2019 AANP DIAGNOSTIC SLIDE SESSION CASE #4

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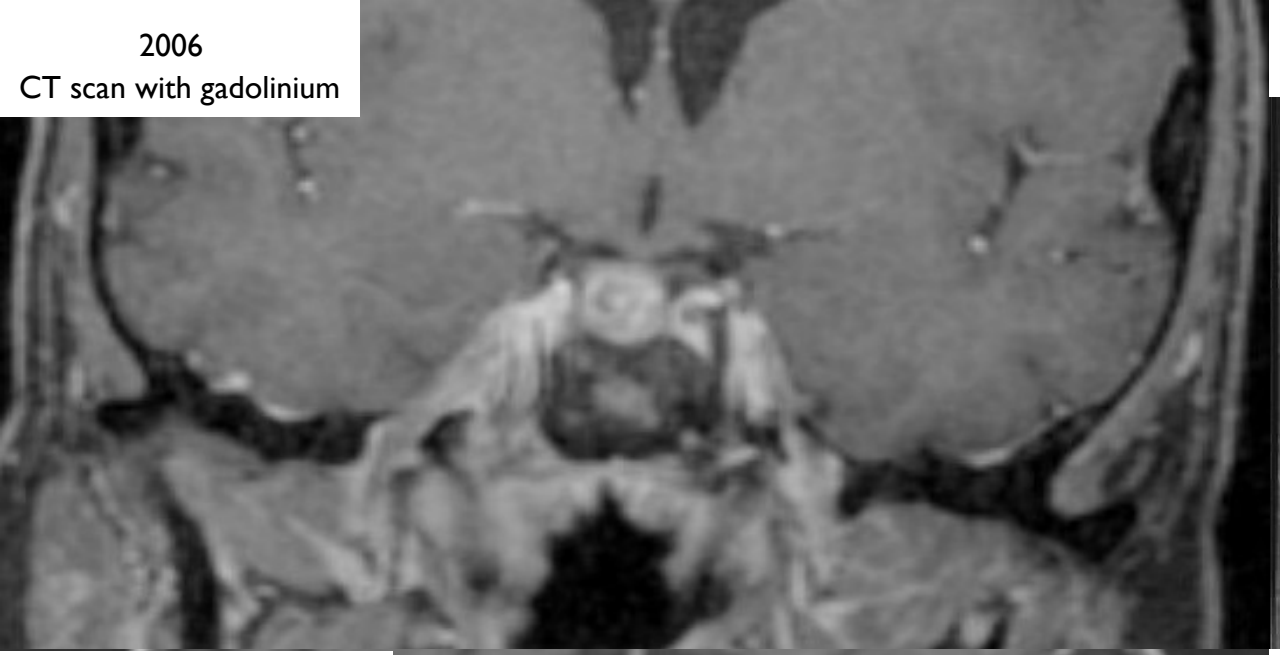
DISCLOSURES

NO RELEVANT FINANCIAL DISCLOSURES

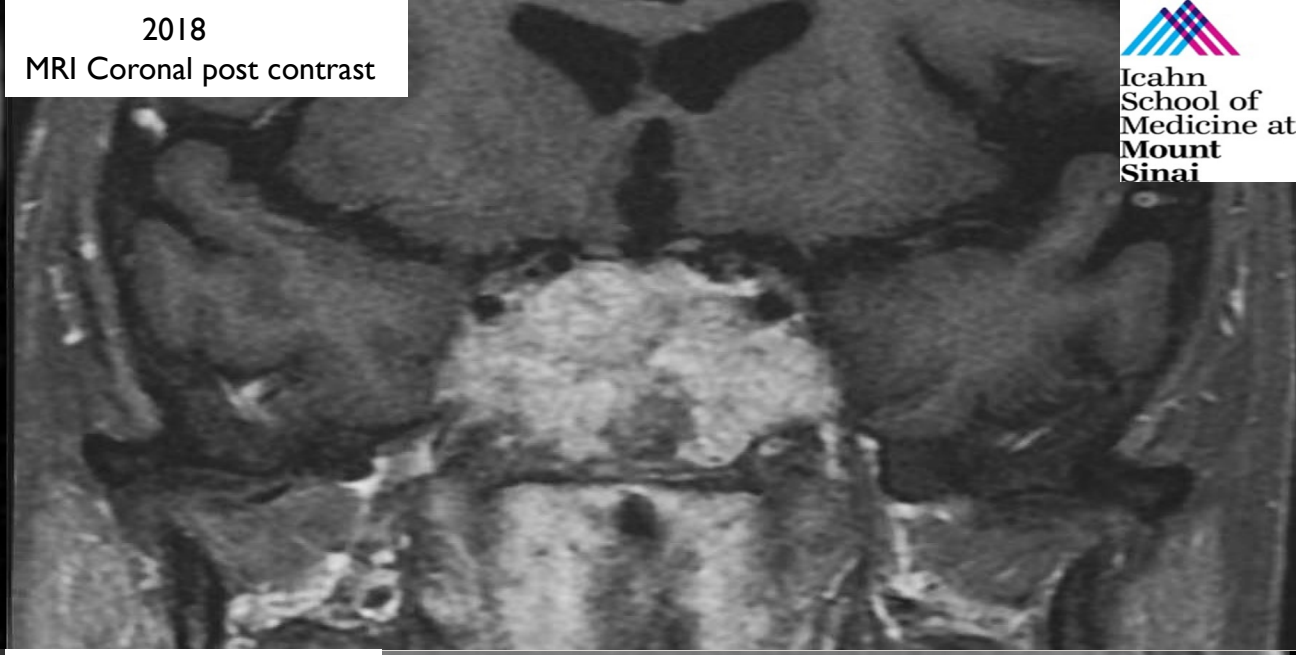
CLINICAL HISTORY

- 67-year-old female with no significant past medical history
- Presented with bitemporal hemianoptic field defect 12 years ago
- Head MRI: A sella/suprasellar heterogeneous mass
- Despite multiple surgical interventions (4 times) and radiation therapy tumor continuously has been grown and extends through the sphenoid, ethmoid and cavernous sinuses as well as upper nasal cavity

