatic tumors, with tumors at least 4 cm in maximum diameter, or in whom a more worrisome diagnosis cannot be excluded.

Keywords Serous cystadenoma · Pancreas · Cystic neoplasms

In 1978, Compagno and Oertel¹ first described 34 cases of serous cystadenoma of the pancreas. In the current era, cystic neoplasms of the pancreas, including serous cystadenoma, mucinous cystic neoplasms, intraductal papillary mucinous neoplasms, etc., are increasingly diagnosed. The increased use of radiography and advances in imaging techniques have led to larger numbers of cystic lesions being identified.^{2–5} For many years, correctly differentiating between a cystic neoplasm and a pseudocyst has been essential in determining correct treatment of these lesions.⁶ More recently, as the divergent natural histories and malignant potentials of the various cystic neoplasms have

been elucidated, differentiating between mucinous cystic neoplasms (MCNs), intraductal papillary mucinous neoplasms (IPMNs), serous cystadenomas, and other less common tumors has become crucial.^{1,7–9}

This high rate of incidental detection of serous cystadenomas and other cystic lesions of the pancreas makes management challenging. First, accurate diagnosis is crucial to rule out mucin-producing cystic lesions and other pancreatic cystic neoplasms that have malignant potential. Second, even when the diagnosis of serous cystadenoma is certain, until recently, there have been no data that allow one to predict if an asymptomatic tumor will grow sufficiently to cause symptoms during the life span of a given patient. This is an important issue because although the mortality of pancreatic resection has decreased markedly in experienced hands, the morbidity remains high and the consequences of loss of pancreatic tissue are not trivial.

Radiographic imaging is a potent tool with which to diagnose serous cystadenoma of the pancreas, but limitations exist. The most widely applicable radiographic test at the current time is helical computed tomography (CT) scanning with thin cuts through the pancreas, which often can provide assistance in the differentiation between serous and mucinous neoplasms. Classic CT findings suggestive of serous cystadenoma include a central scar with the “honeycomb” appearance of microcysts found in the more common microcystic variant of serous cystadenoma. However, the rarer oligocystic or macrocystic variants may be more difficult to differentiate from mucinous tumors based

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J. F. Tseng (✉)
Division of Surgical Oncology and Endocrine Surgery,
Department of Surgery,
University of Massachusetts Medical School,
Worcester, MA 01655, USA
e-mail: tsengj@ummc.org

on CT findings.^{10–14} Other modalities such as magnetic resonance image and magnetic resonance cholangiopancreatography may be more useful in differentiating mucinous tumors such as IPMT from serous cystadenoma.³ In blinded studies, the ability of radiologists to accurately distinguish serous neoplasms has ranged from 23 to 82%, although component cysts smaller than 2 cm have been found to be significantly associated with serous tumors, and peripheral tumor calcification has been found to be significantly associated with mucinous tumors.^{15–18} In the near future, additional techniques including F-18-fluorodeoxyglucose positron emission tomography may help distinguish benign and malignant pancreatic cystic lesions.^{19,20}

Endoscopic ultrasound has been proposed as an ideal imaging technique for pancreatic cystic lesions.^{21–23} Ultrasound can readily characterize cysts, and high resolution imaging of the pancreas can be achieved through endoscopic means. Needle aspiration of pancreatic cystic lesions can be used to obtain fluid for cytology, and cyst fluid tumor markers can be used for diagnostic purposes. Cyst fluid carcinoembryonic antigen values are universally low in serous cystadenomas, trend higher in mucinous lesions, and are generally even more elevated in mucinous cystadenocarcinomas.^{23,24} Although cytologic samples diagnostic of serous cystadenoma are obtained in less than 50% of cases, when such samples are positive, the specificity is high. Clinical acumen and radiologic testing can often be used to differentiate cystic neoplasms from pseudocysts. However, when the operative or non-operative plan hinges upon differentiating a serous from a mucinous cystic neoplasm, cyst fluid analysis via endoscopic ultrasound or CT-guided aspiration and biopsy is particularly useful.²⁵

As opposed to pancreatic pseudocysts, serous and mucinous cystic tumors have an epithelial lining. The epithelium of IPMNs and MCNs is made up of columnar mucin-producing epithelium. However, MCNs, which occur almost exclusively in women, are devoid of communication with the ductal system and supported by ovarian-type stroma, whereas IPMNs arise in the main pancreatic duct or its major branches. In contrast, serous cystic tumors are lined by an inconspicuous single layer of either cuboidal or flattened cells. The cytoplasm of the cells is either clear or eosinophilic, and the nuclei are usually centrally located, small, and hyperchromatic. Mitoses are conspicuously absent in serous cystic tumors.

