NCI Thyroid FNA Conference

Subcommittee IV

Terminology

Papillary Carcinoma and Its Variants

Subcommittee IV

Terminology

Agenda Item

- Morphologic Criteria: What are the diagnostic criteria for the diagnosis of papillary thyroid carcinoma (should they be divided into minor and major criteria) and its variants?

Web Site Posts / Controversies

- Too complicated for me.

Web Site Posts / Controversies

- Papillary carcinoma, of course, is based on nuclear attributes. The nuclei tend toward oval in shape with thin membranes.
- The chromatin is classically very fine and evenly dispersed (powdery). Nucleoli are inconspicuous. Classically, a subjective number or % of the nuclei (perhaps best defined as not rare and randomly scattered in a specimen) have longitudinal grooves.
- Less often, pseudo-inclusions are prominent. One does not need to see true or even vaguely papillary structures and/ psammoma bodies to make this diagnosis, although it is comforting to see them. Multinucleated giant cells and cells with squamoid cytoplasmic appearances help round out the picture.
- I think it is important for the pathologist to search diligently for these features, mostly the nuclear ones. I think we may dx an inconsequential tumor, but it is better than missing one.

Web Site Posts / Controversies

- The criteria may be.
- 1- adequate cellularity - whatever that is determined to be.
- 2- follicular cells (cohesive epithelial cells - papillae, sheets, follicles, etc)
- 3- the same nuclear features one uses histologically, aside from the clearing that we won't get to see -
- The problem is that the histologists don't agree about minimal criteria.

Web Site Posts / Controversies

- **I think that this forum should recommend minimal criteria for a "positive" diagnosis...**

1. **Enlarged oval nuclei with small eccentric nucleoli**
2. **Pale chromatin**
3. **Longitudinal nuclear grooves**
4. **At least a rare intranuclear pseudo-inclusion.**
5. **To me, these are MAJOR features. Do all of these major features need to be present for a "positive" diagnosis or can other "minor" features (e.g. bubble gum colloid, giant cells, papillary formation psammoma bodies, squamoid cytoplasm) [which ones and how many] be used in combination to arrive at a "positive" diagnosis?**

- **This has the potential to become a complex algorithm, but one that is so basic for thyroid cytology that it should be addressed.**

Papillary Thyroid Carcinoma (PTC) Definition

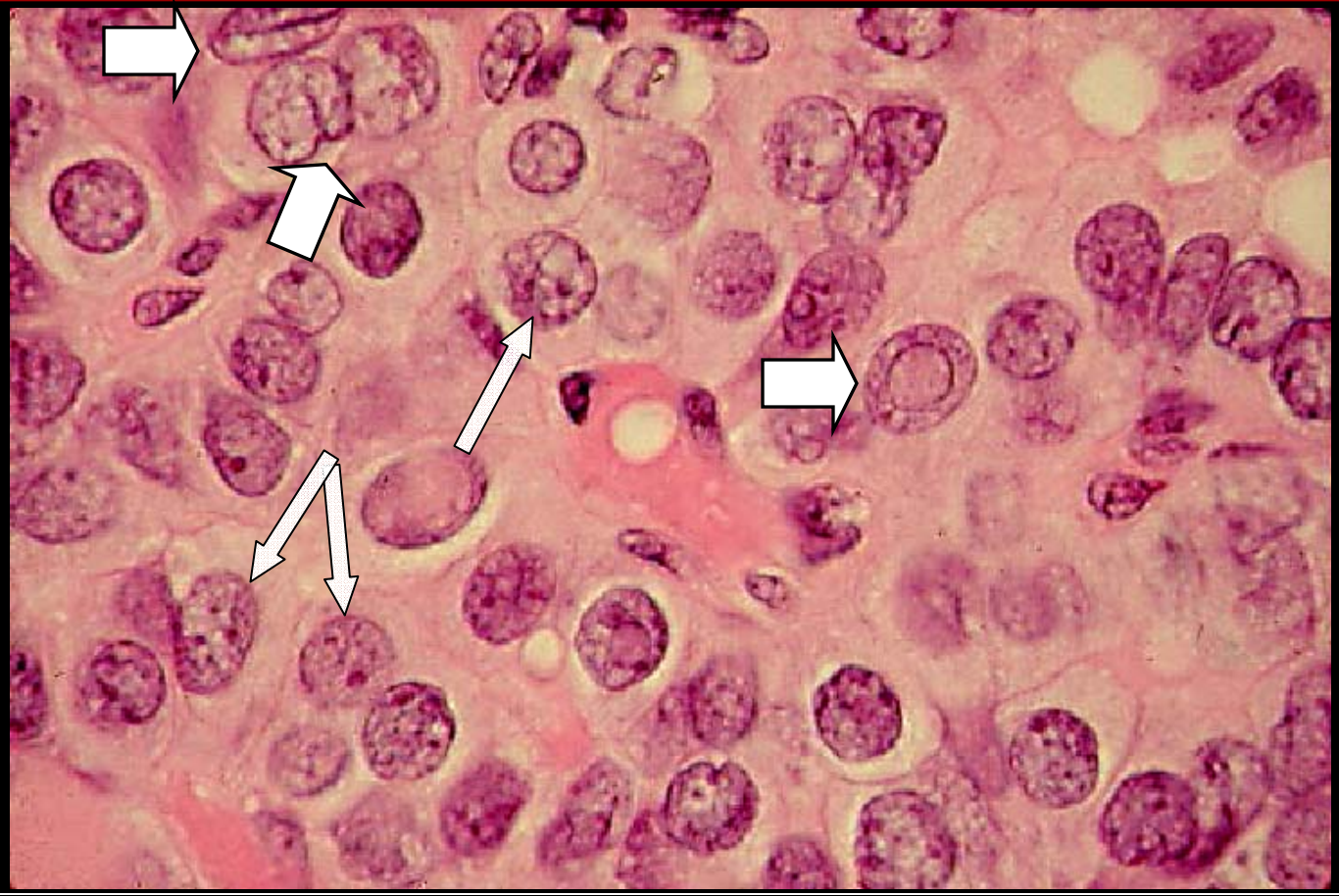
"A malignant epithelial tumour showing evidence of follicular cell differentiation and characterized by distinctive nuclear features"

WHO 2004

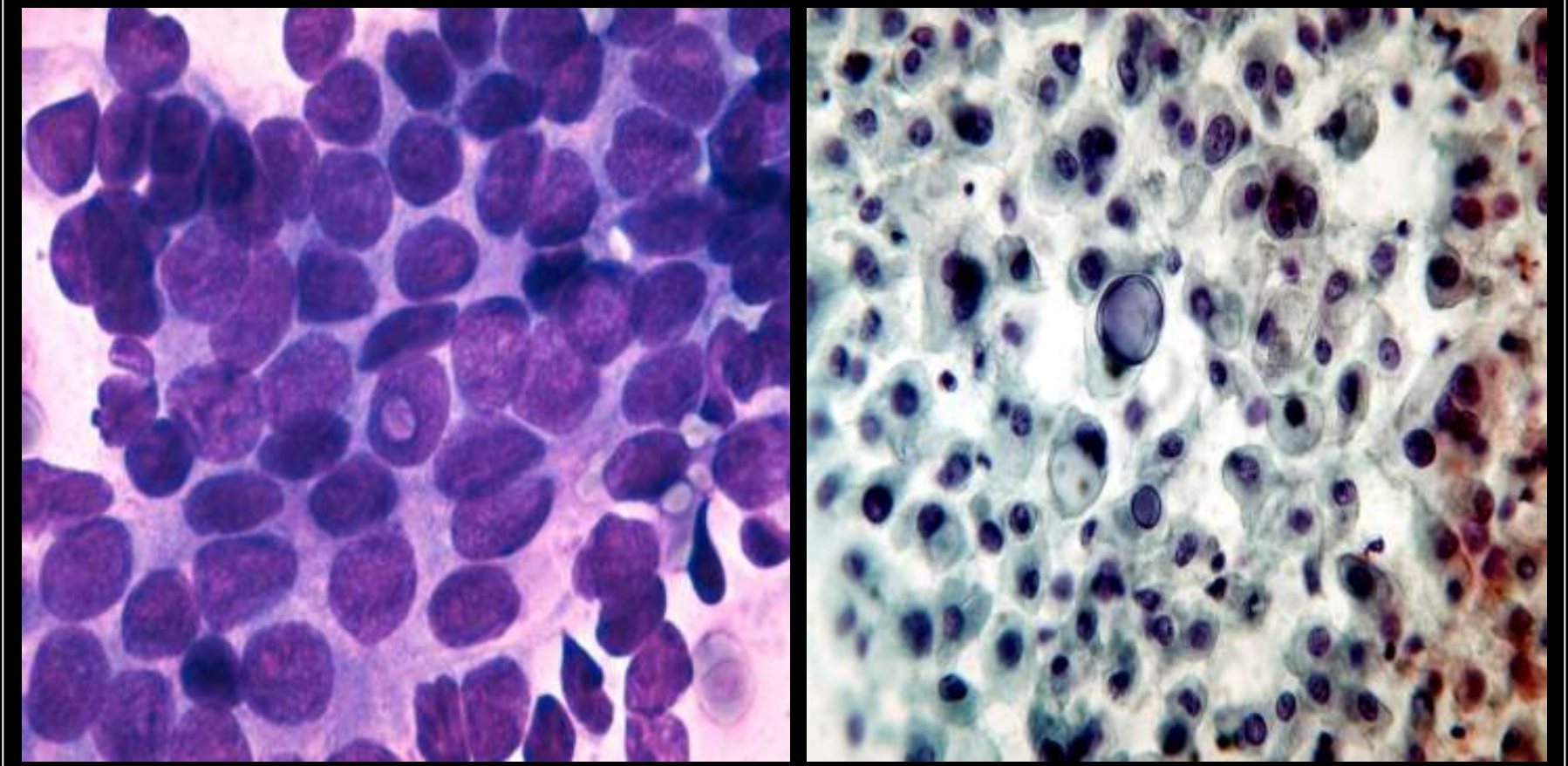
Papillary Thyroid Carcinoma (PTC) Nuclear Criteria

