

# Cystic Pancreatic Neoplasms

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Senior Talk

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# Our Case

- A 77y/o Caucasian male with a history of Htn and GERD complaining of vague upper abdominal pain and early satiety.
- Meds included HCTZ, doxazosin, and pantoprazole.
- Social history + for 1 alcoholic drink daily
- Vital signs were normal, physical exam revealed no abnormalities.



# Our Case Continues

- Laboratory tests revealed no abnormalities.
- CT revealed a cystic lesion in the pancreatic duct at the junction of the body and tail, with evidence of ductal dilation from head to tail and a fluid filled structure 2cm in diameter that appeared contiguous with the duct. There was also atrophy of the surrounding pancreatic tissue.



# What Next?

- On endoscopy the ampulla was enlarged and showed mucin extruding through the orifice.
- Endoscopic ultrasound showed diffuse dilation of the pancreatic duct to 3mm (normal 1-2mm), and a smooth walled cystic lesion that appeared to communicate with the dilated duct.
- FNA revealed thick mucin with cellular debris and epithelial cells with a moderate degree of cellular atypia. Low levels of amylase and elevated levels of tumor markers CEA and CA 72-4 were found



# Goals

- Discuss the different types of cystic pancreatic neoplasms
  - Reviewing their distinguishing characteristics, pathogenesis, natural history, and prognosis
- Evaluate different diagnostic strategies including: CT, MRI, MRCP, ERCP, EUS, Fluid Analysis
- Examine the treatment strategies available
- Review outstanding questions and areas for further research



# Introduction to Cystic Pancreatic Neoplasms

- Represent around 5-15% of cystic pancreatic lesions
  - Other 90% mostly pseudocysts, but also includes developmental (simple/true/retention) cysts, mucin producing ductal adenocarcinomas, abscesses, neuroendocrine tumors, and lymphoepithelial cysts.
- Also represent <10% of pancreatic neoplasms
  - Others include: ductal adenocarcinoma, neuroendocrine tumors, and acinar-cell cystadenocarcinoma.



# Classification of Cystic Pancreatic Neoplasms

- Solid and Pseudopapillary Neoplasm
- Serous Cystadenoma
- Mucinous Cystic Neoplasm
- Intraductal Papillary Mucinous Neoplasm (IPMN)



# How Do These Patients Present ?

- Many discovered incidentally on imaging studies such as CT, MRI, and abdominal ultrasound
- Symptoms may include: recurrent pancreatitis, jaundice, chronic abdominal pain, early satiety.
  - Usually caused by obstruction of pancreatic or biliary duct either by the tumor itself or by mucous in the case of IPMN
- Occasionally a mass is palpated on abdominal exam