Most serous cystadenomas are microcystic, forming a honeycomb-like appearance, but macrocystic variants have been described frequently in the literature.^{11,12,14} The vast majority of these tumors are benign, with only a handful of case reports of serous cystadenocarcinomas.^{26–31} Operative resection is generally carried out for symptoms, large size, or the inability to distinguish a serous cystic neoplasm from

a mucinous lesion, which has greater malignant potential. Some authors have recommended resection for all cystic neoplasms of the pancreas,^{27,28,32} whereas others advocate a more selective approach.^{5,10}

In 2005, we reviewed 106 patients at the Massachusetts General Hospital presenting with serous cystadenoma of the pancreas from 1976 to 2004.³³ Mean age at presentation was 61.5 years. Seventy-five percent of patients were female. Interestingly, the mean age of males was >7 years greater than that of females, and males had larger tumors at presentation, suggesting a delay in diagnosis in men. No cystadenocarcinomas were identified in the MGH series. Forty-seven percent of patients were asymptomatic. The most common symptoms were abdominal pain (25%), fullness/mass (10%), and jaundice (7%). Mean tumor diameter was 4.9 ± 3.1 cm, which did not vary by location. Tumors <4 cm were less commonly symptomatic than tumors ≥ 4 cm (22 vs 72%, $p < 0.001$). Twenty-four patients had serial radiography, and tumor growth curves were calculated. The median growth rate in the patients who had serial radiography was 0.60 cm/year. For tumors <4 cm at presentation ($n = 15$), the rate was 0.12 cm/year, whereas for tumors ≥ 4 cm ($n = 9$), the rate was 1.98 cm/year ($p = 0.0002$).

The reasons why larger tumors appear to have a faster rate of growth than smaller tumors remain unclear. Whether serous cystadenomas that present at and grow to larger dimensions differ biologically, and perhaps bear a greater propensity for malignant degeneration²⁷ compared to their smaller counterparts, remains an open question.

The following guidelines may be useful to the clinician with a suspected serous cystadenoma of the pancreas. Patients should be diagnosed with serous cystadenoma based upon a compatible clinical presentation and characteristic radiographic evidence. When this concordance is not present, endoscopic ultrasound should be utilized.

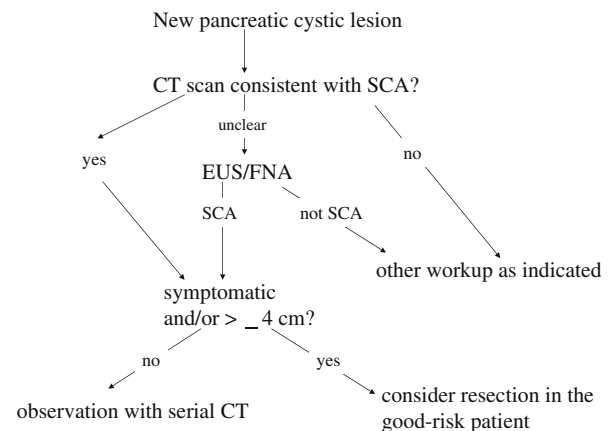


Figure 1 Diagnostic and management algorithm for suspected serous cystadenoma of the pancreas (after Tseng et al.³³) sCA (serous cystadenoma).

Patients with the above criteria who are asymptomatic and have tumors less than 4 cm in maximal diameter are candidates for non-operative management, with clinical follow-up and serial imaging (Fig. 1). The interval between serial imaging is subject to debate, but 2 years may be reasonable. Patients with symptoms attributable to their tumors, patients in whom a mucinous or other potentially malignant tumor cannot be comfortably excluded, and patients with serous cystadenomas measuring 4 cm or more in maximal diameter who are reasonable surgical candidates should be offered resection. This recommendation to proceed with surgery in asymptomatic patients with larger tumors is based both on their more rapid growth rate as well as in a more than threefold increase in the likelihood of developing symptoms.

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