# CASE 5

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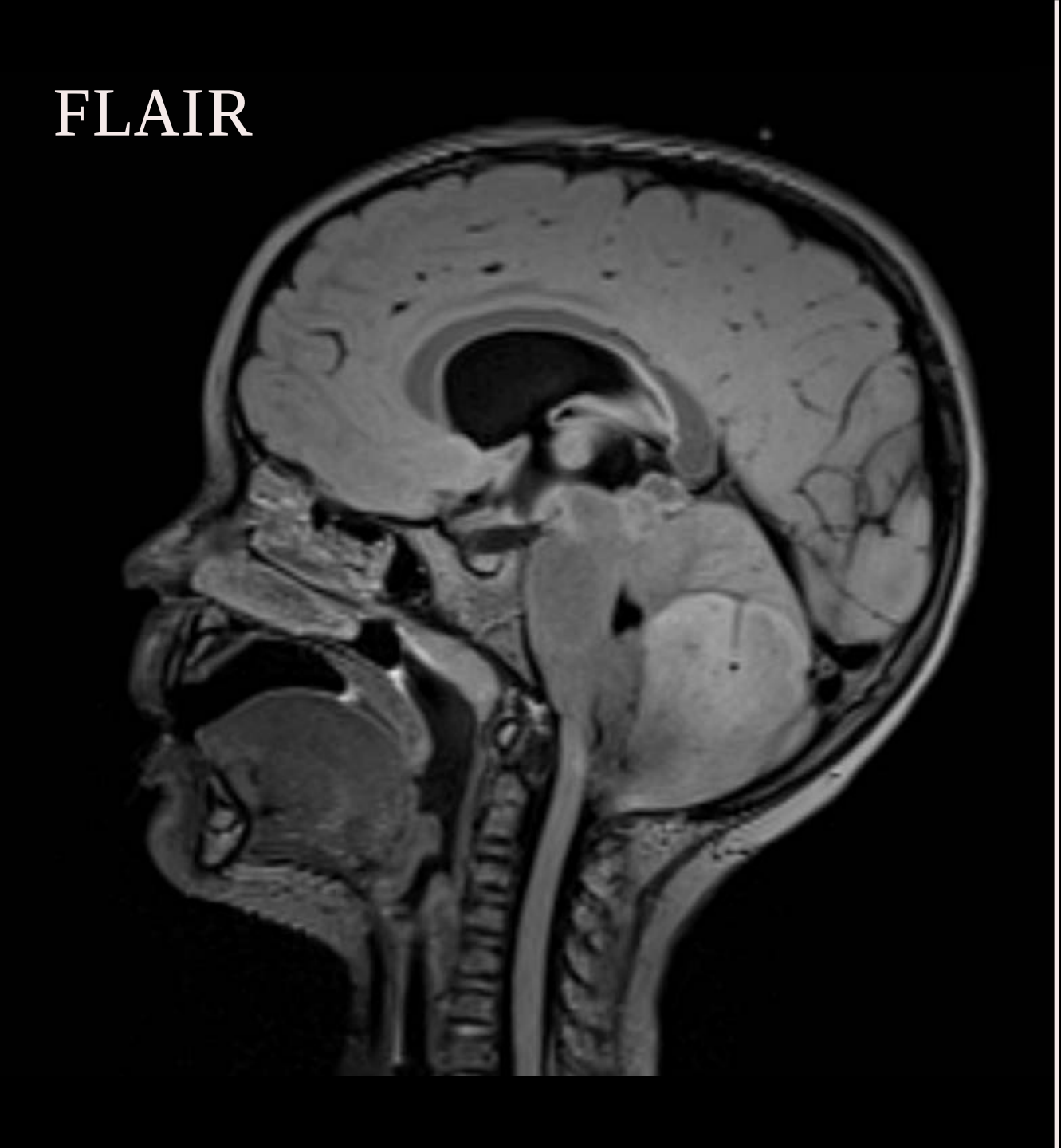