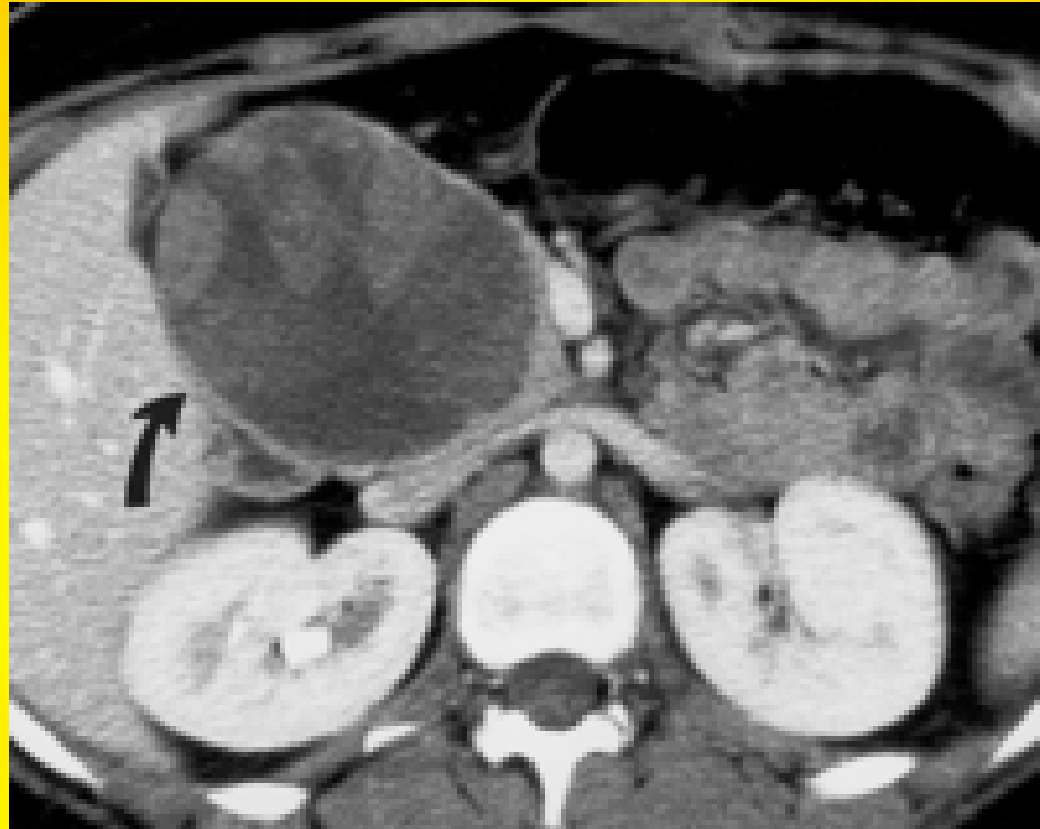


# Solid Pseudopapillary Neoplasms

- <10% of cystic pancreatic neoplasms
- Occur predominantly in young women
- Can be locally invasive, but low-grade potential for development of metastatic disease.
- When metastases are found they are usually in the liver or peritoneum.
- High rate of cure with surgical resection



# Solid and Pseudopapillary Neoplasm



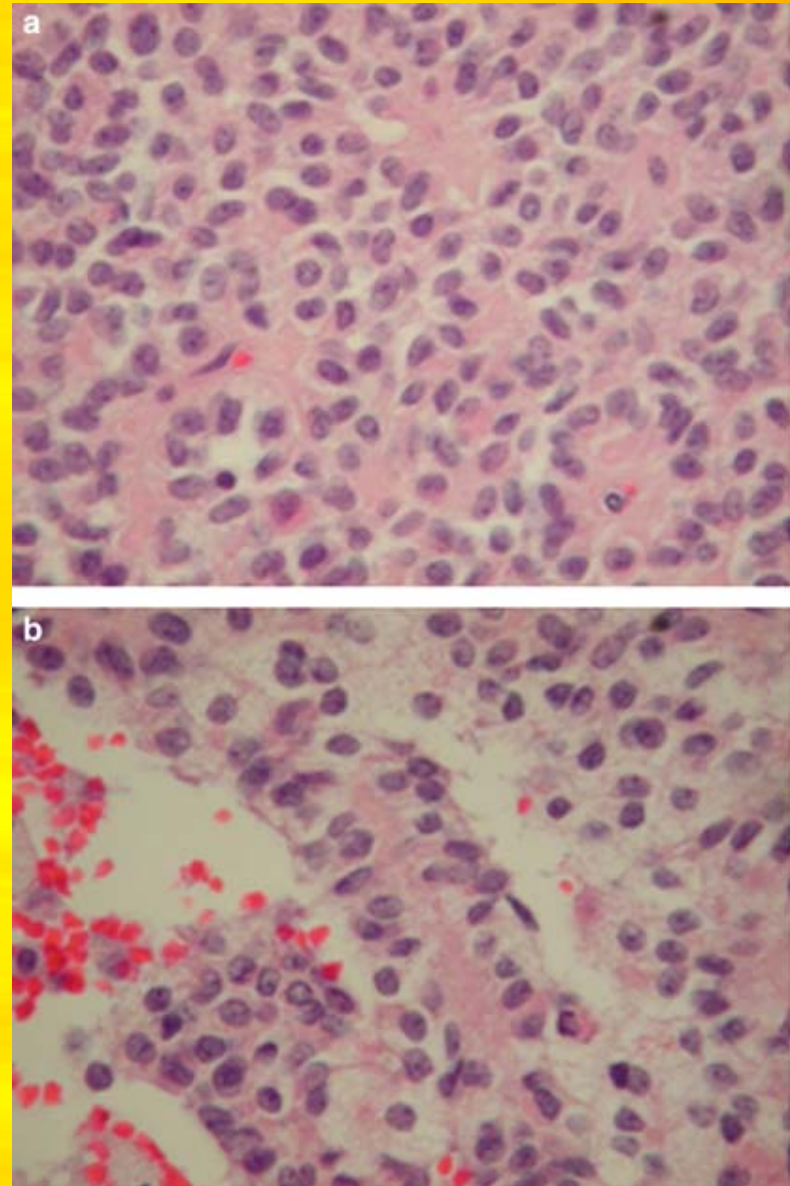
16 year-old girl with mid epigastric pain found to have a solid and pseudopapillary neoplasm. CT scan shows a complex mass (arrow) in the head of the pancreas (9).

# Solid and Pseudopapillary Neoplasm



# Solid and Pseudopapillary Neoplasm

H & E stain from 2 separate areas of a solid and pseudopapillary neoplasm. A. shows an area of solid tumor growth, while B. demonstrates a pseudopapillary structure



# Solid and Pseudopapillary Neoplasm

- With their propensity for young women of reproductive age, role of sex hormones has been examined.
  - 77 of 95 samples (81%) tested in multiple studies for progesterone receptor were positive
  - Multiple studies of alpha subtype of estrogen receptor have been negative
  - Small study by Geers et al showed 5/5 sample positive for beta subtype of ER



# Quick Review of Solid and Pseudopapillary Neoplasm

- Most rare of cystic pancreatic neoplasms
- Occur predominantly in young women
- Can be locally invasive but rarely metastasize
- Sex hormone receptors may play a role in pathogenesis
- Should be removed surgically if possible