2006
CT scan with gadolinium



2018
MRI Coronal post contrast



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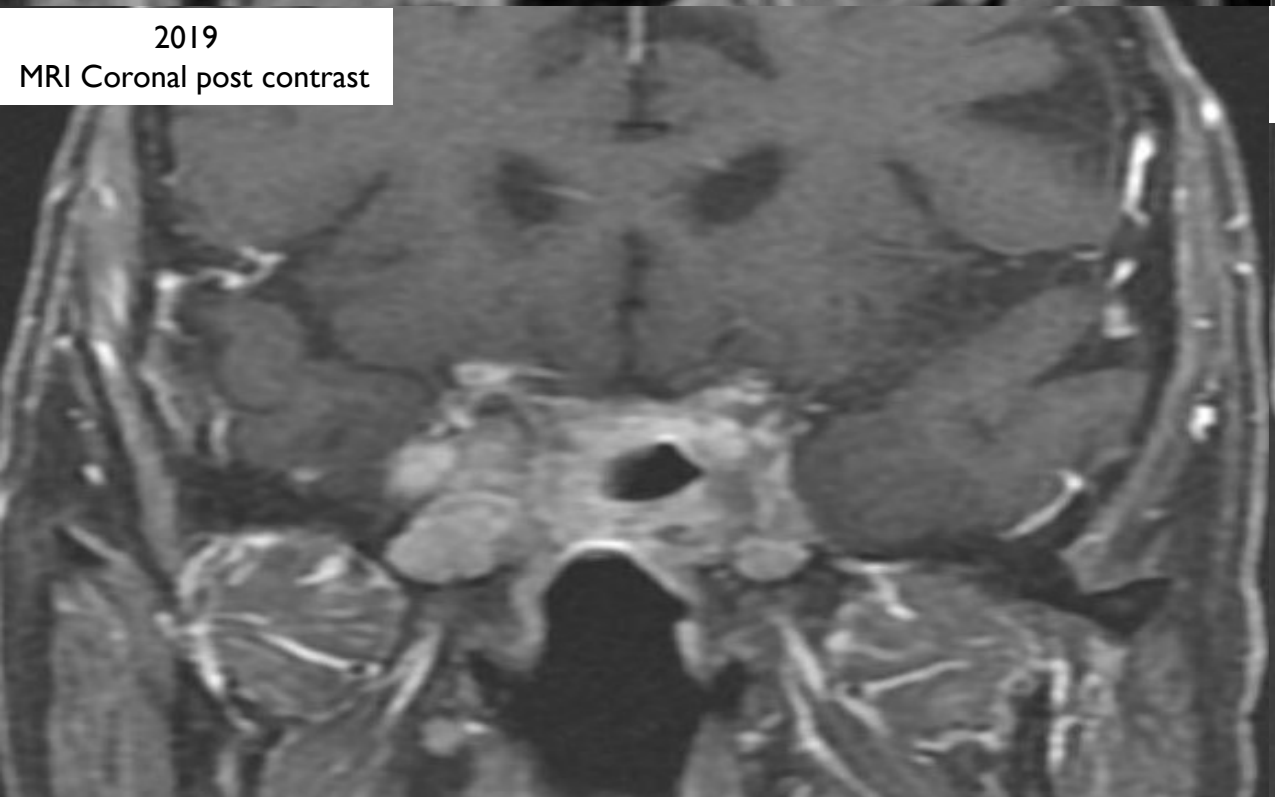
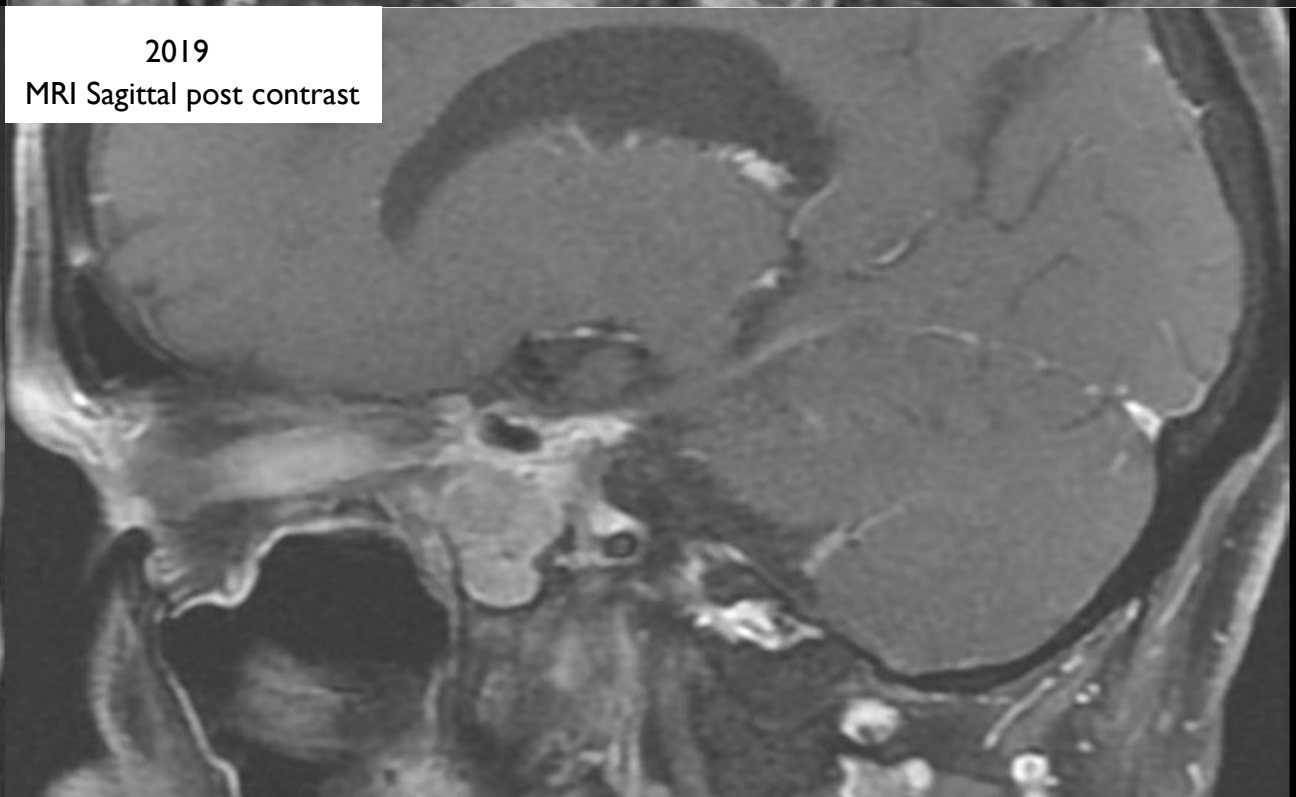
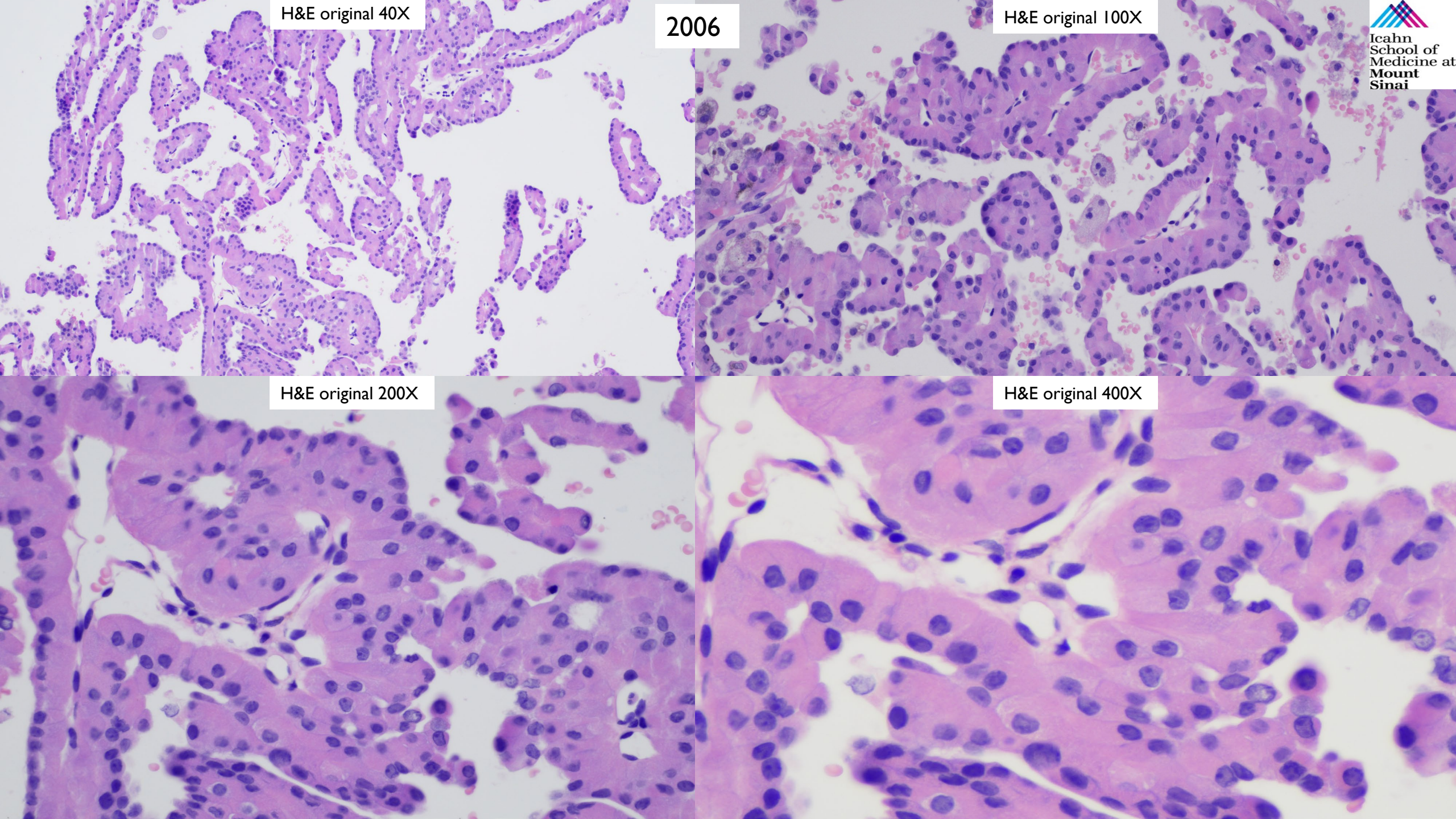
2019
MRI Coronal post contrast