Washington University in St. Louis

2021 Diagnostic Slide Session

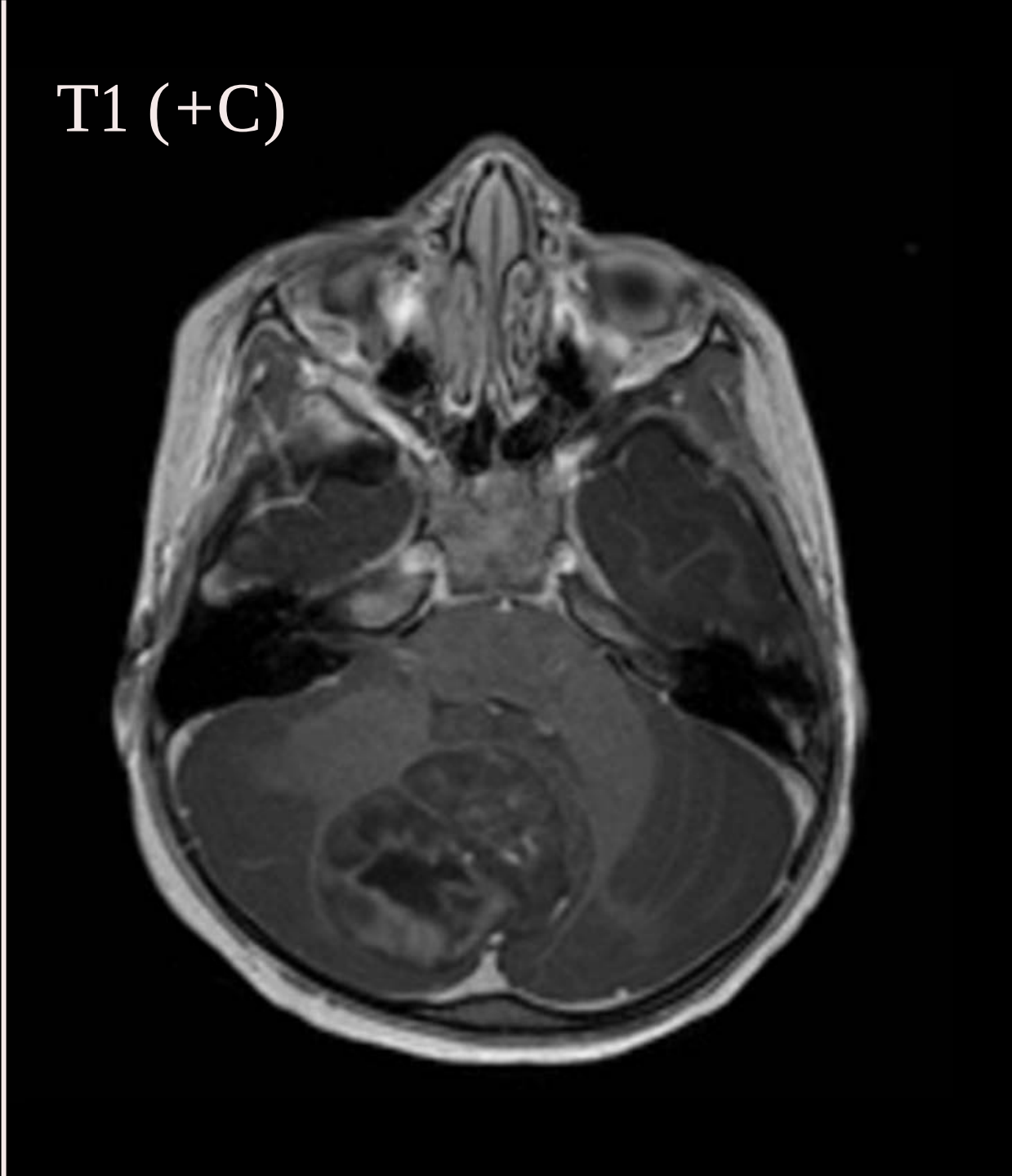
# History

- 