- Nuclear enlargement and elongation
- Irregular nuclear contours that result in nuclear grooves and cytoplasmic pseudoinclusions
- Peripheral margination of chromatin with clearing of nucleoplasm
- Multiple micronucleoli

Papillary Thyroid Carcinoma (PTC) Nuclear Criteria - Histology



Papillary Thyroid Carcinoma (PTC) Nuclear Criteria - Cytology



Papillary Thyroid Carcinoma (PTC) Nuclear Criteria - Cytology

Papillary Thyroid Carcinoma (PTC) Variants

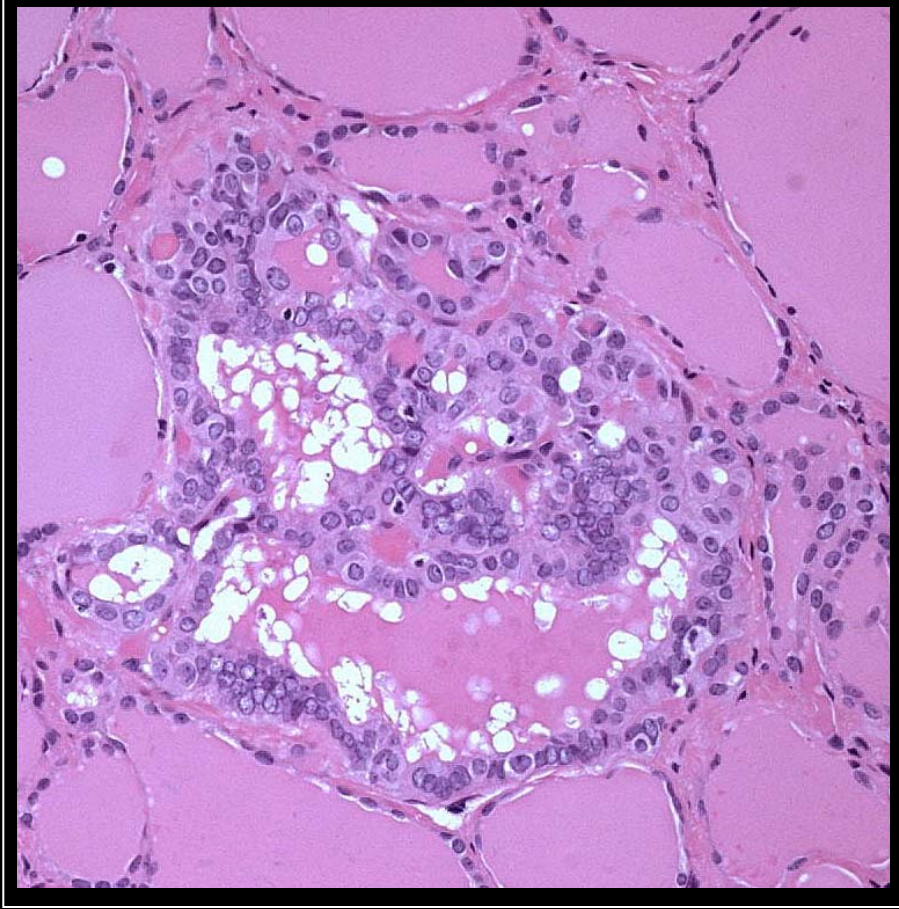
Variants determined by

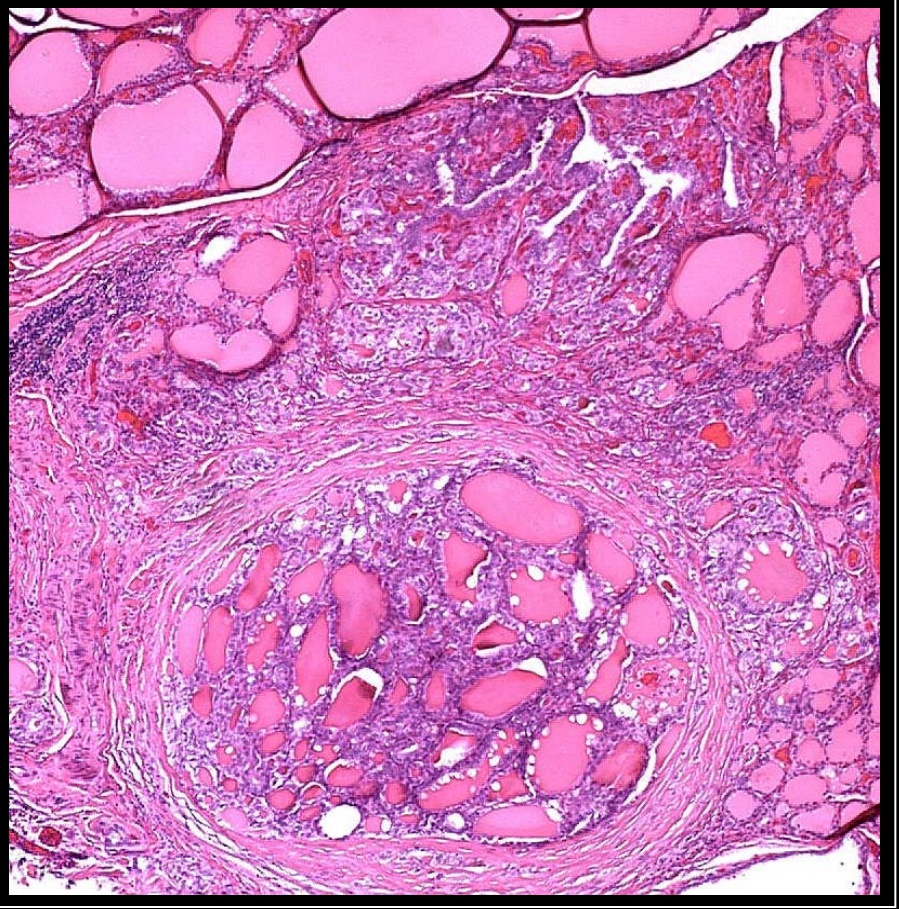
- Size
- Architecture
- Cytology

Papillary Thyroid Carcinoma (PTC) Size Variant

- *Papillary Microcarcinoma*
  - *PTC ≤ 1 cm*
  - *Any architecture*
  - *Any cytology*
- *Clearly not a cytologic diagnosis!*

Papillary Microcarcinoma (PMC)

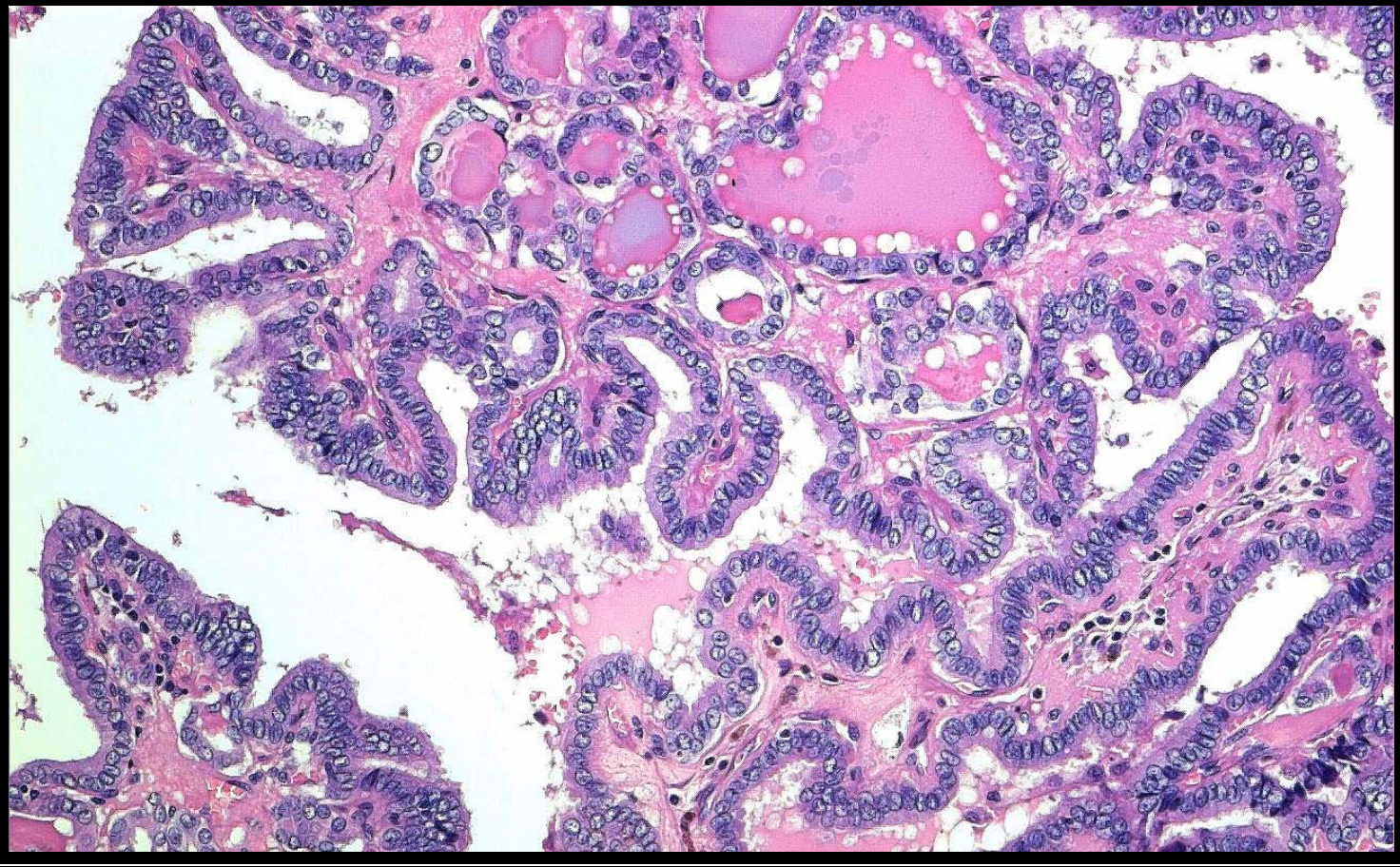




Papillary Thyroid Carcinoma (PTC) Architectural Variants

- *Classical variant: papillary architecture*
- *Follicular variant: follicular architecture*
- *Cribriform-morular*
  - *Thought to be pathognomonic of FAP-associated disease*
- *Solid variant: solid sheets and nests lacking papillae or follicles*