2019
MRI Sagittal post contrast




H&E original 40X
2006
H&E original 100X
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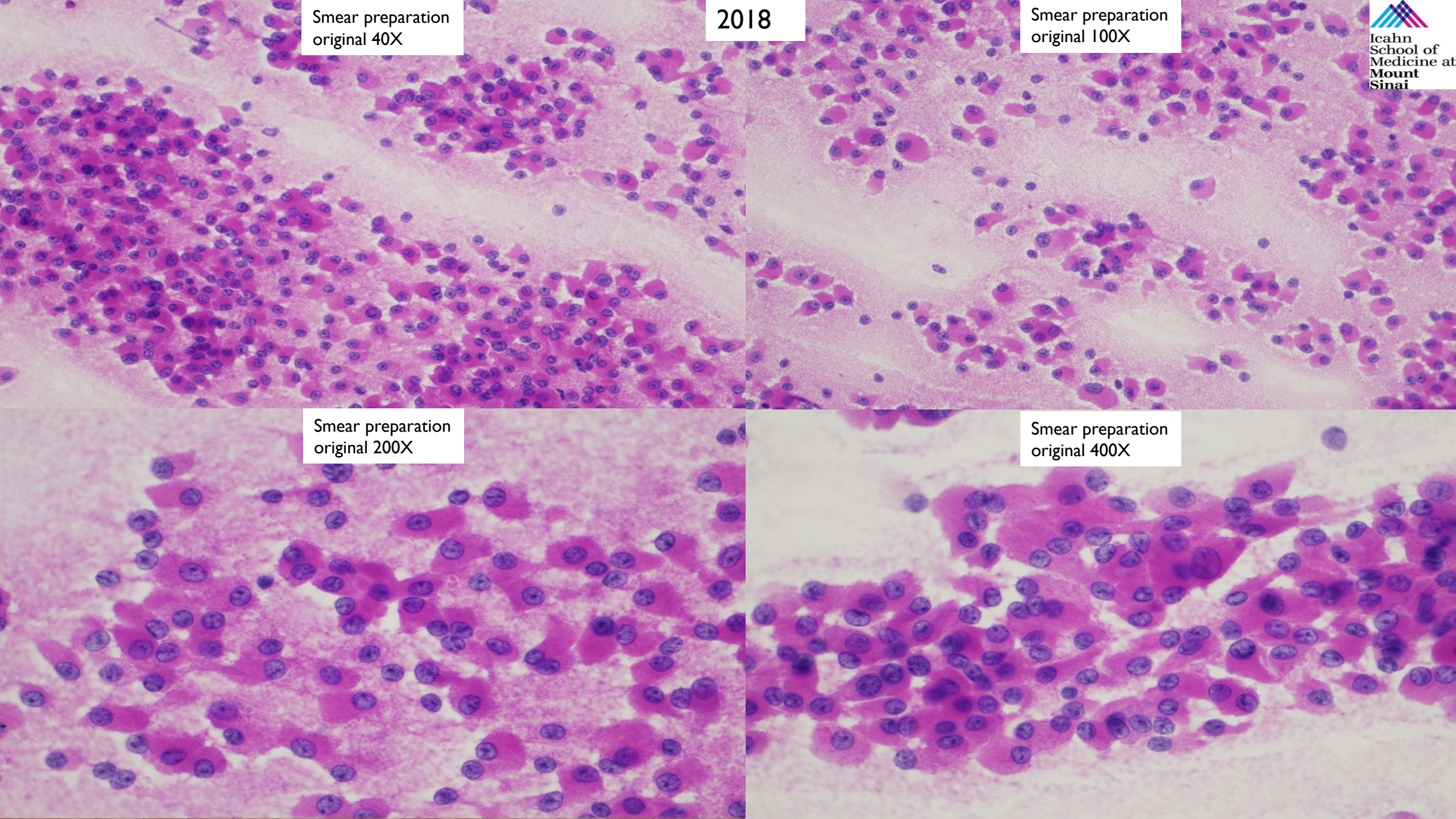
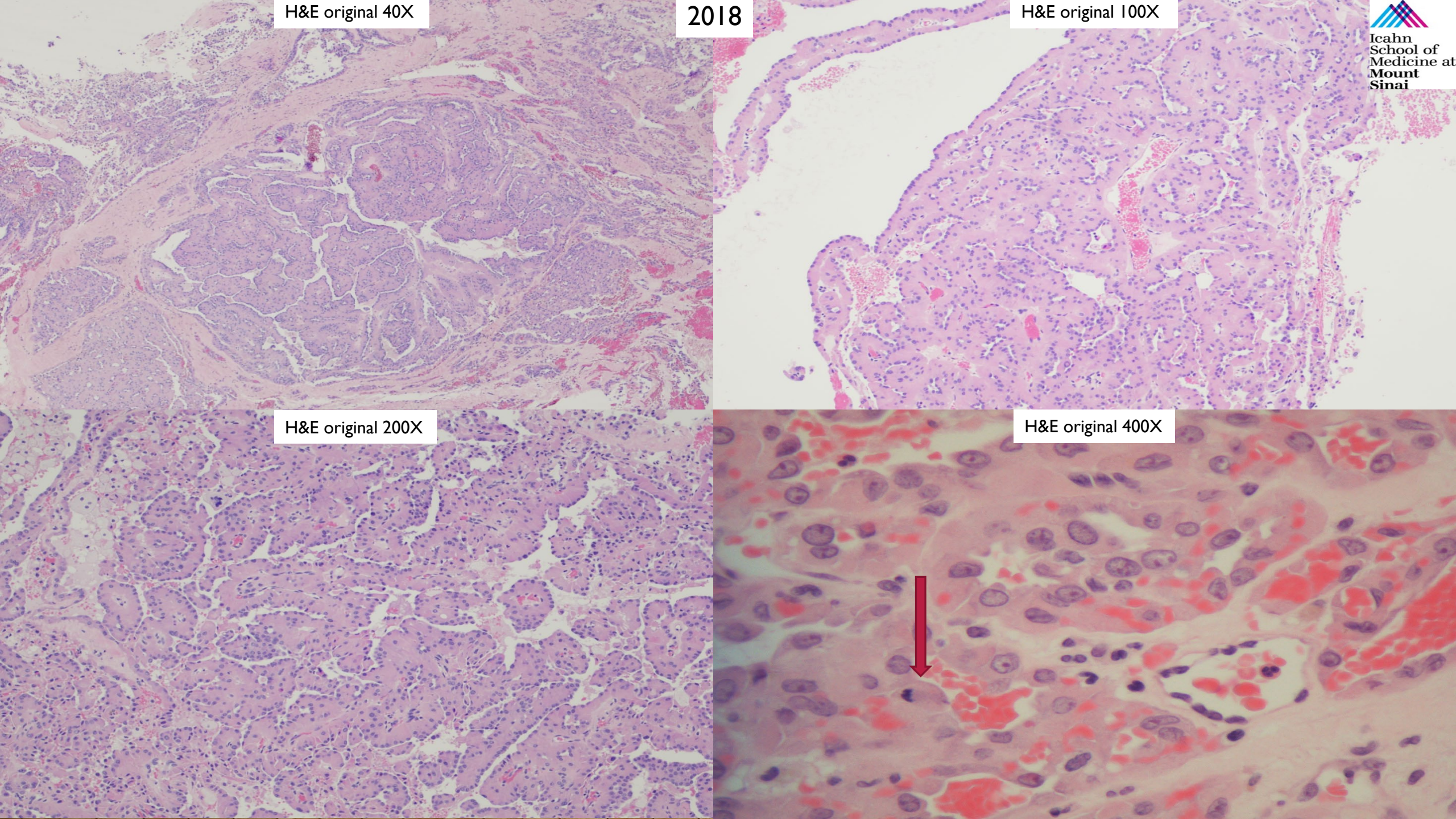
H&E original 200X
H&E original 400X