3-year-old girl presented with three weeks of headache, nausea, and vomiting
- Head CT performed at an outside hospital showed a hypoattenuating mass in the posterior fossa
- Patient transferred to St. Louis Children's Hospital, where Brain MRI w/ contrast was performed:

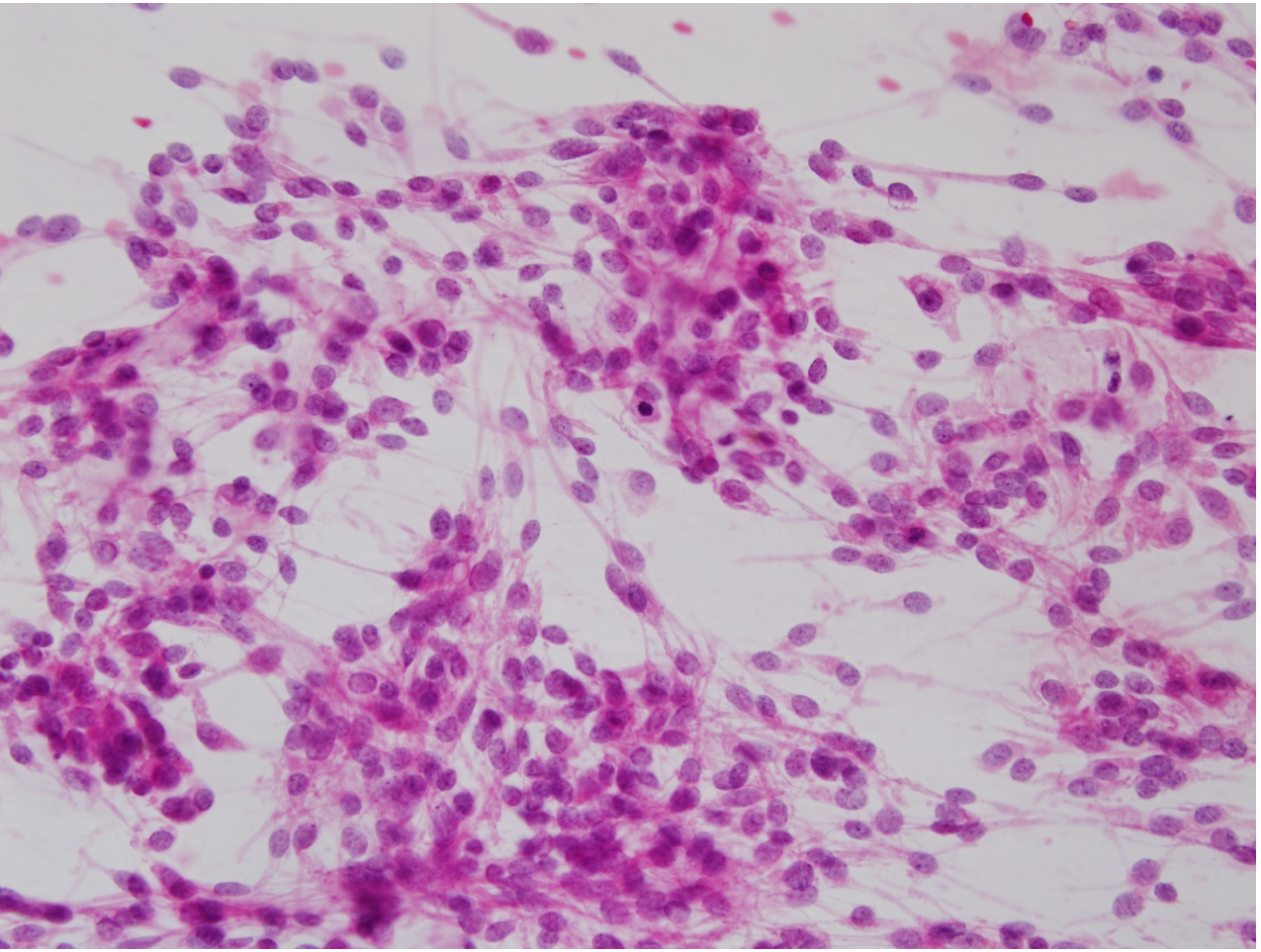
FLAIR

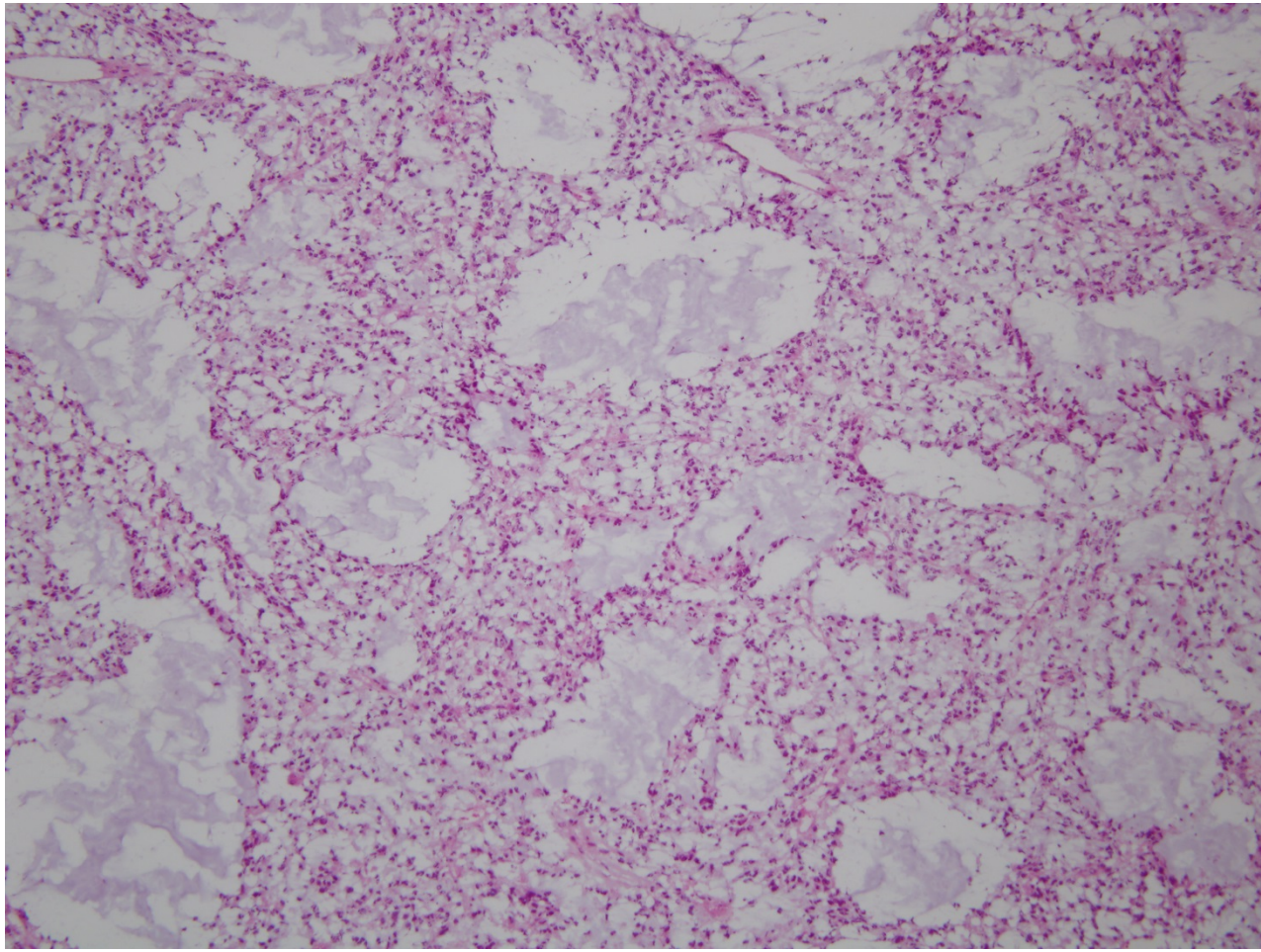


