Pancreas
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Disclosures
None

Outline
• Very basic anatomy and histology
• Brief word on FNA procedures

• CYTOMORPHOLOGY
  - Benign components
  - Inflammatory processes
  - Benign & pre-malignant tumors
  - Malignant tumors
Normal pancreas
- duct
- acini
- islets
Normal duct cells

Normal acinar cells

Benign ductal sheets - Giemsa

Gastric epithelium with mucus
Pancreas: FNA procedures

- Intra-operative FNA (palpation)
- Transabdominal FNA
  - ultrasound guidance
  - CT guidance
- ENDOSCOPIC ULTRASOUND-GUIDED FNA (EUS-FNA)

Upper GI endoscopy

The Endoscope

Ultrasound probe and needle
CT scan performed for lung cancer surveillance

EBUS image of 2cm pancreatic tail cyst

Same cyst at EUS
Acute pancreatitis: Syndromes

- **Acute edematous pancreatitis**
  - Early treatment ...
  - Low mortality

- **Acute hemorrhagic pancreatitis**
  - Pancreatic necrosis
  - Enzymatic digestion of pancreas
  - Peri-pancreatic enzyme leak
  - Medical emergency
  - High mortality

FNA plays no part in diagnosis of acute pancreatitis

Severe abdominal, back pain
High amylase, later lipase
Hemolysis, DIC and ARDS
Diffuse fat necrosis → calcification
Peripheral vascular collapse
Acute onset renal failure
Shock, death

High power: Acute pancreatitis with loss of parenchyma,
Duct erosion, numerous polymorphonuclear leucocytes
Chronic pancreatitis: Morphology

Gross: Hard gland with dilated ducts, visible calcification

Microscopic:
- Fibrosis of parenchyma
- Reduced number and size of acini
- Relative sparing of islets early
- Dilatation and/or fibrosis ducts
- Later loss of islets

Chronic pancreatitis: Massive fibrosis

Chronic pancreatitis: Calcification

Chronic pancreatitis:
- Total loss of acini
- Duct proliferation
- Loss of acini, sparing of islets, dense fibrosis, lymphocytes
- Islets of Langerhans remain
Images of Chronic pancreatitis

Chronic pancreatitis
- few epithelial cells, inflammatory cells, fibrin, histiocytes

Pancreatic Pseudocyst

- Follows pancreatitis, trauma
- Localized collection liquefied necrotic tissue, altered blood, inflammation
- Lacks epithelial lining "pseudo"-cyst, 2-20cm
- Cytomorphology: Fluid aspirate with necrosis, rare if any epithelial cells, blood, fibrin, inflammatory cells and foam cells.
Auto-immune pancreatitis

A clinical and radiologic mimic of cancer

- Raised gammaglobulins, IgG or Ig4
- Serum antibodies
- Diffuse enlargement of pancreas
- Diffuse narrowing of pancreatic duct
- Mild symptoms without acute attacks
- Rare calcification or cysts
- Effective steroid therapy
- FNA: cellular stroma and lymphoid infiltrates
  : false positive reports, epithelial atypia

Pancreatic Neoplasms:
Simplified formal classification

- Exocrine - Serous neoplasms
  - Mucinous cystic neoplasms
  - Intraductal neoplasms
  - Pancreatic intra-epithelial neoplasia
  - Invasive ductal carcinoma
  - Acinar neoplasms
- Endocrine neoplasms
- Non-epithelial neoplasms - eg lymphoma
- Metastatic malignancies


My approach today

- Ductal adenocarcinoma and variants
- Mucinous neoplasms
  - Intraductal papillary mucinous neoplasm
  - Mucinous cystadenoma
- Pancreatic endocrine neoplasm
- Rare tumors - acinar carcinoma
  - serous cystadenoma
  - solid pseudopapillary neoplasm
Invasive ductal cancer: Incidence and survival

- Fourth highest incidence in USA (lung, breast, colon)
- M > F and B > W, middle/older ages
- National Cancer Institute 2008 figures
  - New cases: 37,680
  - Deaths: 34,290
- Dismal prognosis in spite of therapy
- Five year survival minimal (<5%)

Invasive ductal cancer: Clinical features

- 60% arise in head, fewer in body or tail
- Risks: alcohol, smoking chronic pancreatitis
- Asymptomatic >> late weight loss, anorexia, pain
- Jaundice if bile duct obstructed in head
- Trousseau’s sign, migratory thrombosis
- Most inoperable at diagnosis, 5% 5yr survival
- Surgery is Whipple’s or partial pancreatectomy
- Chemotherapy, radiation therapy, palliative

Cytomorphology: Adenocarcinoma

- Cellularity usually high
- Disorderly monolayer sheets
- Single columnar cells and small clusters
- Scant or mucinous cytoplasm
- Nuclear enlargement, pleomorphism
- Irregular nuclear outlines
- Chromatin granular, pale and marginated
- Nucleoli and mitotic figures
Low power - high cellularity