Smear preparation original 40X
2018
Smear preparation original 100X
Icahn School of Medicine at Mount Sinai
Smear preparation original 200X
Smear preparation original 400X


H&E original 40X
2018
H&E original 100X
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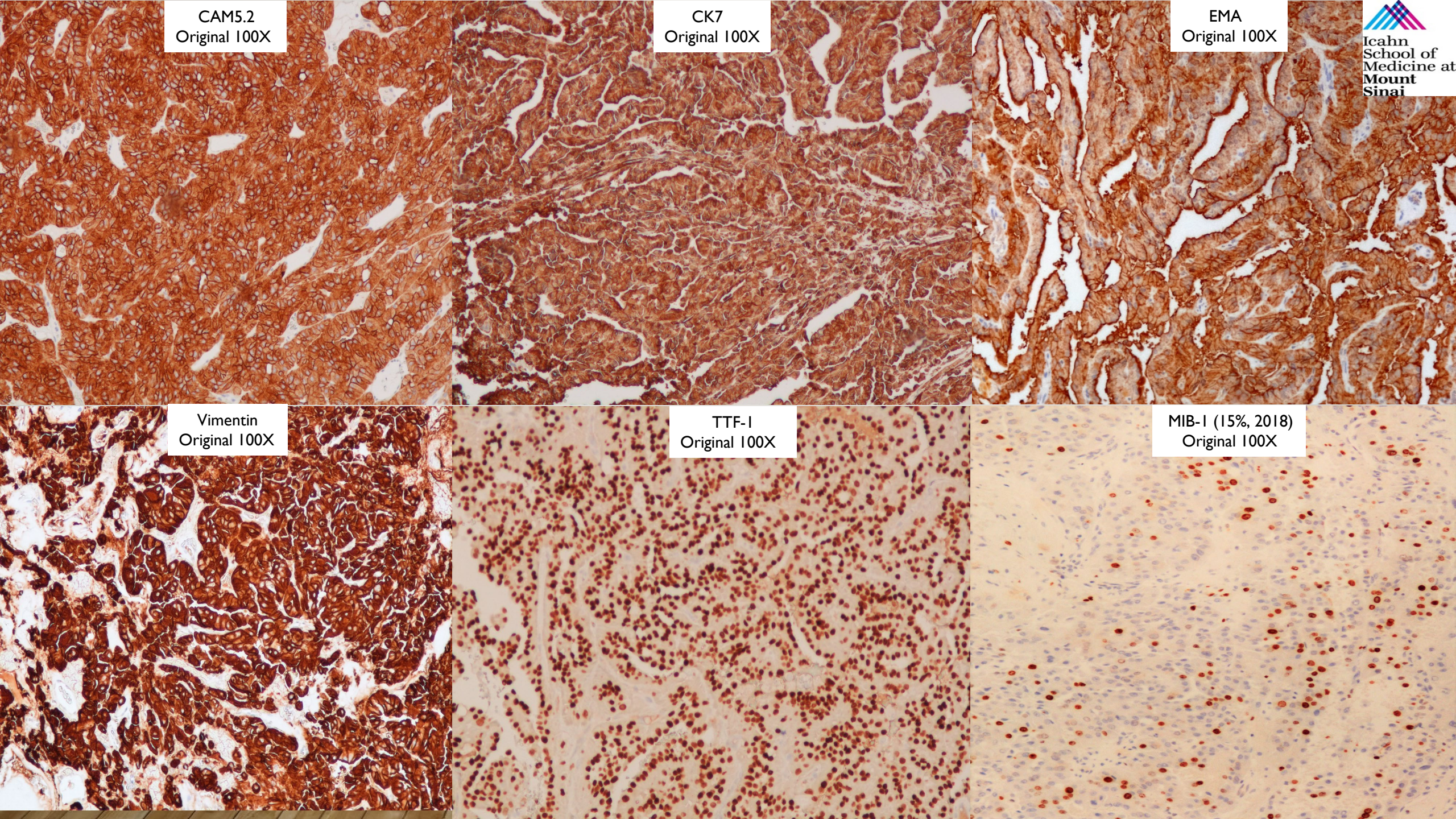
H&E original 200X
H&E original 400X

DIFFERENTIAL DIAGNOSIS


CAM5.2
Original 100X
CK7
Original 100X
EMA
Original 100X
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Vimentin
Original 100X
TTF-1
Original 100X
MIB-1 (15%, 2018)
Original 100X

Immunohistochemistry study

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Test	Result
AE1/AE3 (Cytokeratin markers)	***Positive***
CAM 5.2 (Cytokeratin markers)	***Positive***
CK7 (Cytokeratin markers)	***Positive***
CK20 (Cytokeratin markers)	***Negative***
TTF-1	***Positive***
Vimentin	***Positive***
EMA	***Positive***
Chromogranin (Anterior pituitary panel)	Negative
Synaptophysin (Anterior pituitary panel)	Negative
Pituitary hormones and transcription factors (ACTH, GH, PRL, TSH, LH, FSH, Pit1, SF1) (Anterior pituitary panel)	Negative
Thyroglobulin (Thyroid panel)	Negative
PAX 8 (Thyroid panel, Renal panel)	Negative
CD117 (Renal panel)	Negative
GFAP	Negative
S100, CD68	Negative
Transthyretin (pre-albumin)	Negative
CEA, Napsin-A	Negative
SOX-10, P63	Negative
Mammaglobin, BRST-2, ER and PR	Retained
P53	1-3% (2006) to 20% (2018)
MIB-1	5% (2006) to 15% (2018)

