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Pancreatic EUS-FNA: Current Topics and Helpful Hints

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Objectives

- Effectively communicate intra-procedurally to the performing gastroenterologist and ensure optimal specimen triage.
- Understand current practice and emerging trends in regard to EUS-guided FNAs of the pancreas.
- Gain insight into the perspective of the gastroenterologist.
- Increase awareness of potential pitfalls of solid and cystic pancreatic lesions using a case-based approach.

Factors that affect success of EUS-FNA

- Endoscopist skill
- Endoscopist experience
- Pathologist skill
- Pathologist experience
- Interaction between cytologist & endoscopist
- Tumor related factors:
  - Tumor visibility
  - Tumor accessibility
  - Tumor vascularity
  - Presence or absence of tumor necrosis

Needle Selection

- Scientific:
  - Needle size
  - Needle tip construction
  - Stylet construction/operation
  - Needle visibility during EUS
- Not-so scientific:
  - Perceived comfort of handle/ease of operation
  - Institutional vendor contracts

Role of Needle Size

- Three sizes currently available:
  - 19g
  - 22g
  - 25g
- Larger gauge needles may garner more tissue, but may also be more traumatic:
  - Bleeding
  - Pancreatitis

Effect of Needle Size on EUS FNA

- Affolter, Schmidt, Matynia, Adler, Factor DDAS 2012
- Meta-analysis of 11 studies on needle size
  - No difference in number of passes overall
  - No difference in needle visibility via EUS
  - No difference in overall penetrability
  - No difference in overall complications

Effect of Needle Size on EUS FNA

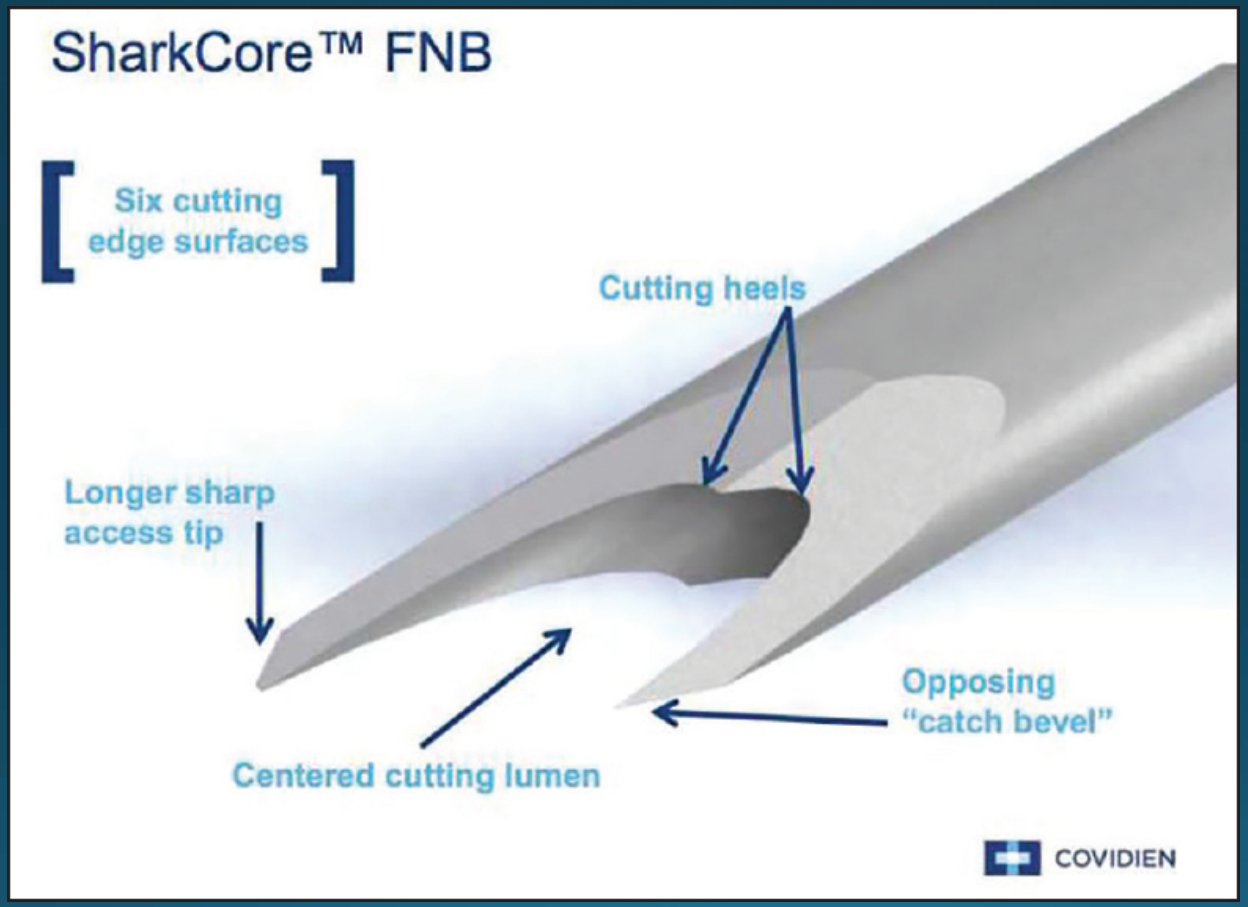
- No difference in adequacy between 19g & 22g
- When 22g and 25g needles compared:
  - 25g needles showed a trend toward greater adequacy but also showed significant heterogeneity overall
- Core needles had lowest technical success rate
  - Evaluated older, more cumbersome core needles

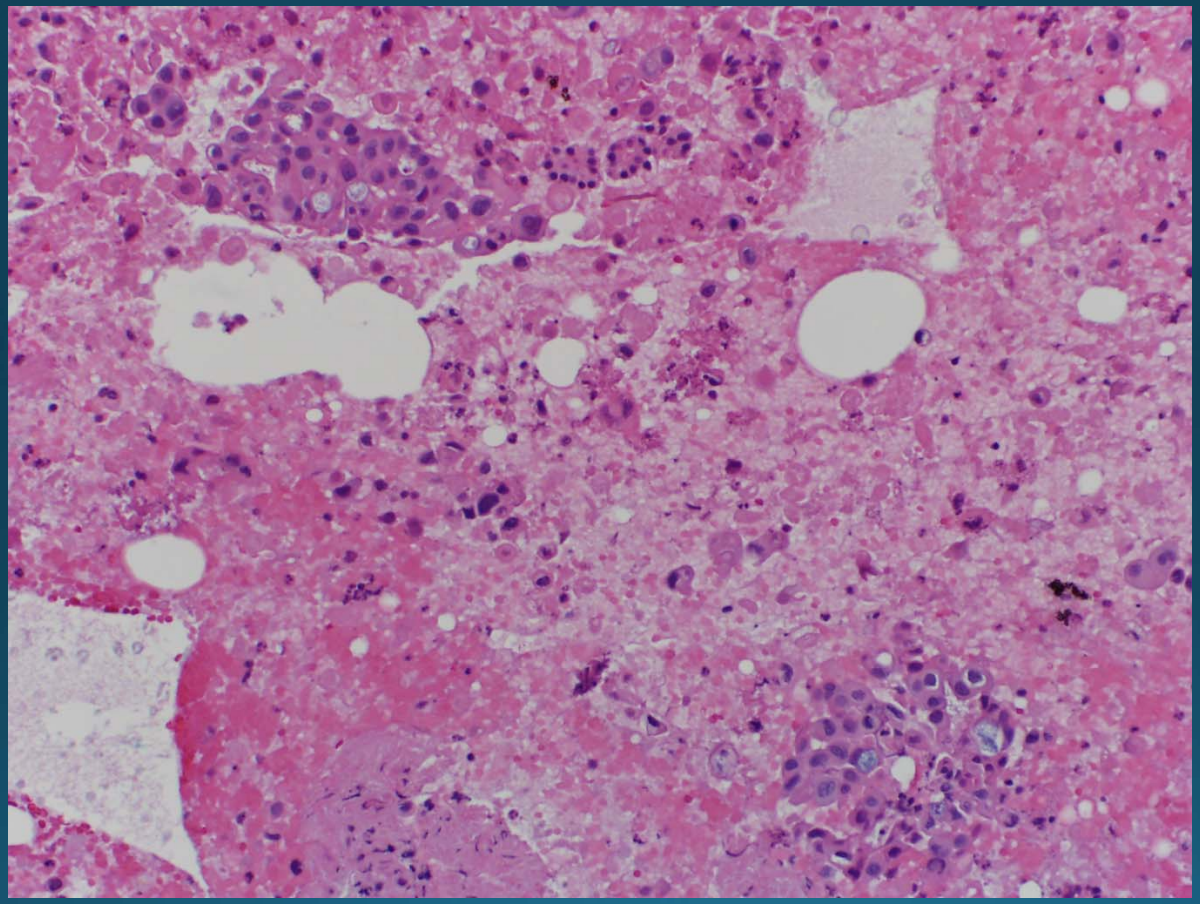
Effect of Needle Size on EUS FNA

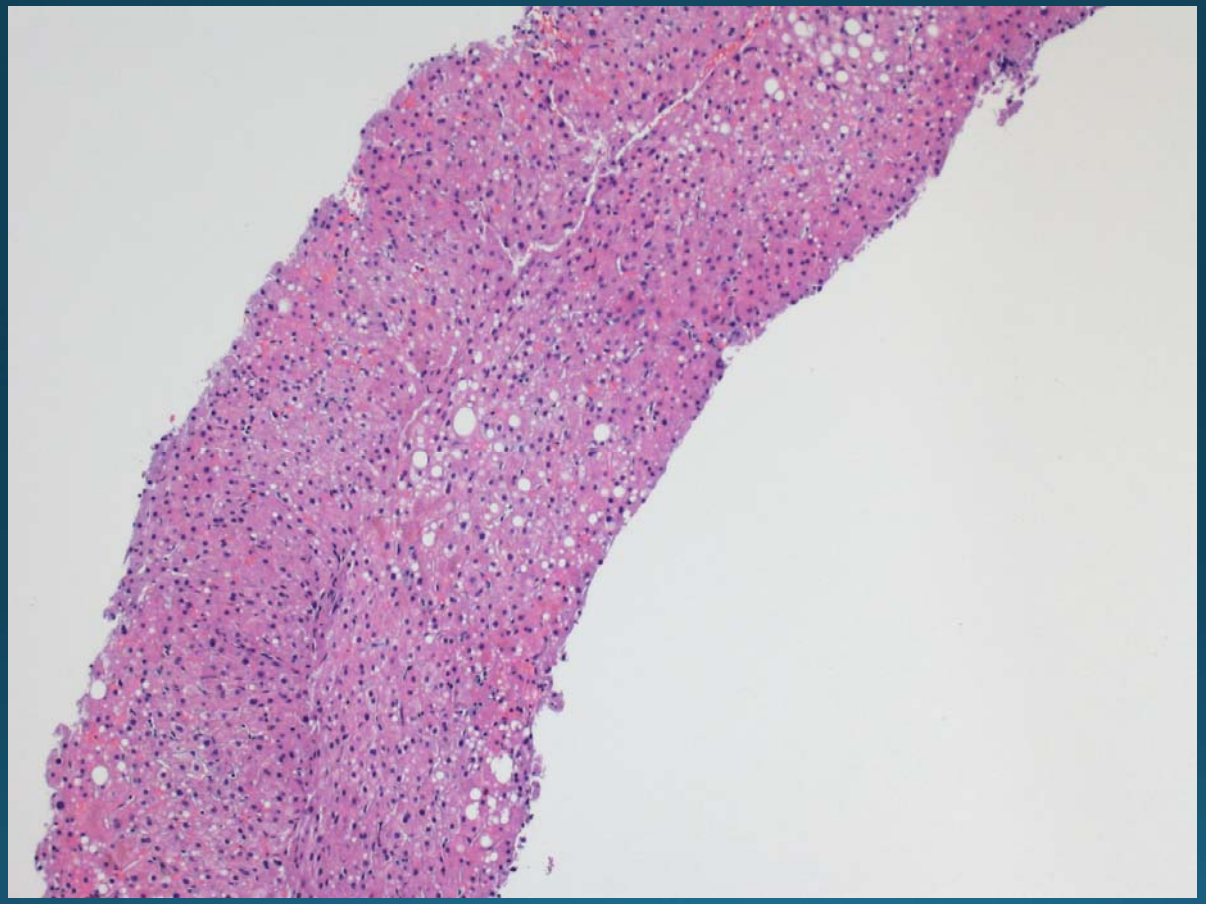
- 25G needles had a slight advantage in adequacy rates
- No overall difference:
  - Accuracy
  - Complication rates
  - Number of needle passes
  - Needle visibility
- Conclusion:
  - **Needle can be selected based on personal preference**

EUS Core Biopsies

- EUS FNA has been standard of care for over 2 decades
- Recent years have seen the development of core needles
- 19, 22, 25 gauge
- Uses
  - Obtain histology of tumors
  - Liver biopsy


SharkCore™ FNB
Six cutting edge surfaces
Cutting heels
Longer sharp access tip
Opposing "catch bevel"
Centered cutting lumen
COVIDIEN





Adler et al EUS 2016

- Retrospective analysis comparing a EUS FNB needle (SharkCore, Covidien, Dublin, Ireland) to a standard cytology needle (EchoTip, Wilson Cook, Winston Salem, NC)
- 30 patients
- The FNA needle required fewer needle passes to obtain diagnostic adequacy than the standard needle [$P < 0.001$].
  - The FNB needle required 1.5 passes to reach adequacy, whereas the standard needle required 3 passes.
  - For cases with cell blocks, the FNB needle produced diagnostic material in 85% of cases, whereas the standard needle produced diagnostic material in 38% of the cases.
  - The FNB needle produced actual tissue cores 82% of the time and the standard needle produced no tissue cores.

Dewitt EIO 2015

- Compared a new EUS needle designed to obtain a tissue cores (ProCore, Wilson Cook, Winston Salem NC) to a much older device (TruCut, Wilson Cook, Winston Salem NC).
- 85 patients undergoing liver biopsy and pancreatic biopsy for a variety of benign and malignant conditions.
- The new EUS core needle specimens had a higher prevalence of diagnostic histology (85% vs. 57%; P=0.006), accuracy (88% vs. 62%; P=0.02), mean total tissue sample length (19.4 vs. 4.3 mm; P=0.001), and mean complete portal triads from liver biopsies (10.4 vs. 1.3; P=0.0004).

Kandel GIE 2016

- Retrospective case-control study comparing FNA to FNB.
- 95% of the specimens obtained from the EUS-FNB group were of sufficient size for histological screening, compared to 59% from EUS-FNA group (P =0.01).
- The median number of passes required to achieve a sample was significantly lower in the EUS-FNB-SC group compared to EUS-FNA group (2 passes vs 4 passes, P = 0.001).

FNA vs. FNB

FNA

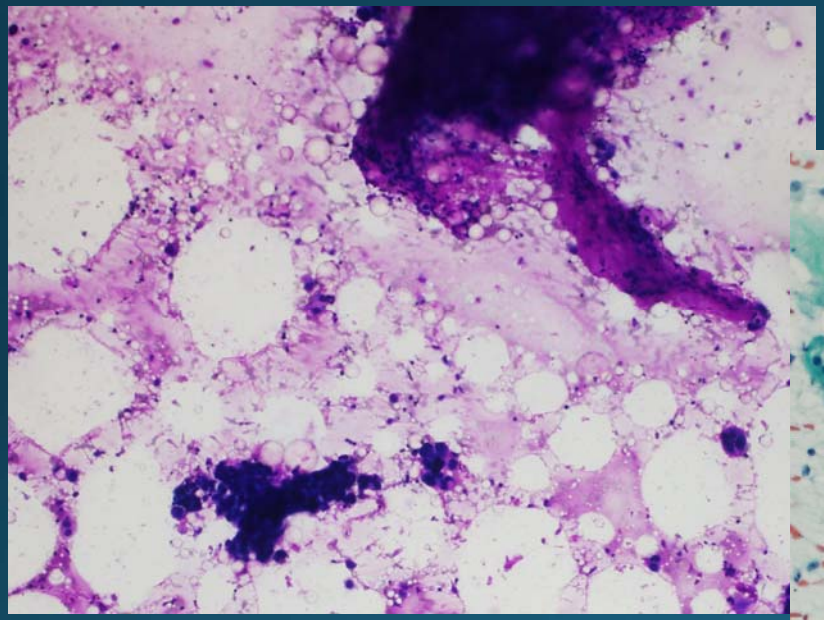
- Simple
- Easy
- Safe
- $$

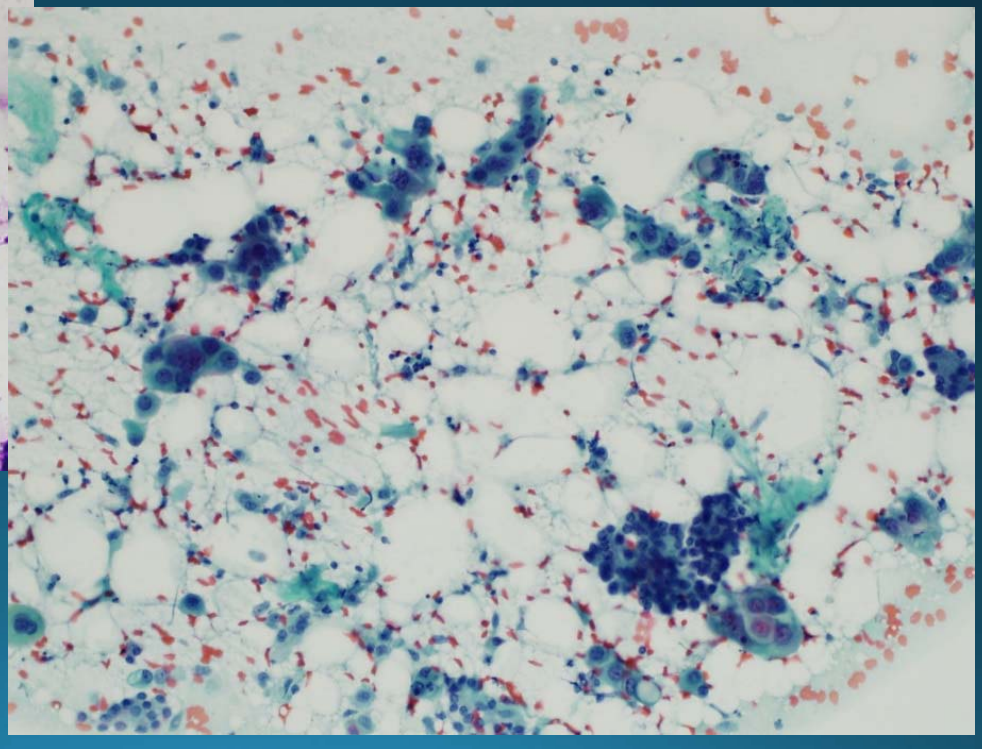
FNB

- Simple
- Easy
- Safe
- $$$

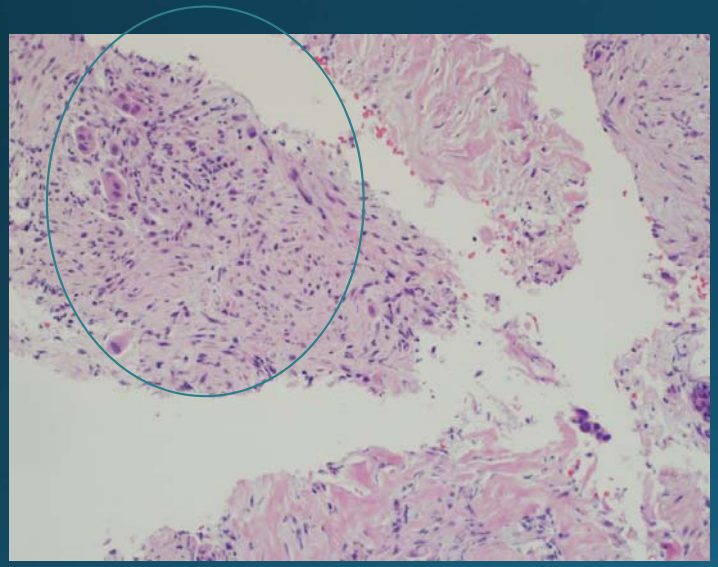
- Maybe you don't need ROSE…

Squash Preparation With New Biopsy Needle Type

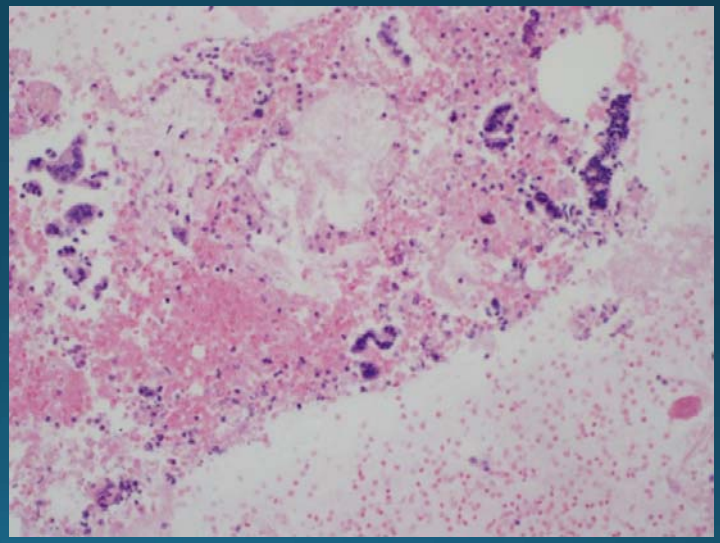




New Biopsy Needle Type



Standard Needle Cell Block



Pathologist View On New Biopsy Needle Type vs Standard Needle

- Nine out of 10 pancreatic malignancies are adenocarcinomas (Cancer 2014;122:399-411)
- Pooled sensitivity and specificity for EUS-FNA for pancreatic ductal adenocarcinoma is 88.6% and 99.9%, respectively [Cytopathology 2013;24(3): 159-71]
- Standard needle 'not broken' with regard to assessment of adenocarcinoma in solid masses….**but**

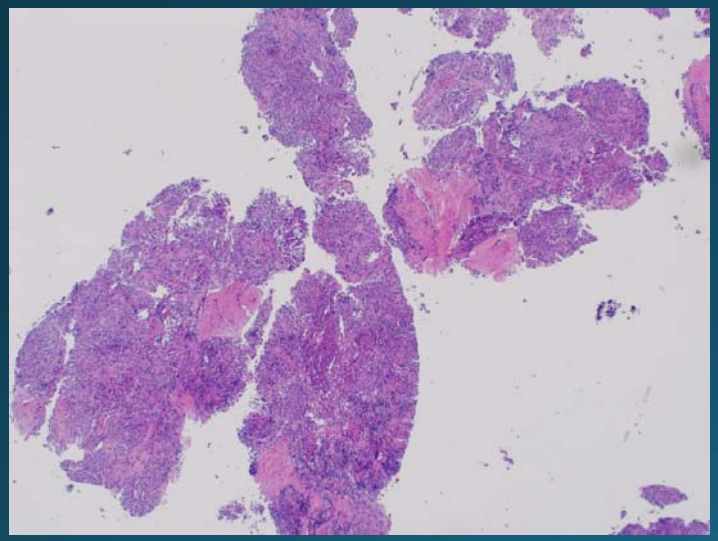
Newer EUS Biopsy Type Needle for Neuroendocrine Tumors

