CASE 2021-9

Diagnostic Slide Session

AANP 2021

6/12/2021

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Clinical History:

- 60 year old female, non-smoker
- no prior history of malignancy or occupational exposures
- Presentation: headache and new onset vision loss in left eye
- Unresponsive to antibiotics and steroids
- Imaging : midline skull base lesion centered within the ethmoid sinus with involvement of the cribriform plate and orbital apex

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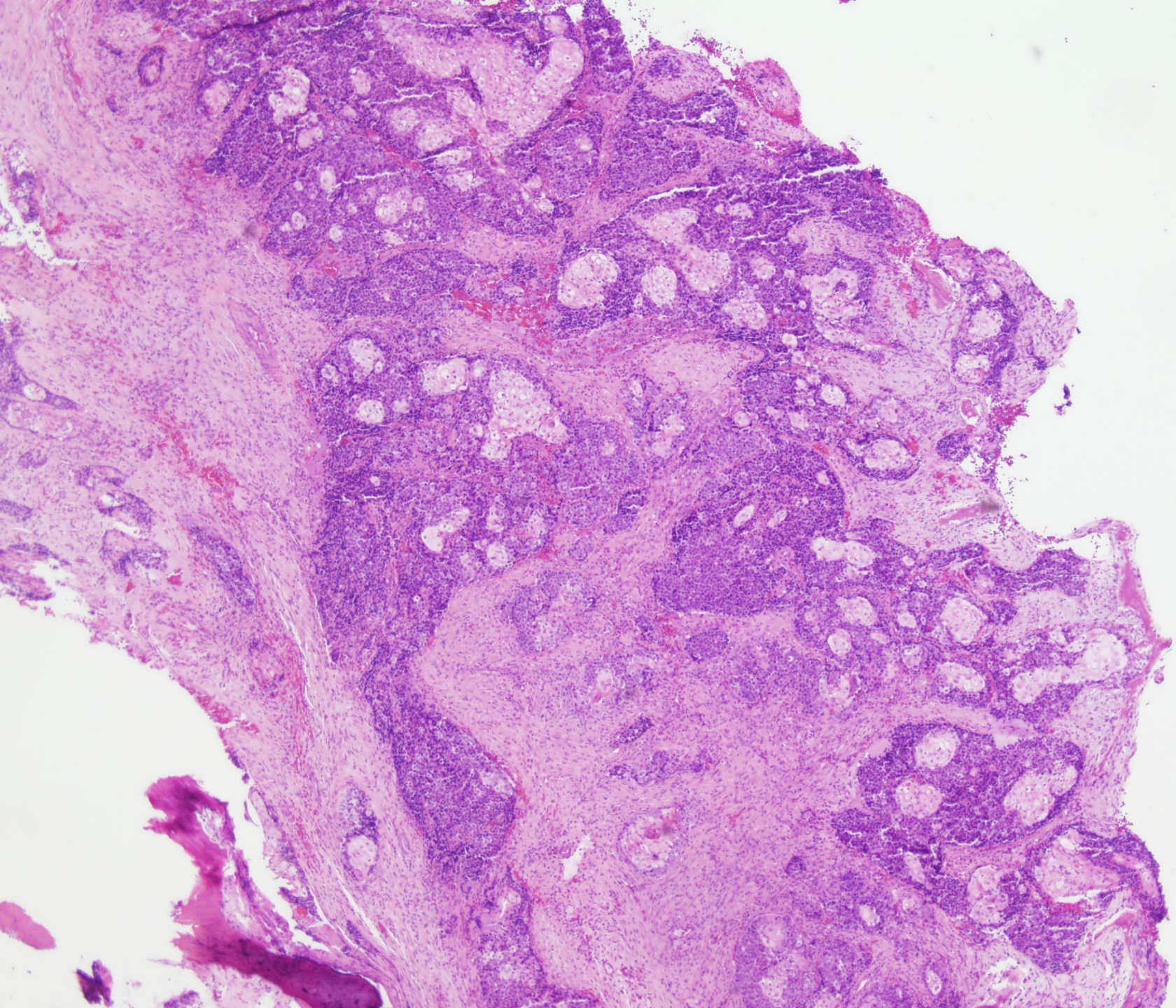