MOLECULAR STUDIES (FOUNDATION ONE)

- **EZH2 Y646H (Y641H)**
- Tumor Mutational Burden: 1 Muts/Mb
- Alteration genes with unknown significance
- EGFR R309Q
- ASXL1 N986S
- EGFR A310T
- MAP3K1 S939C
- MST1R G1385V
- SMO P59Q
- ZNF703 A401_H402ins

Mediates transcriptional silencing
Gain of function mutations (Y646/641)
Non-Hodgkin lymphoma
Promising therapeutic target in germinal center lymphomas

Kim KH et al. Targeting EZH2 in cancer. *Nat Med.* 2016;22(2):128–134

DIFFERENTIAL DIAGNOSIS

- Metastatic carcinoma
  - Unusual complication of systemic cancer (1% of pituitary tumors)
  - Elderly patients with diffuse malignant disease
  - Breast and lung
  - Posterior pituitary
- Metastatic oncocytic papillary carcinoma
  - Clinical imaging did not detect a primary malignancy outside of the sella/supra sella
  - Papillary nasopharyngeal adenocarcinoma (TTF-1 -)
  - Cytokeratin, TTF-1 and Vimentin expression: thyroid, salivary gland, kidney
- Pituitary adenoma with papillary and oncocytic feature
  - Expression of neuroendocrine, hormonal and transcription markers
  - Pituitary oncocytoma (oncocytic null cell adenoma)

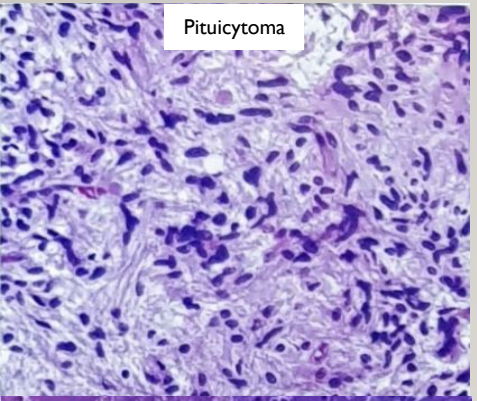
Komninos J et al, Tumors Metastatic to the Pituitary Gland: Case Report and Literature Review, *The Journal of Clinical Endocrinology & Metabolism*, Volume 89, Issue 2, 1 February 2004, Pages 574–580
Pineda-Daboin, K et al. Nasopharyngeal adenocarcinomas: A clinicopathologic study of 44 cases including immunohistochemical features of 18 papillary phenotypes. Annals of Diagnostic Pathology, 2006.10(4), 215-221.

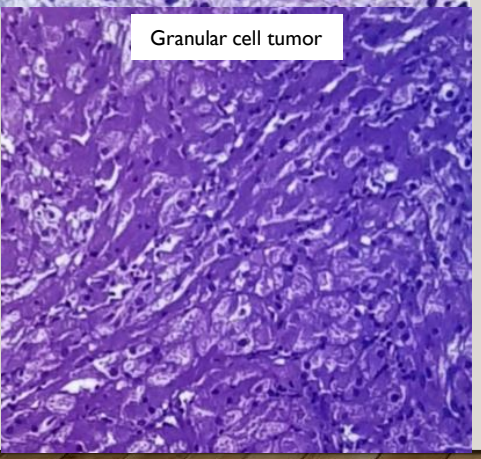
Niveiro M et al. Oncocytic transformation in pituitary adenomas: Immunohistochemical analyses of 65 cases.Arch Pathol Lab Med. 2004;128:776–80
Lloyd RV, Osamura RY, Kloppel G, Rosai J. WHO classification of tumours of the endocrine organs. 4. Lyon: International Agency for Research on Cancer; 2017: 14-54

DIFFERENTIAL DIAGNOSIS (CONTINUED)

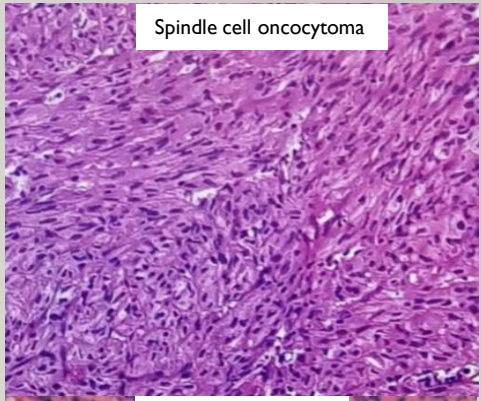
Tumors of posterior pituitary

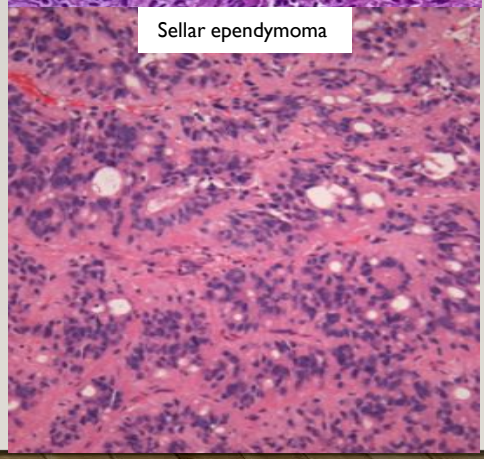
Derived from pituicytes
Five types of pituicyte: light, dark, granular, oncocytic, or ependymal (Takei et al)
TTF-1 positive, variably positive for GFAP, S100, Vimentin, and EMA
Negative for Chromogranin A, Synaptophysin, adenohypophyseal hormones