PTC Classical Type: Histology

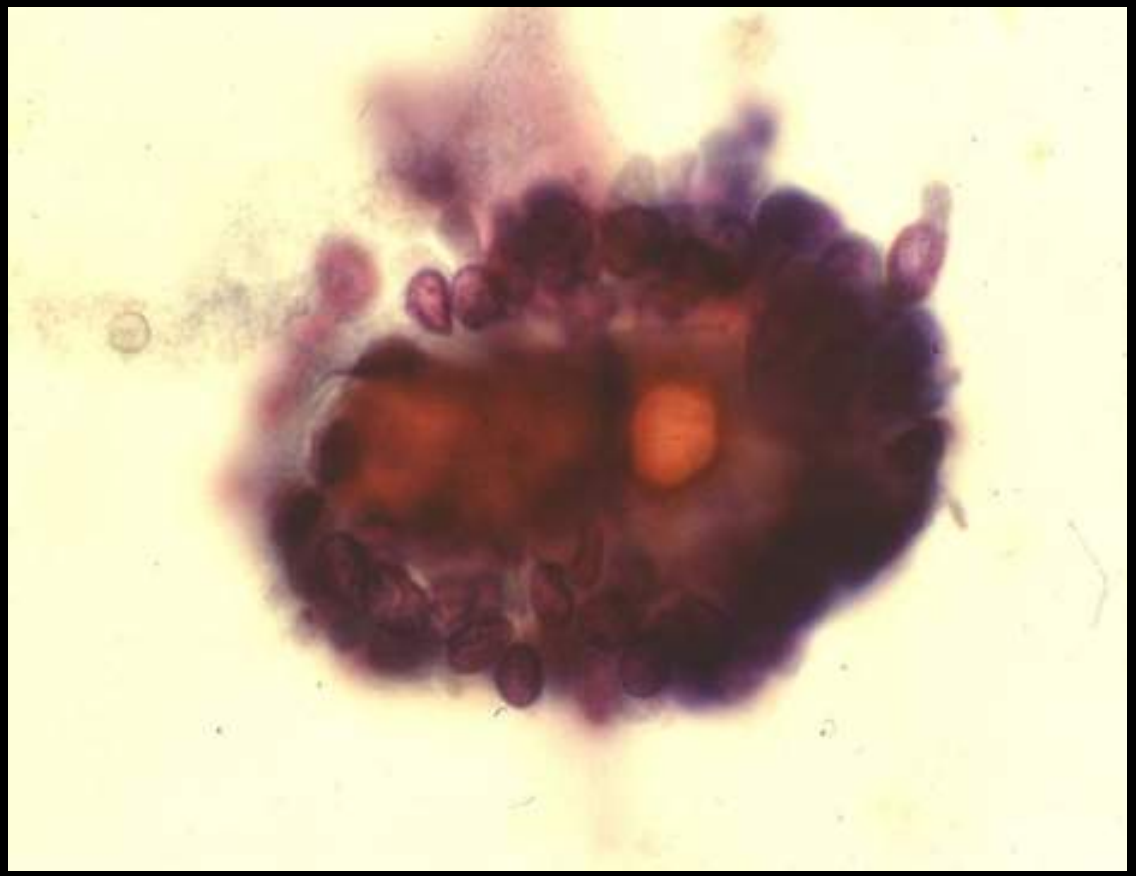


PTC Classical Type: Cytology

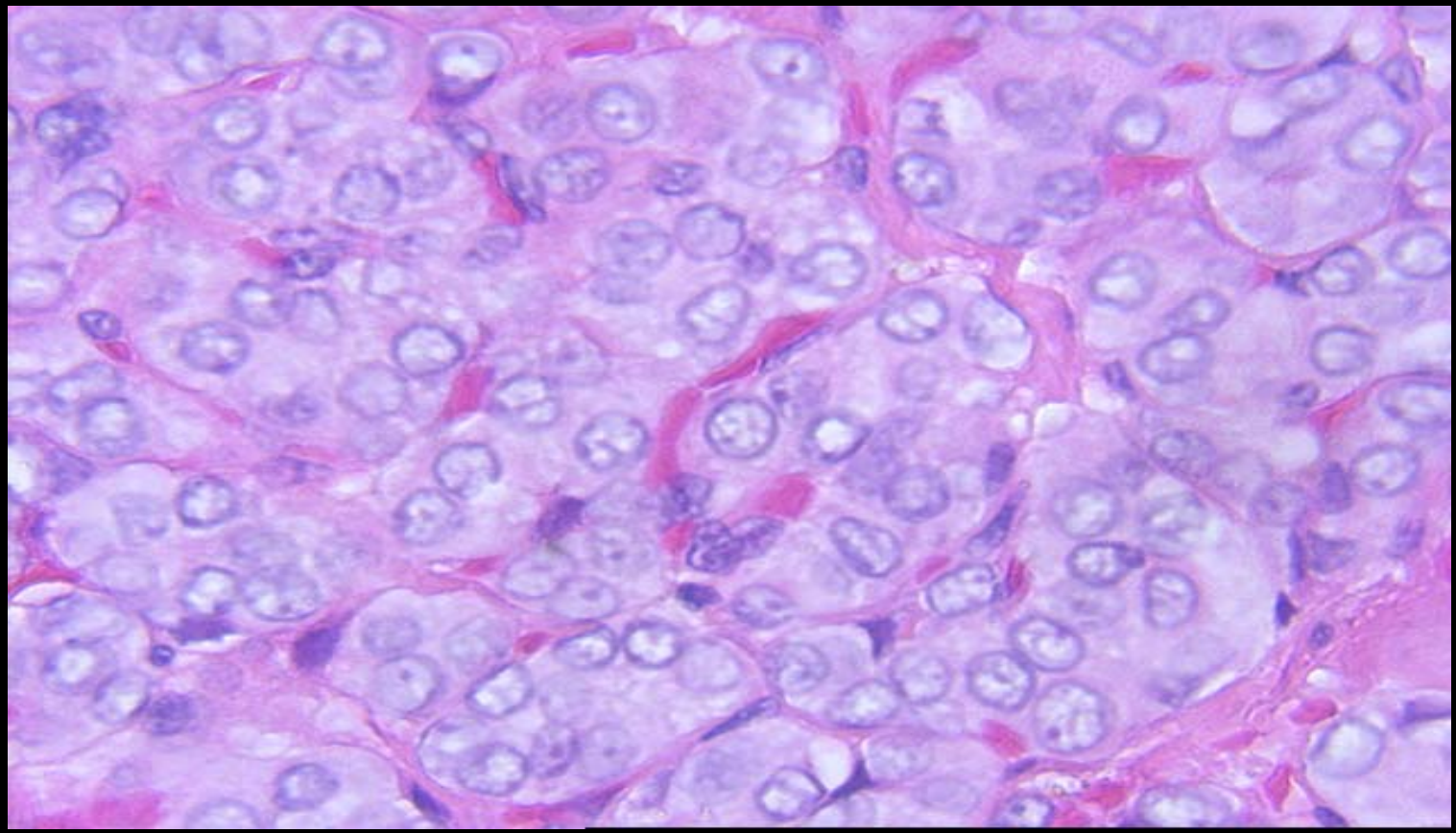
Papillae with fibrovascular cores

PTC Classical Type: Cytology

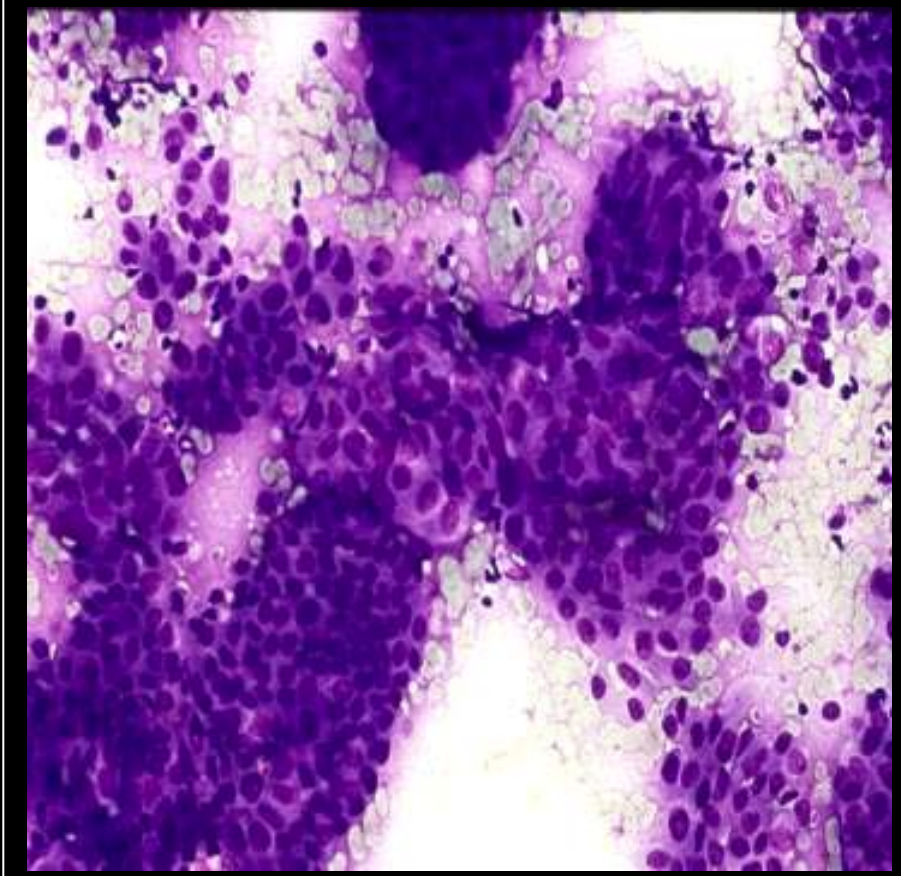
Psammoma body

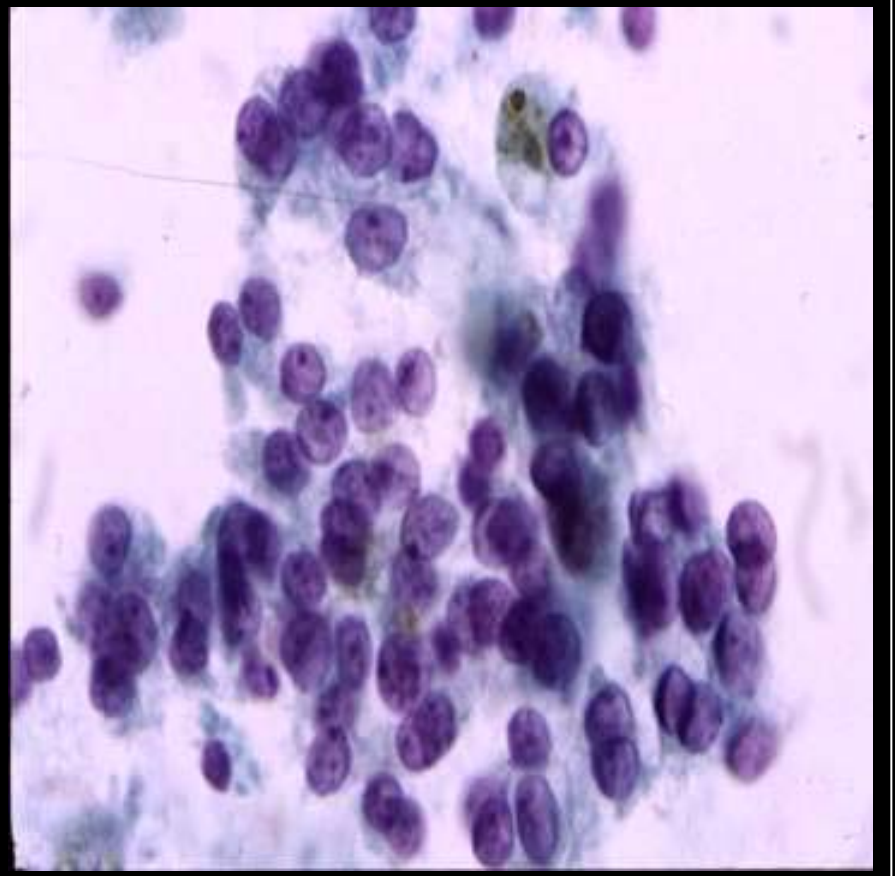


PTC Follicular Variant: Histology

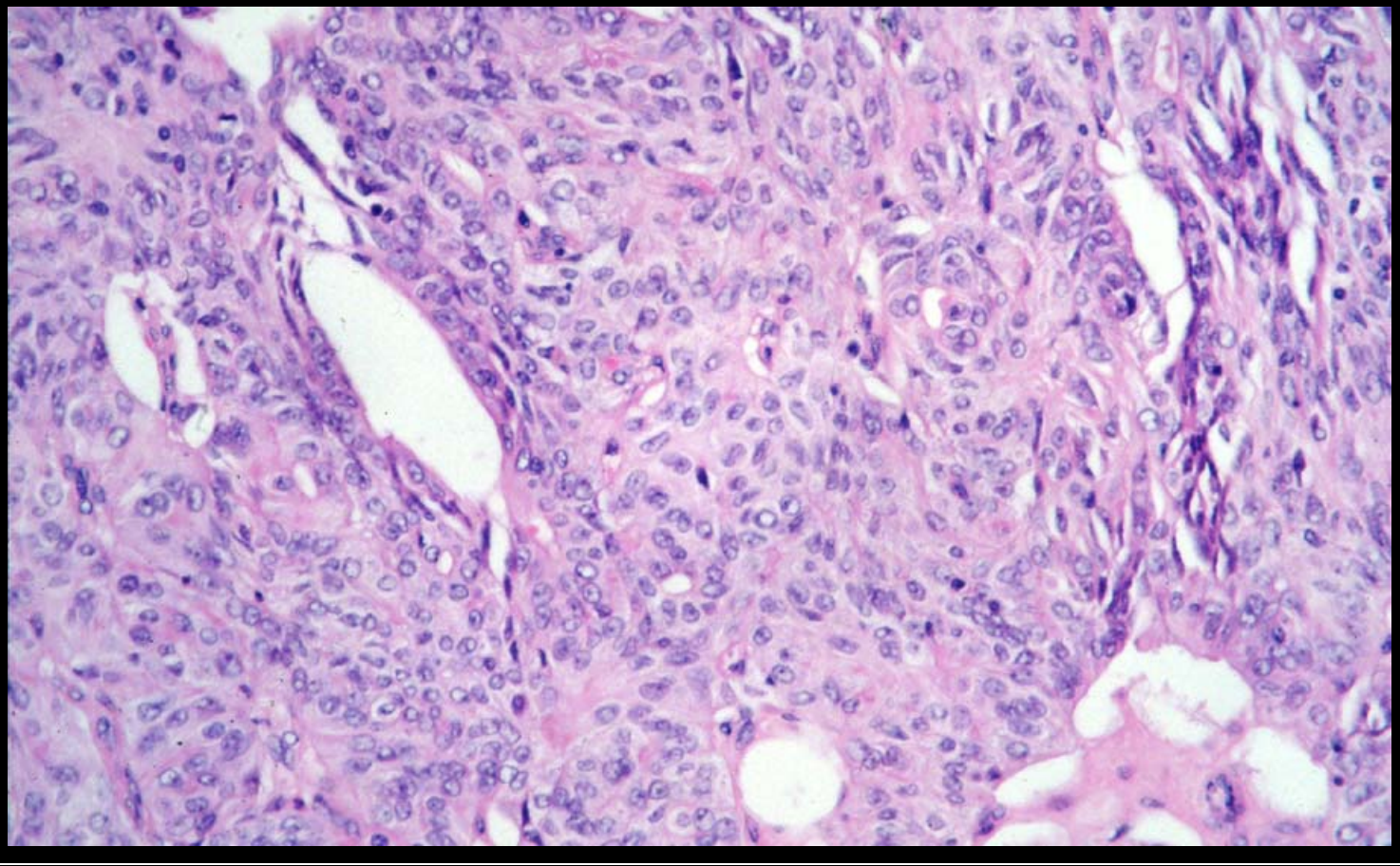