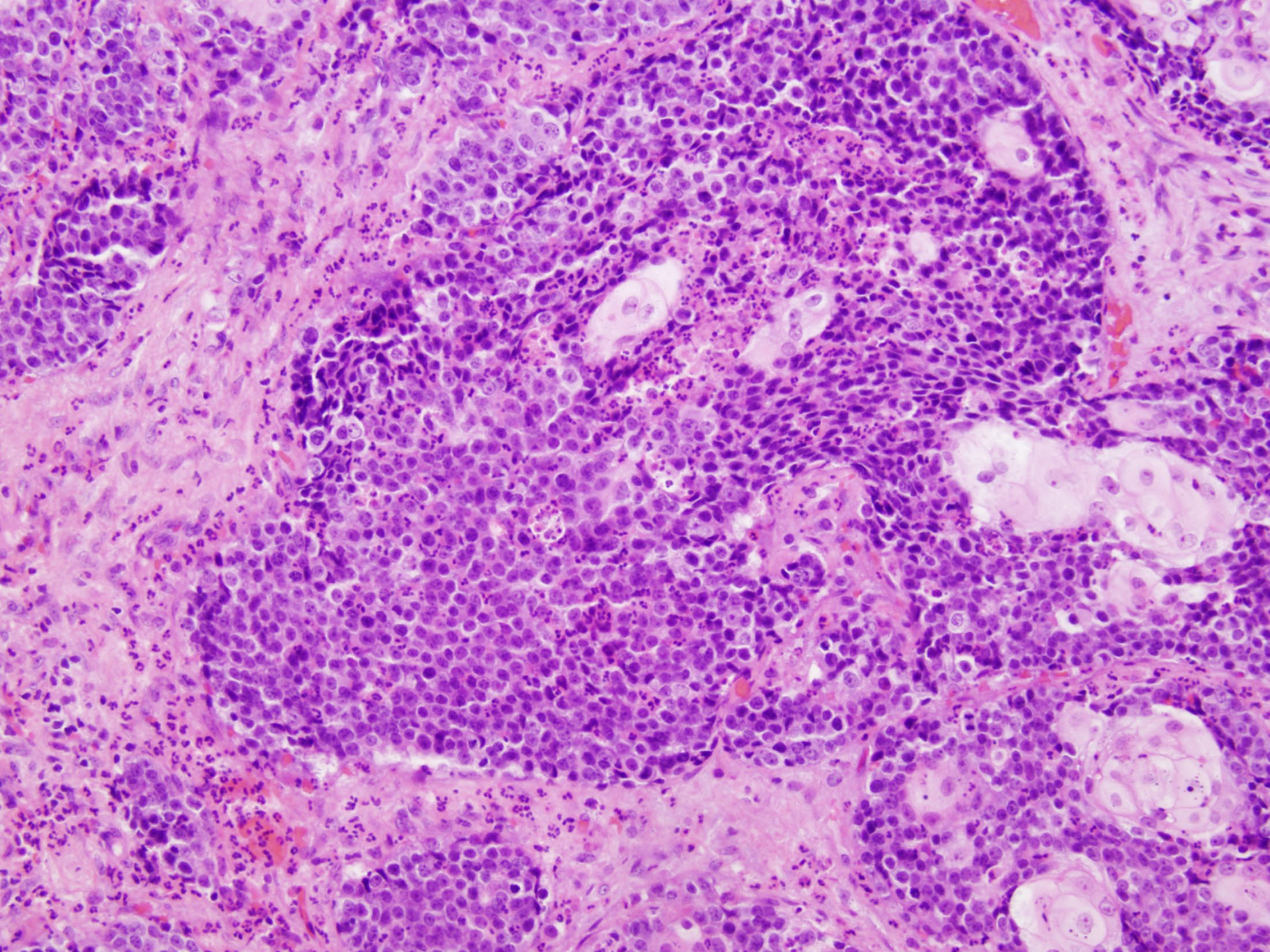

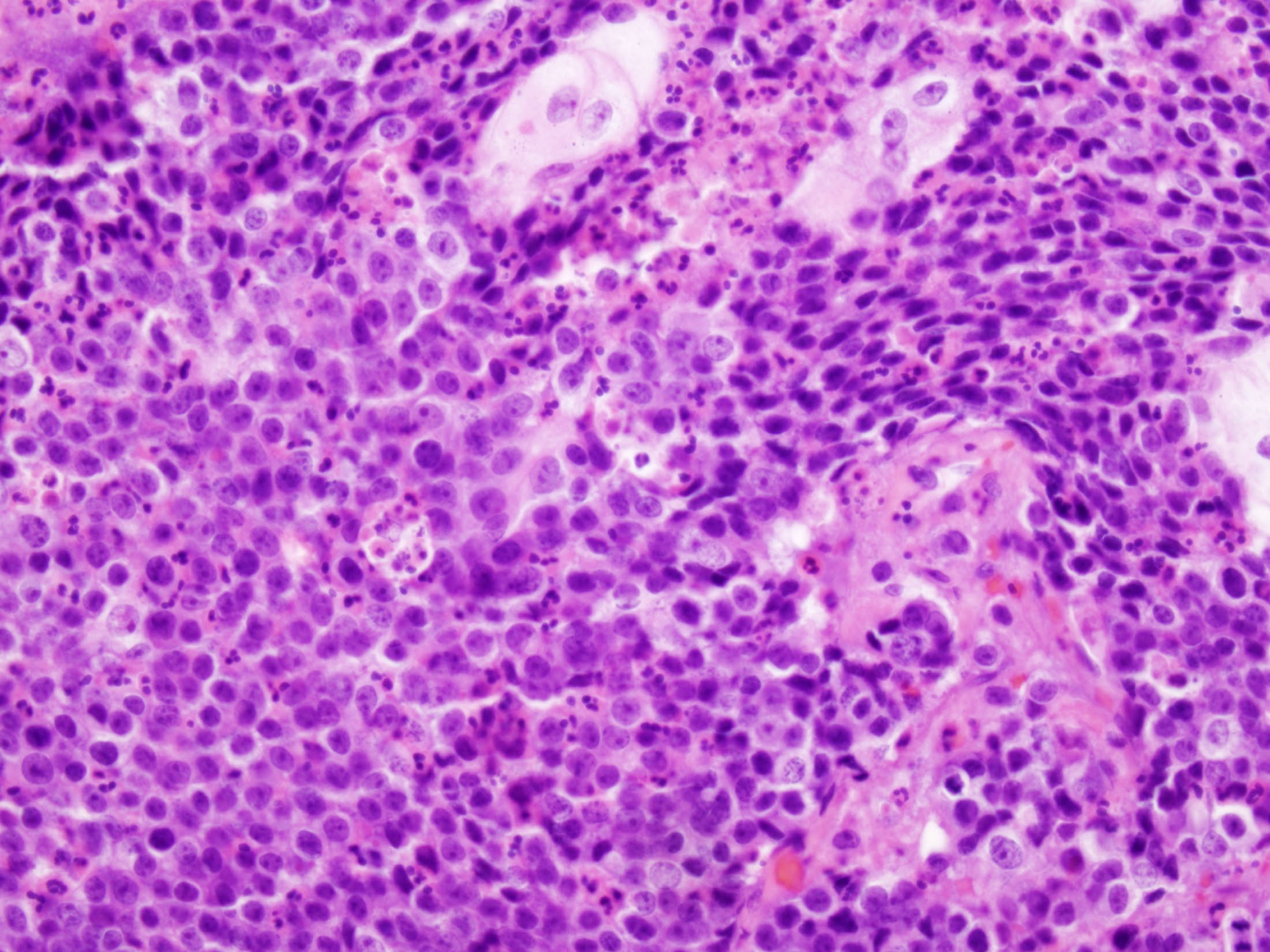