T1 (+C)



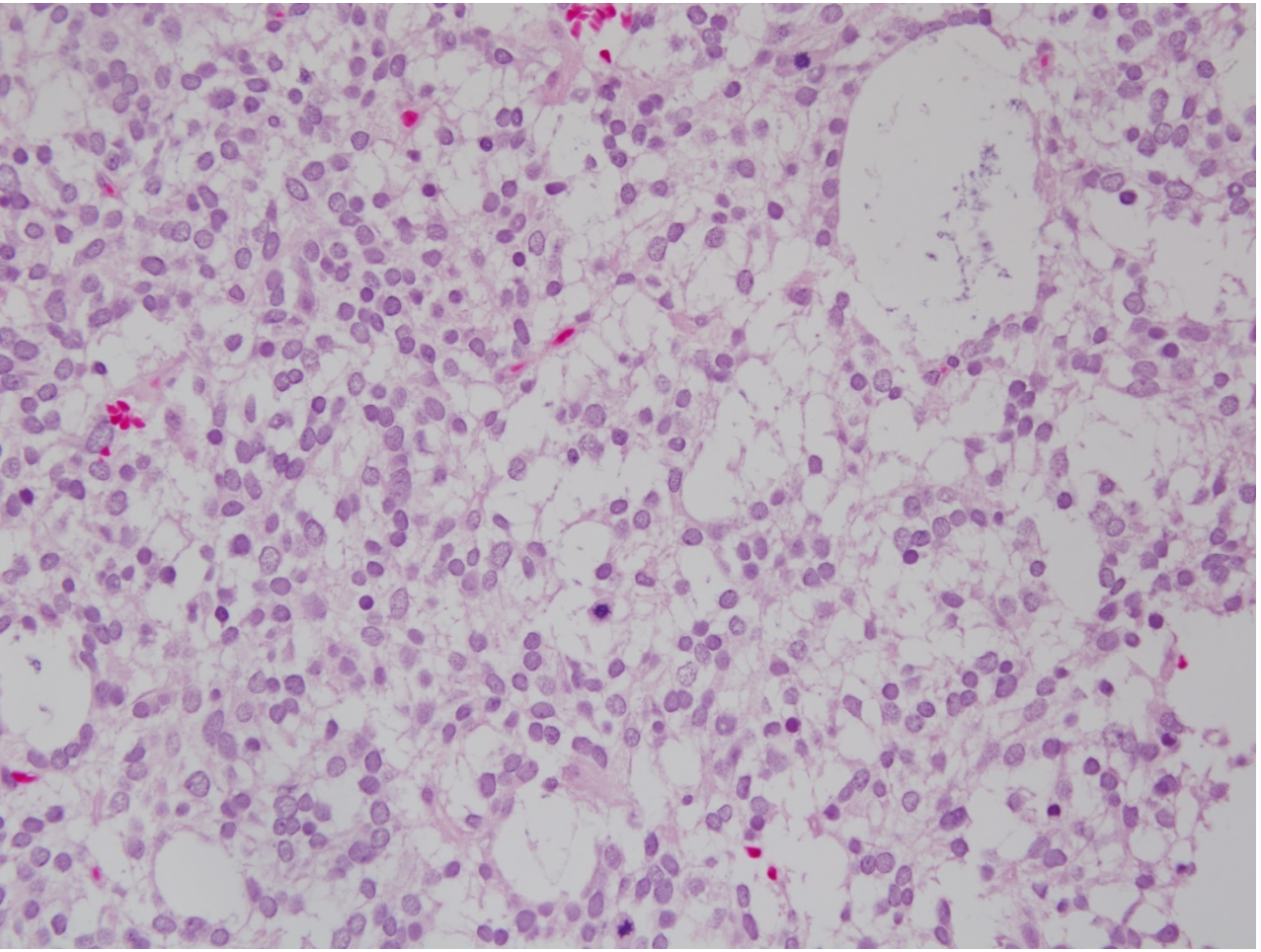
# Intraoperative Consultation

