

Pathologic Quiz Case

A 52-Year-Old Woman With Jaundice and History of Necrotizing Pancreatitis

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A 52-year-old woman presented with jaundice, weight loss, and generalized pruritus. Her past medical history was significant for necrotizing pancreatitis with pseudocyst formation 10 years prior to the current presentation and a 2-year history of a cyst in the head of the pancreas. A computerized tomographic scan demonstrated a large, calcified, 10-cm mass in the head of the pancreas that involved the duodenum. There was also marked dilatation of the entire biliary tree, including the intrahepatic ductal system as well as the common bile duct. No radiologic evidence of vascular invasion by the pancreatic mass was

noted. An ultrasound-guided fine-needle aspiration was performed using a 22-gauge Franseen needle. Smears were air dried and stained with Diff-Quik or were wet fixed in ethanol for subsequent Papanicolaou staining.

On gross examination, the aspirate had a smooth, glistening appearance. Cytopathologic examination showed abundant mucinous material, degenerated inflammatory cells, and rare 3-dimensional fragments of benign-appearing epithelium (Figure 1). Higher magnification showed cytologic atypia with enlarged, crowded, hyperchromatic nuclei (Figure 2). Numerous single cells with large solitary intracytoplasmic vacuoles consistent with mucin were also noted (Figure 3). These cells occasionally had indented nuclei simulating signet ring cells.

The patient was taken to the operating room and was found to have a large cystic pancreatic lesion extending to the retroperitoneum and encasing visceral vessels. A biopsy of the mass was performed, which revealed scattered loosely cohesive groups of epithelium and cells with large cytoplasmic vacuoles in a mucinous background (Figure 4).

What is your diagnosis?

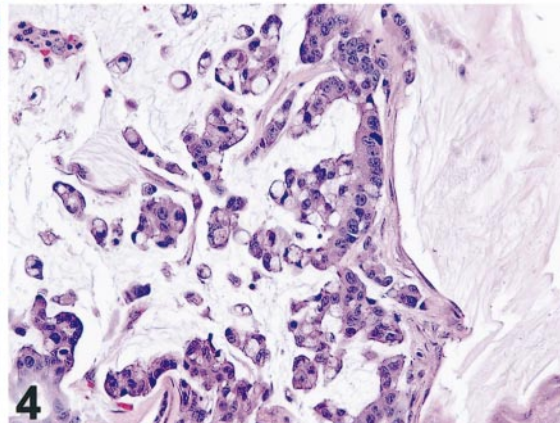
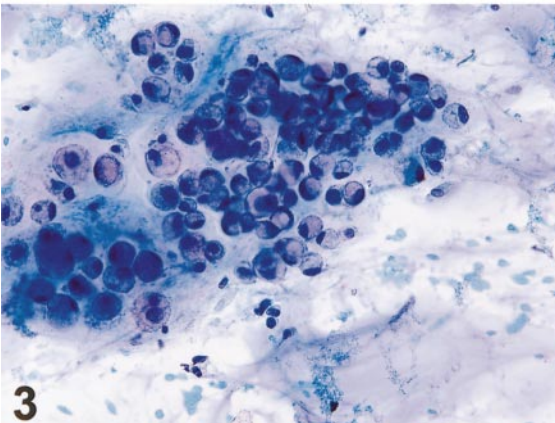
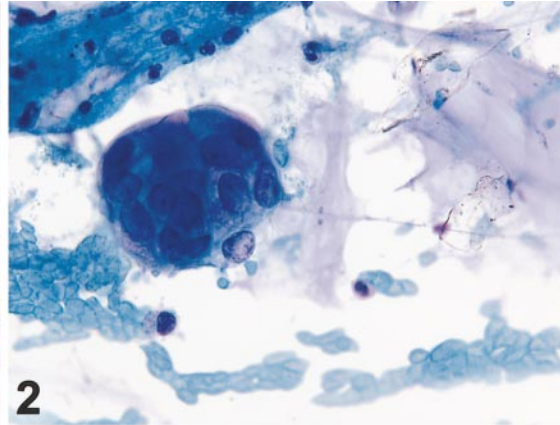
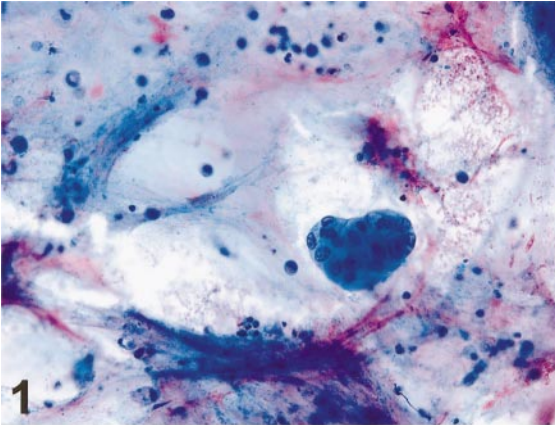
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Pathologic Diagnosis: Primary Colloid Carcinoma of the Pancreas