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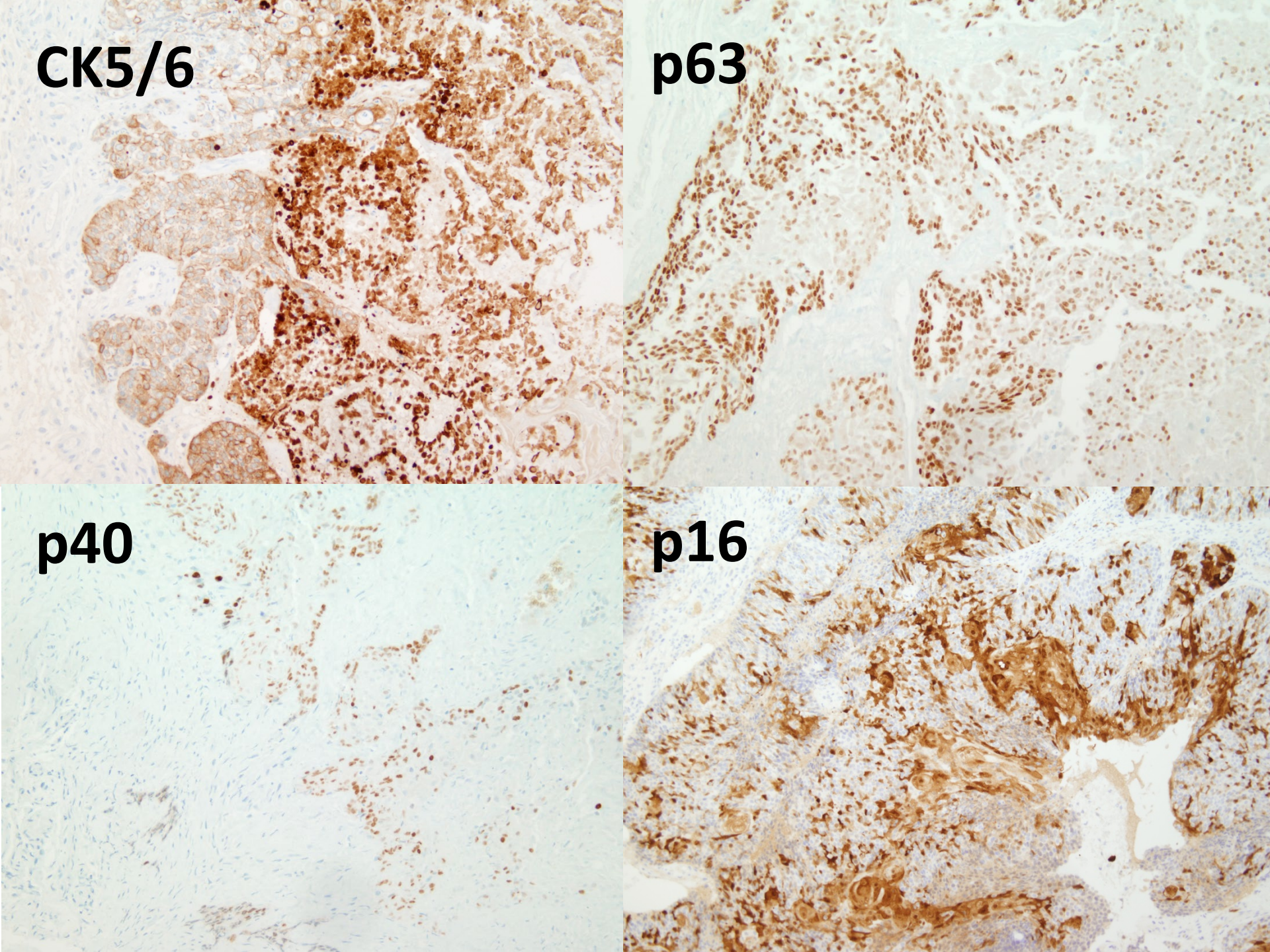
- Audience discussion