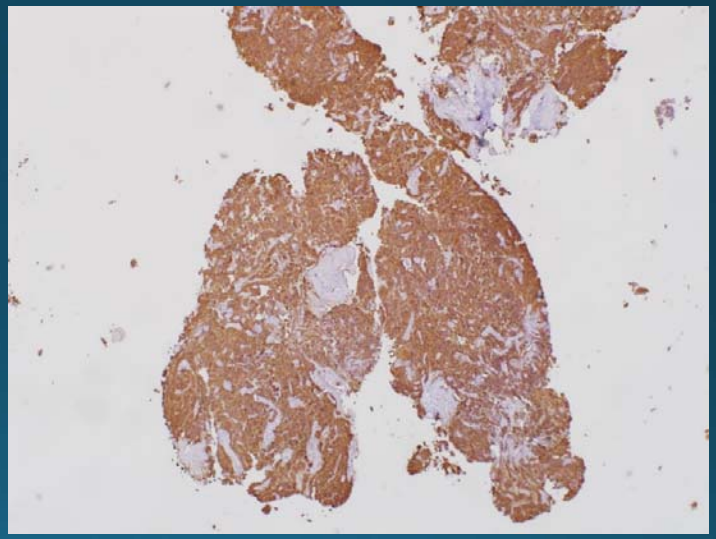
- 15 year retrospective data at our own institution found only 66% sensitivity for EUS-FNA diagnosis of pancreatic NET
- Recently we conducted a pilot study on 20 patients to evaluate value of new biopsy needle type with respect to diagnosis of NET (unpublished)
- Slight trend towards more definitive reporting in new biopsy needle type compared with standard needle type

Production of Diagnostic Material in Cell Blocks

Diagnostic Material Produced	Standard Needle	New Biopsy Type Needle	Total
Yes	6	10	16
Cores/Core fragments/Large clusters	6	8	14
Single cells only	0	2	2
No	4	0	4
Total	10	10	20

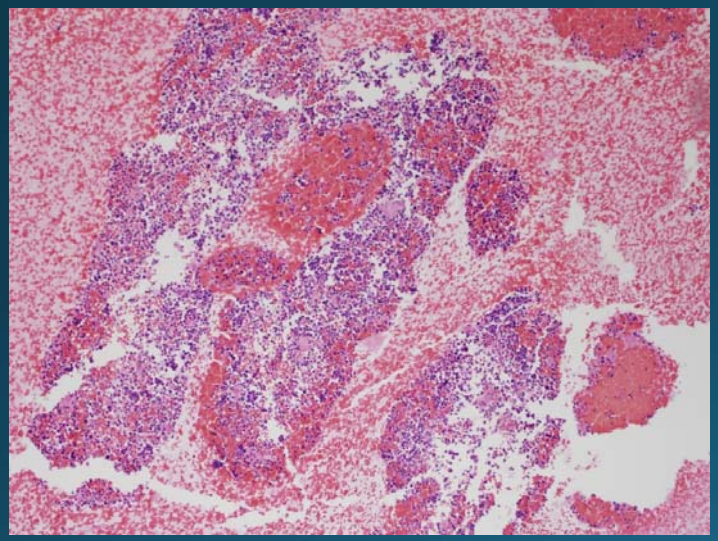
New Core Needle Type

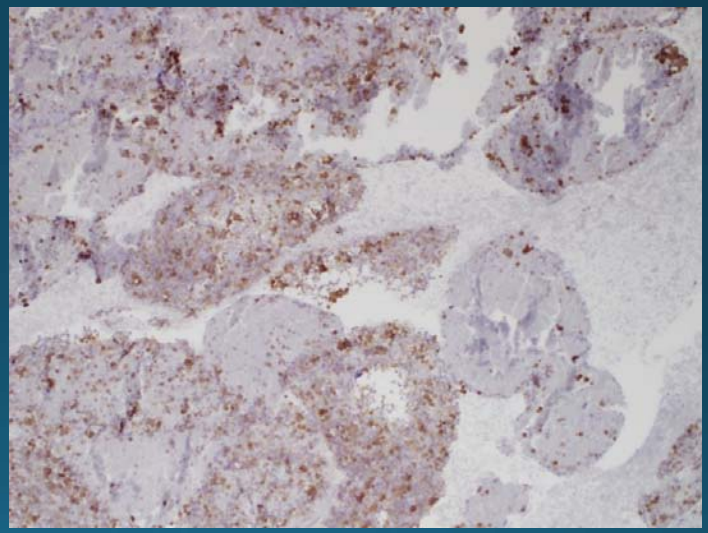




Synaptophysin

Standard Needle Type



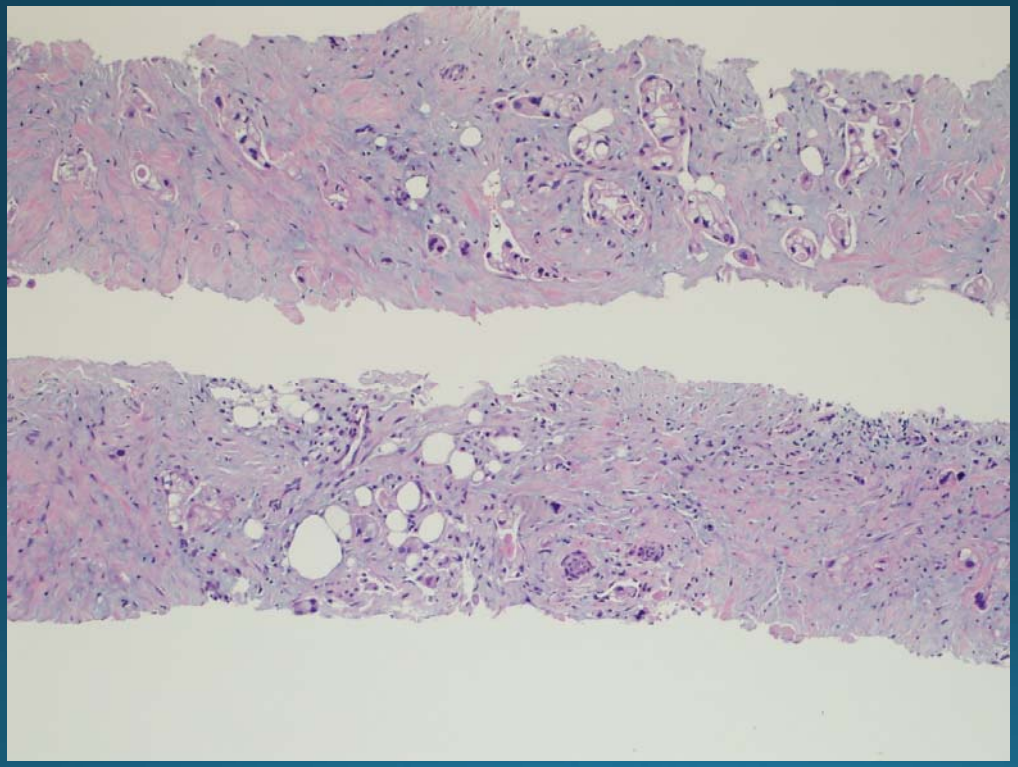


Synaptophysin

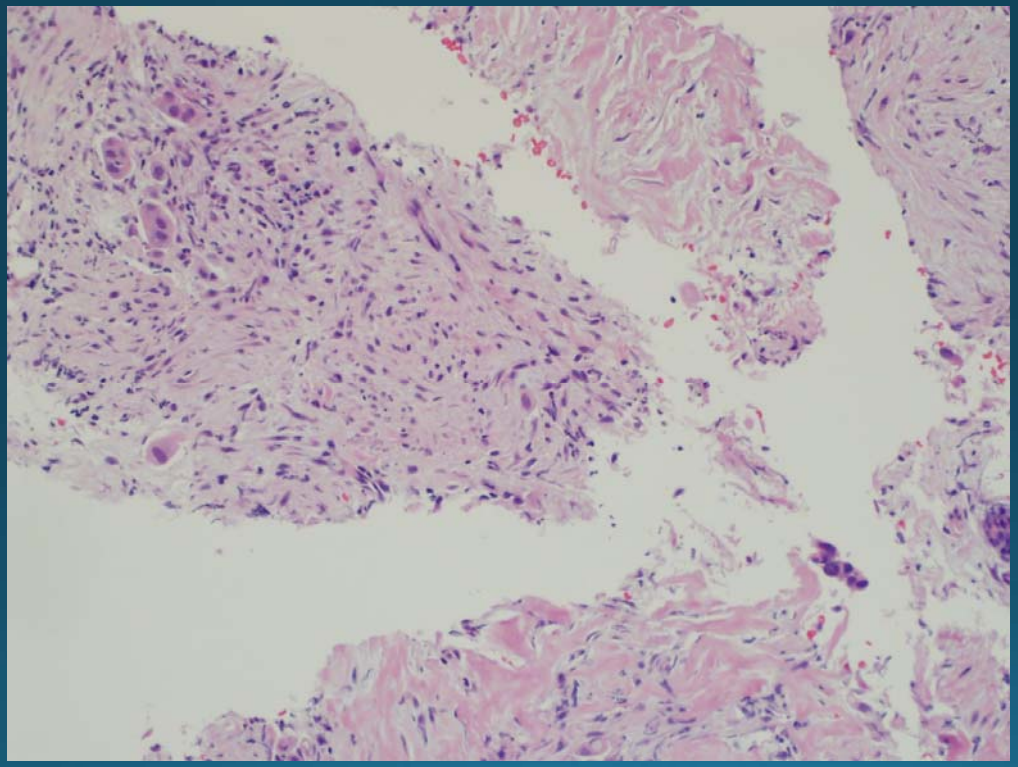
Pathologist View On New Biopsy Needle Type vs Standard Needle

- Based on preliminary experience I think having this option for tumors that fall into cytomorphologic differentials, possible metastases, or stromal tumors is useful
- NET, Acinar cell carcinoma, Solid pseudopapillary tumor, Plasmacytoma differential
- GIST, schwannoma, leiomyoma differential
- But I believe only needed in select case types
- Can be part on ROSE determination

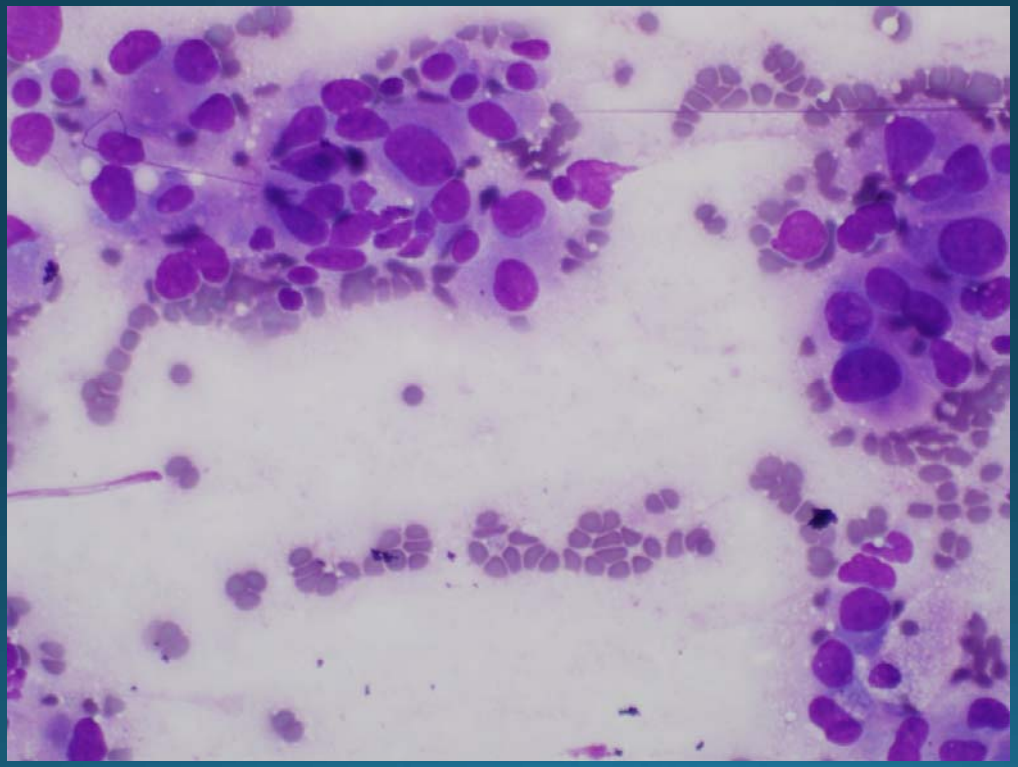
Although you can get this….



Sometimes you get this….



And I prefer this to the latter



Goals of ROSE in FNA Cytology

- Optimize aspirate smears.
- Inform the operator of specimen adequacy.
- Avoid the need for repeat procedures.
- Garner a preliminary diagnosis.
- Determine whether ancillary studies are required to render a diagnosis and appropriate the specimen accordingly.

How to Determine the Effect of ROSE

- Optimal studies are those that compare the performance of 2 cohorts (with and without ROSE).
- Studies that are conducted at a single institution.
  - Minimizes operator and assessor variability
  - Minimizes variation in technique (needle size/type)

Systematic Review and Meta-Analysis on Impact of ROSE on Adequacy (Multiple Body Sites)

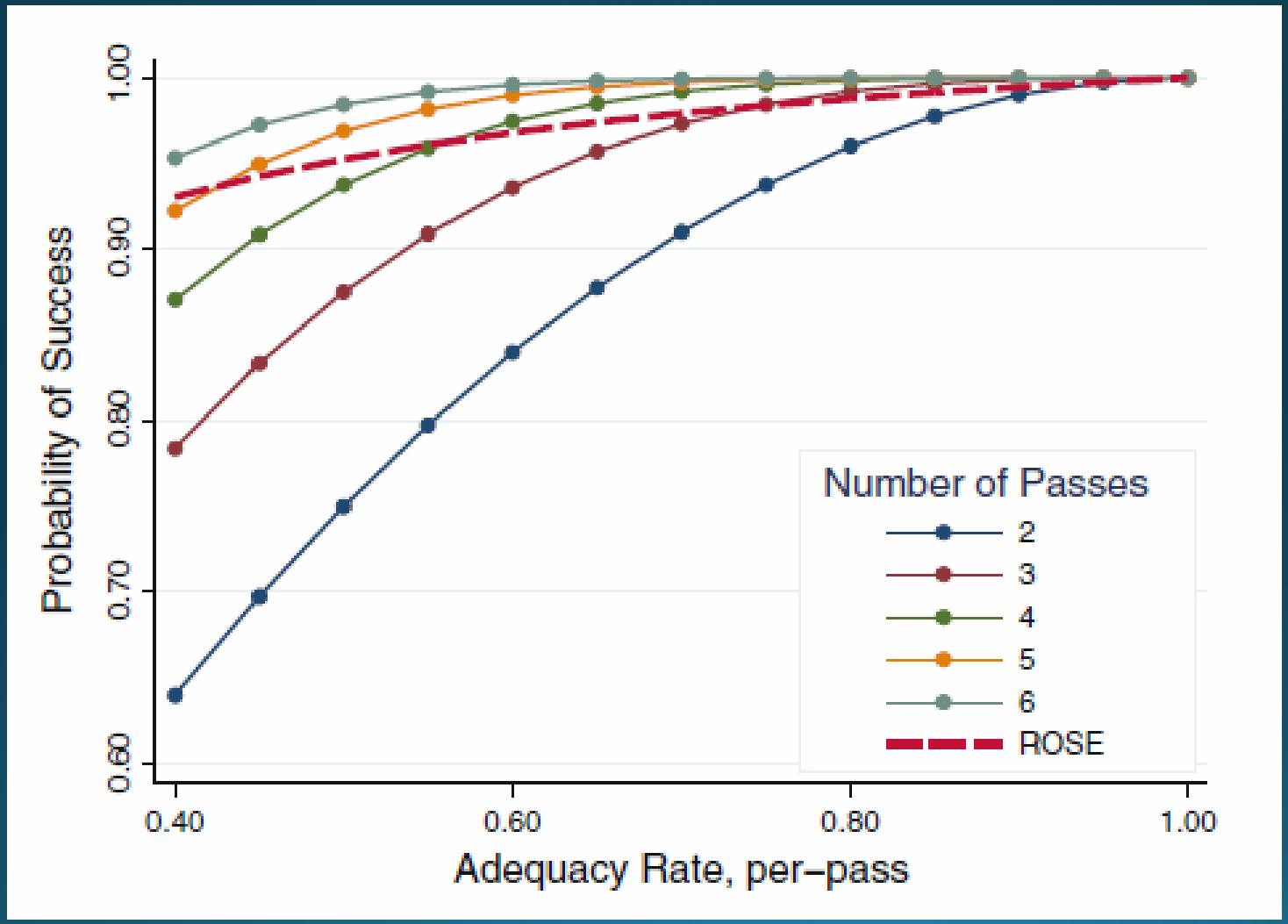
- All anatomic sites included
- 25 articles met our inclusion criteria (MEDLINE and EMBASE) from 9 anatomic sites
- Findings:

  - Overall ROSE improves per case adequacy rate by 12%
  - ROSE had a statistically significant impact on adequacy in 6/9 anatomic sites studied
  - Non-ROSE adequacy rate was the most significant confounder

Schmidt et al. *Am J Clin Pathol* (2013);139:300-308

ROSE Versus Non-ROSE (How It's Impact Relates to Initial Adequacy)

Study	Without ROSE Success Rate	With ROSE Success Rate	Difference with Implementation of ROSE
Alsohaibani	14/22 (63.6%)	14/22 (63.6%)	0%
Cleveland	24/24 (100%)	198/200 (99%)	-1.0%
Iglesias-Garcia	76/87 (87.3%)	94/95 (98.9%)	+11.6%
Klapman	35/48 (72.9%)	79/85 (92.9%)	+20%
Total	311/395 (78.7%)	509/569 (89.4%)	+10.7%
Nguyen (abstract)	22/56 (39.3%)	54/55 (98.2%)	+58.9%
Saleh (EUS-guidance not specified)	15/23 (65.2%)	8/12 (66.7%)	+1.5%
Total	348/474 (73.4%)	571/636 (89.8%)	+16.5%


Probability of Success
0.60
0.70
0.80
0.90
1.00
0.40
0.60
0.80
1.00
Adequacy Rate, per–pass
Number of Passes
2
3
4
5
6
ROSE

Collins, Murad, Wang, Bernadt. Cancer Cytopathol. 2013;121:518-524

- 3 year look back at cohorts of 379 and 377 patients undergoing EUS-FNA with and without ROSE, respectively
- Use of ROSE decreased the percentage of repeat procedures by 50% (11 with ROSE, 22 without)
- The second biopsies performed in the ROSE cohort had a higher rate of definitive diagnosis (63%) compared with non-ROSE cohort (27%)

Conclusions of ROSE Impact on EUS-Guided Pancreatic FNA

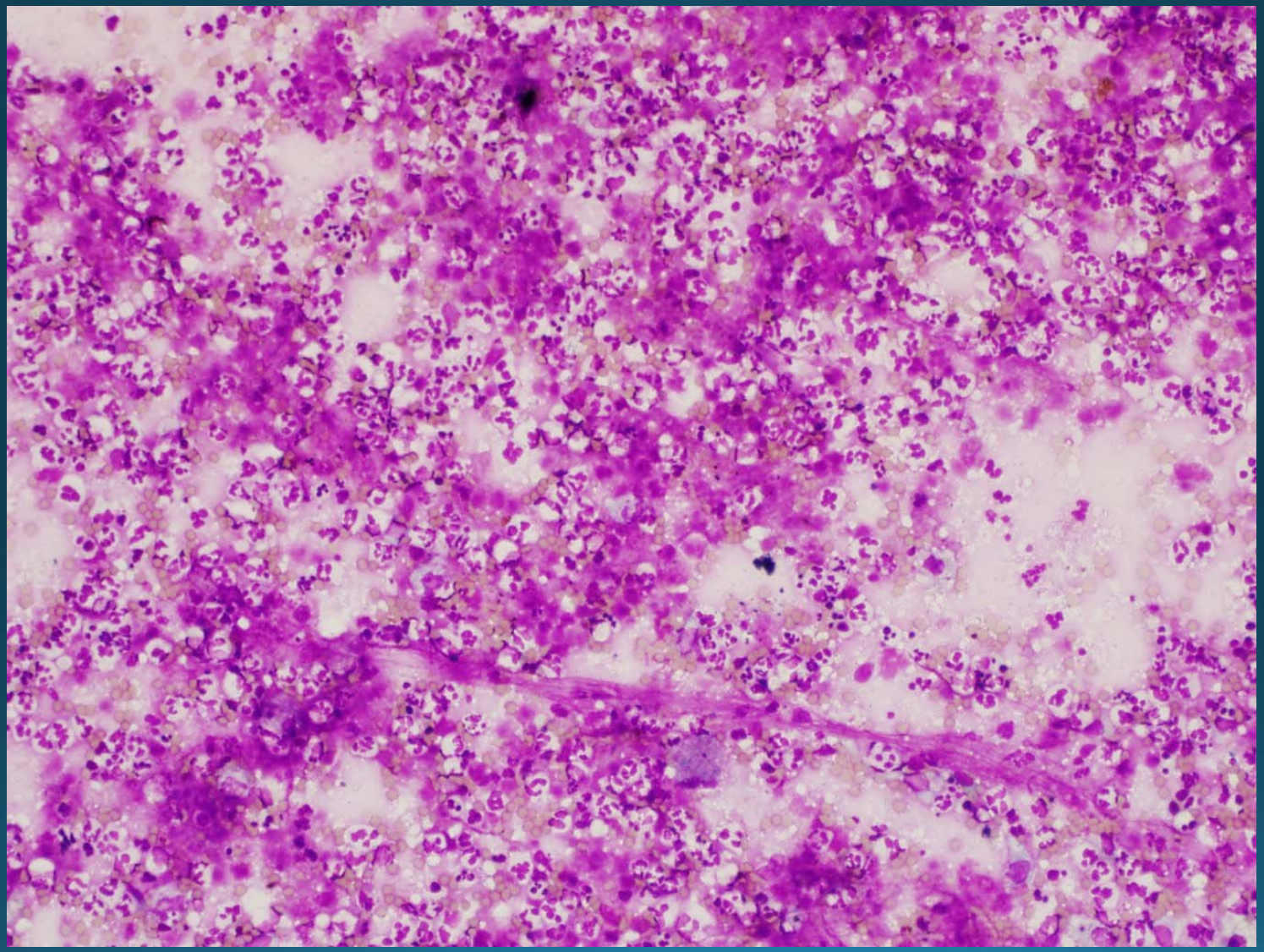
- ROSE frequently can have a statistically significant impact on adequacy rates when implemented at locations where the per-case adequacy rate without ROSE is low (<90%)
- ROSE appears to decrease the rate of need for repeat biopsy
- ROSE can allow for communication to endoscopist to utilize core biopsy needle type in selected cases where robust cores are needed for IHC
- Does not seem to minimize procedure time, risk of procedure