Primary colloid carcinoma (CC) is a rare subtype of adenocarcinoma of the pancreas characterized by production of extensive mucin. Although CC of other organs such as the breast, colon, and prostate have been studied extensively,¹⁻³ there are only a limited number of reported accounts on CC of the pancreas.⁴⁻⁷

Although the clinicopathologic characteristics of the pancreatic CC (location, gender distribution, age, and clinical presentation) are similar to those of conventional-type pancreatic adenocarcinoma, recent studies have suggested that it may have a better prognosis.⁷

Grossly, CCs are often large cystic masses with copious mucoid material. Fine-needle aspiration is an extremely useful adjunct to radiology in the evaluation of cystic lesions of the pancreas.⁸ Cytologically, abundant mucin is seen admixed with fragments of benign-appearing glandular epithelium or single cells. Cytopathologic distinction from other mucinous neoplasms (such as an intraductal pancreatic mucinous neoplasm [IPMN]) can be difficult. Incidentally, on initial cytopathologic evaluation, the current case was interpreted as consistent with a mucinous cystic neoplasm with focal marked atypia, and the possibility of adenocarcinoma was suspected. Subsequent evaluation, however, revealed cytologic features (marked nuclear enlargement, hyperchromasia, and signet ring-type cells) consistent with adenocarcinoma. Histologically, the cystic areas in CC are lined either by flattened mucin-producing cells or by simple connective tissue strands. The tumors have well-defined pools of mucin and free-floating mucinous epithelial cells. Occasionally, signet ring cells (as seen in our case) may be identified in the mucin.

The differential diagnosis of CC on fine-needle aspiration includes mucinous cystadenocarcinoma, IPMN, conventional-type ductal adenocarcinoma with mucinous features, and signet ring adenocarcinoma. The clinicopathologic features of CC of the pancreas have not yet been well characterized, because cases of CC are often associated with mucinous cystic neoplasm or IPMN.⁶ On histopathologic examination, the current case also revealed an associated IPMN. There are conflicting reports as to whether colloid differentiation may be an independent variable in survival studies.^{6,7}

Adsay et al⁷ examined 17 cases of CC, 9 in men and 8 in women. The mean age of the patients was 61 years. Of these cases of CC, 10 were originally classified as mucinous ductal adenocarcinoma and 4 as mucinous cystadenocarcinoma. The tumors had abundant mucin, with malignant cells amid the mucin pools. Regional lymph node metastasis was seen in 8 cases. Molecular studies showed *K-ras* mutations (codon 12) in 4 of 12 cases.⁷

In the study by Adsay et al,⁷ the 5-year survival of CC patients was 57%. The authors compared the CC cases

with 82 cases of typical ductal adenocarcinoma and found that although the patients with CC presented with larger tumors, they presented at a lower stage ($P = .01$). The authors also reported that the prognosis of CC cases was significantly better than that of the typical ductal-type pancreatic adenocarcinomas. At 5 years, CC patient survival was 57% versus 12% for the typical ductal adenocarcinoma.⁷ Other studies have also shown that CC arising in association with IPMN has a favorable prognosis.⁹

In contrast to the study by Adsay et al,⁷ other authors have reported that colloid differentiation was not an independent predictor of patient survival.⁶ Seidel et al⁶ described 39 cases of pancreatic and periampullary carcinoma with colloid differentiation. Colloid carcinoma patients had 2- and 5-year survival rates of 69% and 29%, respectively. The authors reported that in a multivariate model, colloid differentiation was not an independent predictor of patient survival. Therefore, CC of the pancreas and periampullary region does not necessarily have a better prognosis than carcinomas without colloid differentiation. Instead, the authors reported that other factors, including location, perineural and vascular invasion, and margins, may be more important.⁶

In conclusion, CC of the pancreas may occur with or without an IPMN and mucinous cystic neoplasm component. Because of asymptomatic presentation or nonspecific symptoms, diagnosis may not be made until a very advanced stage. Imaging studies play a pivotal role in the diagnosis of CC, and the best modalities include computerized tomography and magnetic resonance imaging. The outcome for patients with CC is dependent on the tumor location and the extent of metastatic spread. Overall, CC of the pancreas may be associated with a better prognosis than ordinary ductal adenocarcinoma. Therefore, an accurate and early diagnosis is very important and can make a difference in successful outcome. Fine-needle aspiration is a useful diagnostic modality and can be used to provide rapid and accurate diagnosis in cases of CC.

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