# Serous Cystadenoma

- Usually small in size and made up of a myriad of small cysts, may also appear solid or oligocystic, and can grow to large sizes
- Lined by a simple cuboidal epithelium of glycogen-rich cells
- Very low potential for malignant disease



# Serous Cystadenoma

- Commonly in middle-aged women in their 60s.
  - Mass General series from 1976-2004 mean age 61 years, 75% female.
- Also associated with von Hippel-Lindeau
  - Chromosomal alterations on von Hippel-Lindeau gene 3p25
  - Series of 156 patients with von Hippel-Lindeau where 9% were dx with serous cystadenoma

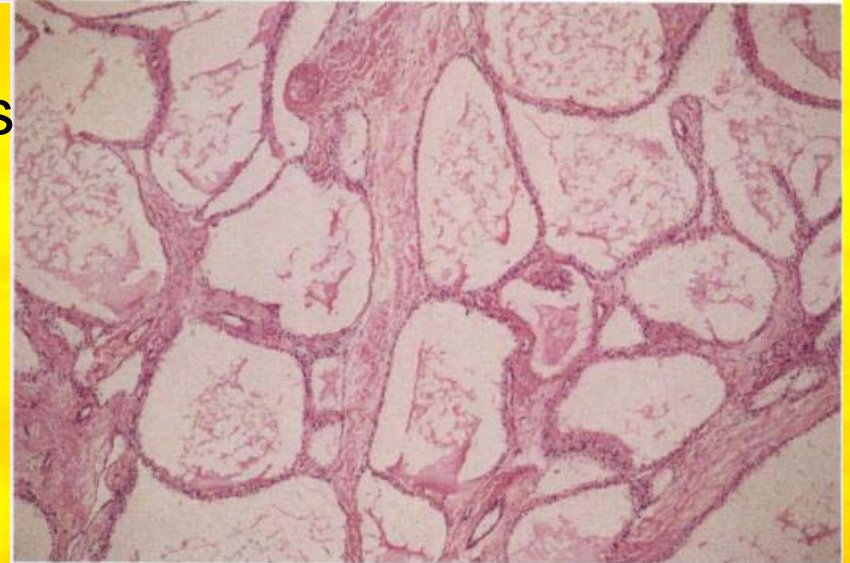


# Serous Cystadenoma

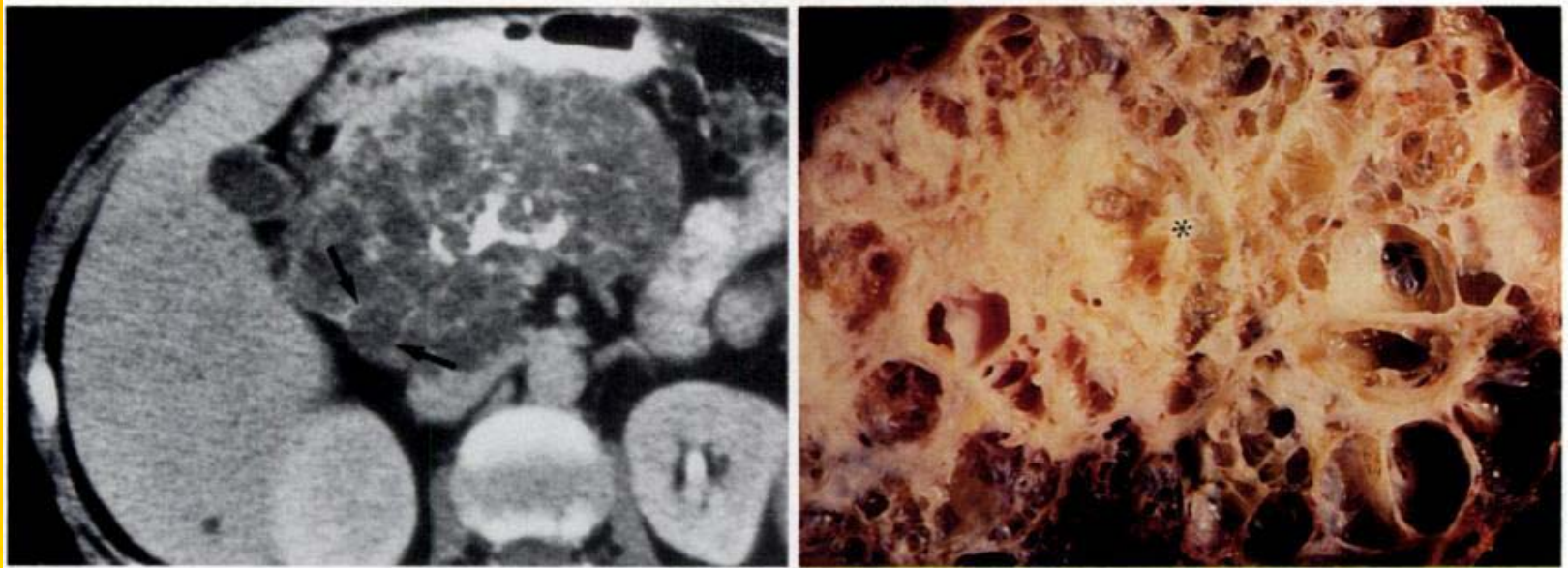


Cut surface of a microcystic adenoma, showing a central stellate fibrotic scar. The cysts are very small and barely visible.