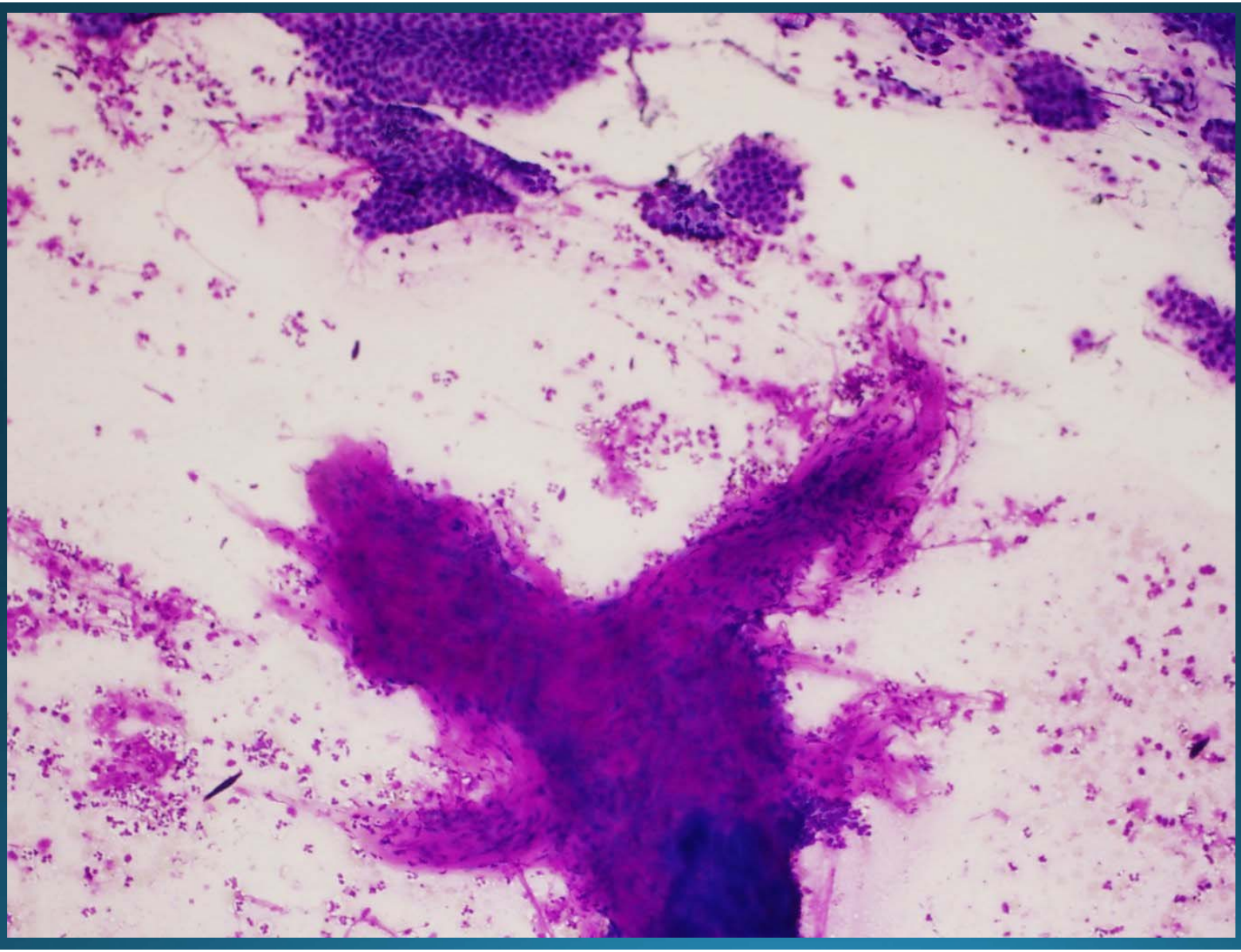
Pitfall 1: Mistaking Reactive Epithelium for Carcinoma

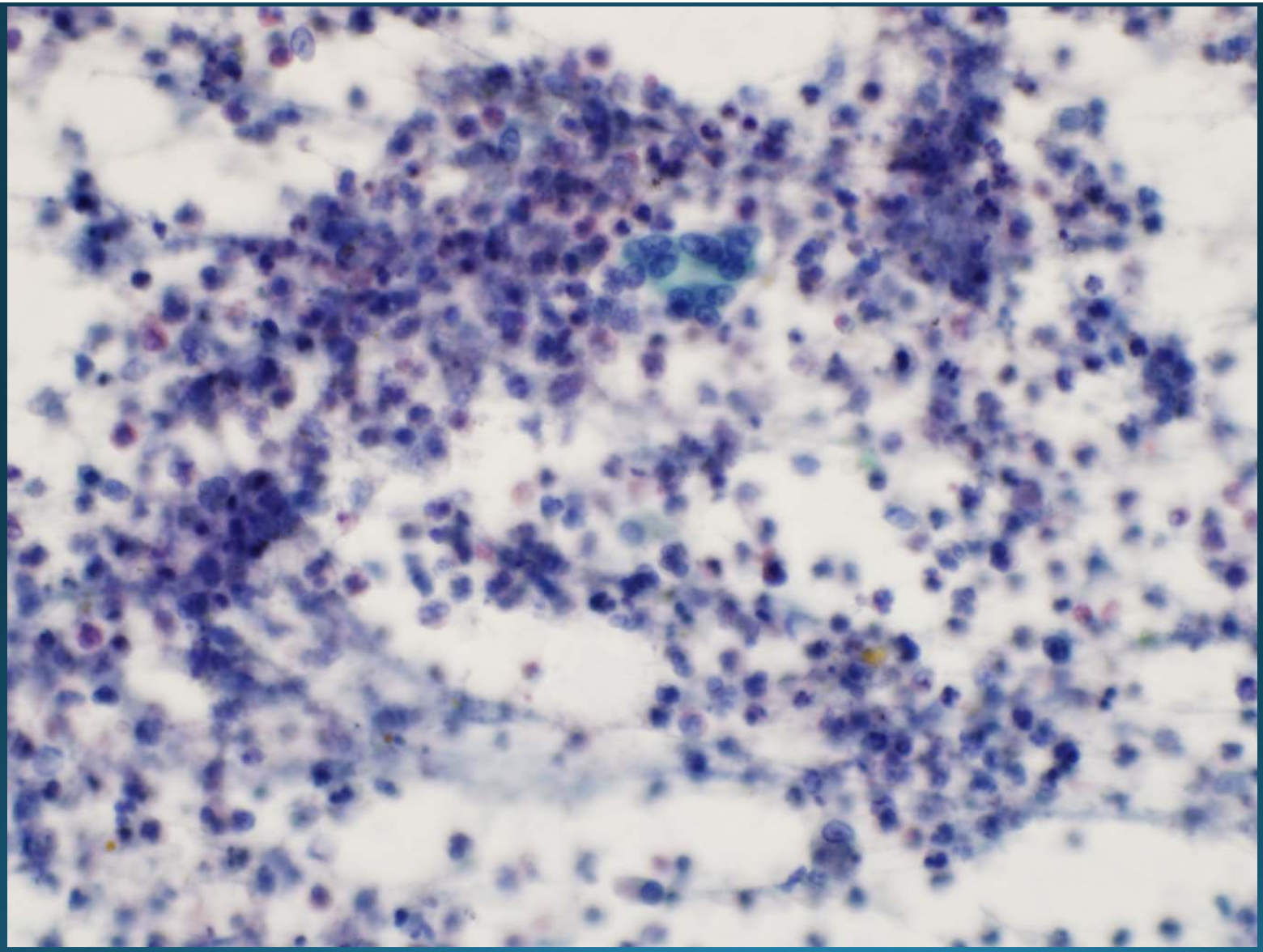
- 65 year old male with ill-defined 5 cm pancreatic head mass
- History of ETOH abuse and chronic pancreatitis

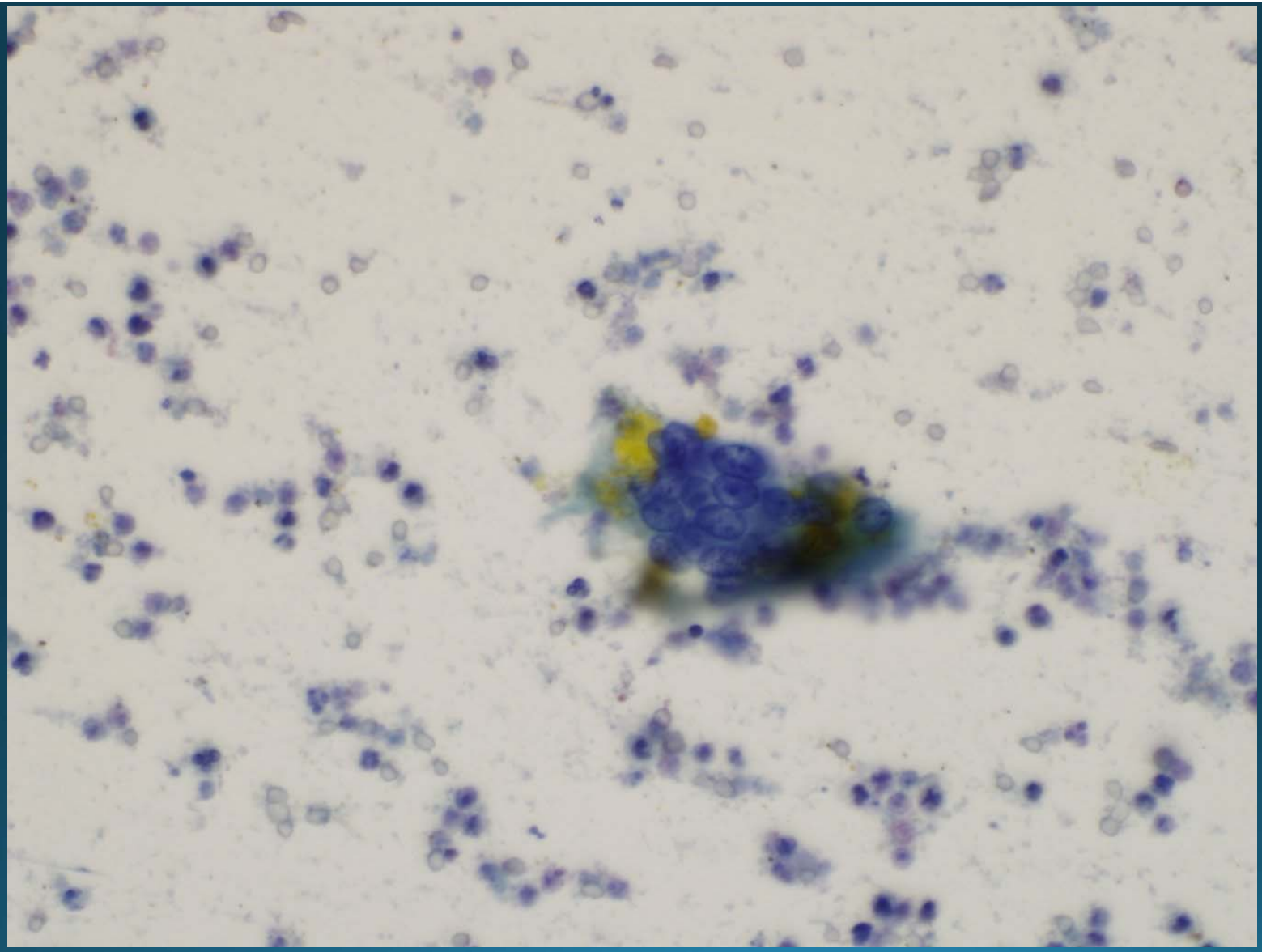

F13
7.5M 5.0 R06 G60 C5


F13
7.5M 5.0 R06 G60 C5

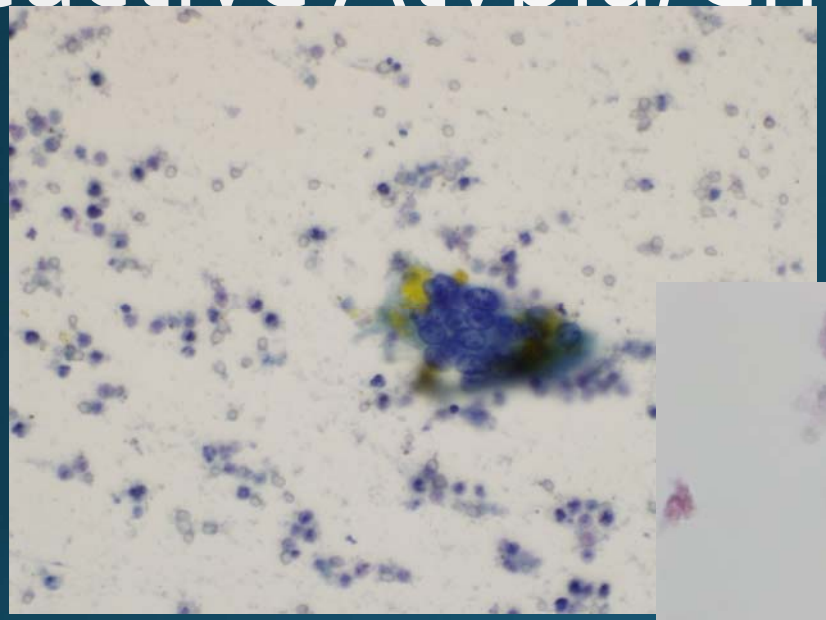






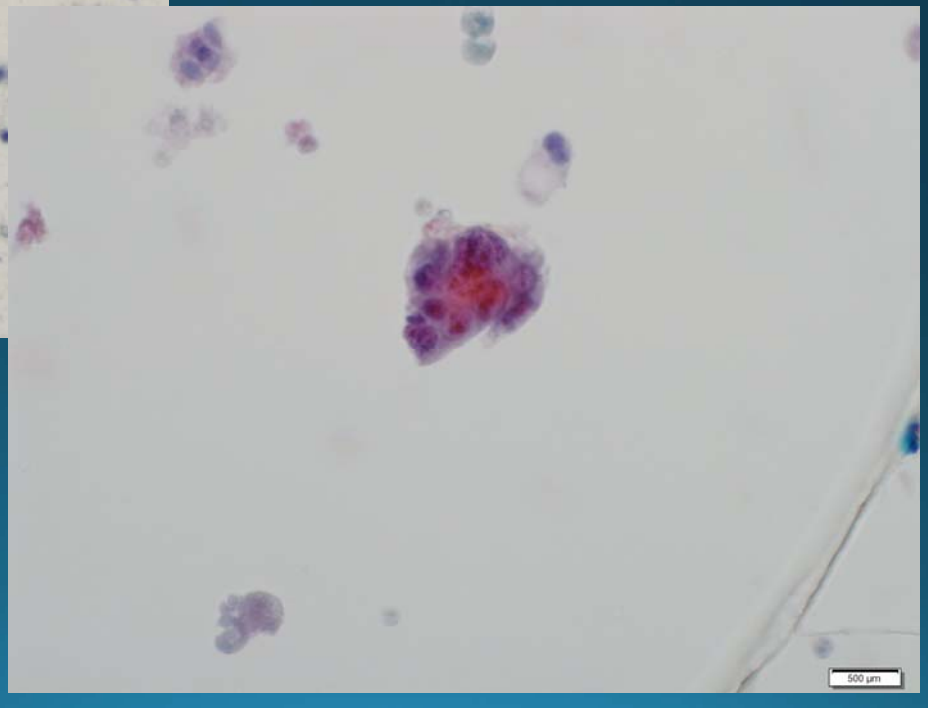


Reactive Atypia/Changes



Reactive

Adenocarcinoma

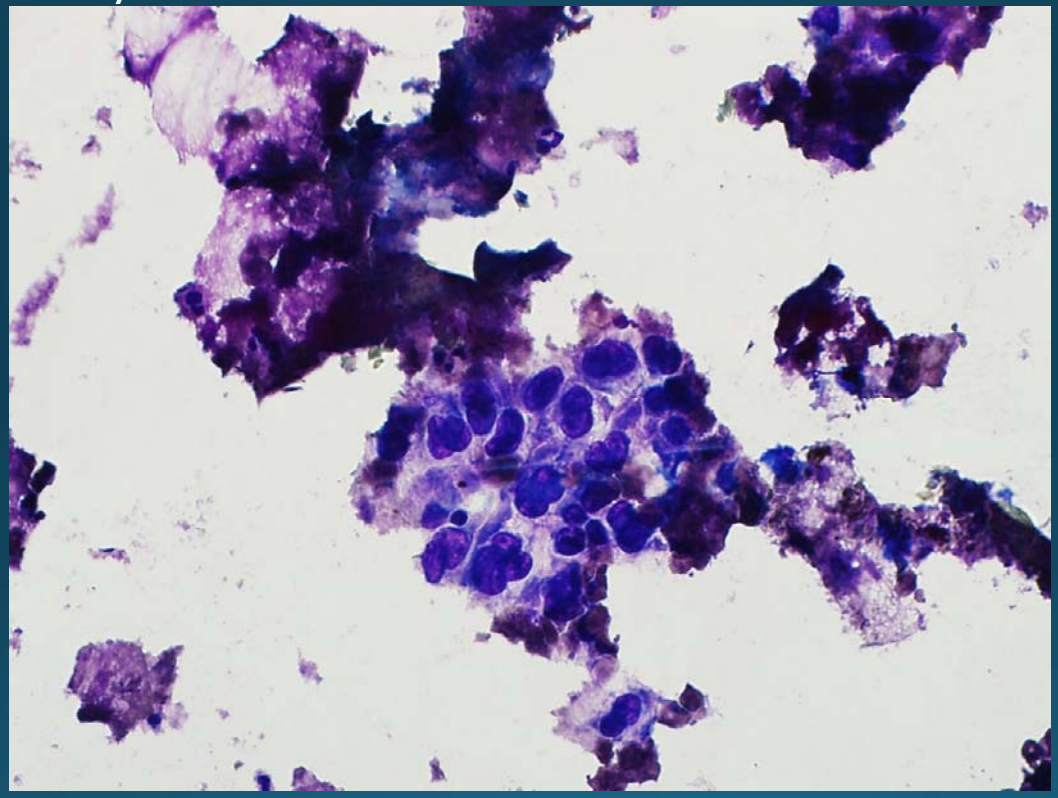


Clues for Reactive Ductal Atypia

- Background inflammation
- Usually more even cell spacing but can tolerate crowding
- Can tolerate nuclear enlargement but nuclei stay round to oval
- Less than 4:1 nuclear size variation in same group
- Low N/C

Cibas and Ducatman. Cytology Diagnostic Principles and Clinical Correlates. 4th Edition. 2014

When to invoke 'Atypical': Pap Society Recommendation

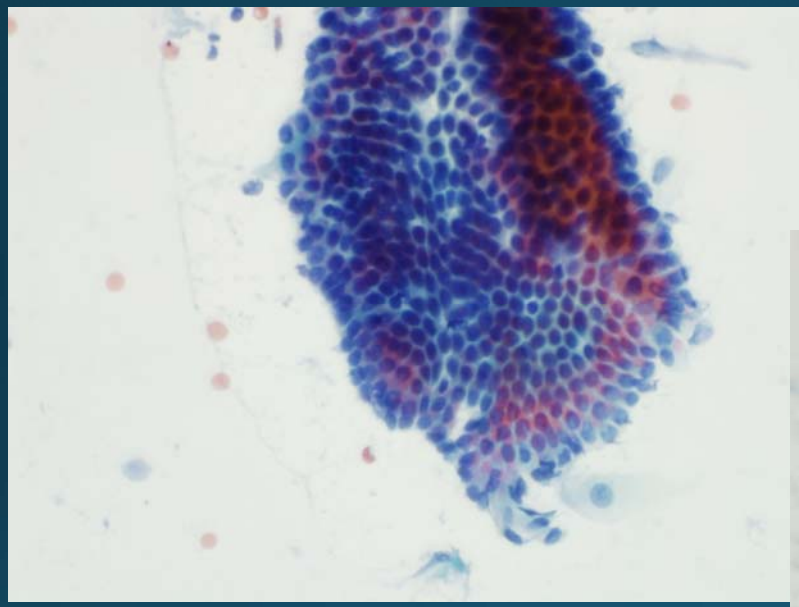


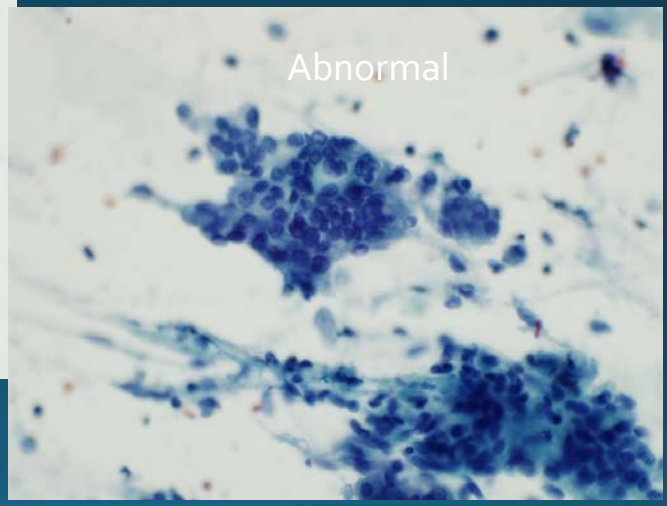
Presence of cellular (nuclear or architectural) features that are not consistent with normal or reactive cellular changes, and are insufficient to classify them as a neoplasm or suspicious for a high grade malignancy. Risk of malignant outcome is 58%-79% based on recent meta-analyses [Diagnostic Cytopathology 2017;45(1):3-13]

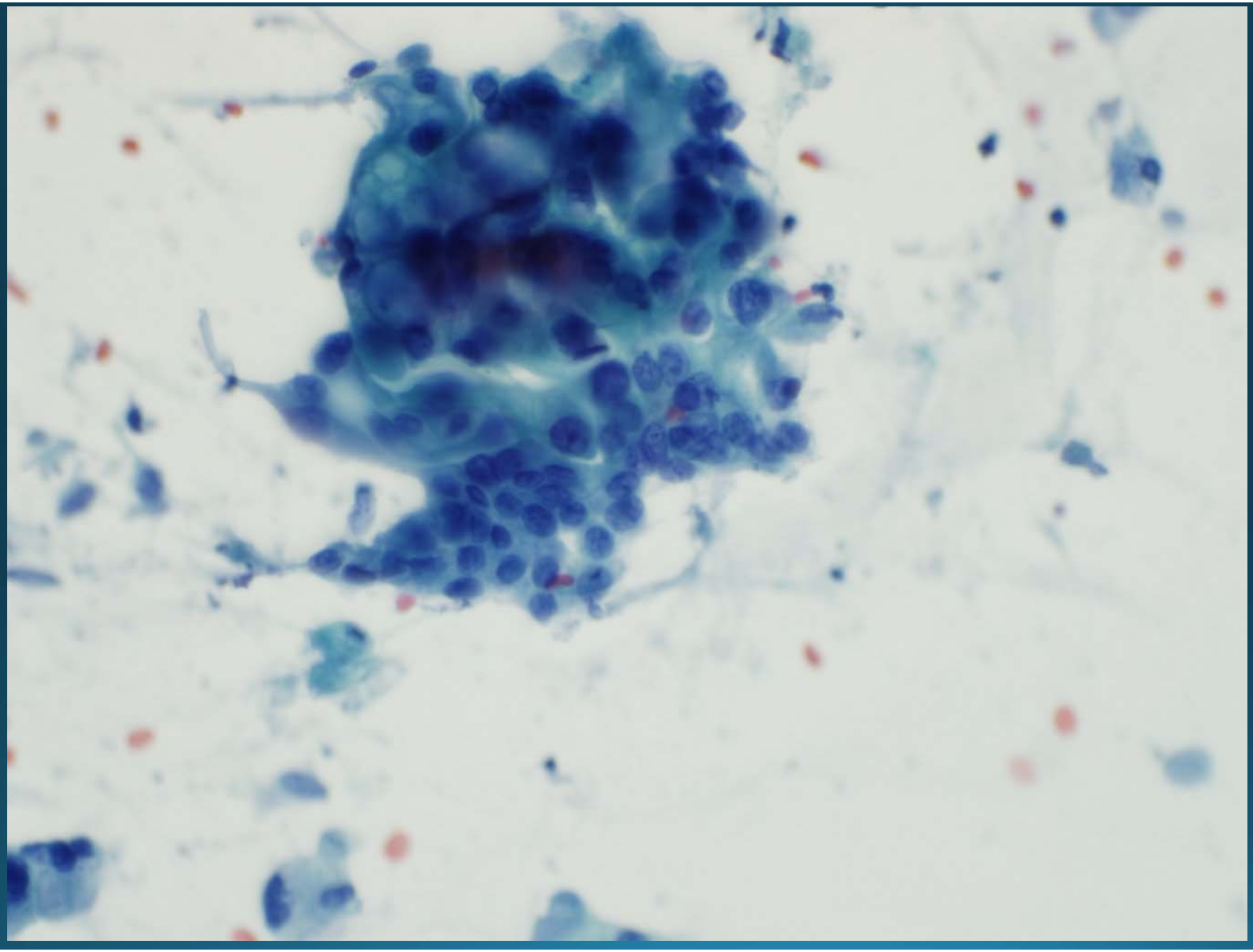
Pitfall #2: The Diagnosis of Well Differentiated Adenocarcinoma

- 70 year old female with a 4 cm mass located in the uncinate with ill-defined borders
- Suggestion of SMA encasement on ultrasound

Normal







Well-Differentiated Adenocarcinoma

- Need good radiologic correlation to ensure solid mass
- Diffuse architectural atypia is often what tips the balance (drunken honeycomb)
- Focal areas of conclusive nuclear features

Climbing the Feature Ladder to Adenocarcinoma

- **Nuclear enlargement (3x size of RBC)**
- **Anisonucleosis (4x nuclear size variation in same group)**
- **Nuclear molding (nuclei don't respect each other)**
- Nuclear contour irregularity
- Chromatin clumping (Pap stain)