PTC Follicular Variant: Cytology

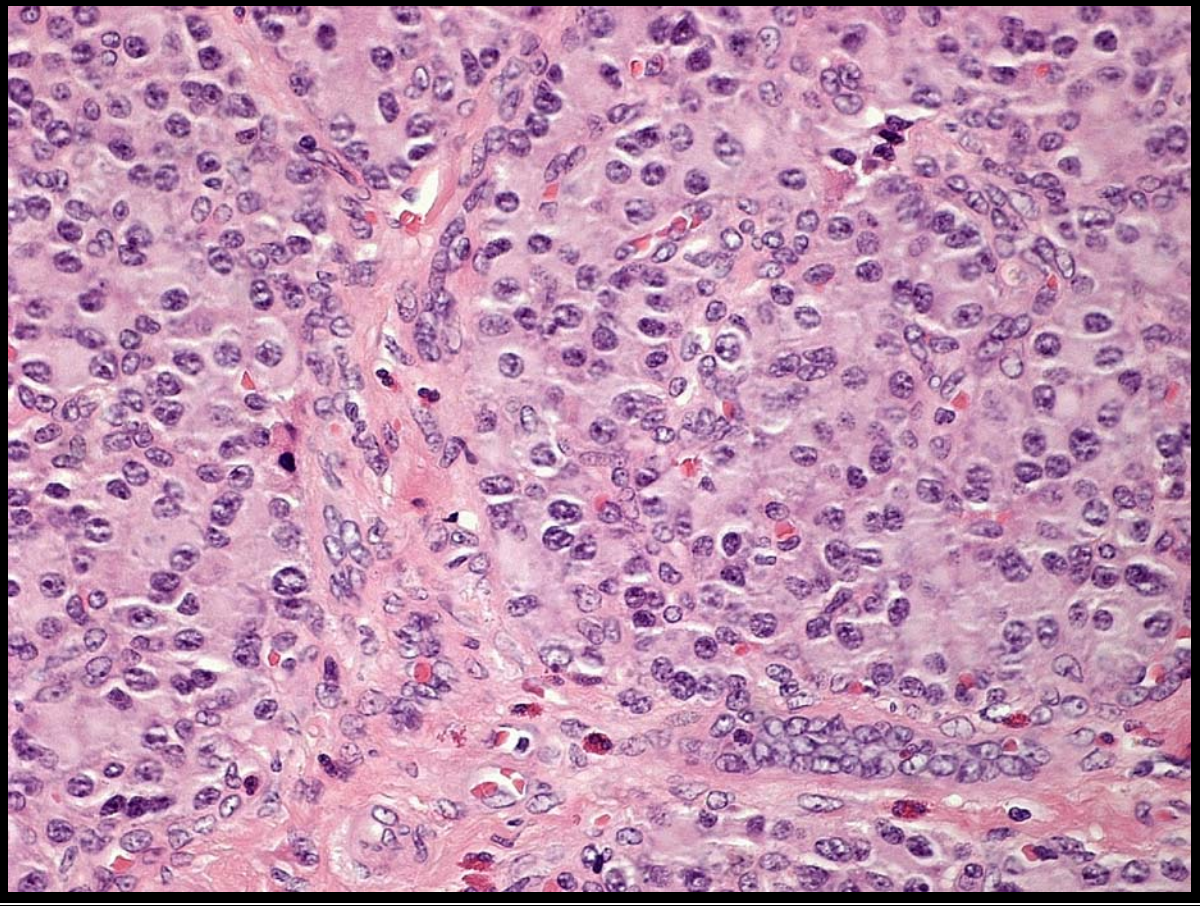




Cribriform-Morular PTC: Histology



Solid Variant PTC: Histology



Papillary Thyroid Carcinoma (PTC) Cytologic Variants

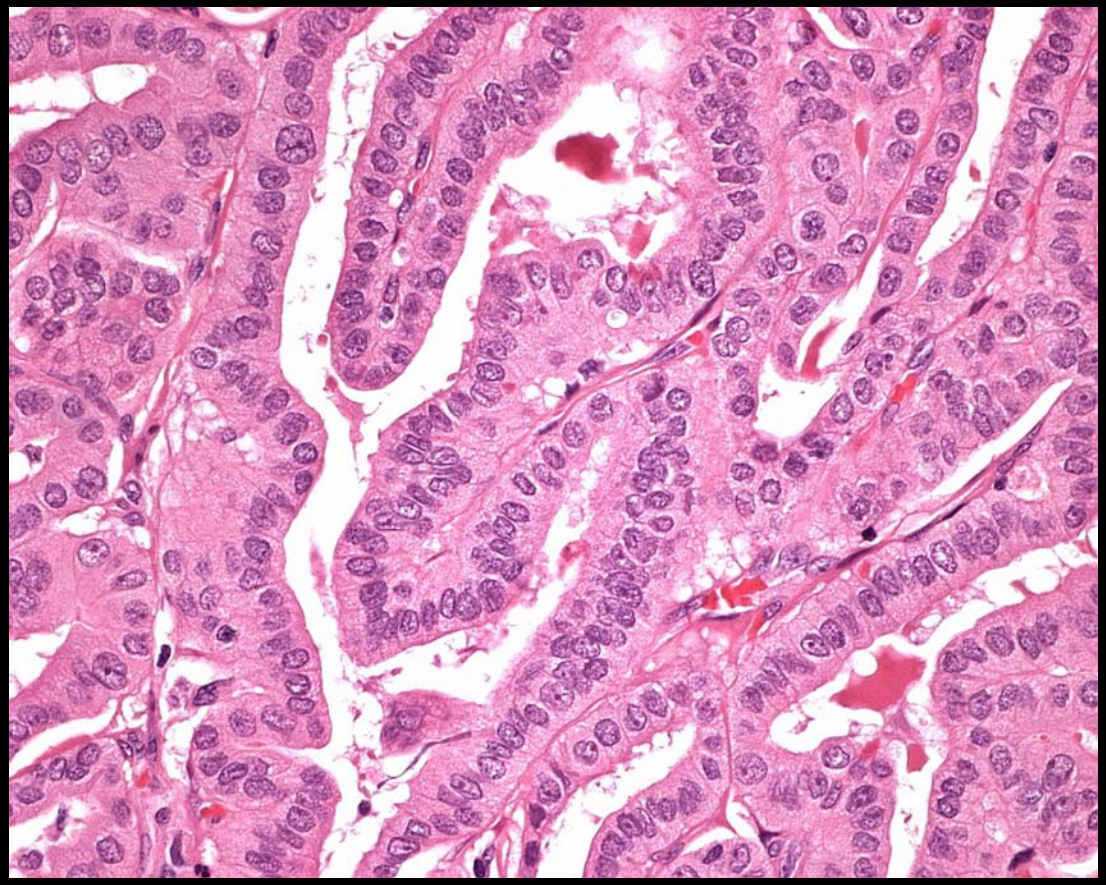
- *Oncocytic: cells with abundant vacuolated mitochondria*
- *Clear cell: various subcellular changes*
- *Tall cell*
  - *Defined as height-to-width ratio >3:1*