Photomicrograph of serous cystadenoma, showing cysts lined by flat cuboidal epithelium without papillae and filled with proteinaceous fluid.



# Serous Cystadenoma



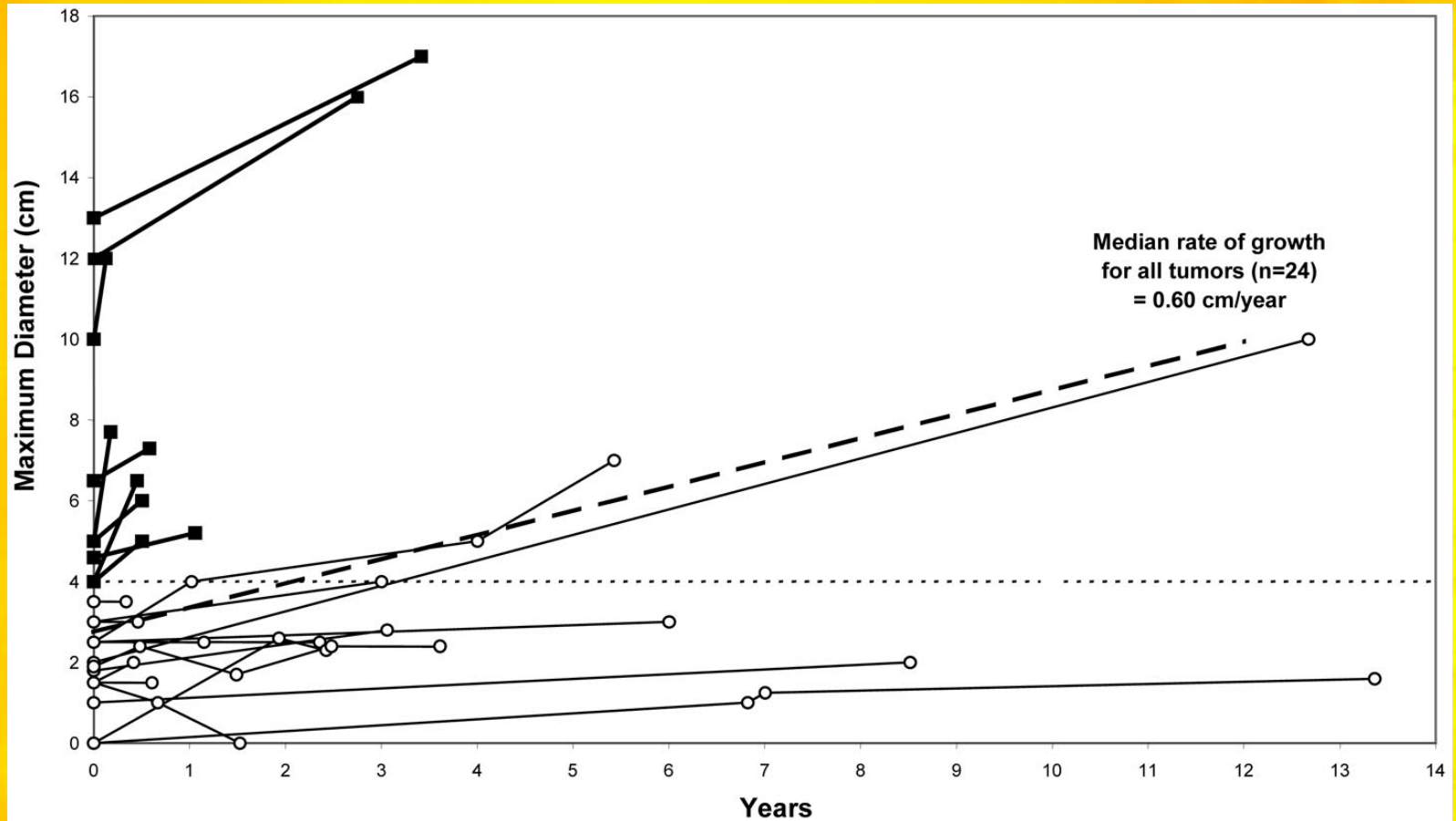
66-year-old woman with no symptoms and an abdominal mass found during routine physical examination. (a) CT scan with large, well-defined mass in the pancreatic head. Honeycombed pattern (arrows) due to fibrous septa. A calcified central scar is seen. (b) Section of the gross specimen shows a multiloculated cystic mass with different-sized cysts and central areas of fibrosis and calcification (\*).

# Management of Serous Cystadenoma

- Based on size and symptoms
- Small, asymptomatic, slow-growing lesions can be monitored
- Mass General series showed that size at presentation influenced growth rates with tumors  $<4$  cm growing more slowly than those  $>4$  cm



# Serous Cystadenoma Growth Rates



Serous cystadenoma tumor growth over time. Open circles = tumors <4 cm at presentation, solid squares = tumors >4 cm at presentation.