- The three bolded criteria had a sensitivity of 98% and a specificity of 100%

Cohen et al. Diagnostic Cytopathol. 1991;7(4):341-45

When to Invoke Suspicious: Pap Society Recommendation

- When some but an insufficient number of the typical features of a specific malignant neoplasm, mainly adenocarcinoma, are present.
- When the morphologic features are sufficiently atypical that malignancy is considered more probable than not
- Risk of malignant outcome with suspicious category ranges for 85% to 96.3% in recent meta-analyses
- Certainly a subset of well-differentiated adenocarcinomas remain in the 'suspicious' category

IHC Markers and Adenocarcinoma: Possible Utility of Robust Cell Block

- Loss of Smad4 immunolabeling
- Smad4 is an immunolabeling surrogate for the product of the gene SMAD4
- Lost in over 50% of adenocarcinomas; never lost in benign epithelium

Pitman MB and Layfield LJ. Cancer 2014;122:399-411

Pitfall 3: PanIN3 Mimicking invasive adenocarcinoma

- 15 year retrospective review of EUS-FNA pancreas cases having follow-up histologic correlation
- 2 cases called adenocarcinoma at FNA ended up being PanIN3 with no invasive carcinoma on histology

Jarboe EA and Layfield LJ. Diagn. Cytopathol. 2011;39:575-581

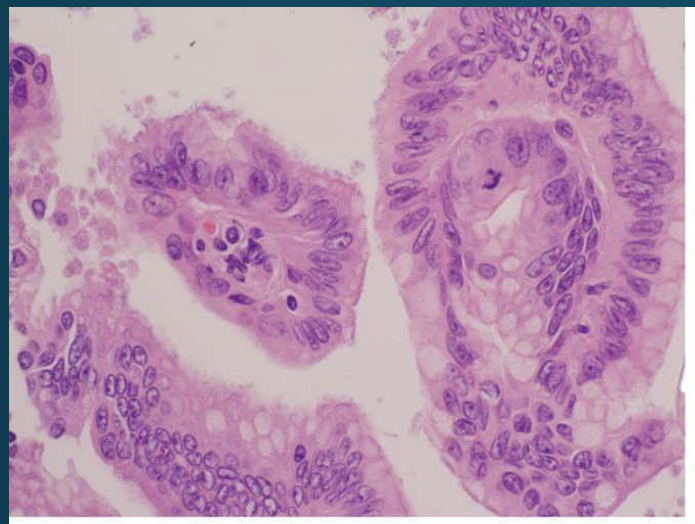


Fig. C-8

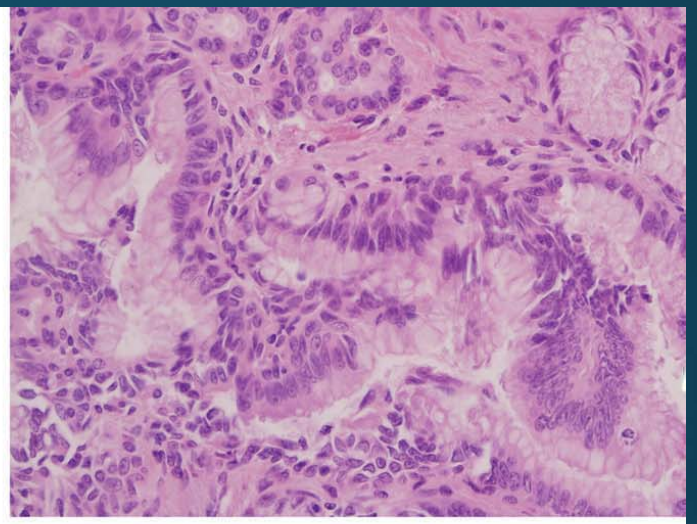
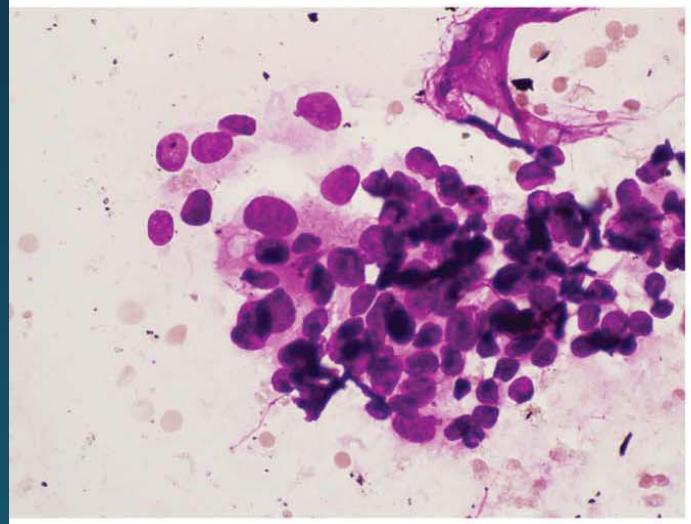
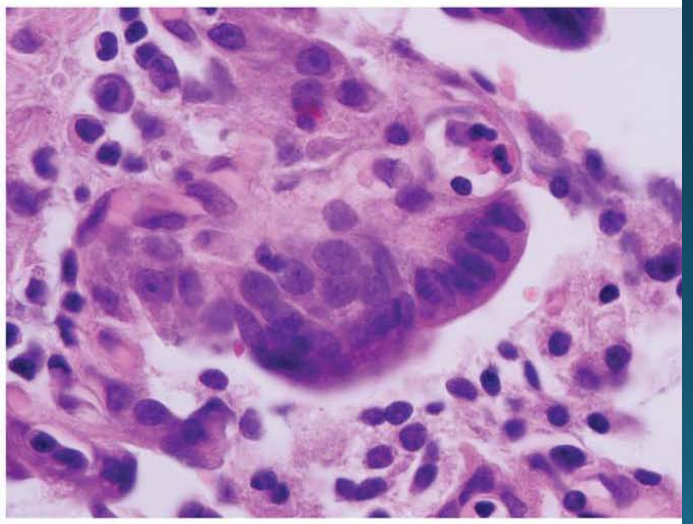


Fig. C-9





Adapted from: Jarboe EA and Layfield LJ. Diagn. Cytopathol. 2011;39:575-581

Pitfall 3: PanIN3 Mimicking invasive adenocarcinoma

- In cases where PanIN was misinterpreted as adenocarcinoma the atypical cells were restricted to a few cell clusters (2-3 per slide) with only rare atypical individual cells
- They met the qualitative criteria for malignancy
- May not have me the qualitative criteria for malignancy

Jarboe EA and Layfield LJ. Diagn. Cytopathol.

Gleeson et al. Gut 2010;59:586-594

- Over a 12 year period included only suspicious or positive FNA results that had resection with no intervening chemo/rads
- For EUS FNAs of the pancreas there was a 2.2% FP risk (5/230)
- 4/5 were chronic pancreatitis
- 1/5 was a pseudocyst
- Upon retrospective review 4 cases were attributed to cytopathologist 'over-interpretation' of atypical cells or histiocytes

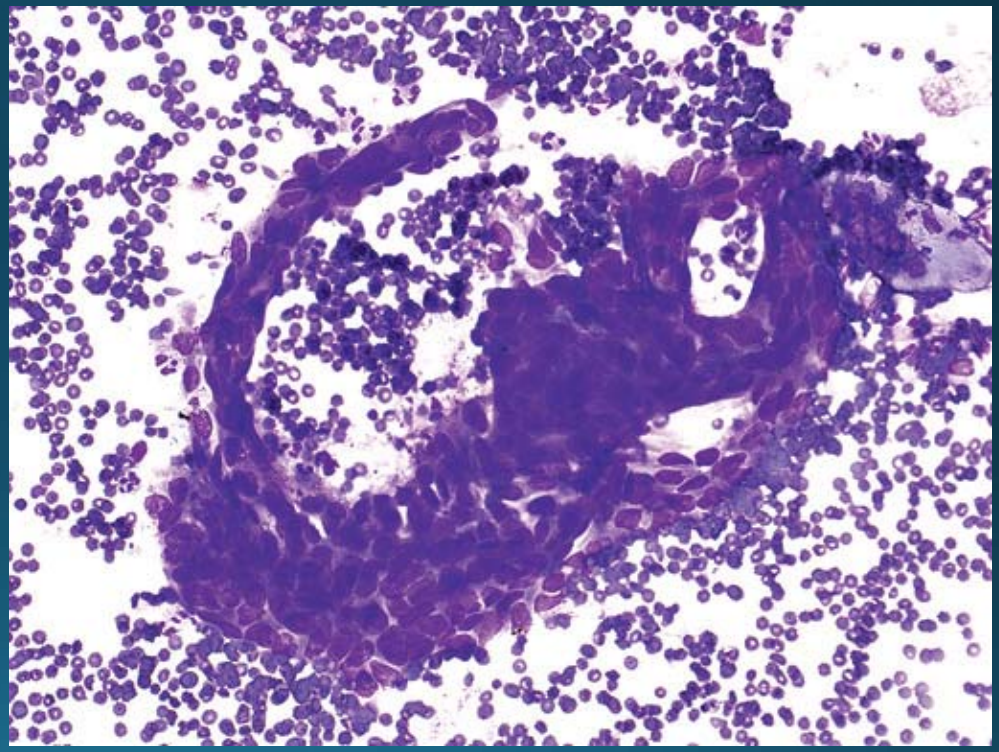
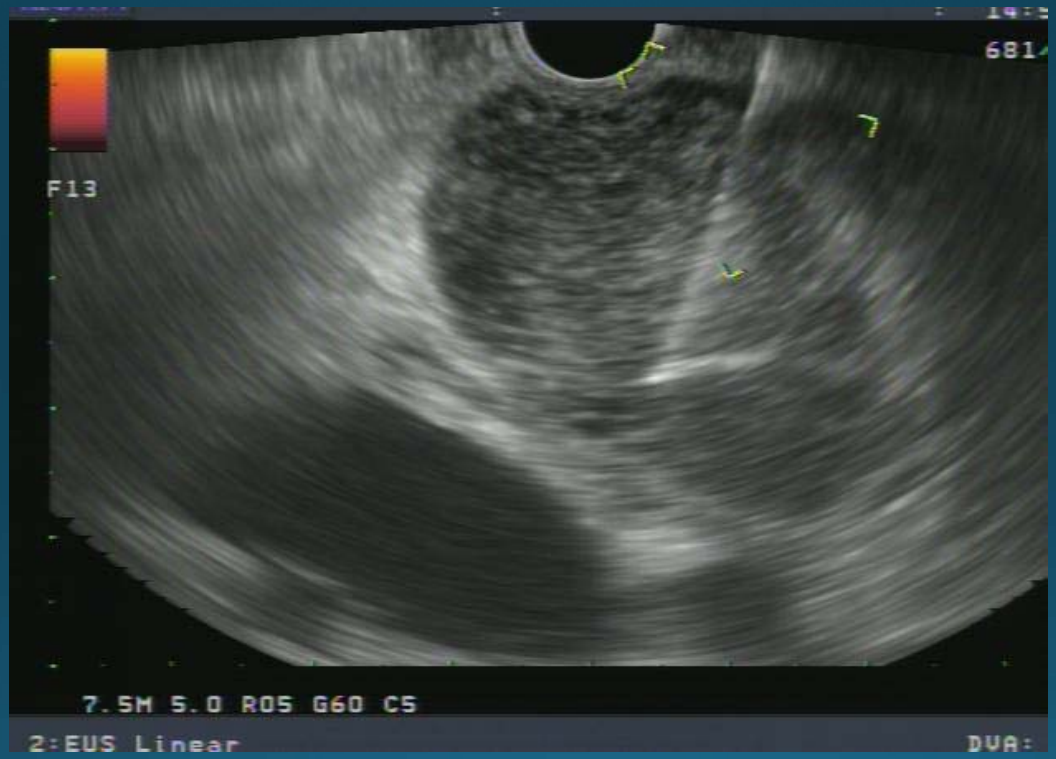
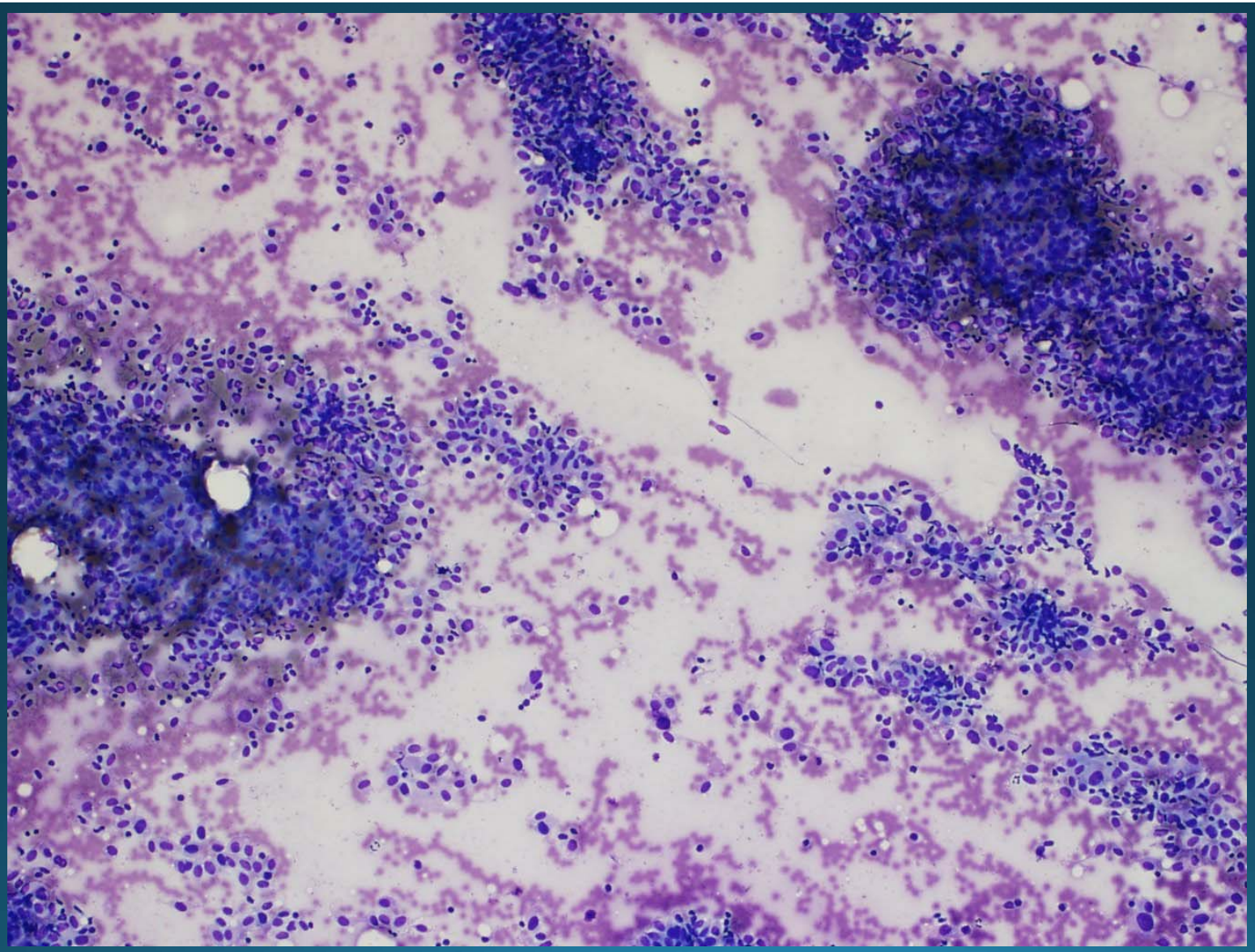


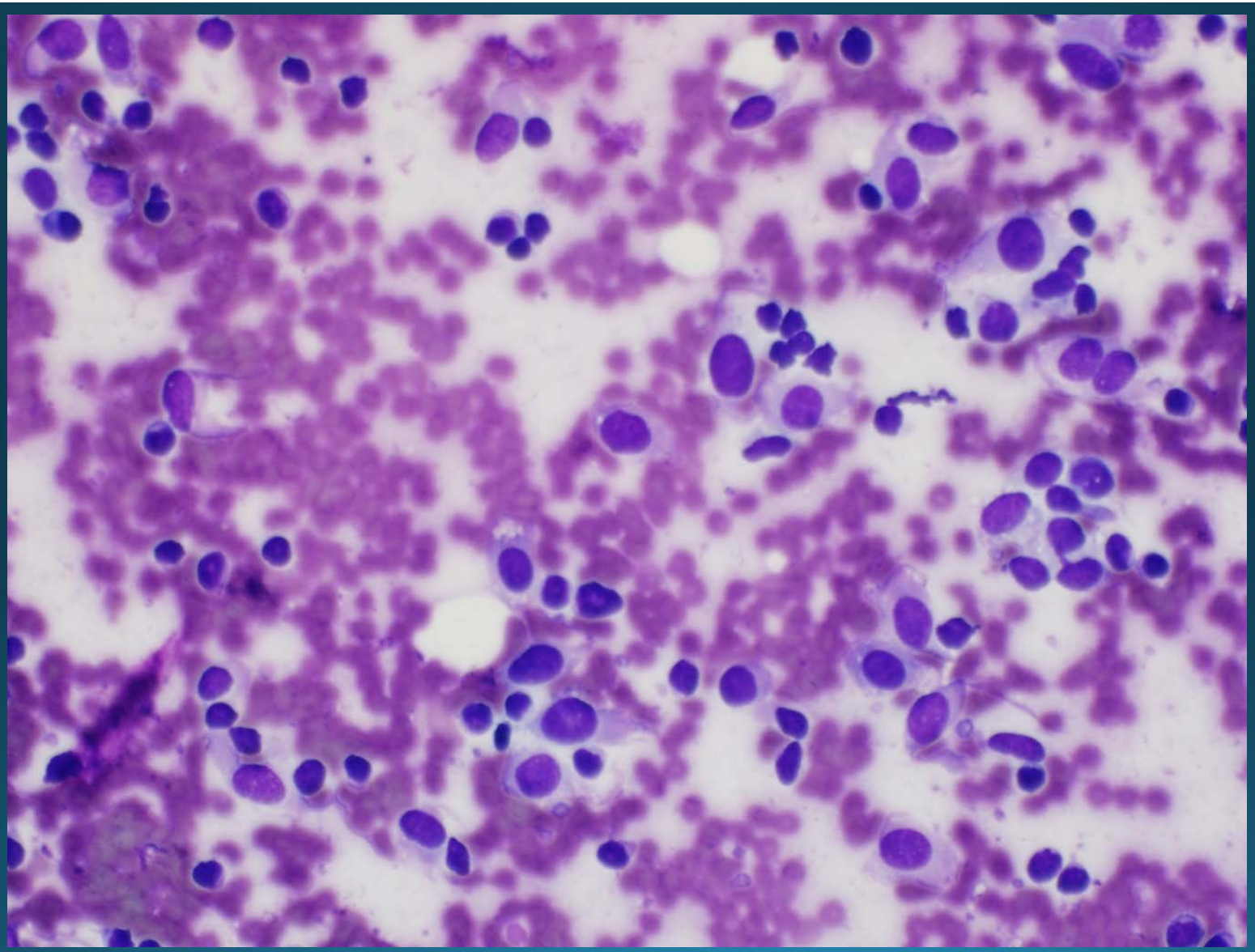
Image adapted from
Gut 2010;59:586-594

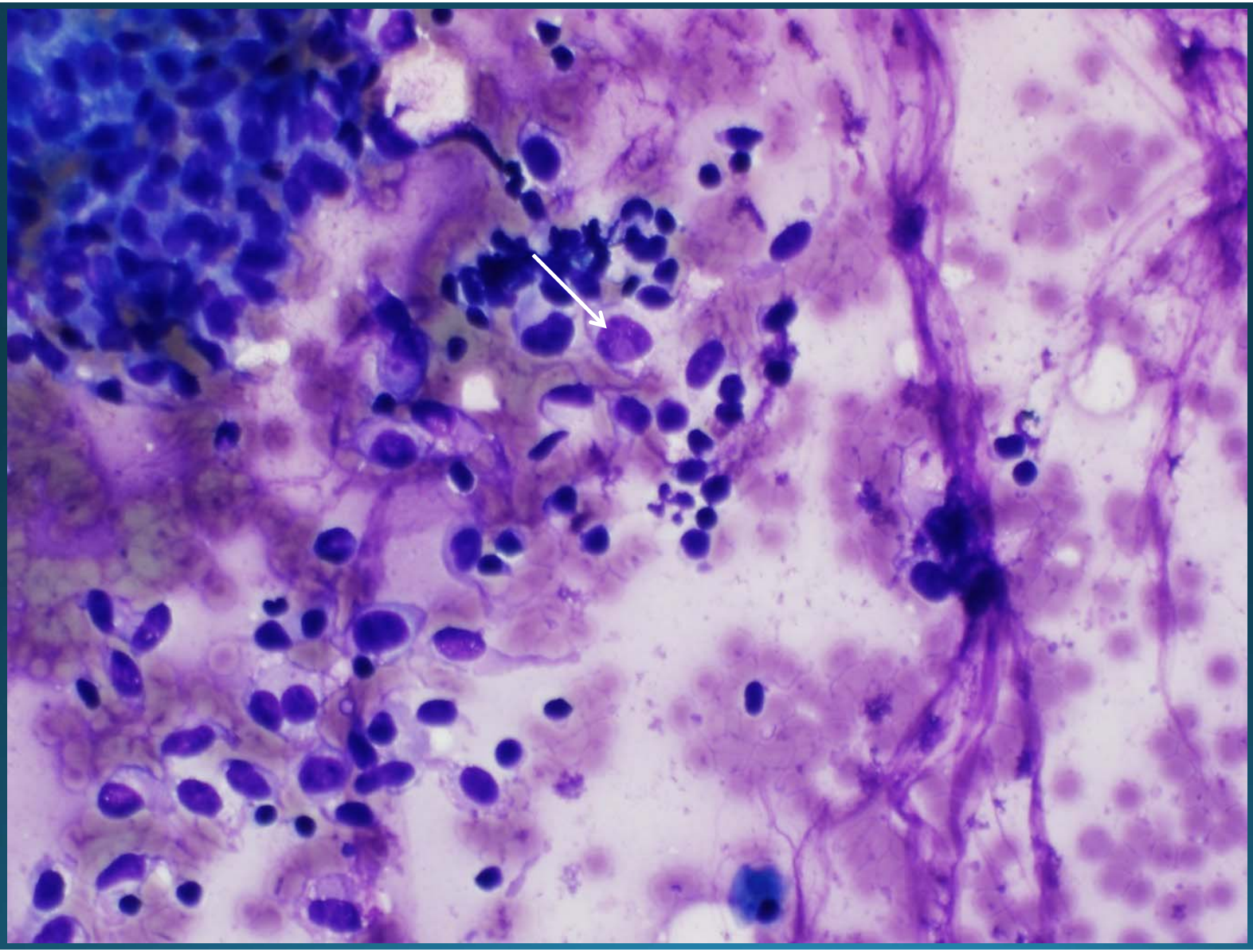
Pitfall 4: Think Outside of Box

- 68 year old male with history of a prior malignancy
- Now with atypical appearing 1.1 cm node in porta hepatis region


F13
7.5M 5.0 R05 G60 C5
2:EUS Linear
DVA:







Melanoma

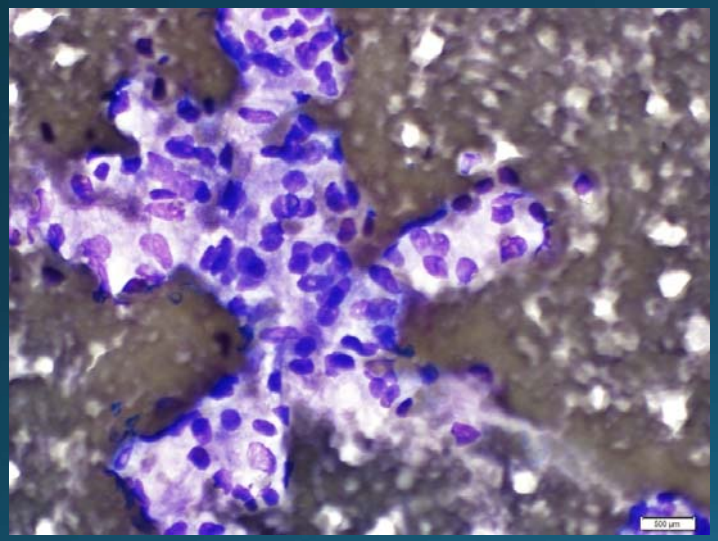
- Can resemble NET
  - Plasmacytoid
  - Loosely cohesive
  - Less chromatin clumping than adenocarcinoma
- Prominent nucleoli one clue
- Intranuclear inclusions are a big clue
- Clinical history on site the biggest clue

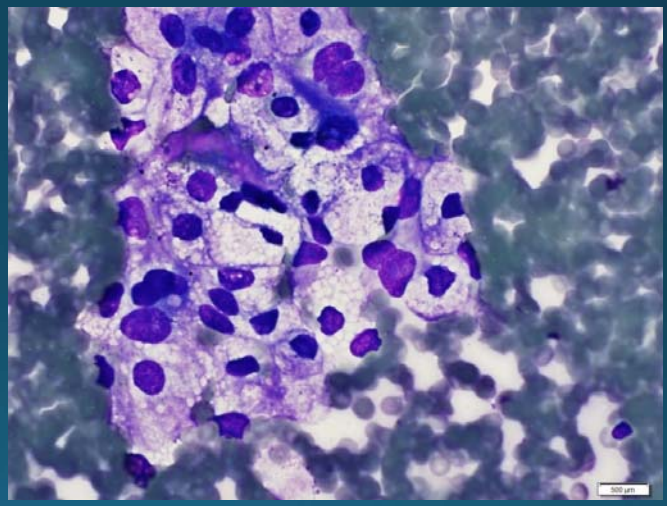
Pitfall 4: Think Outside of Box. Metastases to the Pancreas

- In case reports of melanoma metastatic to pancreas the primary site remains occult in 2.4-8.7%
- Can appear as either a solid or cystic lesion
- Usually have evidence of other intrabdominal metastases (nodal)
- Of all metastases to pancreas, renal cell carcinoma is the most commonly reported

DeWitt JM et al. Endoscopy 2003;35:219-222.