- *Columnar cell*
  - VERY tall cells with pseudostratification and secretory or “endometrioid” appearance

Papillary Thyroid Carcinoma (PTC) Oncocytic Variants

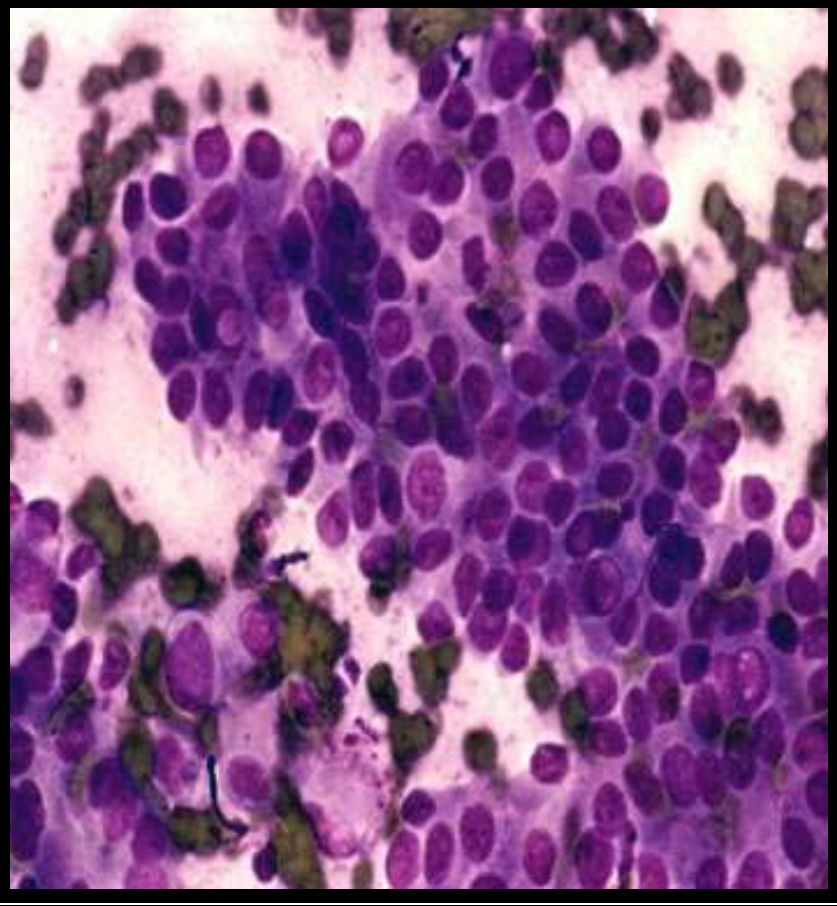
- *Classical PTC with oncocytic change*
- *"Warthin-like" PTC*
  - *Classical papillary architecture*
  - *Stromal lymphoplasmacytic infiltrate*
- Follicular variant PTC with oncocytic change