Pituicytoma


Granular cell tumor

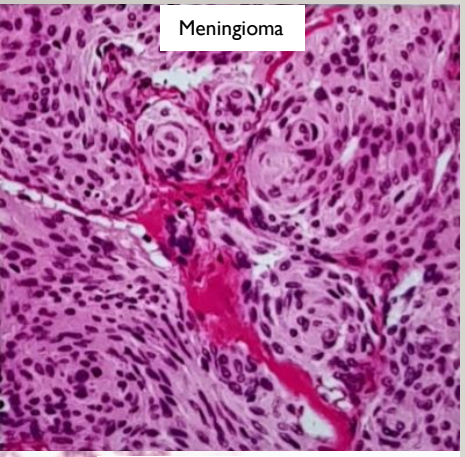
- Pituicytomas
  - Short fascicles of bipolar spindle cells
  - Strong S100 positivity, positivity for CD68
- Granular cell tumor
  - large cells with eosinophillc granular cytoplasm
  - positivity for CD68
- Spindle cell oncocytoma
  - Fascicle and lobules of spindle to epithelioid tumor cells with oncocytic cytoplasm
- Sellar ependymoma
  - Perivascular pseudorosettes
  - Focal expression of cytokeratin, dot like EMA


Spindle cell oncocytoma

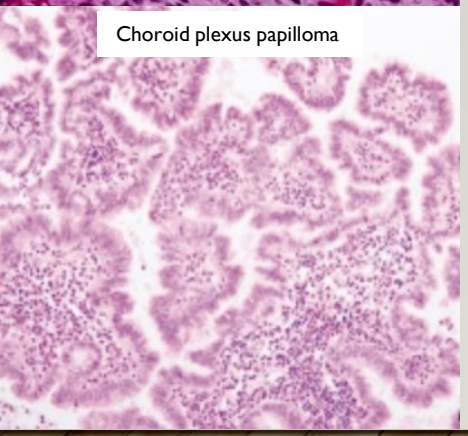

Sellar ependymoma

Lloyd RV, Osamura RY, Kloppel G, Rosai J. WHO classification of tumours of the endocrine organs. 4. Lyon: International Agency for Research on Cancer; 2017: 14-54
Mete O et al, Spindle cell oncocytomas and granular cell tumors of the pituitary are variants of pituicytoma. Am J Surg Pathol. 2013;37:1694–1699
Takei et al. Ultrastructural study of the human neurohypophysis. II. Cellular elements of neural parenchyma, the pituicytes. Cell Tissue Res 2015; 205:273–287

DIFFERENTIAL DIAGNOSIS (CONTINUED)



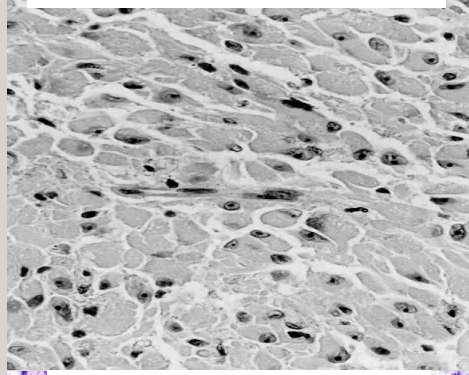
Meningioma



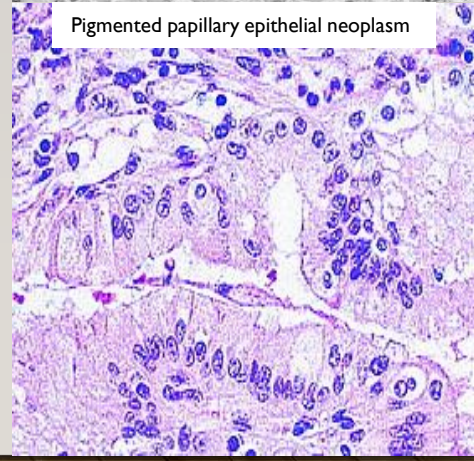
Choroid plexus papilloma

- Meningioma
  - Cytokeratin negativity
- Choroid plexus papillomas
  - Only two cases reported in sella region
  - Thought to developed from ectopic choroid plexus tissue
  - Positive for Vimentin, Cytokeratin, and transthyretin
  - Variably positive for S-100, EMA,GFAP
- Oncocytic neoplasms arising from salivary gland rests in the pituitary (Hampton et al. 1997)
- Pigmented papillary epithelial neoplasm of the pituitary fossa with oncocytic and papillary regions (Fuller et al. 2001)
  - Fibrovascular cores lined by columnar, cells with oval nuclei and nucleoli. Many contained granular, brown, Fontana-positive pigment
  - Positive for transthyretin, S100, CEA, HMB-45, vimentin, CAM 5.2
  - Negative for all pituitary hormones, chromogranin, EMA, and GFAP