Metastatic RCC to Pancreas

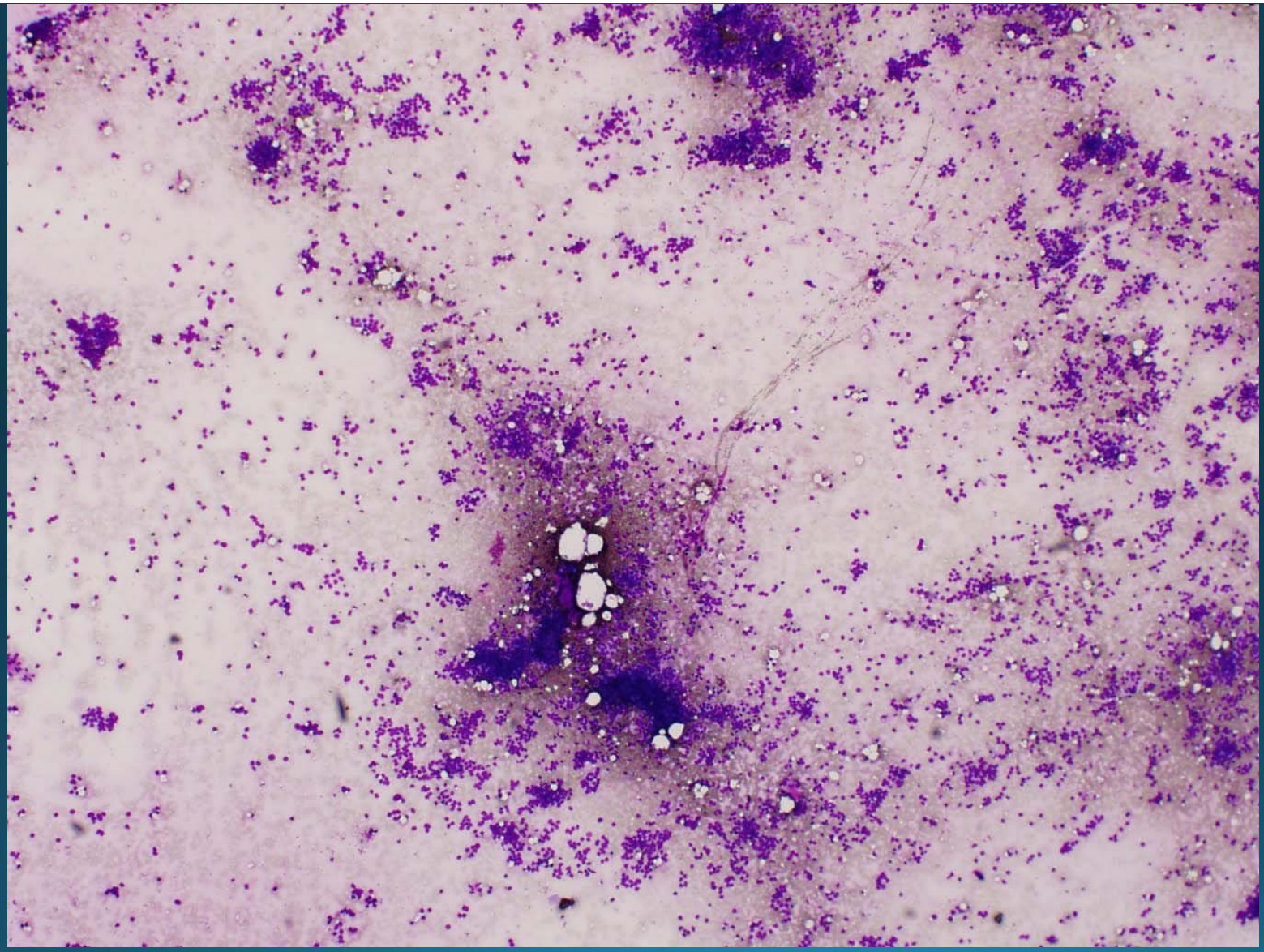


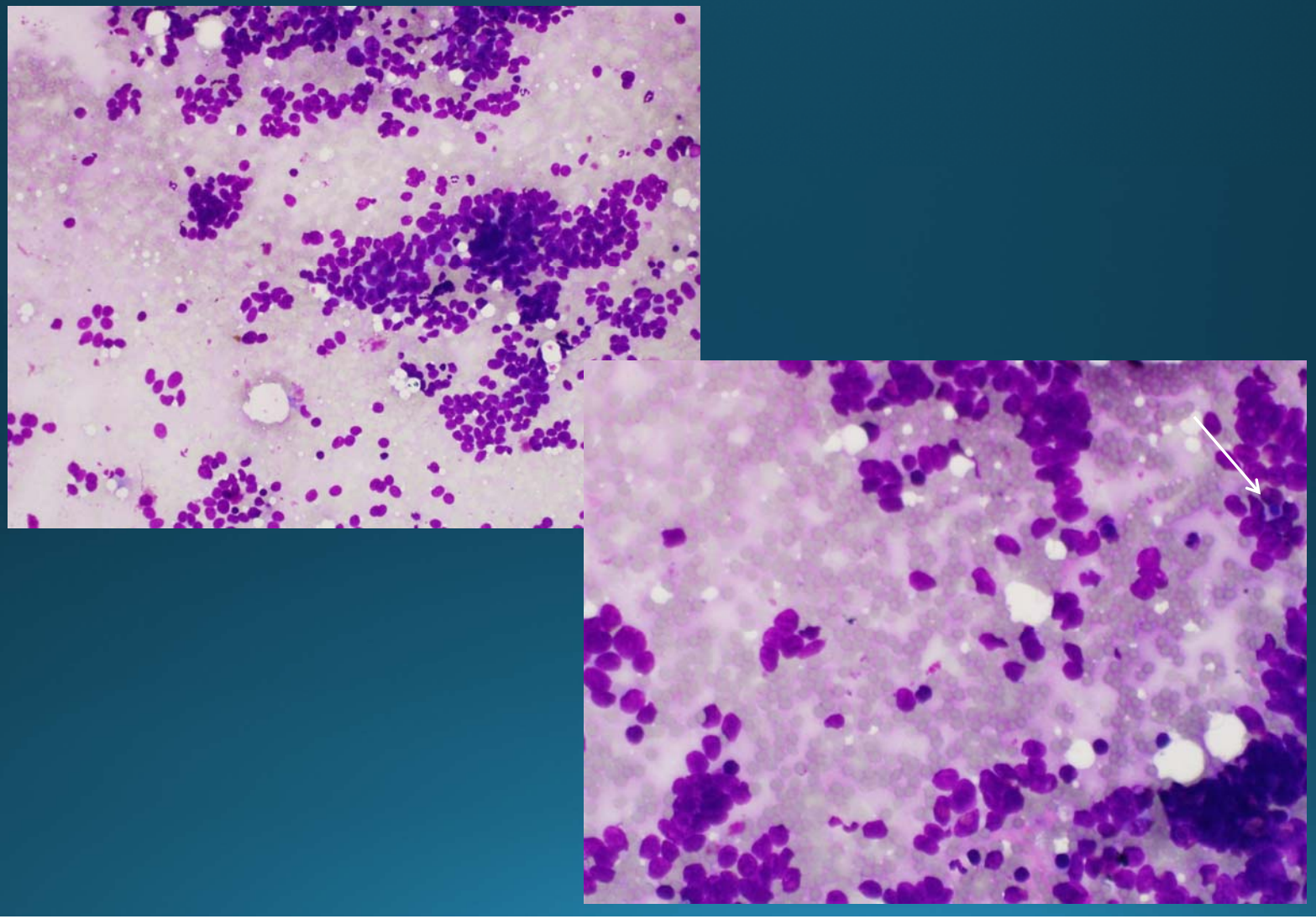


Pitfall 4: Think outside the box

- 61 year old male with 3 distinct ~2 cm masses within the pancreas and extensive peri-pancreatic LAD
- "Very unusual for a pancreatic primary"


F13
7.5M 5.0 R05 G60 C5



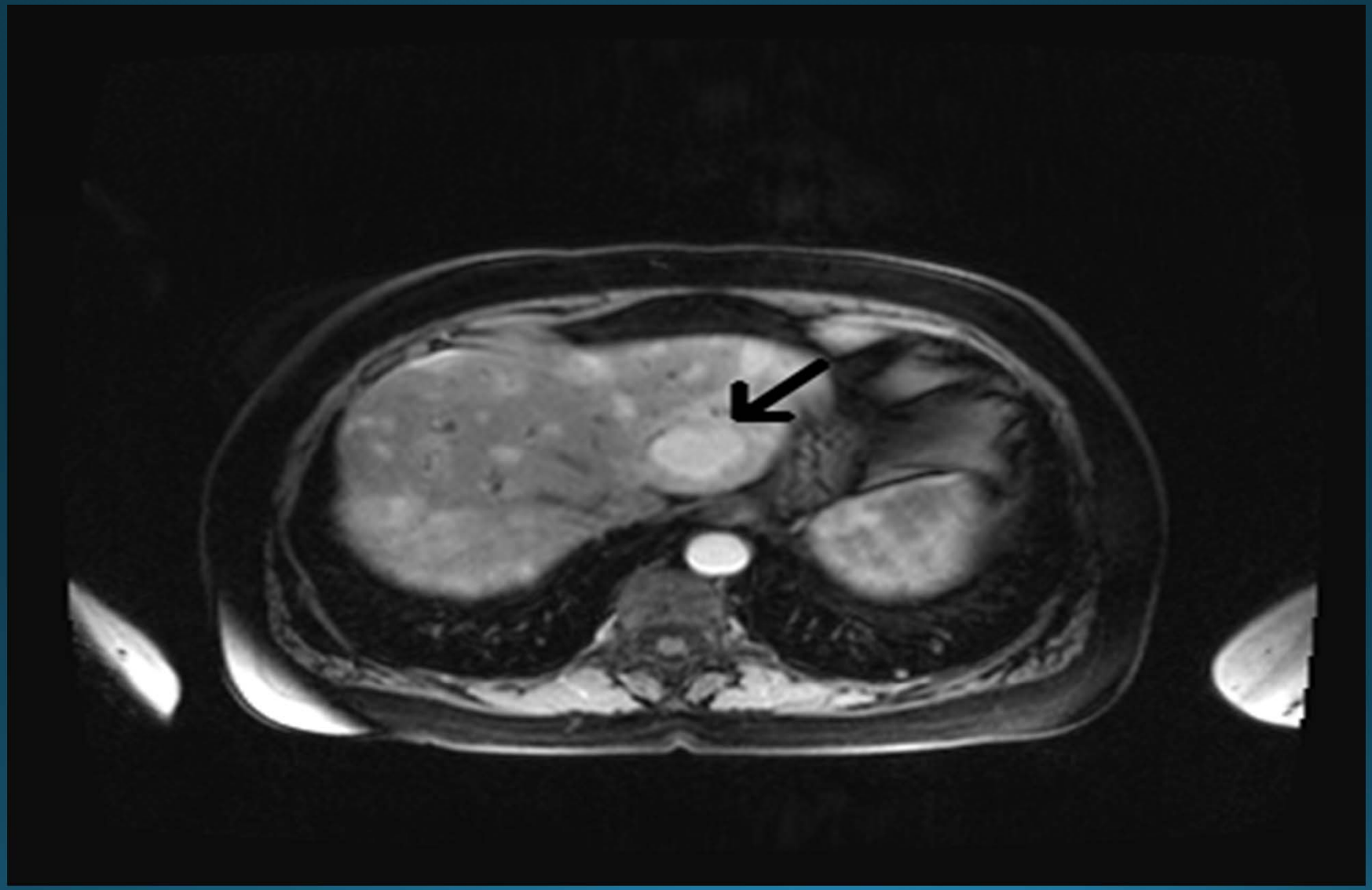


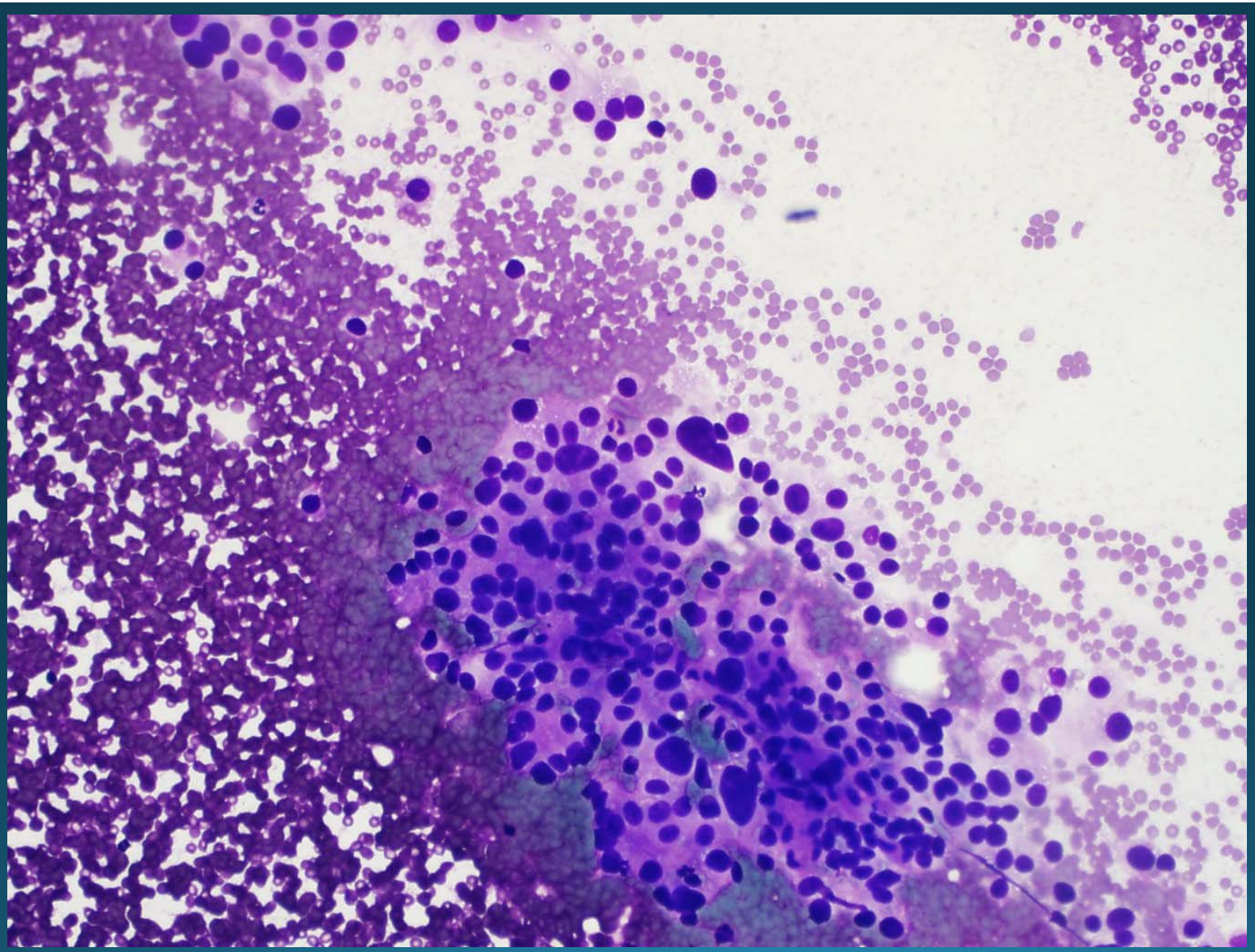
Pitfall 4: Small Cell Carcinoma

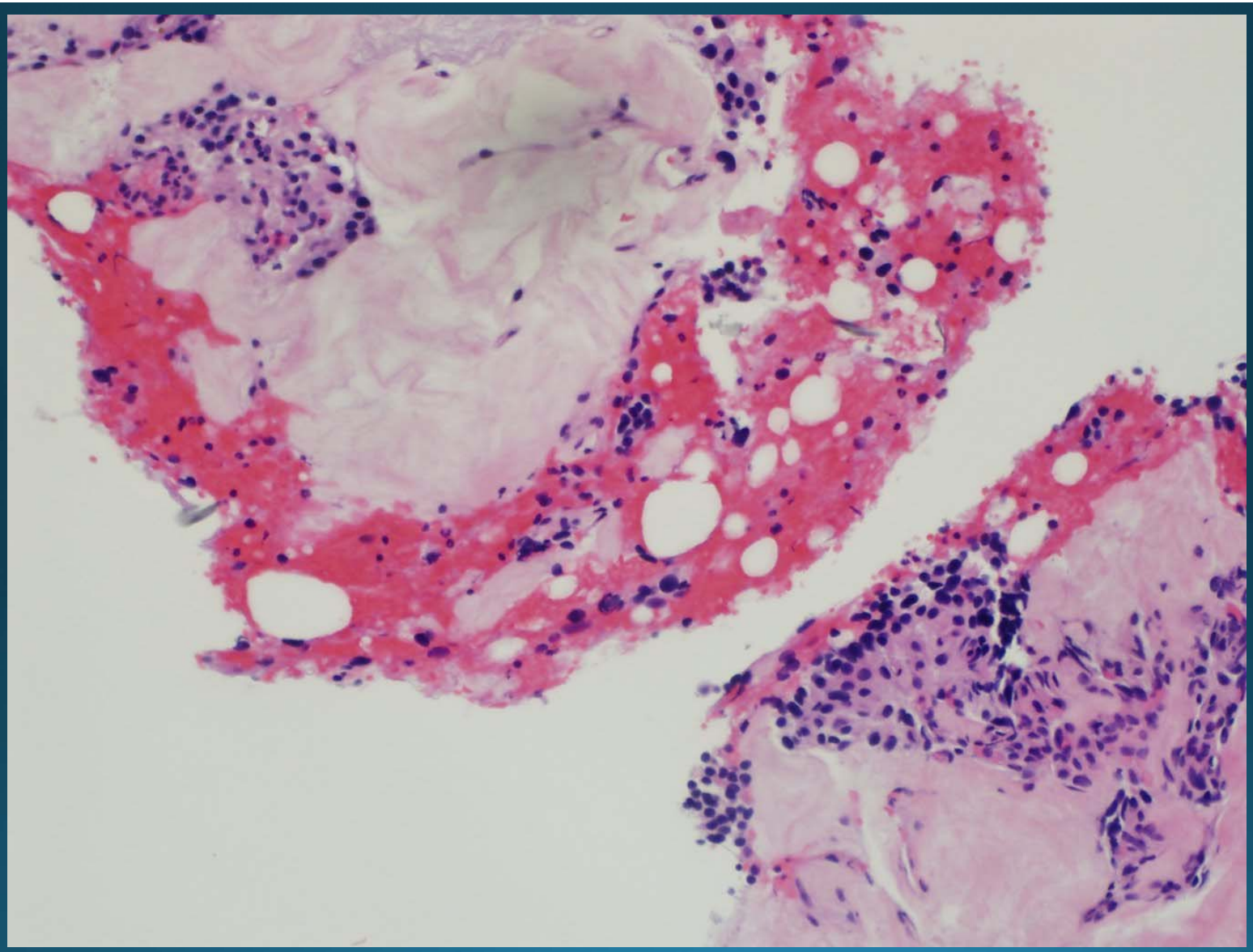
- Cellular smears
- Loosely cohesive to dispersed cells
- Minimal cytoplasm
- Nuclear molding
- Perinuclear blue bodies
- Homogenous chromatin
- Can be primary, but usually metastatic

Pitfall 4: Think Outside the Box

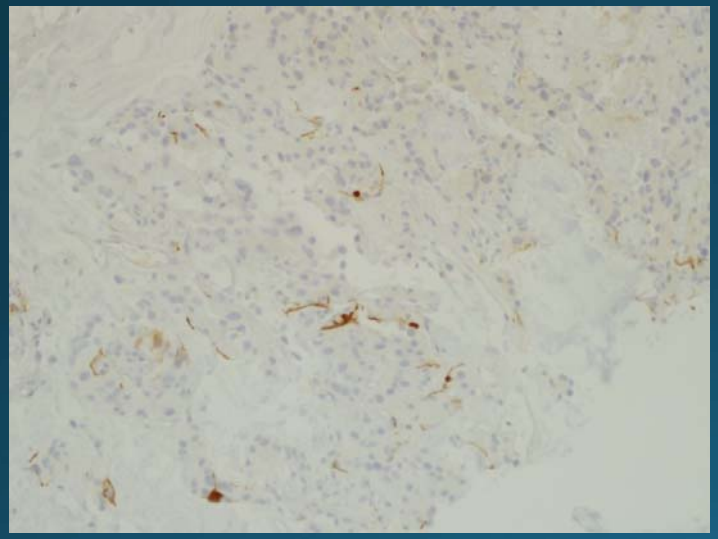
- 35 year old female with a history of a carotid body paraganglioma
- Now with a liver lesion