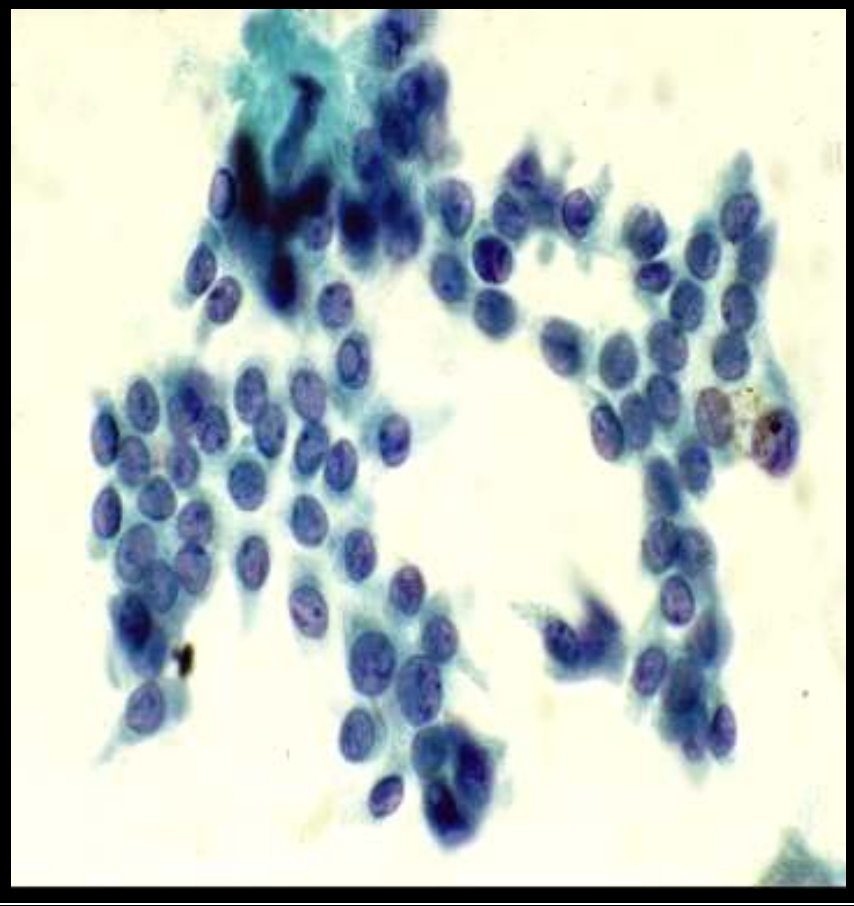
PTC Oncocytic Variant: Histology

Classical



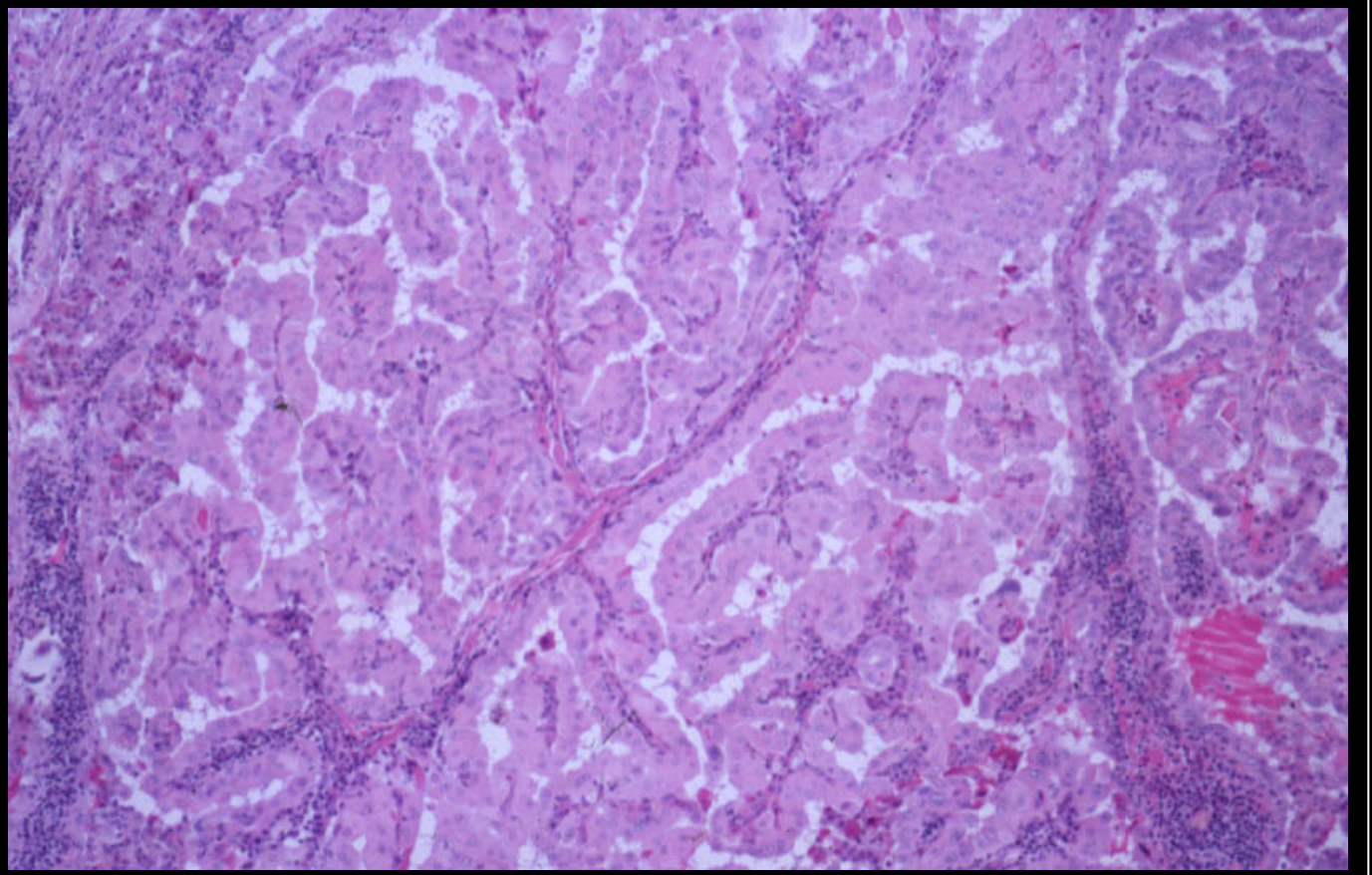
PTC Oncocytic Variant: Cytology



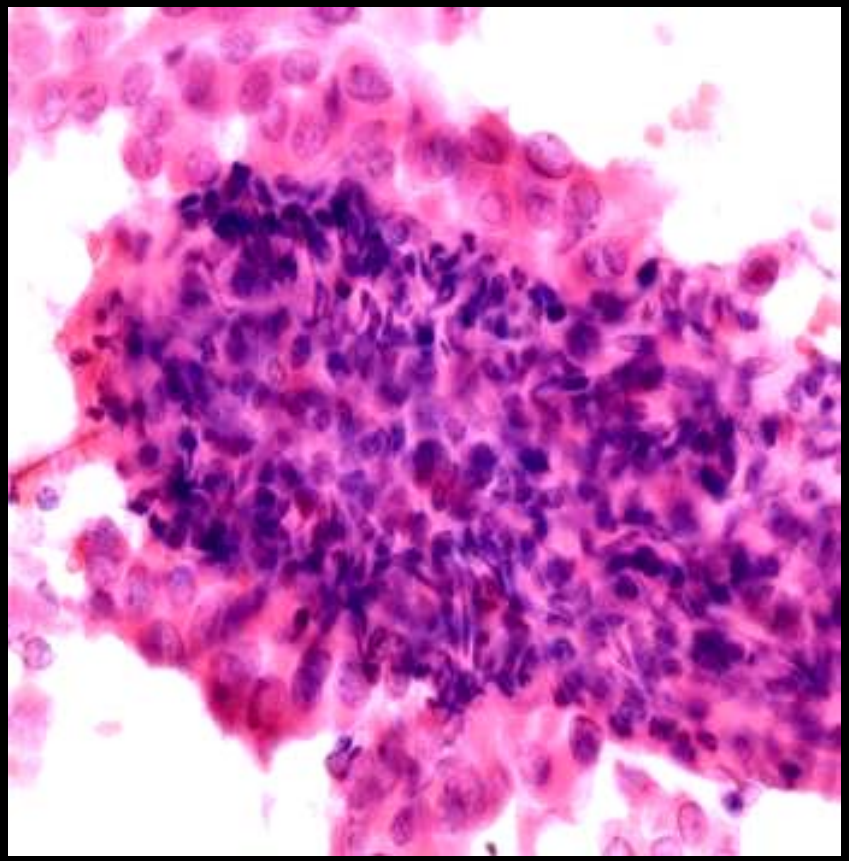


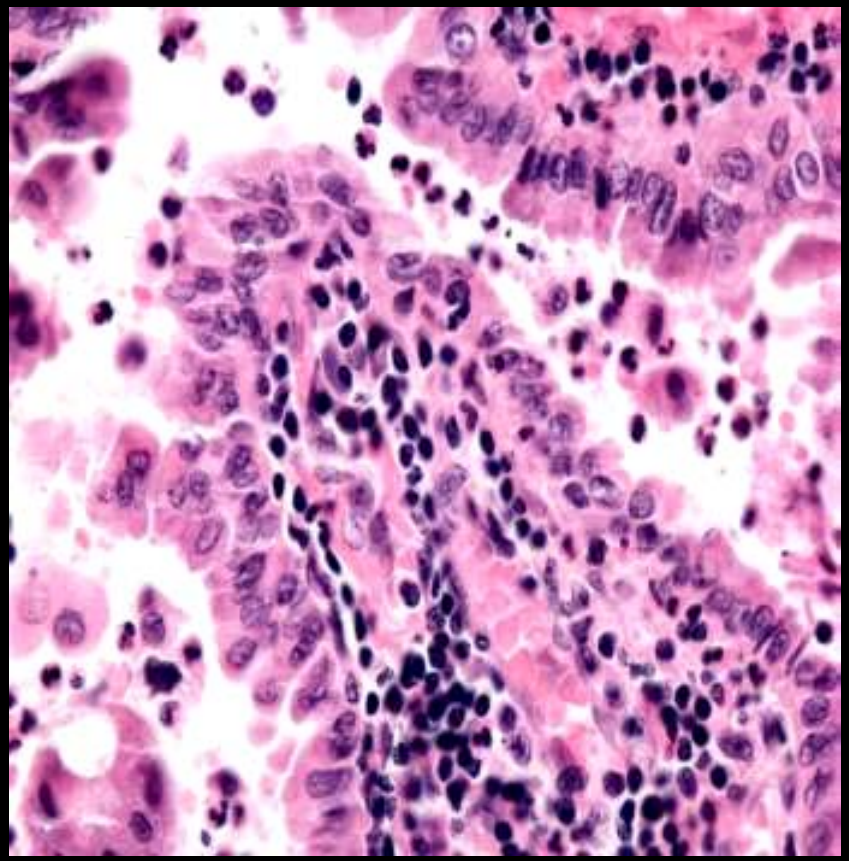
PTC Oncocytic Variant: Histology

Warthin-like

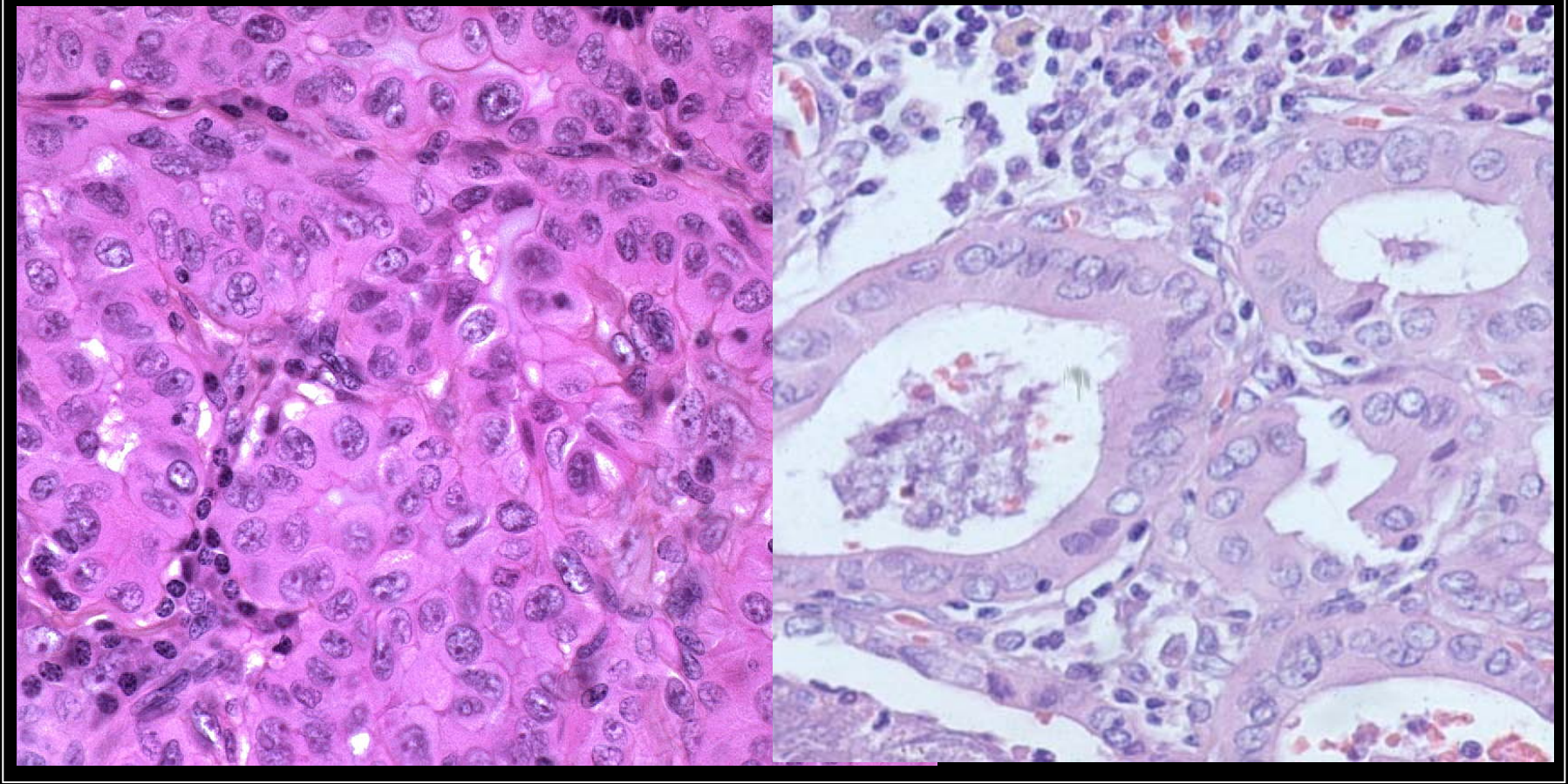


Warthin-like PTC: Cytology

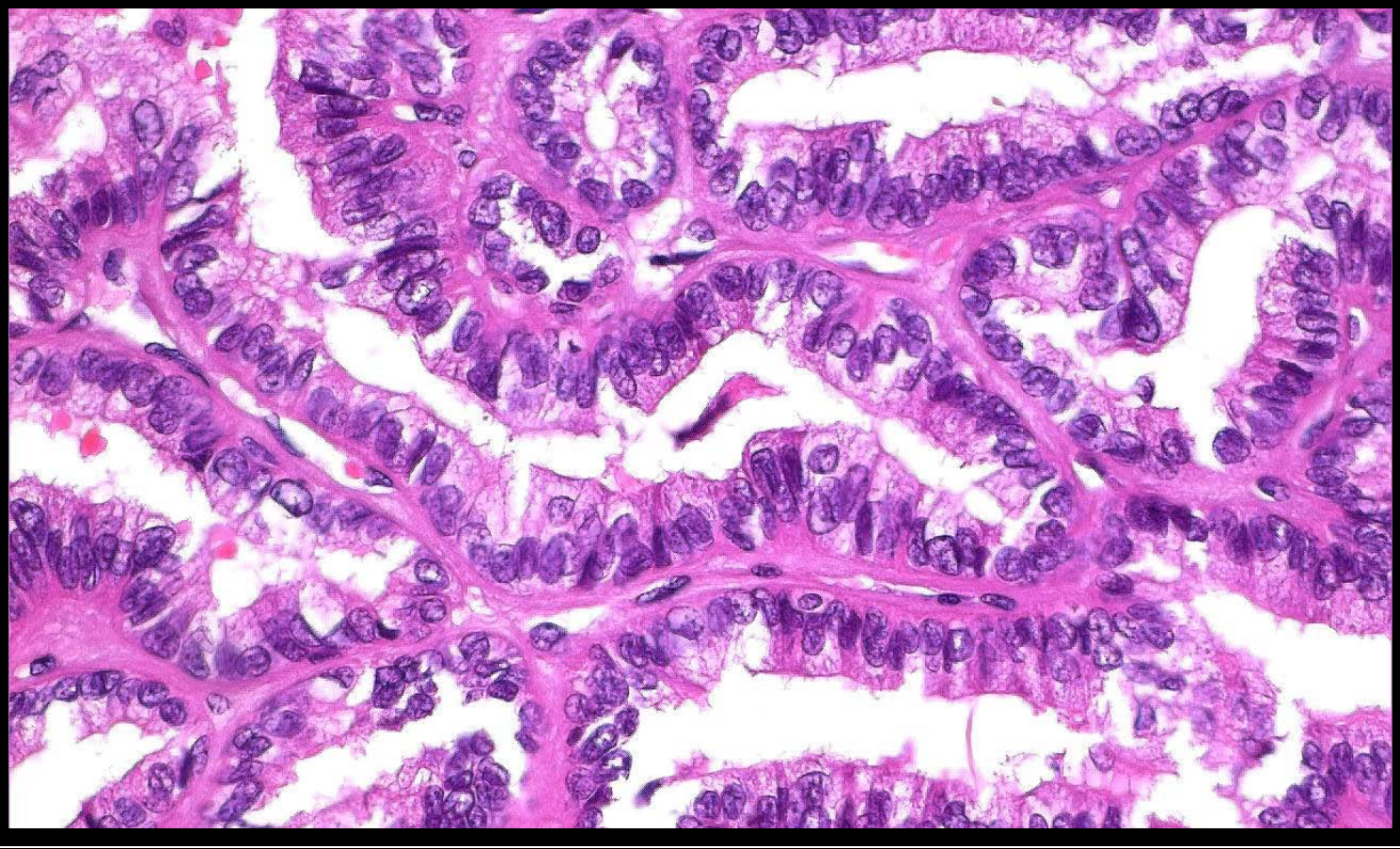




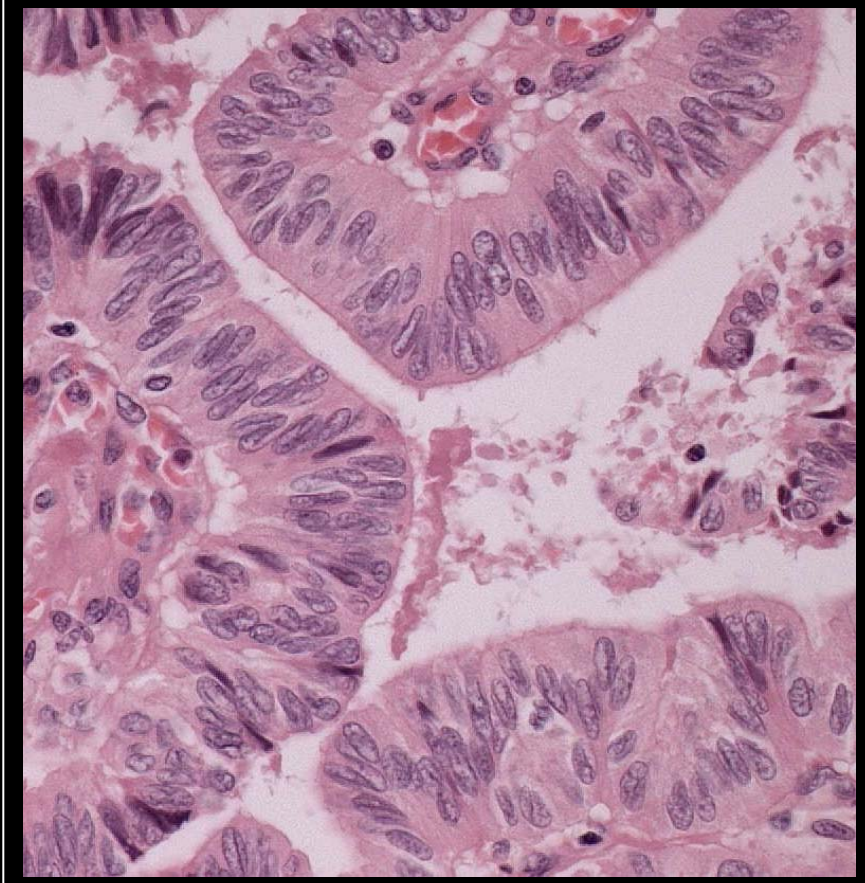
FVPTC Oncocytic Variant: Histology

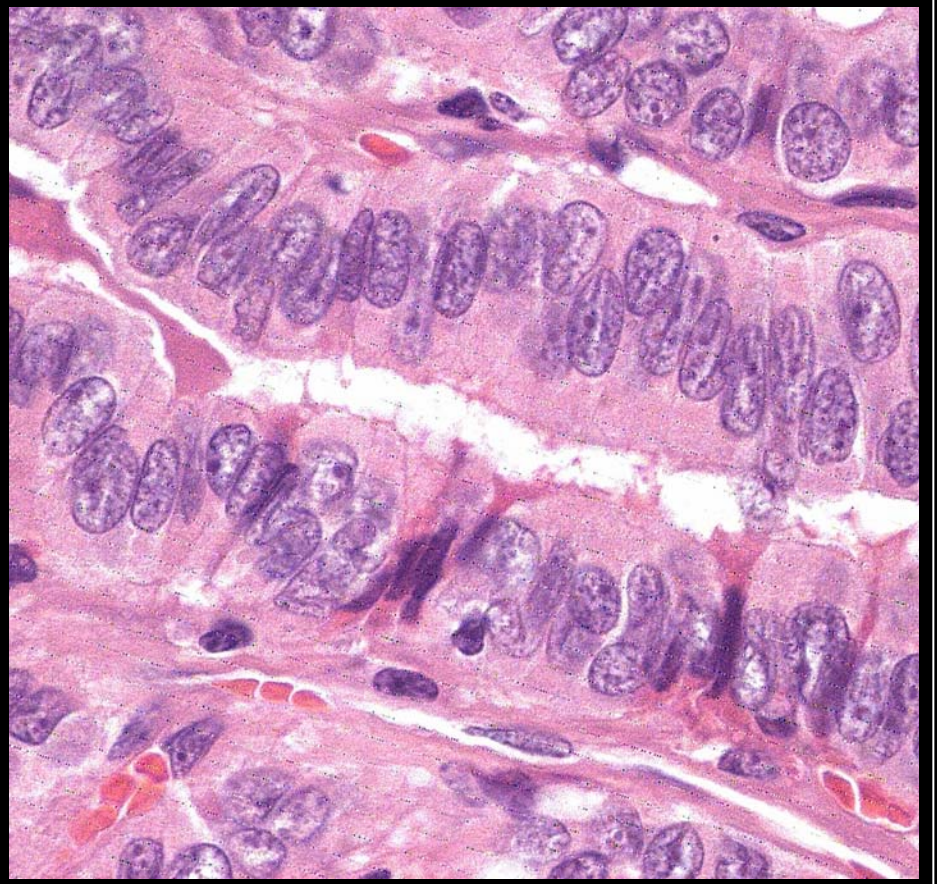


PTC Clear Cell Variant: Histology

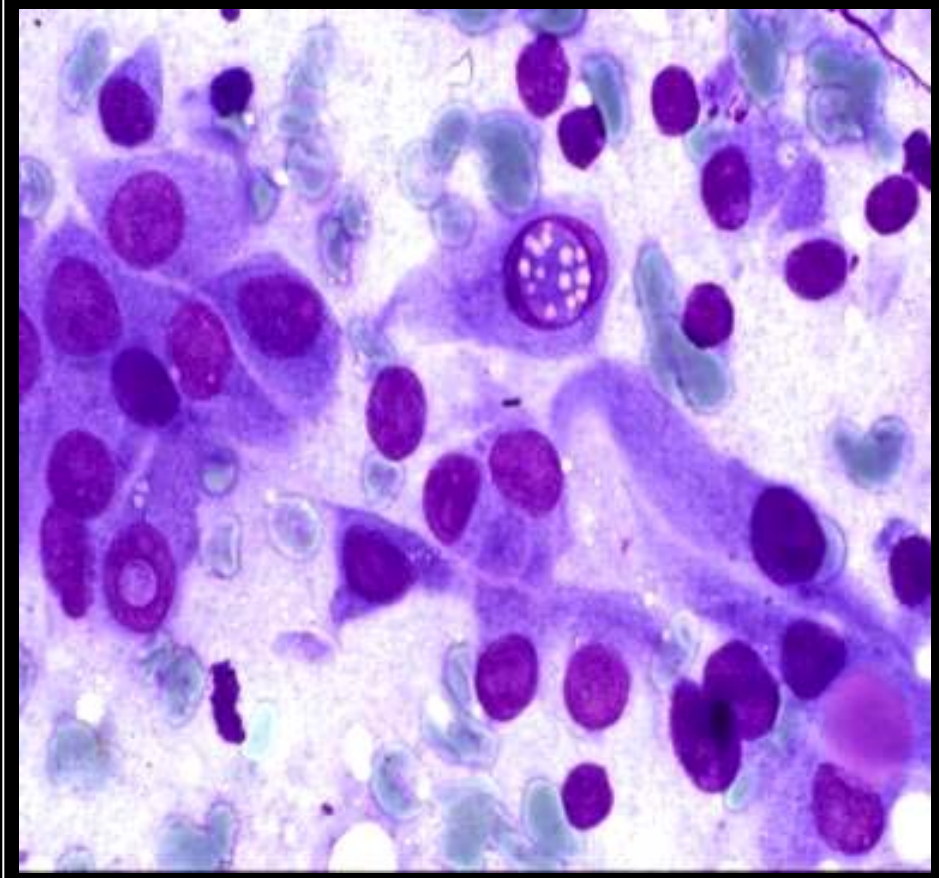


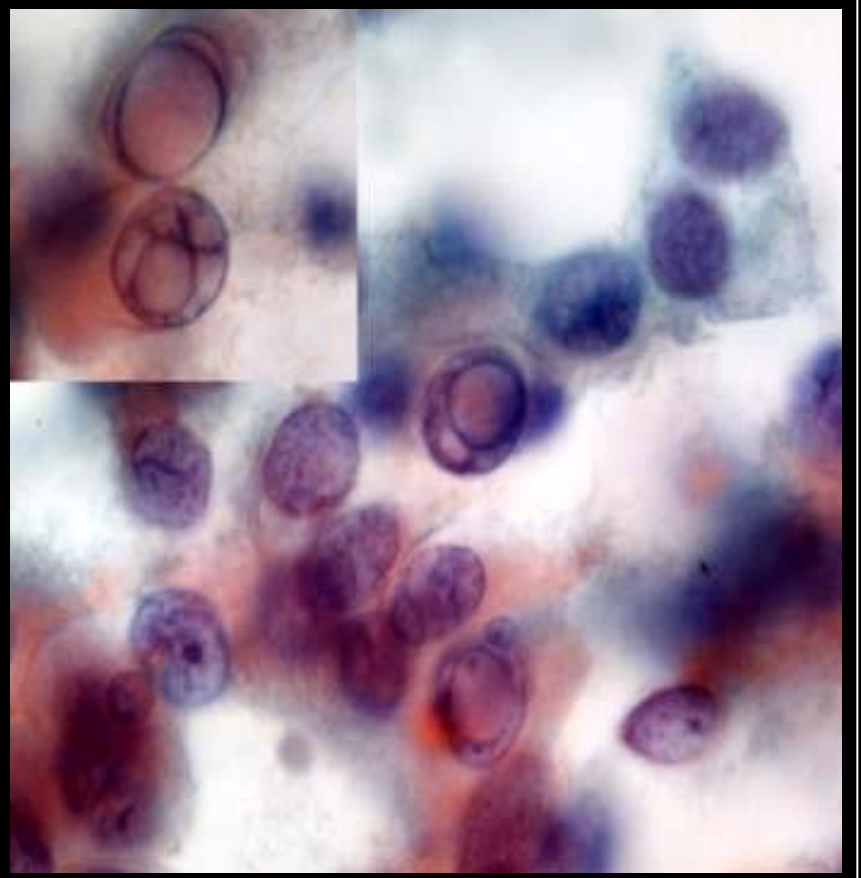
PTC Tall Cell Variant: Histology



