The Pathologist and the Pancreas: Implications for Staging and Treatment

Or
What do Patient’s Need from the Pathology Examination in 2018

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Outline

• Approach to the gross specimen
  • Frozen section
  • Determining primary site
  • Effect of neoadjuvant therapy

• What’s new in staging criteria-AJCC 8th Edition

• Challenges in biomarker analysis
  • Small samples, competing needs, primary vs metastatic sites

• Need for institution wide approach to tissue banking
FIGURE 28.1. Tumors of the head of the pancreas are those arising to the right of the superior mesenteric-portal vein confluence. Tumors of the body of the pancreas are those arising between the left border of the superior mesenteric vein and the left border of the aorta. Tumors of the tail of the pancreas are those arising between the left border of the aorta and the hilum of the spleen.
Primary Site

• Distinguishing pancreatic, cholangiocarcinoma, ampullary and duodenal primary tumors can be challenging

  • Large tumors involve overlapping sites

• Origin matters
  • Prognosis: Ampullary > Cholangiocarcinoma > Pancreatic adenocarcinoma
  • Adjuvant chemotherapy options
  • Use of neoadjuvant largely reserved for pancreatic adenocarcinoma
Changes in the Definitions of AJCC TNM Classifications

AJCC TNM 7th Edition

AJCC TNM 8th Edition

28. Exocrine Pancreas

4 Definitions of AJCC TNM

4.1 Definition of Primary Tumor (T)

4.2 Definition of Regional Lymph Node (N)

4.3 Definition of Distant Metastasis (M)

The terms pM0 and Mx are NOT valid categories in the TNM system. Assignment of the M category for clinical classification may be cM0, cM1, or pM1. Any of the M categories (cM0, cM1, or pM1) may be used with pathological stage grouping.

M Category M Criteria

cM0 No distant metastasis

cM1 Distant metastasis identified by FNA or core needle biopsy only.

pM1 Distant metastasis, microscopically confirmed
Pancreatic Ductal Adenocarcinoma is Spread to the Peripancreatic Soft Tissue in the Majority of Resected Cases, Rendering the AJCC T-Stage Protocol (7th Edition) Inapplicable and Insignificant: A Size-Based Staging System (pT1: ≤2, pT2: >2–≤4, pT3: >4 cm) is More Valid and Clinically Relevant

- Spread present in 91% of 223 Whipple specimens
- Median and 3-year survival rates of this size-based protocol were 26, 18, 13 months, and 40 %, 26 %, 20 %, respectively (p < 0.0001).

Implications of Tumor Staging in Setting of Neoadjuvant Therapy

• Embed entire pancreas to ensure accurate assessment of residual tumor and lymph node status

• Complete pathologic response associated with increased DFS and OS compared to near complete and limited response
  • He et al. Ann Surg 2018, Johns Hopkins- no details of path exam

• Inflammatory response: Should this be characterized for prognostic purposes?
  • Nejati et al. Pancreas 2017;46-1180-1187, MD Anderson
  • Quantitative immunohistochemistry on 136 cases TMA
  • High CD4+ tumor infiltrating lymphocytes associated with high CD8+
  • High CD4+ and high CD8/FOXP3 ratio associated with increased DFS and OS
Challenges in Biomarker Analysis

• Triage of tissue for molecular signatures
  • Clinical trials, chemotherapeutic choices, translational investigations

• In 70% of patients biopsy represents only tissue available for study
  • Either primary or metastatic sites

• Competing demands for small amounts of tissue
  • Tumor profiling, PD-L1, MMR, other trials-mesothelin
  • Investigational assays: stromal markers, immune cells

• Potential for different results in primary tumors and metastasis

• 2016-17: 51 requests for molecular profiling
  • Oncomine assay-mutations/amplifications in 134 genes and gene fusions (23)
  • 24 primary pancreas tumor (FNA, biopsy or resection)
  • 19 were liver, remainder other sites (eg, peritoneal, omental)
  • 14 (28%) insufficient
What Do Patients Need From the Pathologist in 2018 and Beyond

• Outstanding patient care and accurate tumor staging (pathology, radiology, endoscopy) as starting point for consideration of options
• Goal is transformation of this disease from a death sentence to prolonged survival
• Forward thinking, coordinated and synergistic approach to tissue based research
• Crucial if Yale is to be a thought leader and change agent in pancreas cancer.
  • Uniform procedures and financial support for state of the art tissue banking, including clinical annotation and serum samples
  • Up front non-clinical samples to be archived for research in all patients