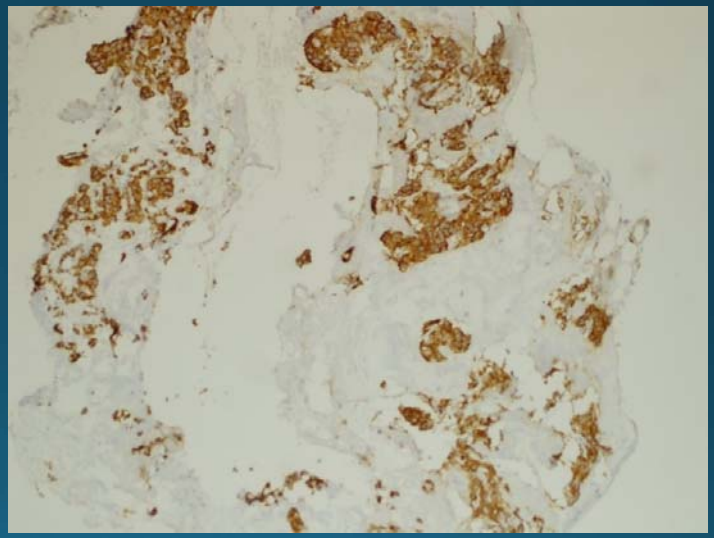




S-100



Synaptophysin



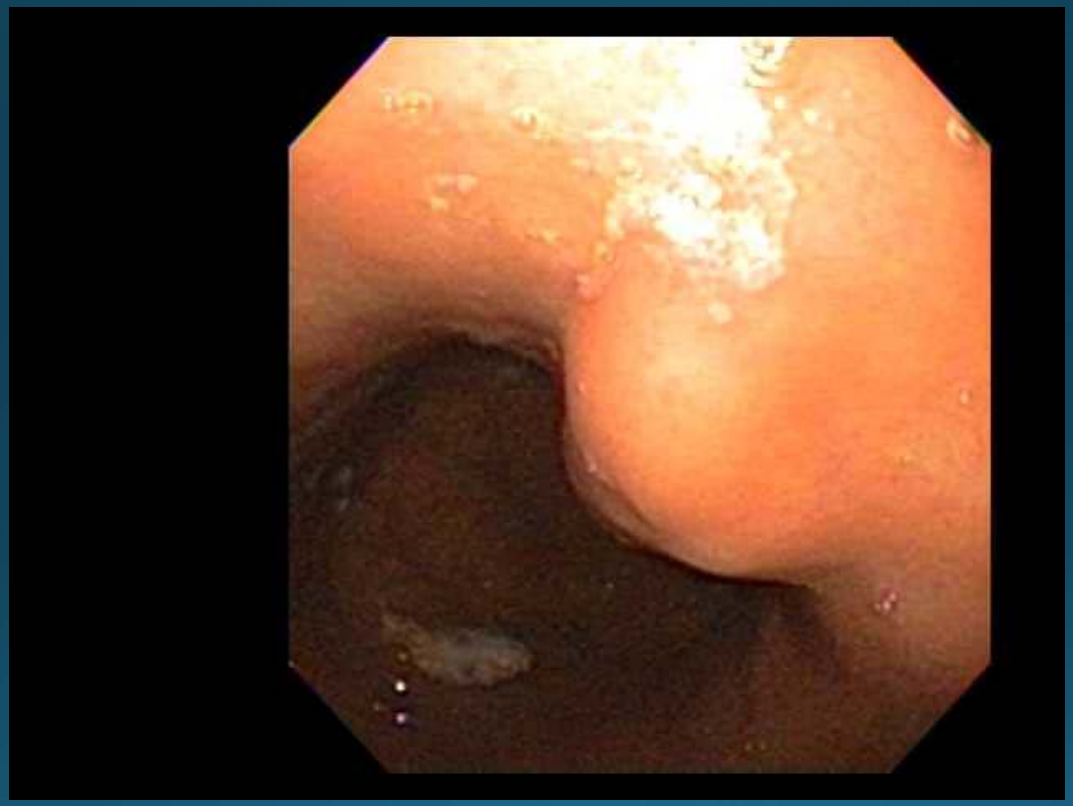
Cytokeratins were negative

Pitfall 4: Paraganglioma

- Cytomorphologic overlap with well differentiated neuroendocrine tumors
  - Loose clusters of round to oval cells
  - Fine granular chromatin
- More frequently stripped nuclei
- Requires immunostain support
  - Cytokeratin-
  - Neuroendocrine marker positive
  - S100+ sustentacular cells
- Evaluating for germline SDH gene mutations is now recommended for risk assessment (SDHB immunostain)

Pitfall 4: Think Outside the Box

- 43 year old female with a 3 cm hypoechoic submucosal lesion in gastric body




ALOKA
HUNTSMAN CANCER CENTER
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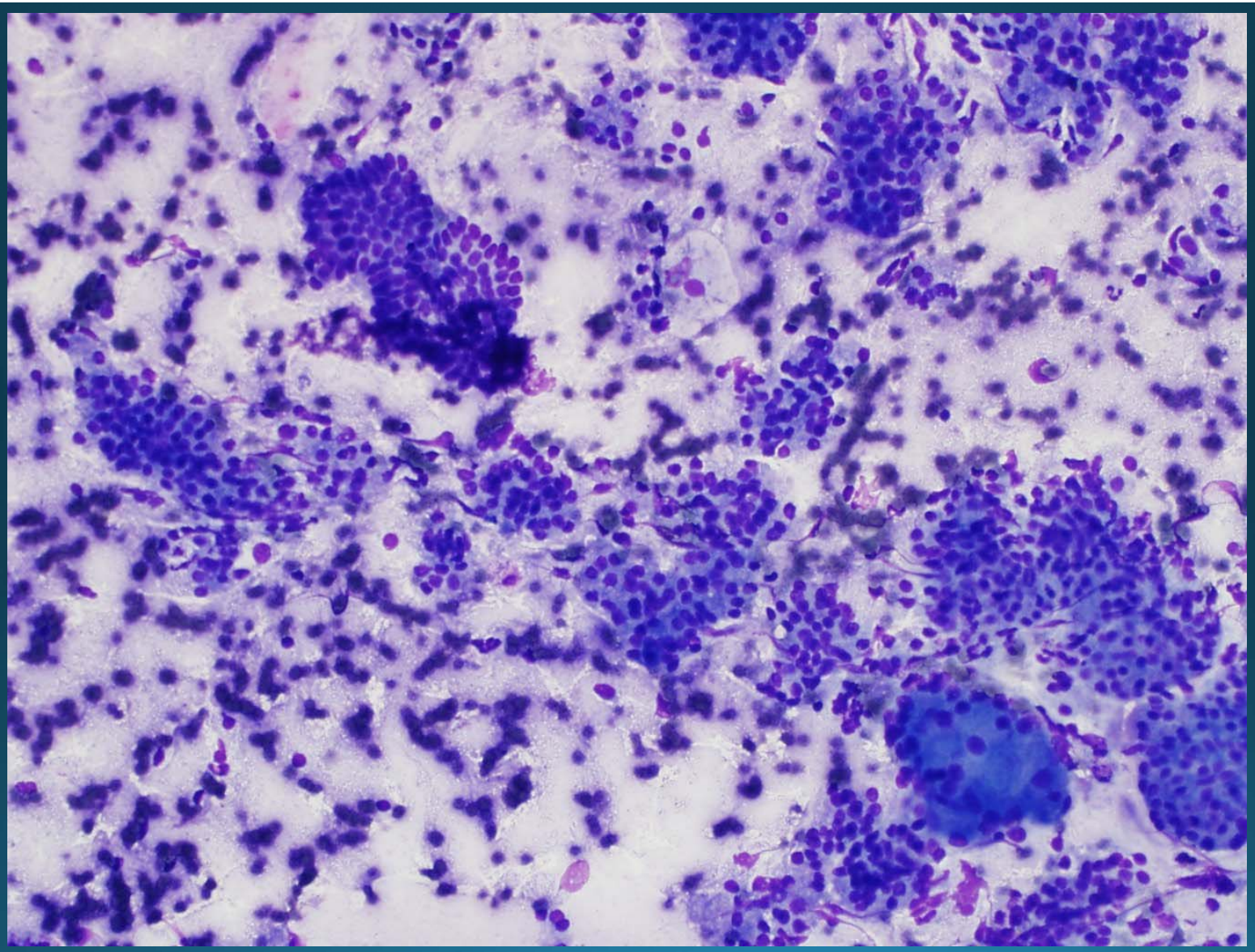
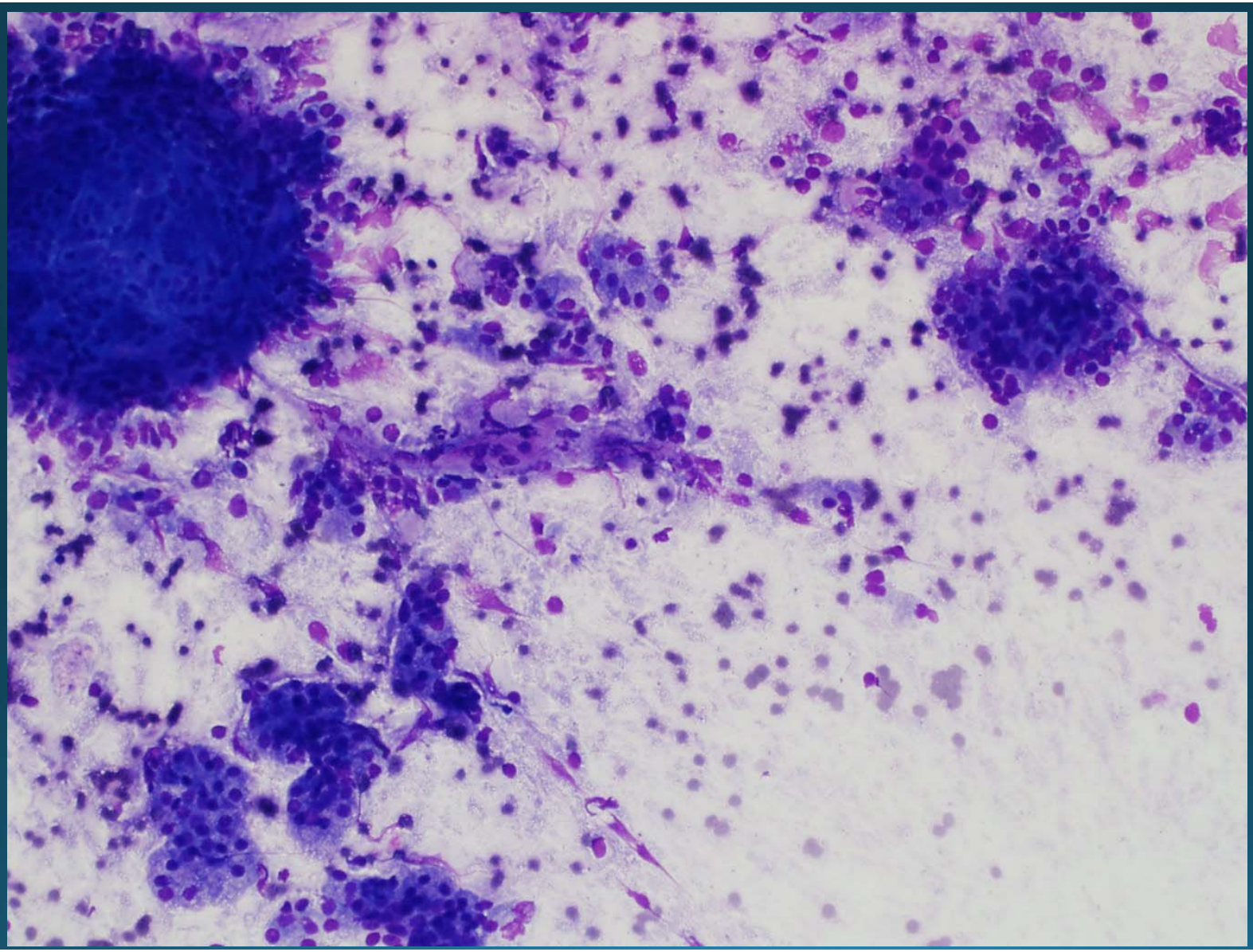
7.50M R5.0 G57 D80 A1
903/906
1:RADIAL160-02
Probe:RAD160
AIP

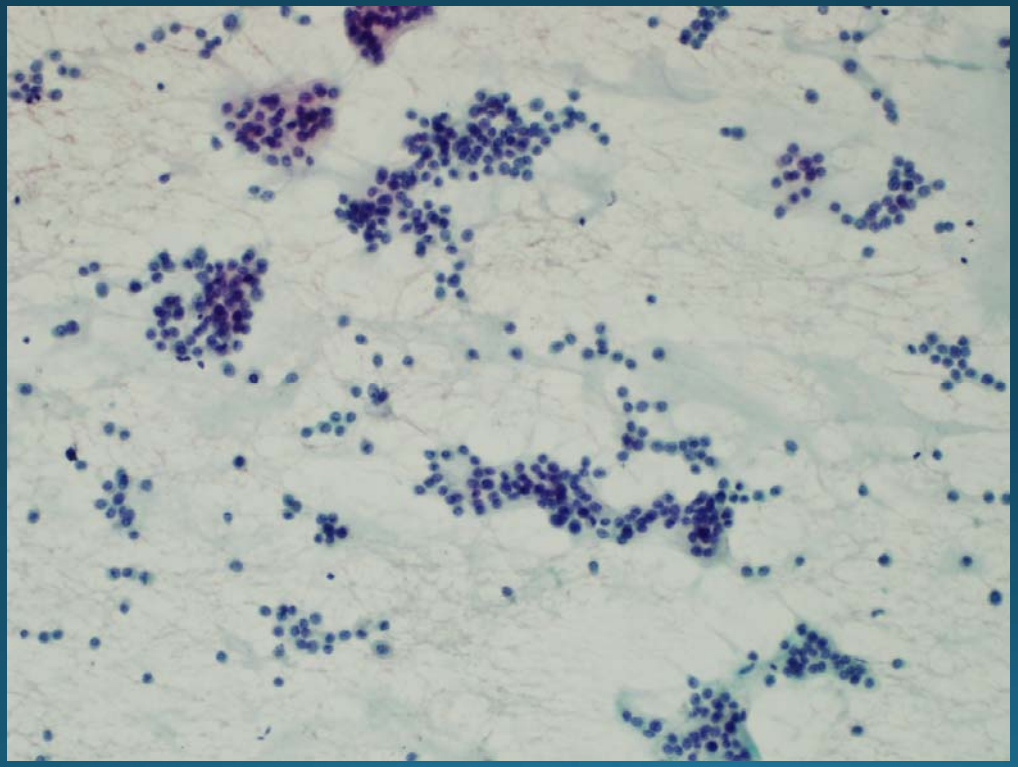




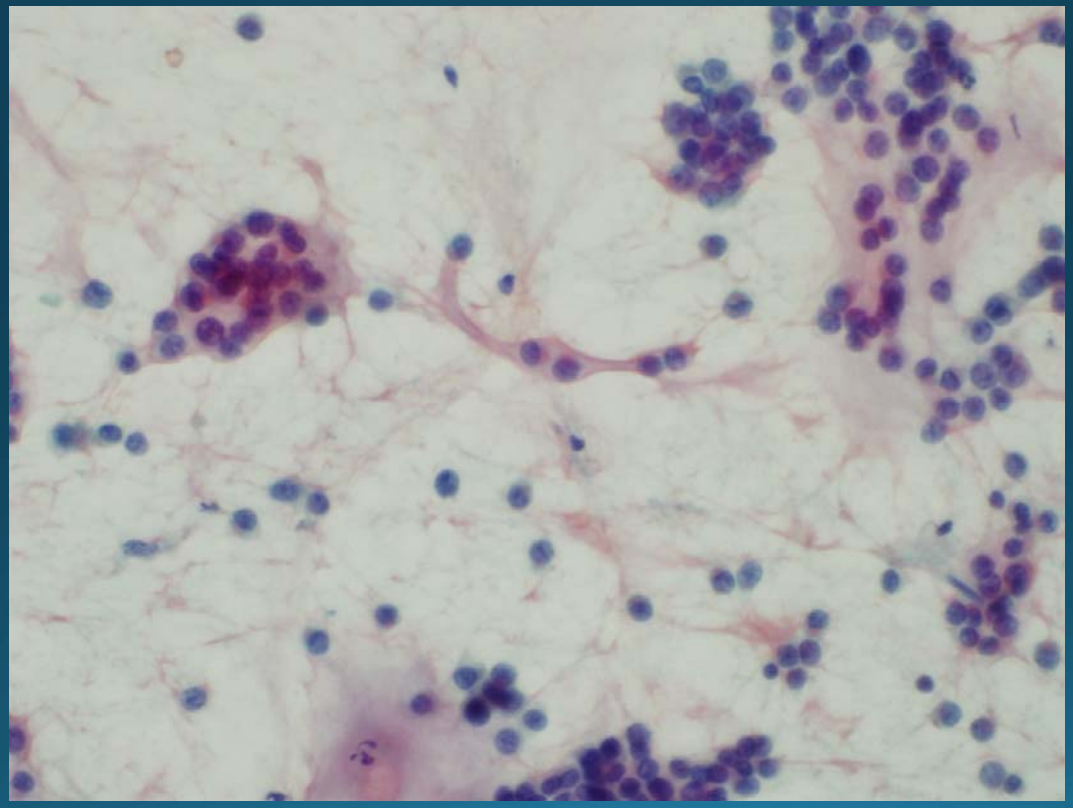
Pitfall 4: Pancreatic heterotopia

- "Doug, why does this look like pancreas?"
- …Oh, right. Heteroptopia.
- Be wary, very cellular

Pitfall 4: Think Outside of Box



Extraskeletal Chondrosarcoma of Pancreas (Case from ASC Diagnostic Slide Seminar 2016)…Seriously outside of box



Pitfall 5: Cystic Lesions of Pancreas

Papanicolaou Society of Cytopathology proposal for reporting pancreaticobiliary cytology:

1. **Nondiagnostic**
2. **Negative for Malignancy** (pancreatitis, pseudocyst, accessory spleen)
3. **Atypical** (insufficient to classify as neoplasm or suspicious for malignancy)
4. **Neoplastic**
    - A. **Benign** (serous cystadenoma, schwannoma)
    - B. **Other** (PanNET, SPN, MCN, IPMN)
5. **Suspicious** (quantitatively or qualitatively insufficient but worrisome for malignancy – generally referring to adenocarcinoma)
6. **Malignant** [Adenocarcinoma (9/10), acinar cell carcinoma, small cell carcinoma, lymphoma, sarcoma, or metastases]

Papanicolaou Society of Cytopathology proposal for reporting pancreaticobiliary cytology with regard to cystic lesions

- Cystic lesions with mucinous epithelium = **Neoplastic (other)**
- Cystic lesions with mucinous epithelium and high grade dysplasia = **Neoplastic (other)**
- Cystic lesions with no mucinous epithelium on cytology with high CEA (>192 ng/mL) = Neoplastic (other)
- Cystic lesions with thick colloid-like mucin = **Neoplastic (other)**
- Cystic lesions with non-mucinous, cuboidal/bland epithelium = **Neoplastic (benign)**
- Mucinous debris of uncertain origin (lesional versus GI contamination) is reasonable

Cancer Cytopathol.
2015;123:488-94

Biochemical and Molecular Tests for Classifying Pancreatic Cysts

Cyst	CEA	Amylase	*KRAS*	*GNAS*
Pseudocyst	Low	High	-	-
Serous cystadenoma	Low	Low	-	-
IPMN	High	Often high	+	+
MCN	High	Can be high	+	-

A high CEA is defined as >192 ng/mL
A high Amylase is generally in the 1000s / A low Amylase is typically <100 ng/mL

Adapted from: Cibas and Ducatman. Cytology: Diagnostic Principles and Clinical Correlates. Fourth Edition. Elsevier Saunders 2014. Page 400.

Examples of Reporting: Pitman et al. Cytojournal. 2014;11(Suppl 1): 3.

Satisfactory for evaluation

Neoplastic: Other

Mucinous cyst fluid with low-grade dysplasia (see note)

Note: Benign-appearing mucinous epithelium is present from this transduodenal FNA in a background of abundant extracellular mucin. (If available, add CEA is elevated at 357 ng/ml supporting the diagnosis).

Satisfactory for evaluation

Neoplastic: Other

Cyst fluid with thick colloid-like extracellular mucin containing cyst debris consistent with a neoplastic mucinous cyst, favor MCN given the clinical and imaging findings of a 45-year-old female with a multiloculated cyst in the pancreatic tail. Scant benign appearing mucinous epithelium is present of uncertain origin, favor gastric contamination. No high-grade epithelial atypia present.

Evaluation limited by scant cellularity

Neoplastic: Other

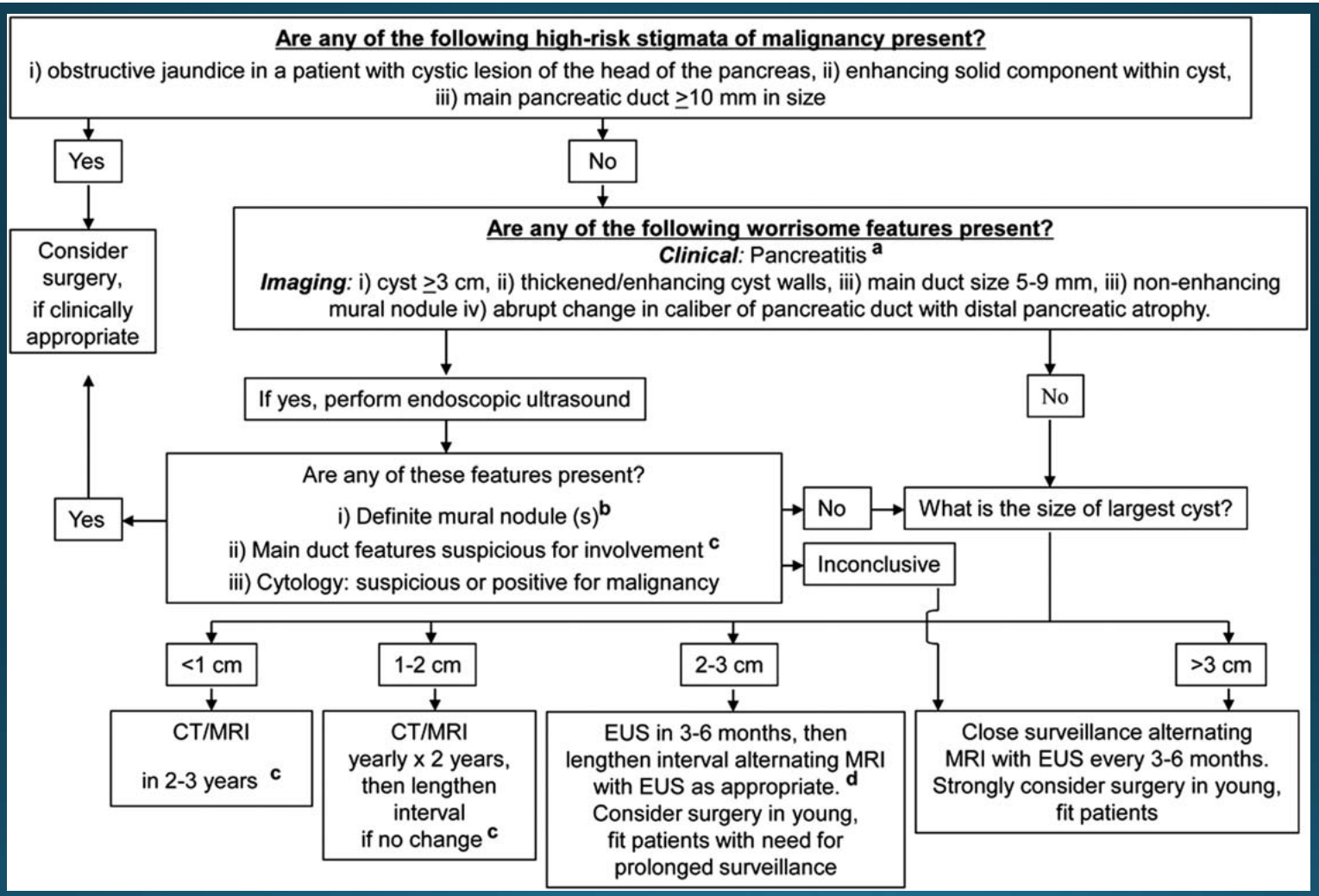
Mucinous cyst fluid with high-grade epithelial atypia (see note)

Note: No thick extracellular mucin is present, but cyst fluid CEA is 1267 ng/ml supporting the diagnosis. In addition, molecular analysis demonstrates a *KRAS* point mutation, which supports a mucinous etiology. The epithelial cells are most consistent with high-grade dysplasia, however, invasive carcinoma cannot be excluded. Correlation with imaging findings required.

