PANCREATIC CYTOLOGY

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Papanicolau Society of Cytopathology
5 Committees and their publications in 2014


Other references

Benefits of a common nomenclature

- Standardization of nomenclature
- Unifies reporting of disease categories
- Contributes to evaluation of interobserver variability
- Improves intraobserver reproducibility
- Better aligns patient management options with interpretations
- Improves patient care
- Universally understanding by clinicians and pathologists
- “Statistics” (economical aspects)

Categories

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Management

- Malignant ......................surgery
- Premalignant
  - Low-intermediate grade..........observation with repeat sampling
  - High grade .....................surgery
- Neoplasm .........................surgery or observation
- Benign .............................medical management
- Endocrine tumors ...............surgery, chemotherapy, observation

Clinical information

- Patient age, gender
- Symptoms
- Anamnesis (important details that may effect diagnosis)
Radiological information

- Localisation of the lesion in the pancreas
- Characteristics of the lesion
  - Size, growth pattern (rounded, infiltrative)
  - Solid or cystic (unilocular, multilocular, solid with cystic component, thickness of the wall, calcifications)
  - Vascularisation
  - Cyst contents: thin, thick, mucinous, viscous, water-clear, brown, ...

NEEDLE TRACT!!! EUS Via?
- Esophagus?
- Gastric wall?
- Duodenum?

Ancillary tests

- CEA
- AMYLASE
- Molecular analyses: KRA, GNAS
- Immunocytochemistry & Immunohistochemistry (cell-block)

Differential Diagnostic Approach

SOLID
- Chronic pancreatitis
- Ductal adenocarcinoma
- Acinar cell carcinoma
- Pancreatic endocrine neoplasm
- Solid pseudopapillary tumor
- Pancreatoblastoma
- Metastasis

CYSTIC
- Pseudocyst
- Serous cyst
- Mucinous cyst (MCN, IPMN)
- Cystic degeneration of typically solid tumors
- Rare cystic lesions
  - Simple cysts
  - Lymphoepithelial cyst
  - Peripancreatic cysts

Important!

- DO NOT DIAGNOSE AS "TUMOR" IF THERE IS NO RADIOLOGIC MASS LESION!!!
- NO MASS LESION: MOST PROBABLY NORMAL ACINAR CELLS/FRAGMENT, NOT ACINAR CELL CARCINOMA OR NEUROENDOCRINE TUMOR!!!
Contamination !!!

- Gastric
- Intestinal
- Contamination or a component of the tumor?

Gastric contamination, cell-block

Cystic lesions

- Direct smears
- Other analyses on fresh undiluted cyst fluid
  - CEA
  - Molecular
  - Cytomorphologic
    - Cytospin
    - Cellblock

Duodenal contamination

Amylase & CEA

- Amylase levels
  - High levels associated with pseudocysts
  - Not increased in serous cysts and MCN

- Elevated CEA: in favour of mucinous cyst
  - Cannot distinguish IPMN from MCN
  - No correlation with malignancy
  - May be increased in duplication cysts, lymphoepithelial cysts

Molecular tests

- KRAS
  - Supports a neoplastic mucinous cyst
  - Does not contribute grading

- GNAS
  - Supports IPMN over MCN
  - No correlation with grade

- RNF43
  - Supports a mucinous cyst
  - Does not distinguish IPMN and MCN

- 3p deletions
  - 3p25, VHL gene, and other 3p deletions supports Serous Cystic Adenoma (SCA)

- CTNNB1 (Beta-catenin) deletion
  - Support Solid Pseudopapillary Neoplasm (SPN)

Suggested Categories (Papanicolau Society of Cytopathologists)

I. NONDIAGNOSTIC
- A specimen that provides no diagnostic or useful information about the lesion sampled.

- Criteria
  - Preparation artifact
  - Obscuring artifact
  - Gastrointestinal epithelium only
  - Normal pancreatic tissue elements in the setting of a clearly defined mass by imaging
  - Acellular aspirates of a solid mass or pancreatobiliary brushing
  - Acellular aspirate of a cyst without evidence of a mucinous etiology (thick mucin, elevated CEA or KRAS mutation)

II. NEGATIVE
- Definition: A sample that contains adequate cellular and/or extracellular tissue to evaluate or define a non-neoplastic lesion that is identified on imaging.

- Includes the presence of normal pancreatic tissue in the appropriate clinical setting such a vague fullness on imaging and no distinct mass lesion.

(Benign pancreas, Chronic pancreatitis, Autoimmune pancreatitis, pseudocyst, lymphoepithelial cyst, accessory spleen)

II. ATYPICAL
- Definition: Cells with cytoplasmic, nuclear, or architectural features not consistent with normal or reactive cellular components of the pancreas or bile ducts, and insufficient features to classify them as a neoplasm or suspicious for a high grade malignancy.