# Quick Review of Serous Cystadenoma

- Most often found in women in their 60s
- Multiple small cysts within one larger mass, characteristically with fibrous septae and a stellate central scar
- Almost universally benign
- Management based on size of mass at presentation and presence of symptoms



# Mucinous Cystic Neoplasm

- Mucin producing tumors which contain a dense mesenchymal ovarian-like stroma which helps differentiate them from IPMN
- Also lack communication with the pancreatic ductal system which is a feature of IPMN
- Almost exclusively found in middle-aged women
  - In one series of 56 pts all were women
  - In a second series 70 of 84 pts (80%) were women

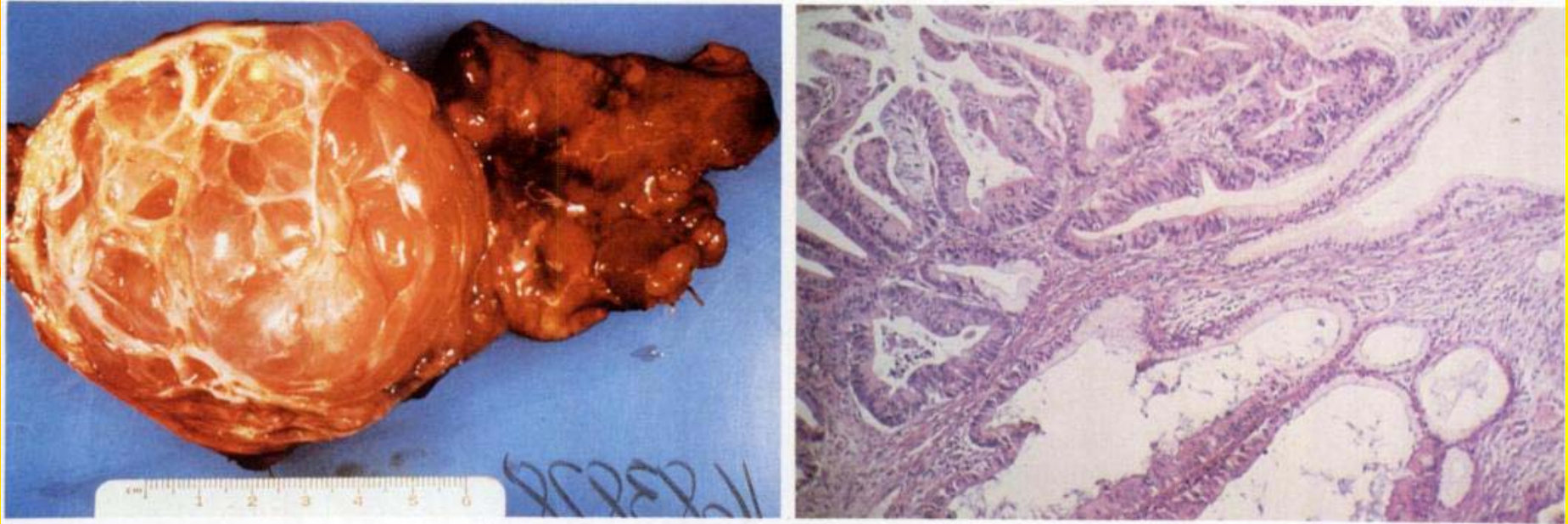


# Mucinous Cystic Neoplasms

- WHO classified into 3 stages: benign (adenomatous), low grade malignant (borderline), and malignant (carcinoma in situ and invasive cancer).
- High malignant potential
  - In one series of 61 pts c/ MCN, 44% adenomatous, 8% borderline, 15% carcinoma in situ, and 33% invasive adenocarcinoma
- Prognosis related to stage at time of resection
  - Survival around 100% at 5 yrs if no evidence of invasion
  - For those with invasion 5 yr survival less than 20%



# Mucinous Cystic Neoplasm



a. Gross specimen of a mucinous cystic neoplasm, manifested as a thick-walled, multilocular cyst with large cystic spaces.

b. Photomicrograph of a mucinous cystic neoplasm, showing columnar epithelium arranged in single rows in some areas and forming atypical papillae in others.