Satisfactory for evaluation

Negative for malignancy

Mucinous cyst debris of uncertain etiology. No high-grade epithelial atypia identified. Correlation with imaging and ancillary studies required

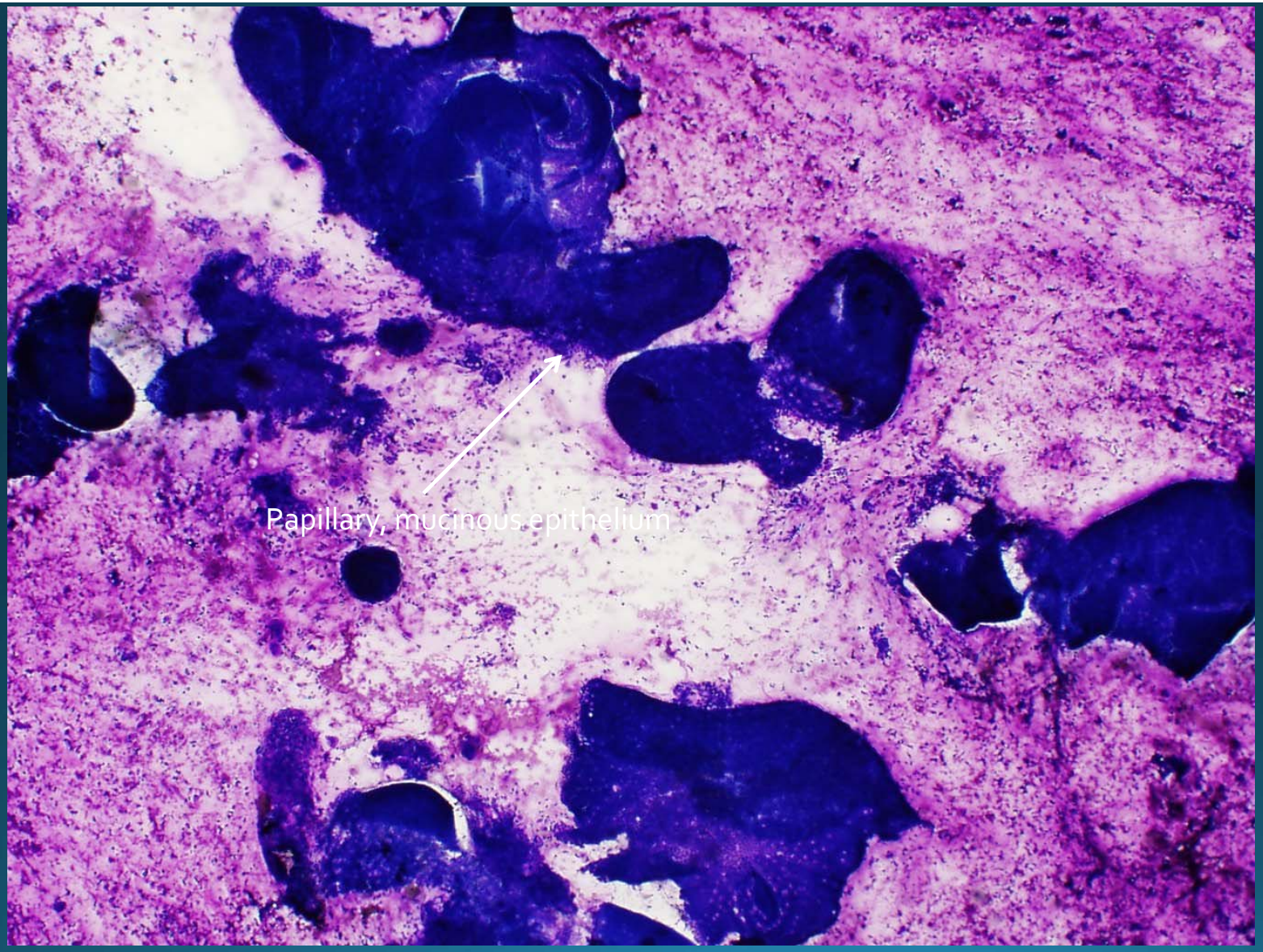


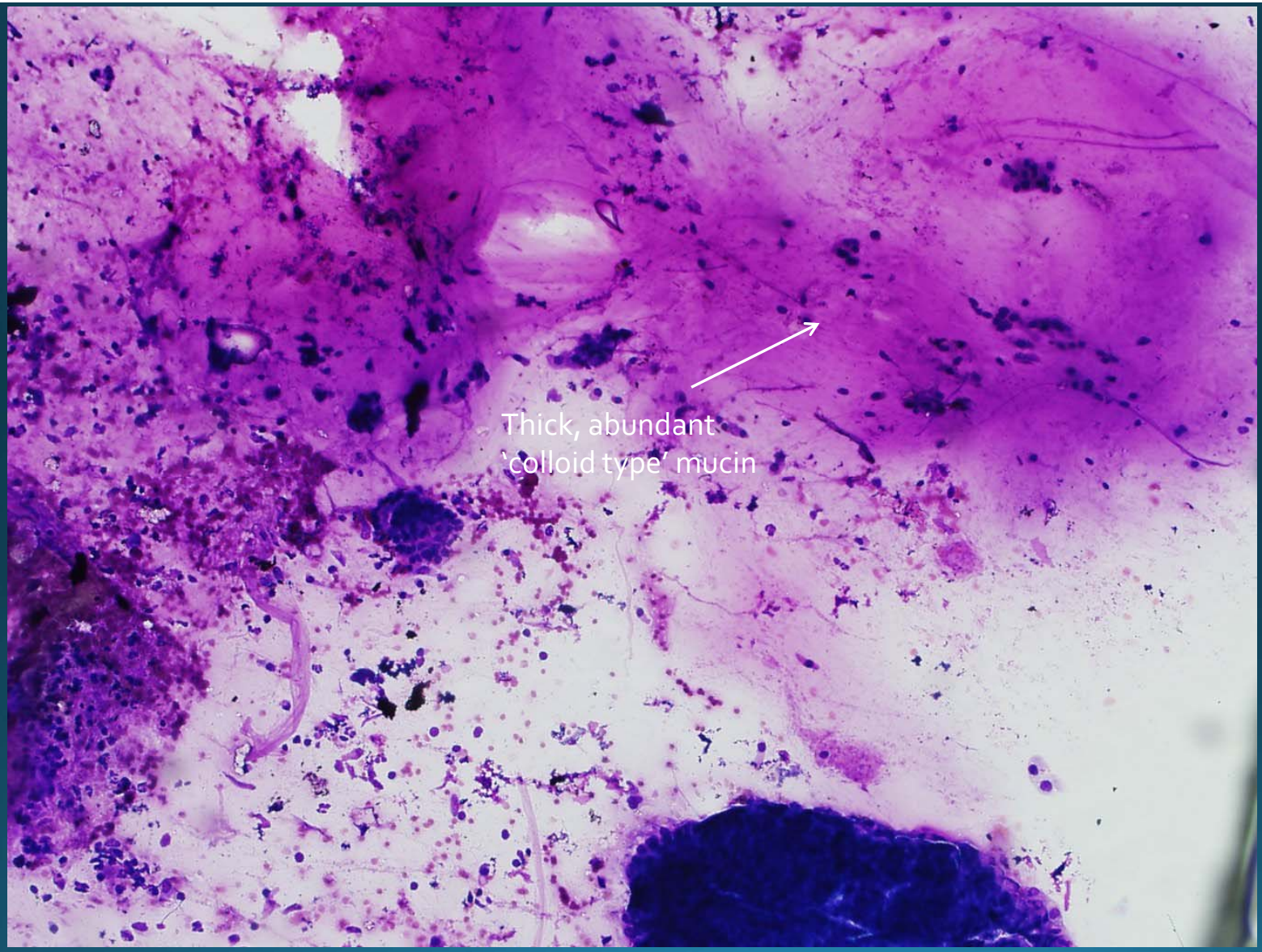
Adapted from: Adler et al. Diagn. Cytopathol. 2014;42:325-332

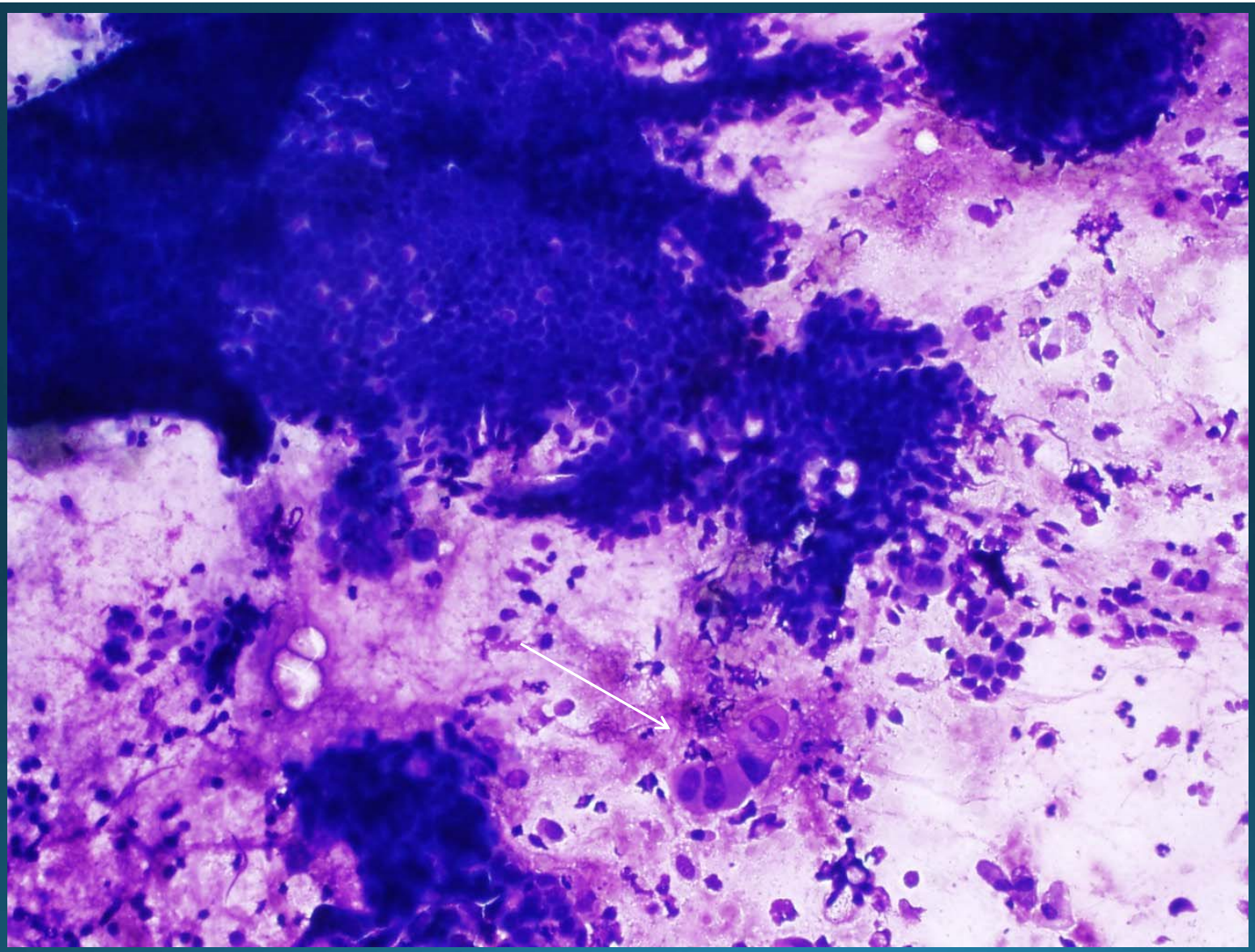
Pitfall 5: Cystic Lesions of Pancreas

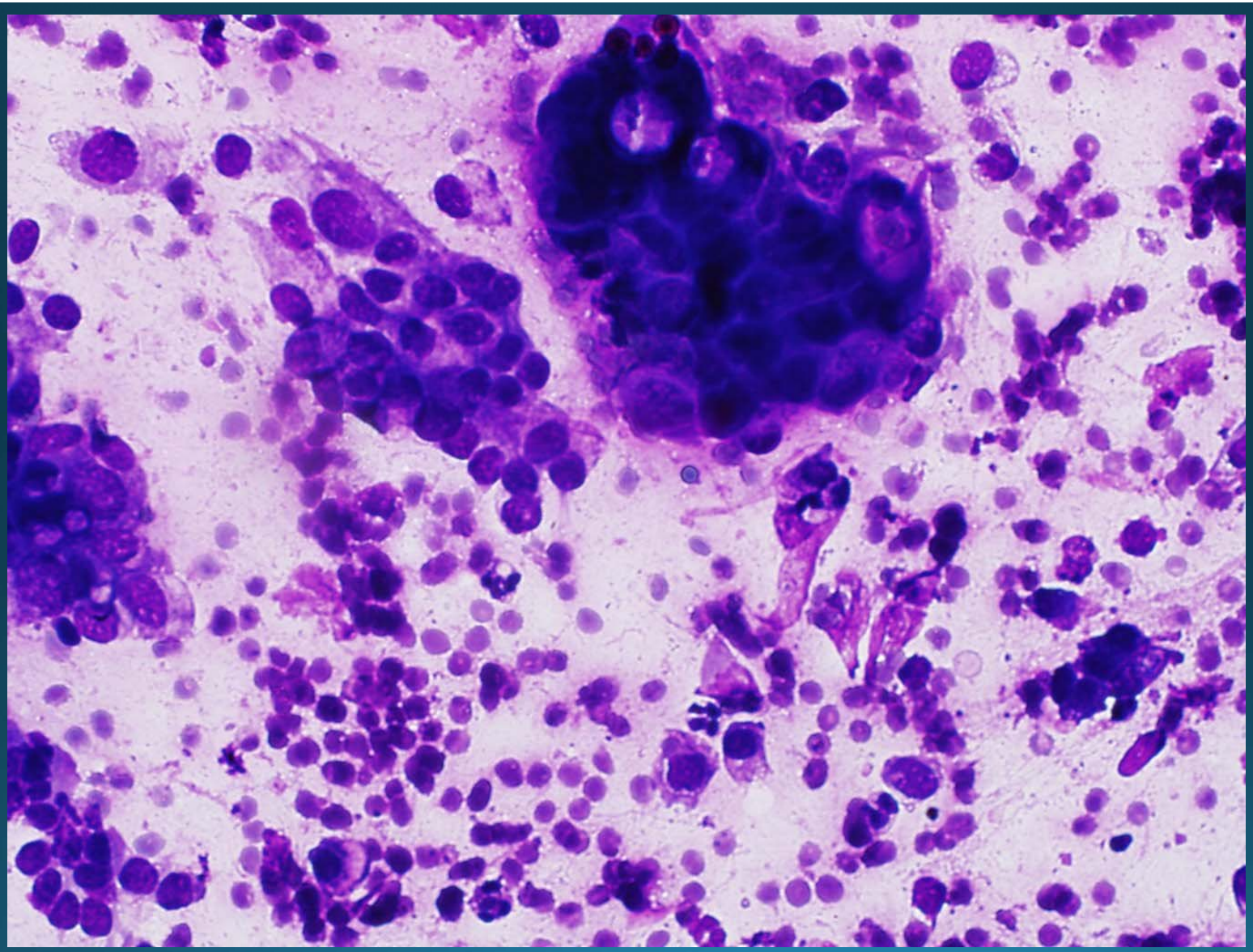
- 72 year old male with multiple cystic lesions of the pancreas and pancreatic duct dilation


681/6
5
.5M 5.0 R04 G60 C5
S Linear
DVA: 7


Papillary, mucinous epithelium


Thick, abundant
'colloid type' mucin





IPMN with High Grade Dysplasia

- Background thick 'colloidal type' mucin
- Abundant mucinous epithelium
- Areas showing anisonucleosis (3-4X), irregular nuclear contours, disorganization (either discohesion or overlap/crowding)

Management for IPMNs

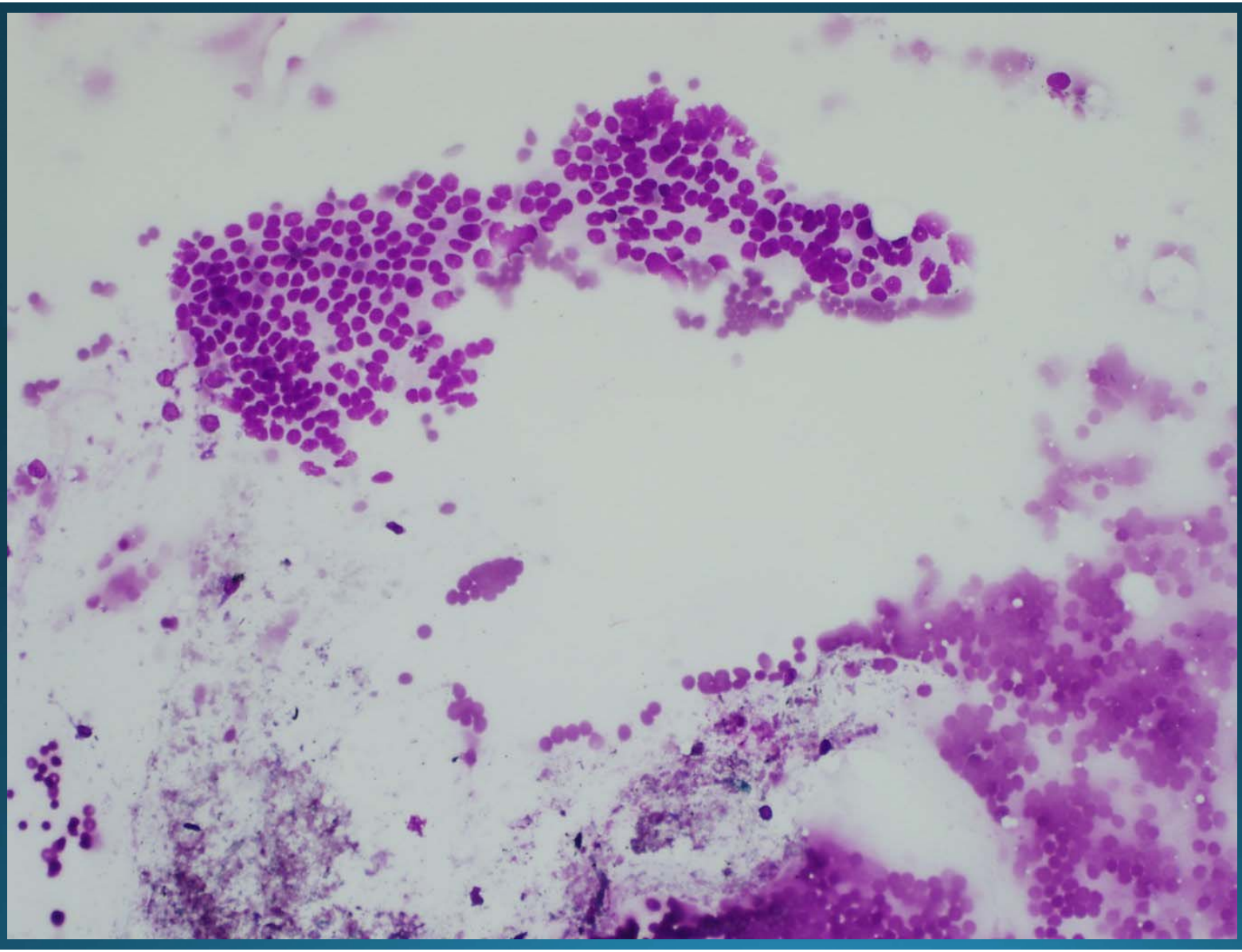
- Main duct are resected
- Those with high grade dysplasia are resected
- Branch duct is bit more controversial
  - Usually foveolar type
  - Demographics, serum markers (CA19-9) may play a role in determining treatment

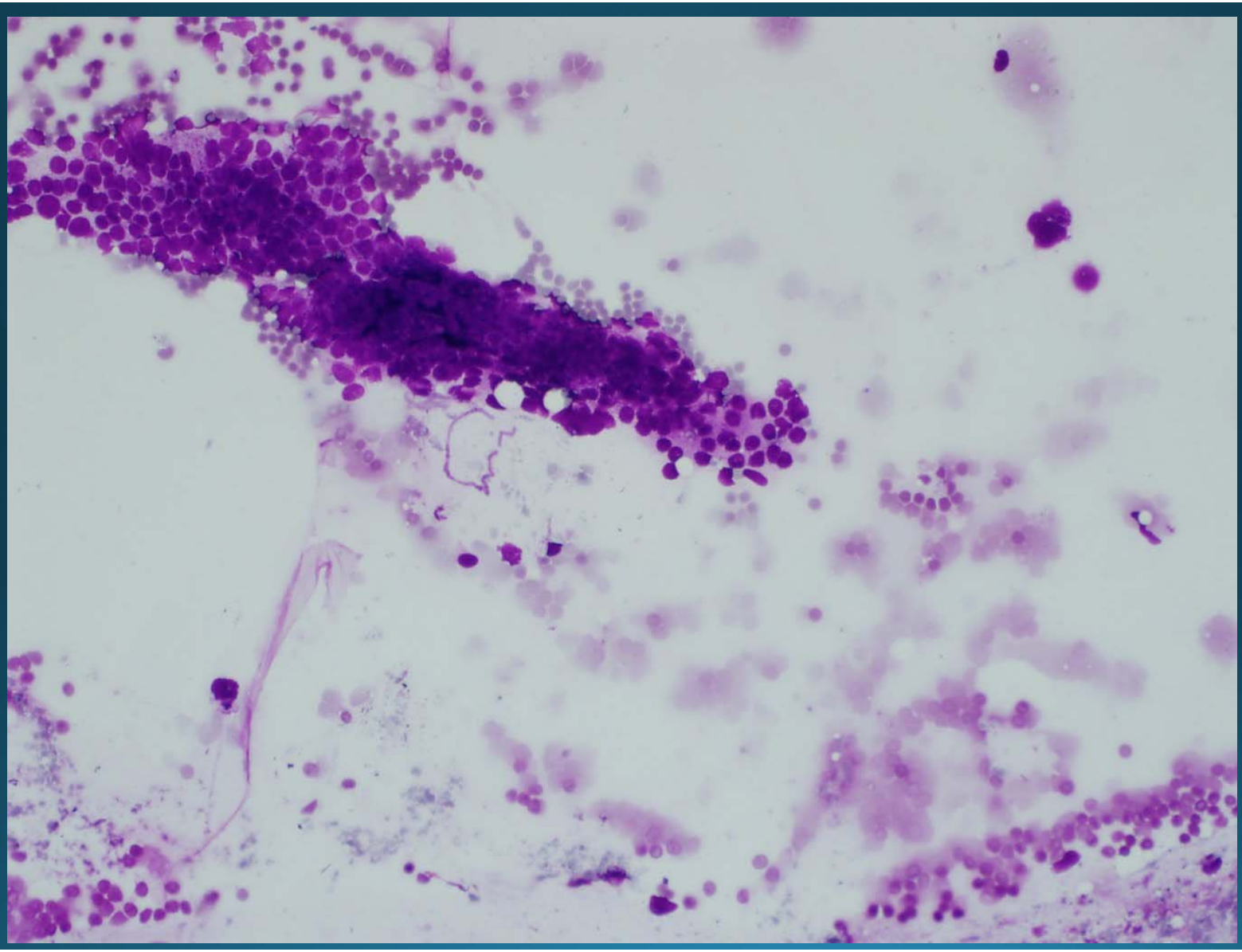
Pitman MB and Layfield LJ.
Cancer 2014;122:399-411