CK5/6
p63
p40
p16

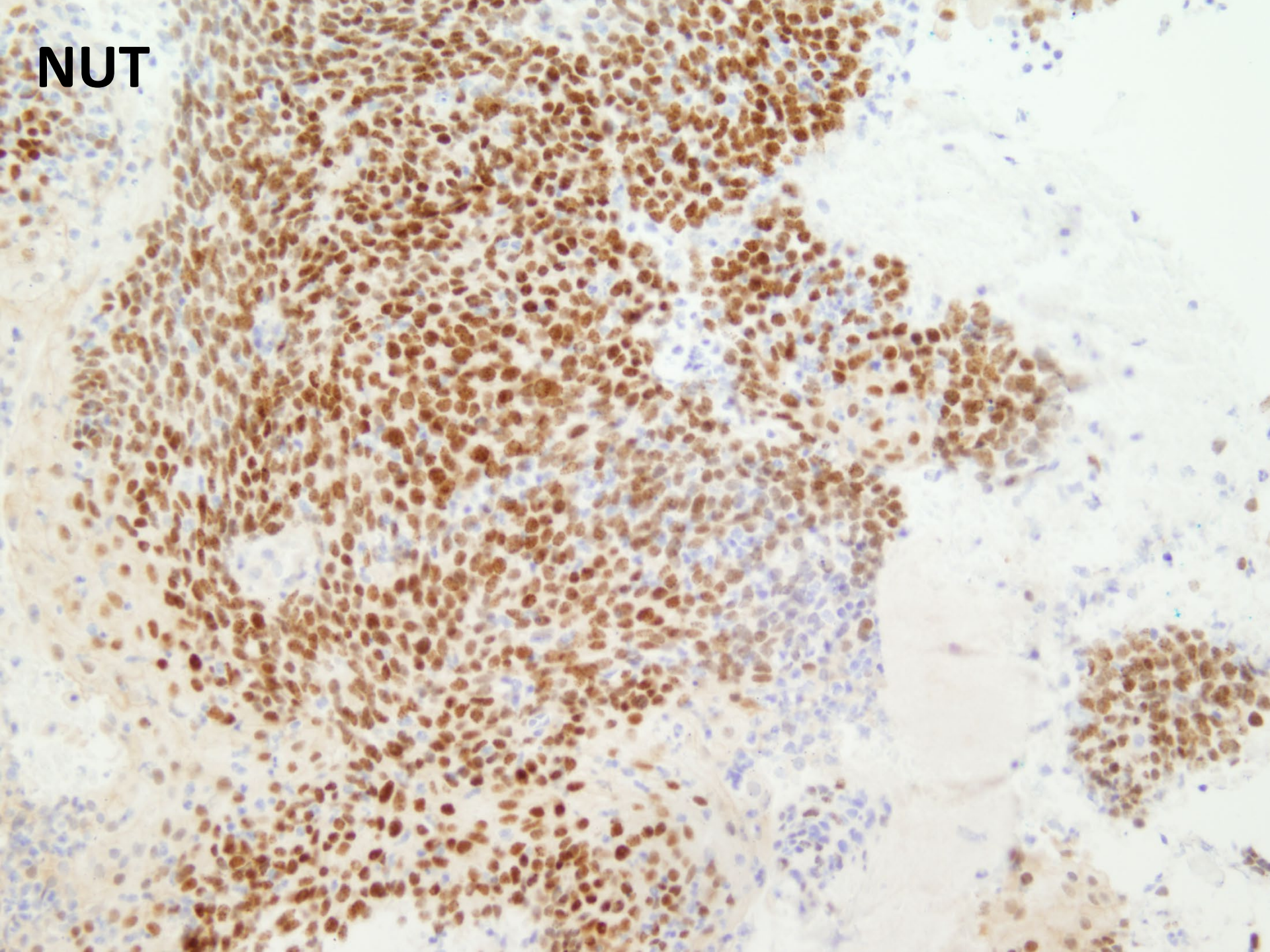
Immunohistochemical stains

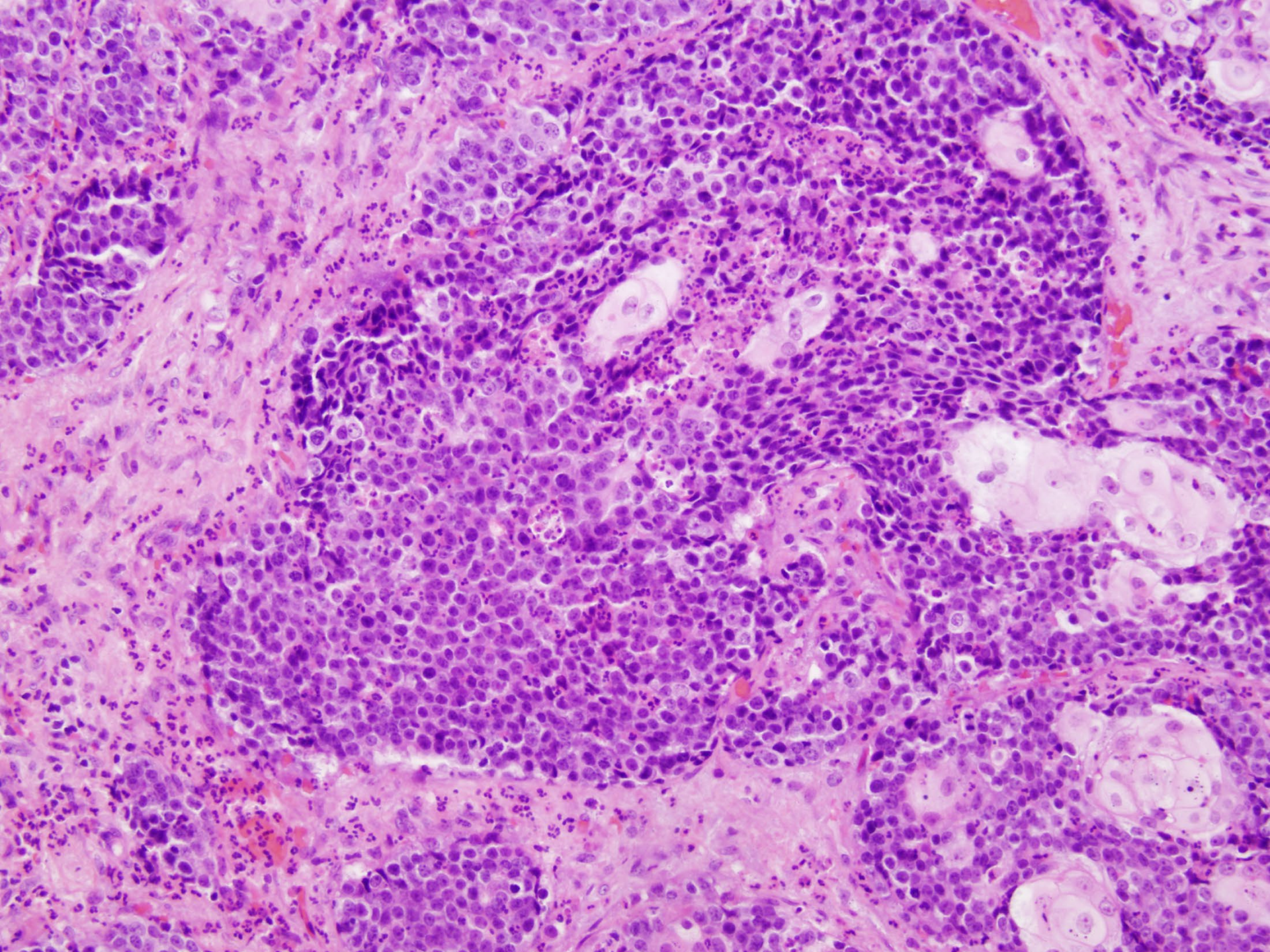
POSITIVE

- CK903
- CK7
- CK5/6
- p40
- P63
- INI-1 (retained)
- (additional (next slide))

NEGATIVE

- Synaptophysin
- Chromogranin
- TTF-1
- PAX-8
- p16 (no block-like reactivity)


NUT



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- Diagnosis: NUT carcinoma

(formerly NUT midline carcinoma)

- Rearrangement involving NUTM1 gene, 15q14
- NUT fusion protein
- Detectable by IHC (sufficient for diagnosis)
  - >50% tumor nuclei in FFPE tissue

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- Frequently misdiagnosed poorly differentiated carcinoma
- Hallmarks: monotony and abrupt keratinization
- Differential diagnosis:
  - Poorly differentiated SCC
  - Ewing sarcoma
  - Hematopoietic neoplasm
  - Sinonasal undifferentiated carcinoma
  - Esthesioneuroblastoma
  - SMARCB1-deficient sinonasal carcinoma

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- Any age group, not restricted to midline
- Poor prognosis, poor response to traditional therapies
- Genetic rearrangement involving NUTM1 → gene fusion (BET-NUTM1) →NUT fusion oncoprotein
- Targeted therapies under investigation
  - BETi
  - HDACi

CASE 2021-9

- When to test for NUT?
  - **All poorly differentiated non-cutaneous carcinomas with a monomorphic appearance**
  - No association with HPV or EBV (of note, p16 IHC positivity in NUT may be misleading), so presence of confirmed viral etiology is enough to exclude

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Bibliography:

- French, C.A. 2018. NUT Carcinoma: Clinicopathologic features, pathogenesis, and treatment. Pathology International. 68: 583-595.
- El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ (Eds): WHO Classification of Head and Neck Tumours, (4th edition, volume 9). IARC: Lyon 2017.