# Mucinous Cystic Neoplasm



**Fig. 13A** —Incidental mass found on lumbar spine MR image in this 80-year-old woman with lower back pain. Large, unilocular mass in pancreatic tail can be seen on CT scan. Notice calcification in wall (*arrow*)

# Mucinous Cystic Neoplasm

- Likely related to mucinous tumors of ovary, liver, retroperitoneum
  - All almost exclusively in women
  - Similar protein staining patterns
  - Similarly high proportions of estrogen and progesterone receptors
  - During 4<sup>th</sup>-5<sup>th</sup> weeks of development primordial gonad and portion of pancreas that becomes body and tail are adjacent



# Quick Review of Mucinous Cystic Neoplasms

- Mucin-producing tumor surrounded by ovarian-type stroma that does not communicate with ductal system
- Almost always in middle aged women
- Appears as unilocular mass almost exclusively in body and tail
- High malignant potential with likely adenoma to carcinoma progression
- May be related to mucinous tumors of ovary, liver, and retroperitoneum
- Should be surgically resected if possible

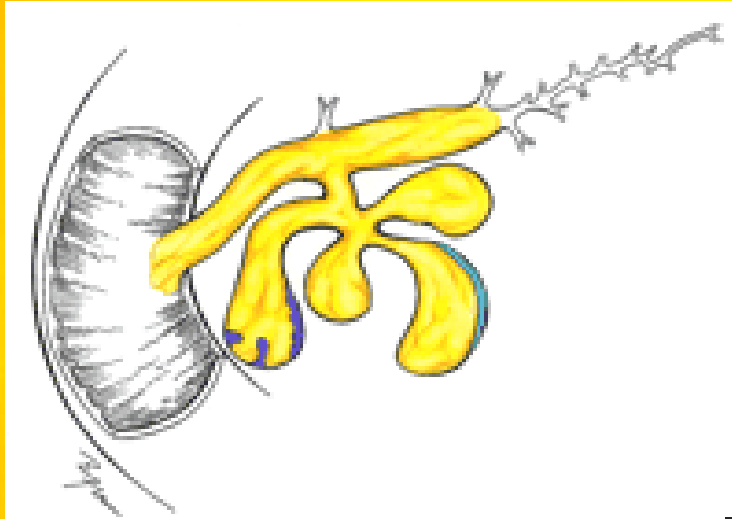


# Intraductal Papillary Mucinous Neoplasm

- Mucinous tumor that communicates with the pancreatic ductal system
  - Divided into main ductal type and branch ductal type
- Shares histologic classification of adenoma, borderline, carcinoma with mucinous cystic neoplasm
  - Adenoma to carcinoma progression likely
- Most common in men in their 60s & 70s



# Branch Ductal IPMN



Side branch IPMN. Abnormal cells in uncinata side branches may take the form of hyperplastic lining (blue) or polypoid projection (purple). Produce large amount of mucus (yellow) that distends side branch system.

ERCP of side branch IPMN in a 38-year-old man presenting with recurrent bouts of epigastric pain. After most of mucus has been removed abnormal side branch (*arrowhead*) can be readily seen.