Pitfall 5: Cystic Lesions of Pancreas

- 70 year old male with a pancreatic cyst


16:08
131
5M 7.5 ROS G60 CS
Linear
DVA:10



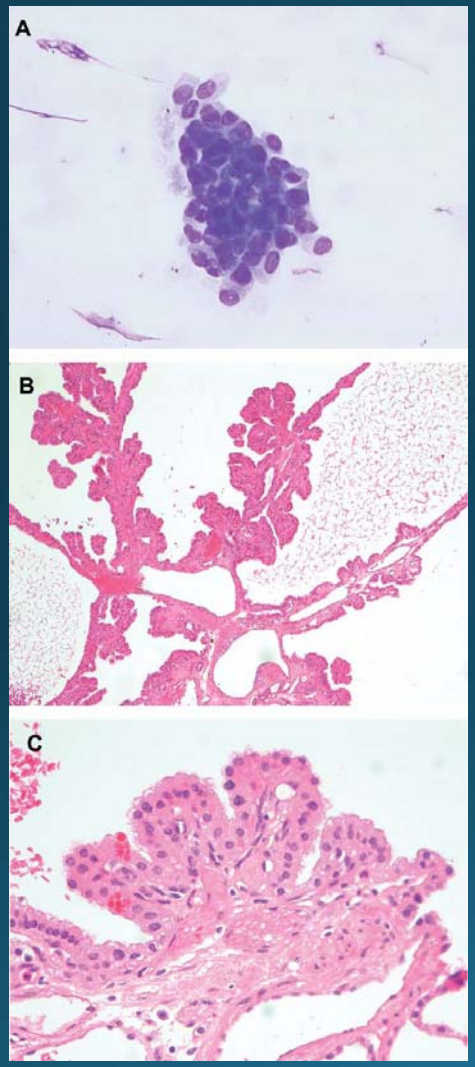


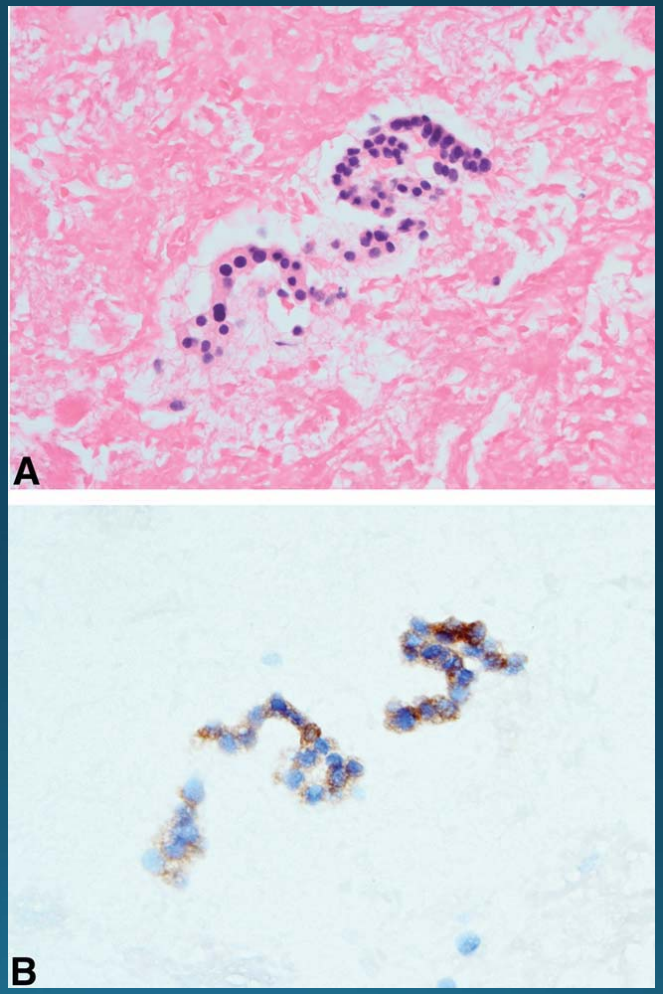
Serous Cystadenoma

- Often scantly cellular (11/15 in one series): Common cause of nondiagnostic cysts
- Round to cuboidal cells in overlapping to flat sheets
- Hemosiderin-laden macrophages (63%, usually not present in cystic mucinous neoplasms)
- Sometimes with clear cytoplasm (glycogen)
- Sometimes with plasmacytoid to oncocytic cells
- Flat strips on cell block
- Alpha Inhibin immunostain supports diagnosis
- PanNET a potential pitfall
- "Scant non-mucinous cuboidal epithelium and hemosiderin-laden macrophages in a non-mucinous cyst fluid consistent with the clinical impression of a serous cystadenoma" (include CEA and amylase results if available)

Pitman et al. Cytojournal. 2014;11(Suppl 1): 3

Salomao et al. Cancer 2014;2014;122:133-9





Images adapted from:
Salomao et al. Cancer 2014;2014;122:133-9

Management of Serous Cystadenomas

- Proposed surgical intervention include symptomatic mass >4 cm, rapid growth, or diagnostic uncertainty

Pitfall 5: Cystic Lesions of Pancreas

- 68 year old male with cystic lesion involving the pancreatic duct and its branches


ALOKA
HUNTSMAN CANCER CENTER
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09.07.'16
12:34:08
MI =0.86 TIS< 0.4 100% 56Hz 1
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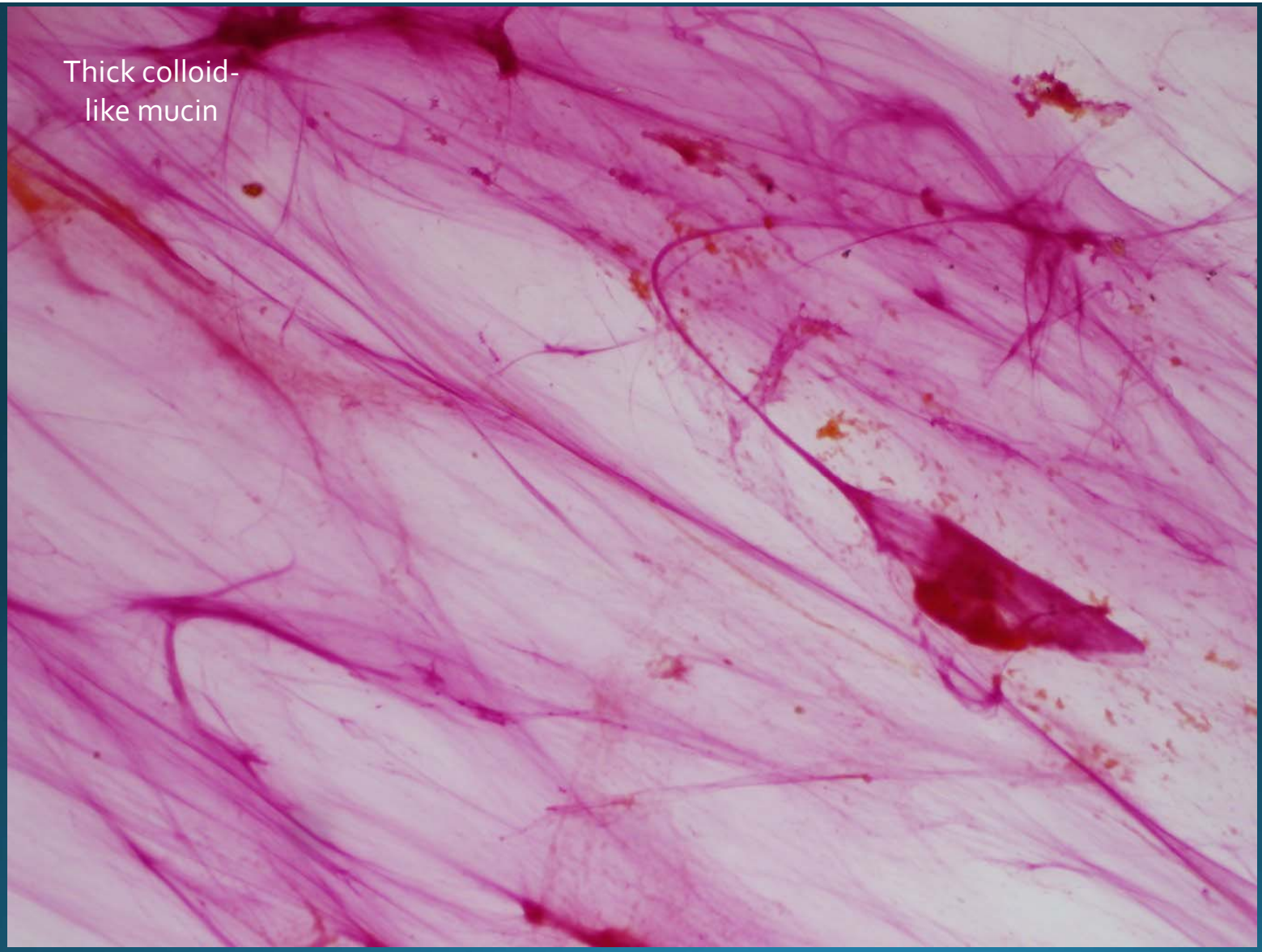
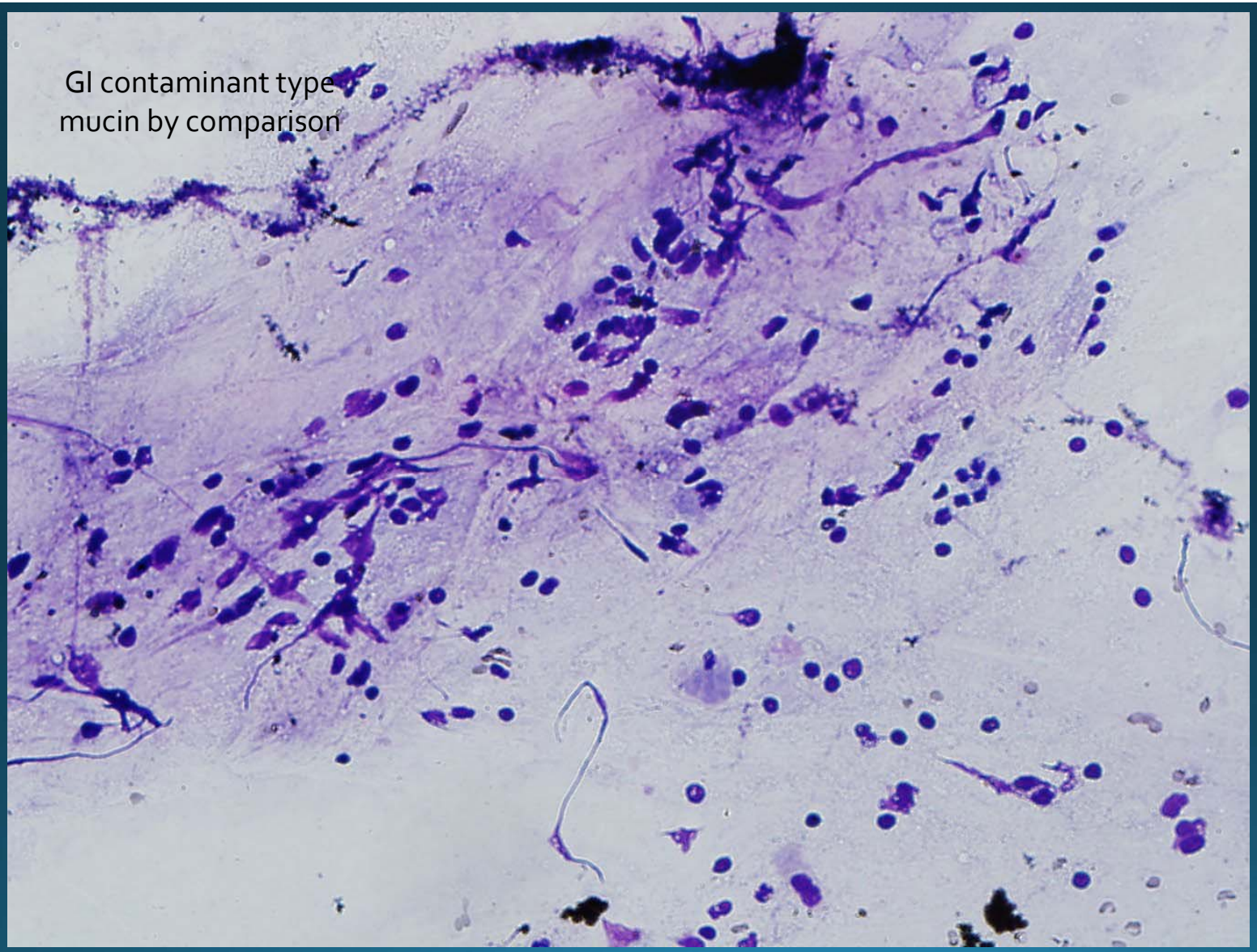
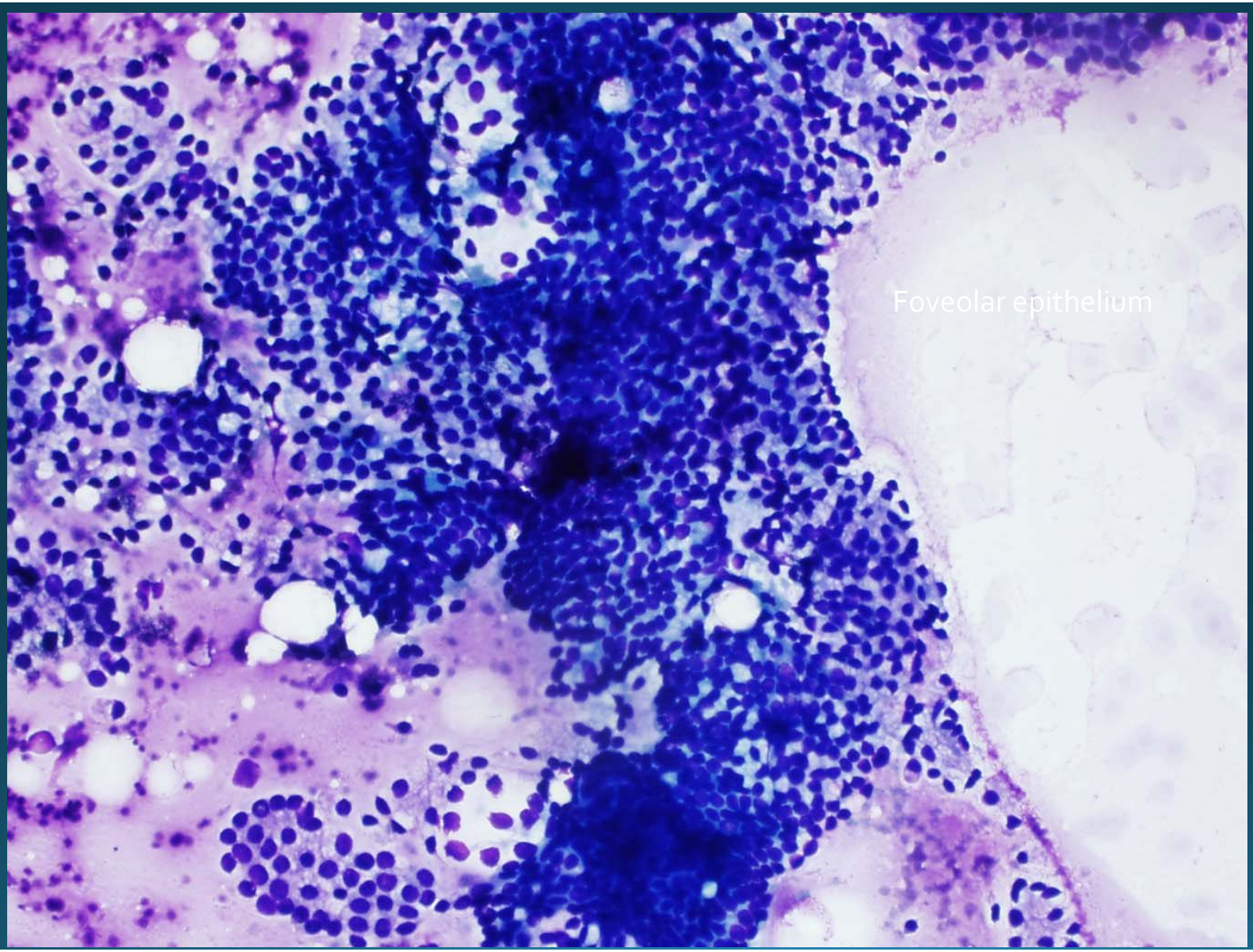
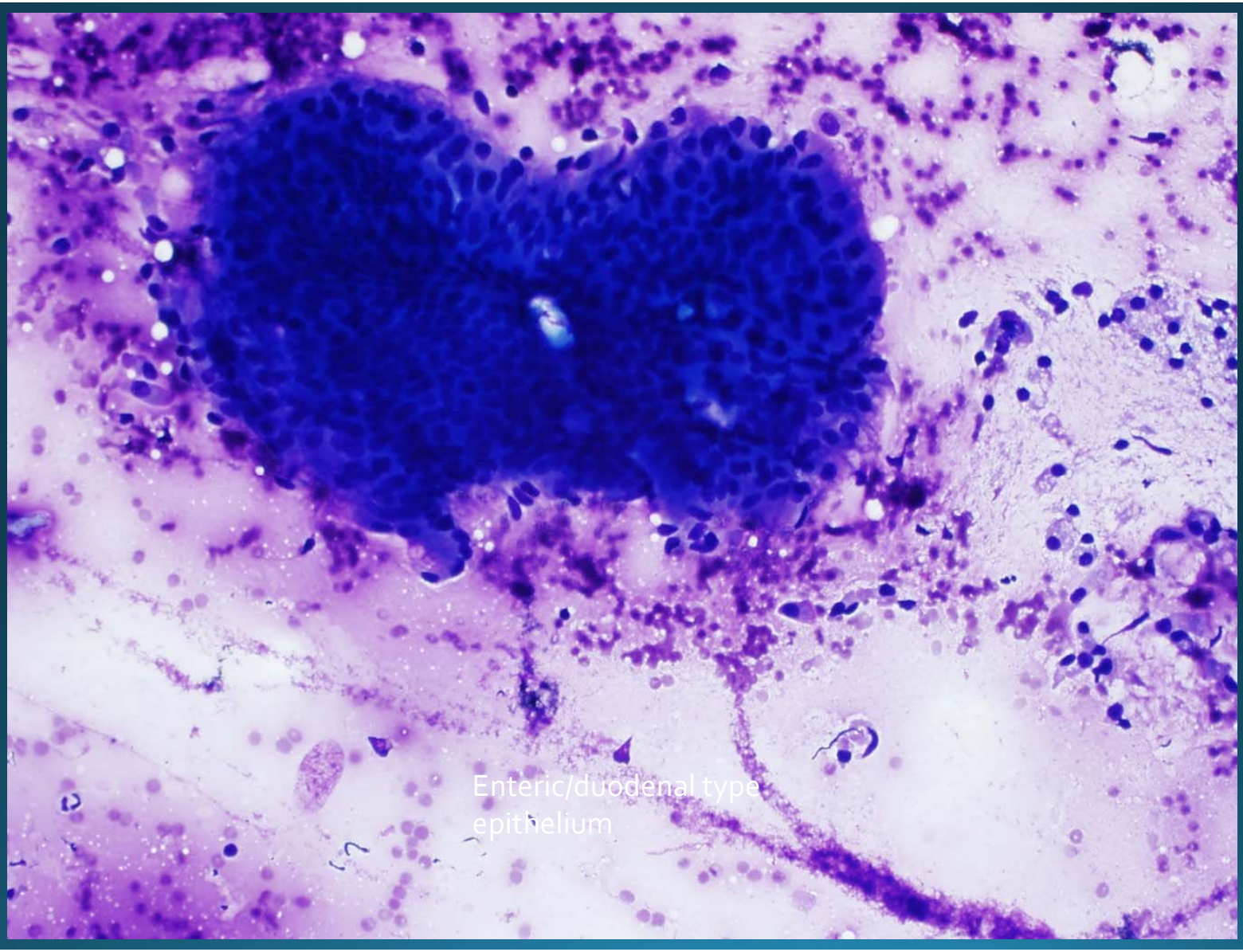
AIP


Thick colloid-
like mucin


GI contaminant type
mucin by comparison


Foveolar epithelium


Enteric/duodenal type
epithelium

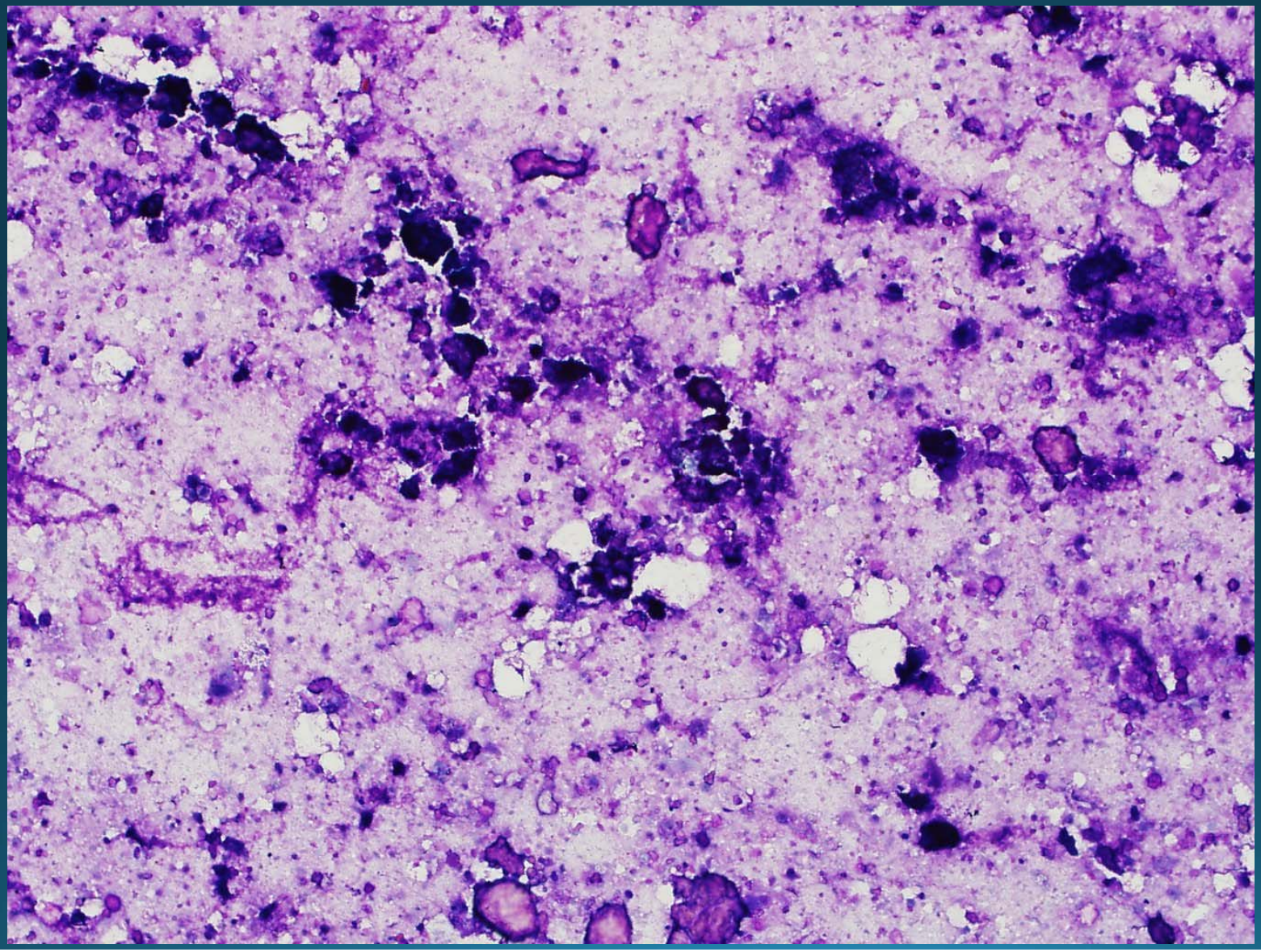
IPMN with No/Low Grade Dysplasia

- Often hard to exclude GI contamination
- Mix of gastric/foveolar epithelium (mucinous cytoplasm, may see pits or naked nuclei) and duodenal/enteric epithelium (non-mucinous with occasional Goblet cells) is indicative of a true cystic mucinous neoplasm
- Thick mucin and CEA >192 ng/mL in absence of epithelium are in keeping with cystic mucinous neoplasm

Pitfall 5: Cystic Lesions of Pancreas

- 37 year old female with a 3 cm cystic lesion in the head of the pancreas


679/682
52Hz
F13
7.5M 5.0 R04 G61 C5



Pseudocyst

- Turbid fluid, nonspecific findings
- FNA: histiocytes, debris, few epithelial cells
  - Necrosis, inflammation, granulation tissue, fibrosis, calcification, cholesterol crystals
  - Repair = some atypia
- Elevated amylase (generally in 1000s) in combination with low CEA (<100)
- Benign category by Pap Society guidelines