Oncocytoma arising from salivary gland rest



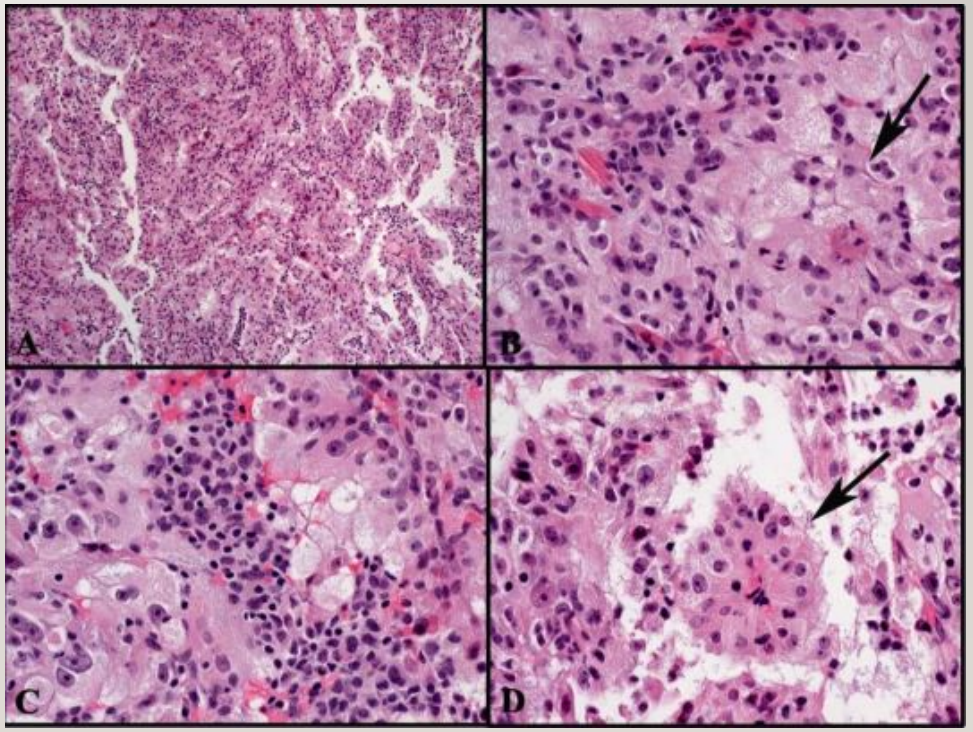
Pigmented papillary epithelial neoplasm



Fuller et al. Pigmented papillary epithelial neoplasm of the pituitary fossa: a distinct lesion of uncertain histogenesis, Arch Pathol Lab Med 2001; 125:1242-1245
Hampton et al. Salivary gland-like tumors of the sellar region. Am J Surg Pathol 1997;21:424–34

DIFFERENTIAL DIAGNOSIS (CONTINUED)

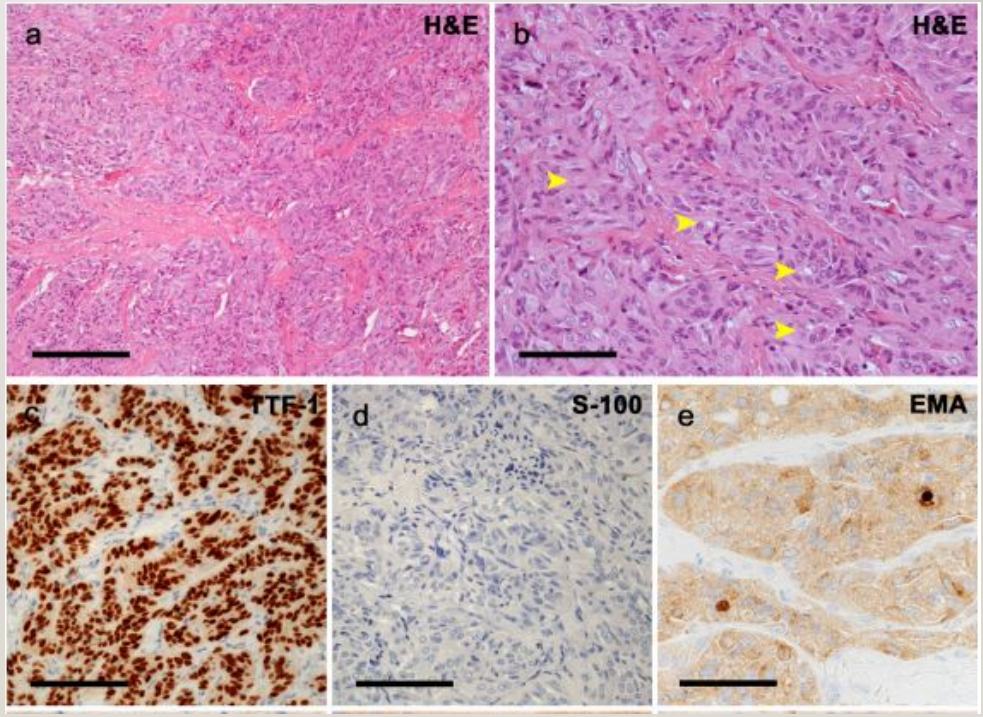
- Ryu et al. 2015
- A TTF1 positive epithelioid oncocytic tumor in the sellar region with focal papillary architecture which was reactive for EMA, CK7, and CAM5.2, and non-reactive for GFAP, CK20, thyroglobulin, CD34, and PAX8 similar to this case, but showed reactivity for S100 and Bcl2 which is not seen in this current case
- This reported case was associated with Birt-Hogg-Dube syndrome which is due to a mutation in the folliculin (FLCN) gene and associated with dermatologic lesions and lung cysts, not seen in this case



Ryu et al. An unusual oncocytic sellar neoplasm in a patient with Birt-Hogg-Dube Syndrome. Columbia International Publishing , International Journal of Neuropathology (2015) 3(1):43-54.

DIFFERENTIAL DIAGNOSIS (CONTINUED)

- Yoshimoto et al. 2015
- A TTF-1-positive oncocytic tumor with epithelioid features and trabecular/follicle formation
- Negative for S100 protein and positive for CAM 5.2 and focally positive for neuronal markers



Yoshimoto et al. TTF-1-positive oncocytic sellar tumor with follicle formation/ependymal differentiation: non-adenomatous tumor capable of two different interpretations as a pituicytoma or a spindle cell oncocytoma. Brain Tumor Pathol. 2015 Jul; 32(3):221-7.

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PAPILLARY ONCOCYTIC PITUITARY TUMOR (POPT): A NOVEL ENTITY?

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- Fuller CE, Smith M, Miller DC, Schelper R, Pigmented papillary epithelial neoplasm of the pituitary fossa: a distinct lesion of uncertain histogenesis, Arch Pathol Lab Med 2001; 125:1242-1245
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- Won Hyung A. Ryu, Leslie Hamilton, Yves Starreveld, and Jennifer Chan. An unusual oncocytic sellar neoplasm in a patient with Birt-Hogg-Dube Syndrome. Columbia International Publishing , International Journal of Neuropathology (2015) 3(1):43-54.
- Yoshimoto T, Takahashi-Fujigasaki J, Inoshita N, Fukuhara N, Nishioka H, Yamada S. TTF-1-positive oncocytic sellar tumor with follicle formation/ependymal differentiation: non-adenomatous tumor capable of two different interpretations as a pituicytoma or a spindle cell oncocytoma. Brain Tumor Pathol. 2015 Jul;32(3):221-7.
- Takei et al. Ultrastructural study of the human neurohypophysis. II. Cellular elements of neural parenchyma, the pituicytes. Cell Tissue Res 2015; 205:273–287

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