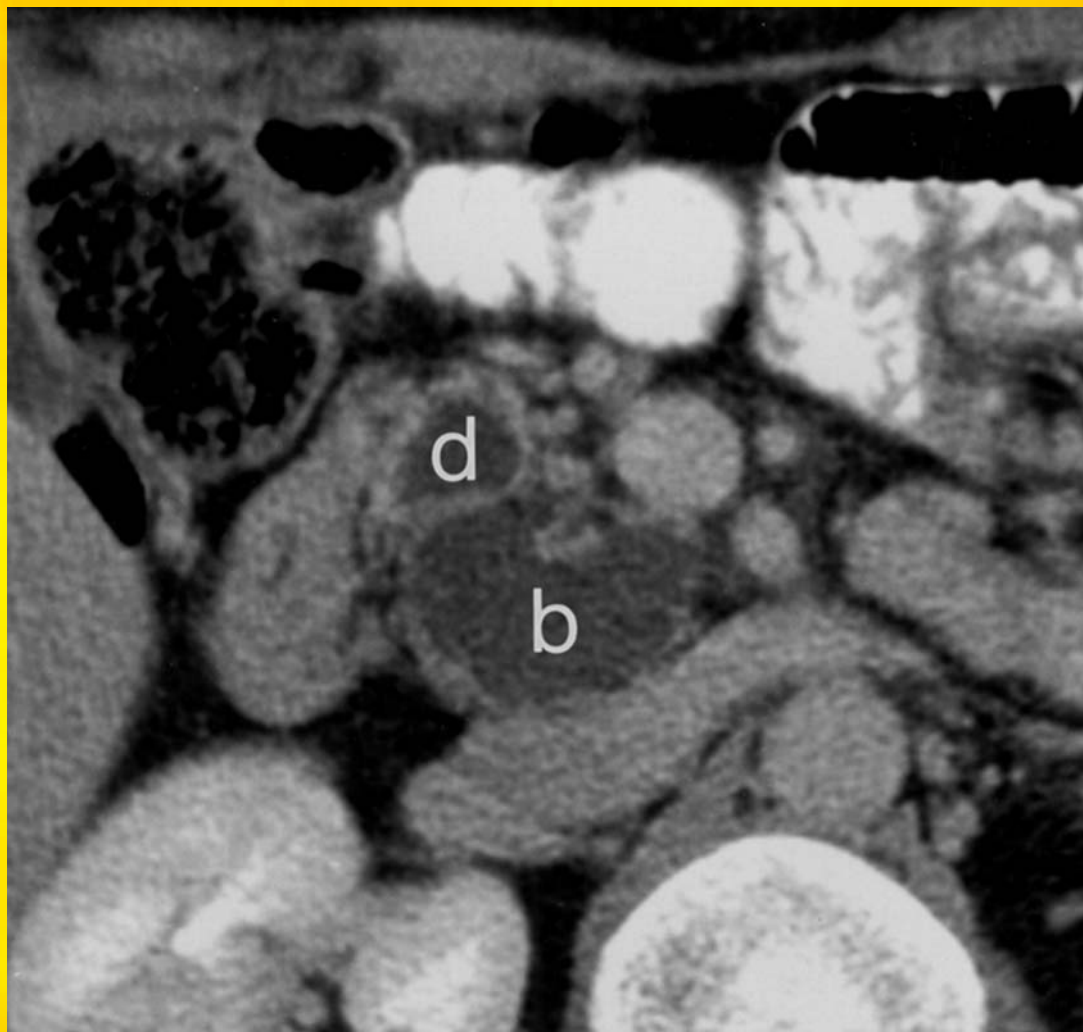


**--Side branch intraductal papillary mucinous neoplasm in 46-year-old man with abdominal pain and pancreatitis**



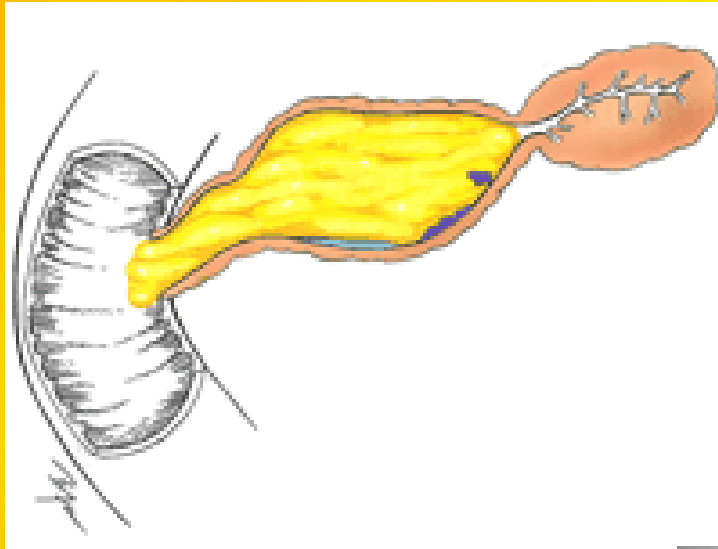
Grogan, J. R. et al. Am. J. Roentgenol. 2001;176:921-929

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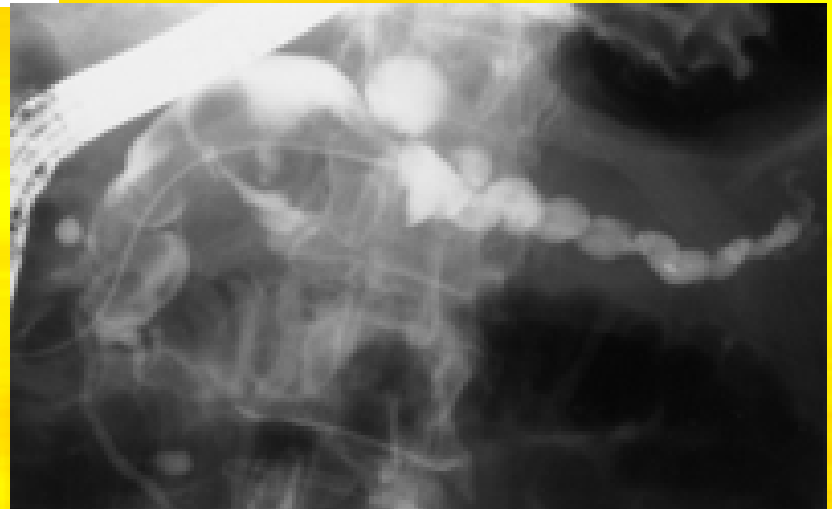
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# Main Duct IPMN



Main duct IPMN demonstrating marked main pancreatic duct distention from mucus (*yellow*) and atrophy of the pancreatic parenchyma.

ERCP of main duct IPMN in a 66-year-old renal transplant patient with abdominal pain and diabetes. There is massively dilated main pancreatic duct with diffuse filling defects.