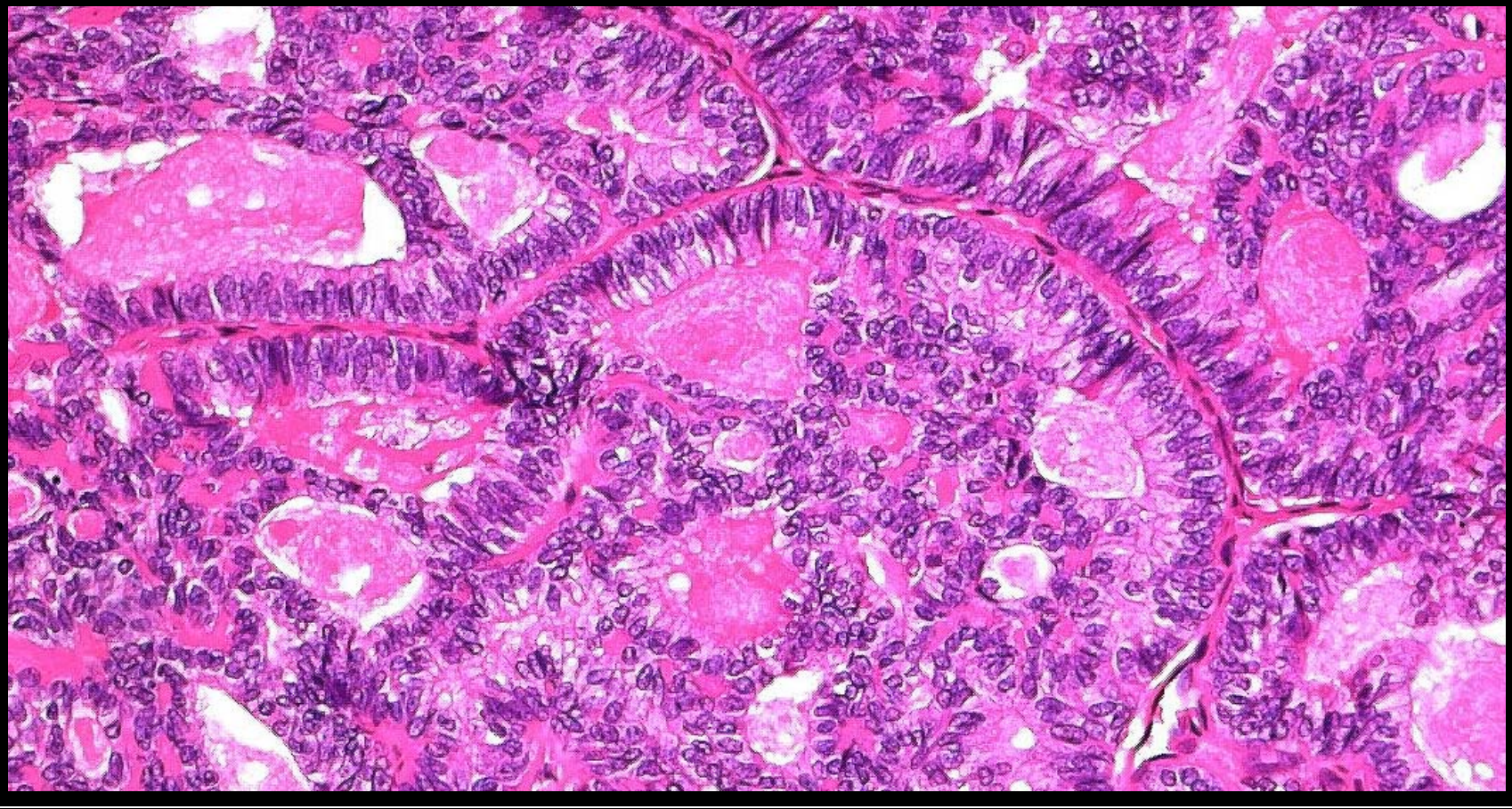


PTC Tall Cell Variant: Cytology





PTC Columnar Variant: Histology



Prognostic Implications of Variants

- *Microcarcinoma: very low risk (aka papillary "microtumor")*
- *Follicular variant: controversial*
- *Cribriform-morular: FAP-associated disease*
- *Solid variant: more aggressive behavior*
- *Tall cell: worse prognosis usually attributed to higher stage at diagnosis (local invasion)*
- *Columnar cell: very aggressive malignancy*

Pathobiological Implications of Variants

- *Classical variant: BRAF mutations*
- *Follicular variant: possibly ras, ret/PTC-3*
- *Cribriform-morular: ? FAP-association*
- *Solid variant: ret/PTC-3*
- *Tall cell: ? Multiple mutations*
- *Oncocytic variants: mitochondrial and GRIM-19 mutations in addition to other mutations specific to PTC*

Conclusions

- Papillary Carcinoma Diagnosis – Major

  <u>Diagnostic Cytologic Features:</u>

  1. **Enlarged, oval "and irregular" nucleus**
  2. **Eccentric and often multiple micro-nucleoli**
  3. **Fine, pale chromatin**
  4. **Longitudinal nuclear grooves**
  5. **Intranuclear pseudo-inclusions**

Conclusions

- Papillary Carcinoma Diagnosis – Minor

  <u>Diagnostic Cytologic Features:</u>

  1. **Papillary cytoarchitecture**
  2. **Syncytial monolayers**
  3. **Dense squamoid cytoplasm**
  4. **“Bubble-gum” colloid**
  5. **Psammoma bodies**
  6. **Multinucleated giant cells**