- The findings do not explain a lesion identified on imaging studies
- Follow-up evaluation is warranted.

III. NEOPLASTIC
- Definition: Benign or malignant neoplasms.

II. ATYPICAL
- Definition: Cells with cytoplasmic, nuclear, or architectural features not consistent with normal or reactive cellular components of the pancreas or bile ducts, and insufficient features to classify them as a neoplasm or suspicious for a high grade malignancy.

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- Follow-up evaluation is warranted.
Atypical

• Mild-moderate cellular atypia, NOS
• Mucinous/ductal epithelium with mild-moderate nuclear atypia (from a solid lesion or not clearly from a mucinous cyst)

IV. Neoplastic

• Benign
• Other

IV. Neoplastic: Benign

• Definition: Cytological specimen sufficiently cellular and representative, with or without the context of clinical, imaging, and ancillary studies, to be diagnostic of a benign neoplasm.

• SCA (Serous cystadenoma)
  • Sparse cellularity
  • Clean or bloody background
  • Flat sheets and loose clusters
  • Bland cuboidal cells
  • Clear, finely vacuolated or granular cytoplasm with indistinct borders
  • Associated hemosiderin-laden macrophages
  • Low CEA, low amylase
  • No KRAS mutation

IV. Neoplastic: Other

• Definition: A neoplasm that is either premalignant such as IPMN or MCN with low, intermediate or high grade dysplasia, or a solid-cellular neoplasm such as well-differentiated PanNET or SPN

• PanNET
• SPN
• Mucinous cyst (IPMN or MCN), not otherwise specified
• Mucinous cyst (IPMN or MCN), with low-grade atypia
• Mucinous cyst (IPMN or MCN) with high grade atypia
• GIST

WHO 2010 classification of the primary neuroendocrine tumors of the gastrointestinal system

• NET G1 (carcinoid) (Neuroendocrine Tumor Gr-1)
• NET G2 (Neuroendocrine Tumor Gr-2)
• NEC (Neuroendocrine Carcinoma, large cell or small cell type)
• MANEC (Mixed Adenoneuroendocrine Carcinoma)
• Hyperplastic and preneoplastic lesions.

• NETs usually show local metastases but NECs are usually much more aggressive tumors and can show widespread metastases
PanNET

- Almost the same classification and grading system as in gastrointestinal system
- "Pancreatic small cell NECs may not express neuroendocrine markers and this does not preclude the diagnosis so long as alternative diagnostic considerations are excluded".
- NET usually p53(-), NEC usually p53(+)
- NET can be positive for CD99. t(11;22) translocation can be helpful in differential diagnosis of PNET.

ENETS (European Neuroendocrine Tumor Society) grading*

- G1
  - mitotic count <2/10HPF and/or
  - Ki 67 index ≤ 2%
- G2
  - mitotic count 2-20/10HPF and/or
  - Ki 67 index 3-20
- G3
  - mitotic count >20/10HPF and/or
  - Ki 67 index >20

Mitotic count in at least 50HPFs

Ki 67 index as a percentage of 500-2000 cells counted in areas of strongest nuclear labelling (hot spots)

Case: Pancreas EUS PanNET

IHC-panel for PanNET/NEC

- Chromogranin-A
- CK8/18
- Gastrin
- Glukagon
- Insulin
- Ki67
- Pancreatic Polypeptid
- Somatostatin
- Synaptophysin
- (Trypsin)
- (Beta-catenin)
GASTRIN

SYNAPTOPHYSIN

ZES

Only mucin: Category?

Case: pancreas MCN?

Case-pancreas tumor: SCPPN

Whipple: PanIN-I-II, IPMN borderline, IP pancreatit, squa metap
V: Suspicious for malignancy

- Definition:
  - A specimen is suspicious for malignancy when some but not all of the criteria of a specific malignant neoplasm are present, mainly pancreatic adenocarcinoma.
  - The cytological features raise strong suspicion for malignancy, but the findings are qualitatively and/or quantitatively insufficient for a conclusive diagnosis.

VI: Positive/Malignant

- Definition: Unequivocal display of malignant cytologic characteristics
  - Adenocarcinoma of the pancreatobiliary ducts, and variants
  - Acinar cell carcinoma
  - High-grade neuroendocrine carcinoma (small and large cell type)
  - Pancreatoblastoma
  - Lymphoma
  - Metastases

Acinar cell carcinoma

Trypsin (It is positive in normal cells also)
IHCC-panel for GIST

- ASMA
- CD34
- C-KIT
- DESMIN
- DOG-1
- Ki-67
- S100

CASE
Old man with a 3 cm tumor in the pancreatic corpus

Renal Cell Carcinoma metastasis

Hvala vam puno na pažnji.