Irregular sheet, cytoplasmic mucin, irregular nucleoli

Crowded sheet, margination
Giemsa – Crowding and nuclear pleomorphism

Nuclear convolutions, cytoplasmic vacuoles

Giemsa, mucus, single tumor cells
Nuclear pallor and grooves

Mucinous adenocarcinoma

Intensive multinucleation
Criteria: Well-Differentiated Ductal Cancer
Lin & Staerkel, MD Anderson, 71/291 cases
Cancer Cytopathology 2003; 99:44-50

1) Anisonucleosis (3-4x)
2) Nuclear membrane irregularity
3) Nuclear enlargement (2x RBCs)
4) Architecture - 2D aggregates, crowding, overlapping, loss of polarity

Of NO use in WD tumors: Single cells, prominent nucleoli, chromatin disturbances, molding, mitotic figures, NC ratio, necrosis

Well differentiated adenocarcinoma

Well differentiated adenocarcinoma
Well differentiated adenocarcinoma

Adenocarcinoma variants

- Adenosquamous carcinoma
- Signet ring adenocarcinoma
- Anaplastic carcinoma
  - with osteoclastic giant cells
  - with pleomorphic giant cells
  - with both!

Adenosquamous carcinoma
Anaplastic carcinoma with pleomorphic giant cells

Intraductal Papillary Mucinous Neoplasm (IPMN)

Seemingly recent tumor!
Middle-aged, older
Main, segmental ducts or both
Mucin-filled dilatation of duct
Complex papillary lining
Endoscopy distinctive
Radiology deceptive
Cytopathology characteristic
Histopathology mandatory
Prognosis favorable (60-90%)
Strong malignant potential
Histopathology essential (main, not branch ducts)

FAHC - IPMN
Invasive IPMN vs solid adenoca

Invasive IPMN vs solid adenoca - no nodes

Invasive IPMN vs solid adenoca - with nodes

Cancer 2010;116, 3369

Low power IPMN – thick papillary fragments

Intracellular and extracellular mucin
High power IPMN – papilla and Cytoplasmic mucin

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**Mucinous Cystadenoma**

Middle-aged females, body and tail
No connection with pancreatic duct
Unilocular, multilocular, mucin-filled
Thick capsule, ovarian-type stroma
Smooth (~papillary) lining
Radiology/cytopathology distinctive
Prognosis intermediate (35-45%)
Adenoma-carcinoma sequence
Excision/histopathology essential

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Further notes: IPMN and MCA

- Spectrum of cytopathology from benign through borderline to malignant
- Cytodiagnosis should reflect that – but "Mucinous cystic lesion" permissible.
- Both entities have high malignant potential
- Histopathology essential in both
- Differential for both is benign gastric epithelium!
Pancreatic Endocrine Neoplasms

- Usually cellular aspirates
- Isolated cells and stripped nuclei
- Pseudorosettes, ribbons and clusters
- Eccentric nuclei “plasmacytoid”
- Low N/C ratios
- Round regular nuclei
- Hallmark is nuclear chromatin granularity
- Chromogranin and synaptophysin positive
Synaptophysin positive PEN

Acinar adenocarcinoma

Rare 1-2% neoplasms, older males
Symptoms deceptive (local, lipase)
Radiology non-specific
Cytology subtle and “bland”
Many differentials to be considered
Histochemistry, ICC, EM essential
Prognosis abysmal (<5%)
SCA: Serous Cystadenoma

- Benign neoplasm, older females, body/tail (centro-acinar, intercalated duct)
- Age 61 yrs, F:M ~3:1
- Microcystic, well defined, sponge-like
- Classic stellate scar, not universal
- 1-25cm, smaller in screened groups
- Malignant transformation negligible
- May be left in-situ, watchful waiting
- May cause obstruction if large
- Recognition should pre-empt surgery

SCA: Cytology and enzymes

- CEA, Ca19.9 are NOT significantly raised
- Fluid is watery, NOT mucinous
- Cells scant, bland++, easily overlooked
- Small sheets, cleared cytoplasm
- Diagnosis is clinico-RADIO-cytological
- Be "SCA conscious", avoid surgery
Benign epithelium – Surgical was diagnosed as serous adenoma

Sneige and Staerkel

**Solid-Pseudopapillary neoplasm of young women (SPN)**

- Still puzzling neoplasm mainly of young women 25yrs (7-70)
- F:M >20:1 expressing progesterone and estrogen
- No similar parenchymal tumor ovaries, elsewhere
- Radiology variable depending on cyst formation
- Mean 10 cm (0.5-25 cm), solid, friable, hemorrhagic
- Histology: Solid vascular>breakdown> pseudopapillae/cysts
- Cytology: Bland epithelial cells, vessel-based,
  Chinese lettering
  Vascular stroma is an integral part of diagnosis
- Neuroendocrine markers neg, Beta catenin, Ckit positive
- Resection curative 80%, peritoneal mets, few deaths*
- *Recent reports anaplastic variants
Initially solid growth

Later pseudo-papillary breakdown

SPN – Papanicolaou stain with faint central stromal cores
Pancreatic lymphoma

- In adjacent nodes > or parenchymal
- Non-Hodgkins > Hodgkins
- Large cell B-lymphomas predominate
- MALT lymphomas well described
- All types have better prognosis cf cancer
- Biopsy often tricky / dangerous
- Flow cytometry and FNA diagnostic

The End