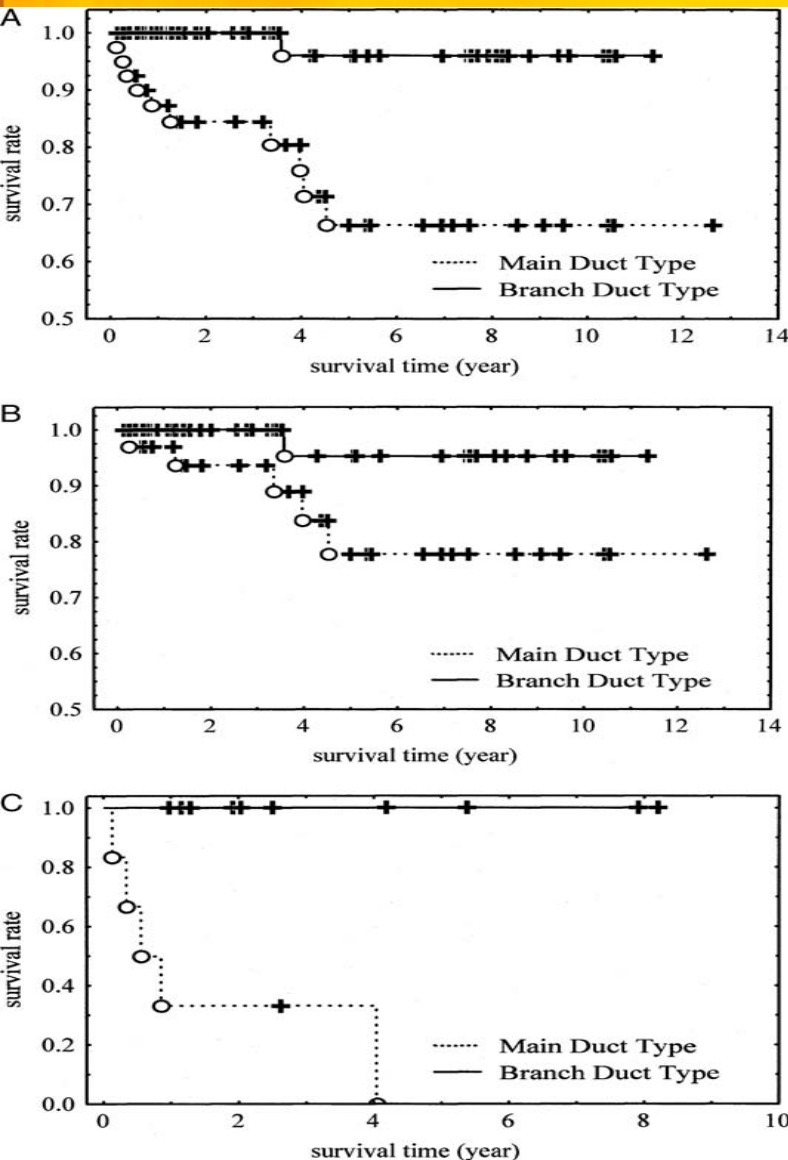


--Main duct intraductal papillary mucinous neoplasm in 66-year-old male renal transplant patient with abdominal pain and recent onset of diabetes



Grogan, J. R. et al. Am. J. Roentgenol. 2001;176:921-929

# IPMN Survival by Type



Survival in IPMN based on morphologic diagnosis

- A. Analysis of all patients. The prognosis in patients with main duct type was significantly worse than in patients with branch duct type ( $P = 0.0012$ ).
- B. Analysis of surgical patients. The majority of the branch duct type surgical patients survived, with the exception of one patient ( $P = 0.0871$ ).
- C. Analysis of nonsurgical patients. All the nonsurgical main duct type patients died due to progression of pancreatic disease while all the branch ductal group survived without evidence of disease progression. ( $P = 0.00077$ ).

The symbols in the figure designate either complete (O) or incomplete cases (+).

# Quick Review of IPMN

- Mucin producing tumor that communicates with ductal system
- More common in men in their 60s & 70s
- Divided into main duct and branch duct types.
- Main duct worse prognosis should be resected
- Some propose that branch duct may be observed



# Difficulties in Diagnosis

- Using Imaging Studies
  - Procacci et al, retrospective analysis of 100 cystic masses, correct identification in only 60%
- ERCP/Endoscopic ultrasound
  - Pancreatic duct obstruction high specificity but low sensitivity for diagnosis of malignancy
  - No criteria identified to predict benign disease



# Cystic Fluid Analysis

- Sperti et al, showed sensitivity of 80% and specificity of 95% for CA 72-4 in differentiating benign from malignant
  - However, these results were not reproducible, with other studies finding that this marker was neither sensitive or specific.
- Kimura et al, sensitivity of 57% AND 69% for CEA and CA 19-9 respectively with specificity of 100%



# Other tests of cystic fluid

- Elevated amylase levels suggestive of pseudocyst
- Cytology very specific but not sensitive
  - Serikawa et al. studied IPMN showed cytology sensitivity of 23.5% for branch duct type and 33.3% for main duct with specificities of 100 and 96.4% respectively
- Small studies in mucinous lesions on telomerase activity and gene mutations like K-ras and p53



# Areas of Future Research

- Preoperative differentiation of the type of lesion and its malignant potential
- Use of alternate treatments for those for whom resection is not possible
  - Chemotherapy
  - Estrogen and Progesterone Receptor modulators
  - Ethanol or radiofrequency ablation



# To Wrap Up Our Case

- The patient was diagnosed with intraductal papillary mucinous neoplasm
- He underwent complete surgical resection which required a total pancreaticoduodenectomy and had an uneventful postop course.
- Tumor histology revealed areas of markedly atypical epithelium consistent with intraductal carcinoma.
- The patient was alive and well without recurrence 2 years later.