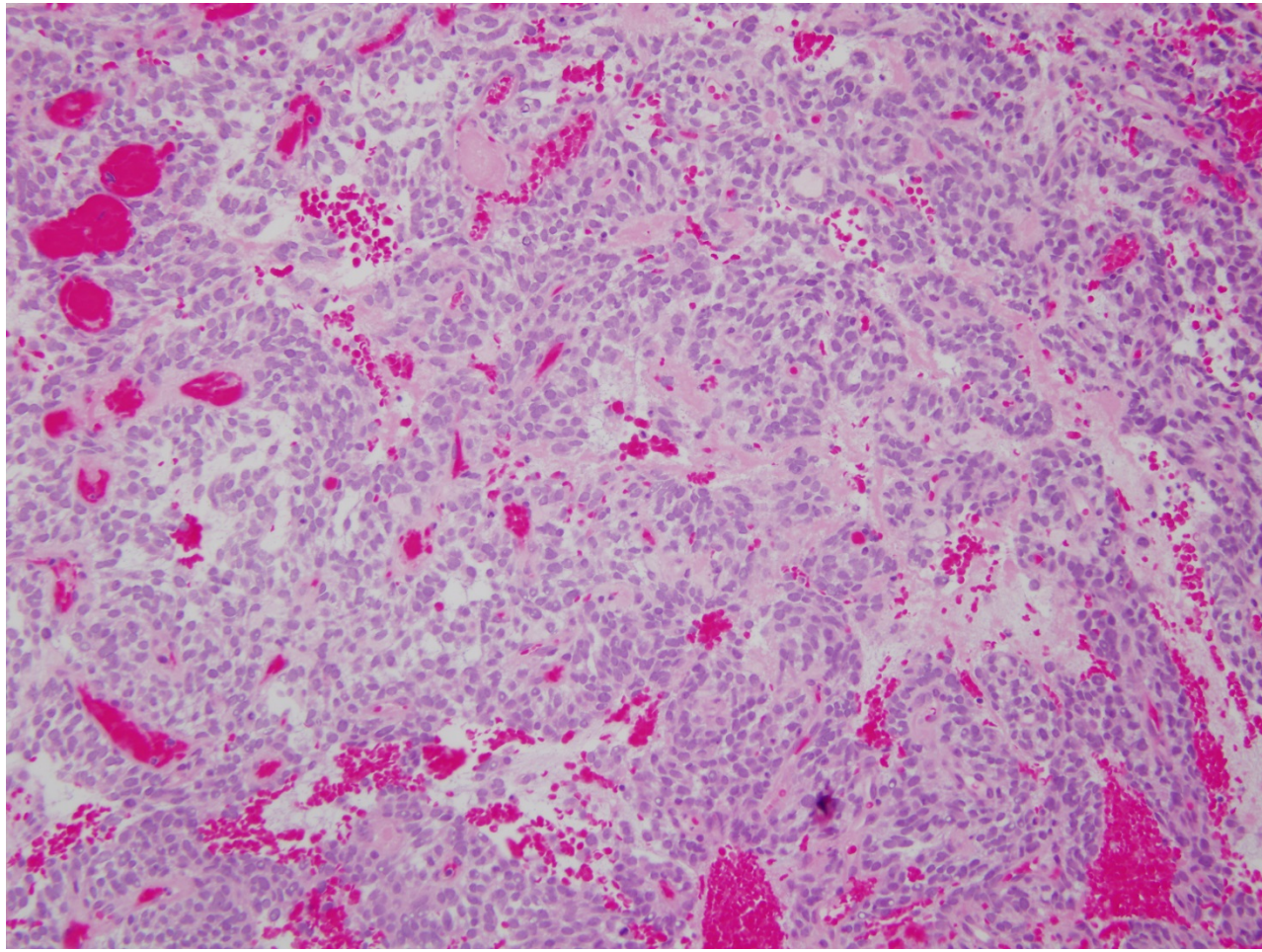




# Permanent sections

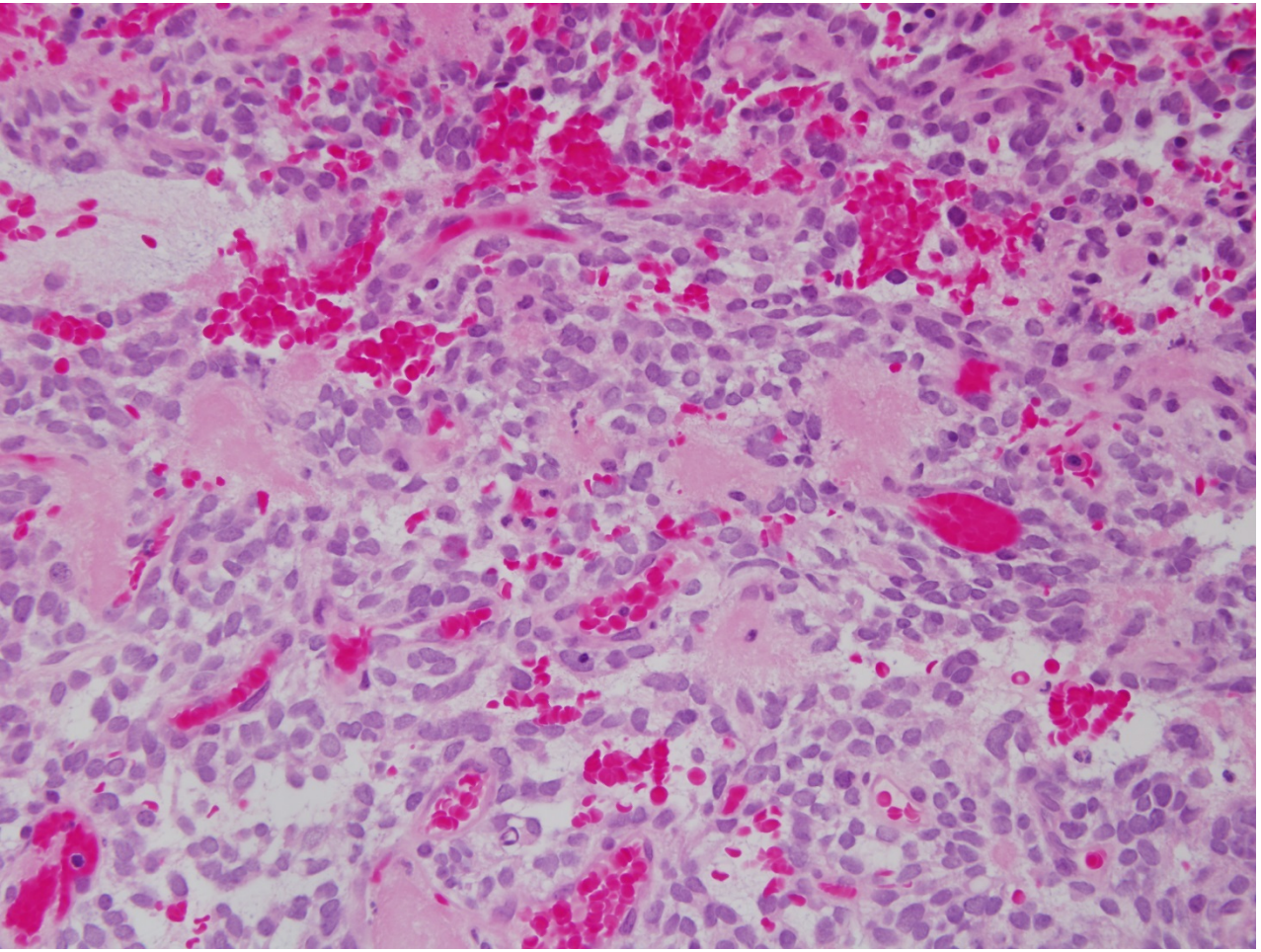
## Tumor heterogeneity

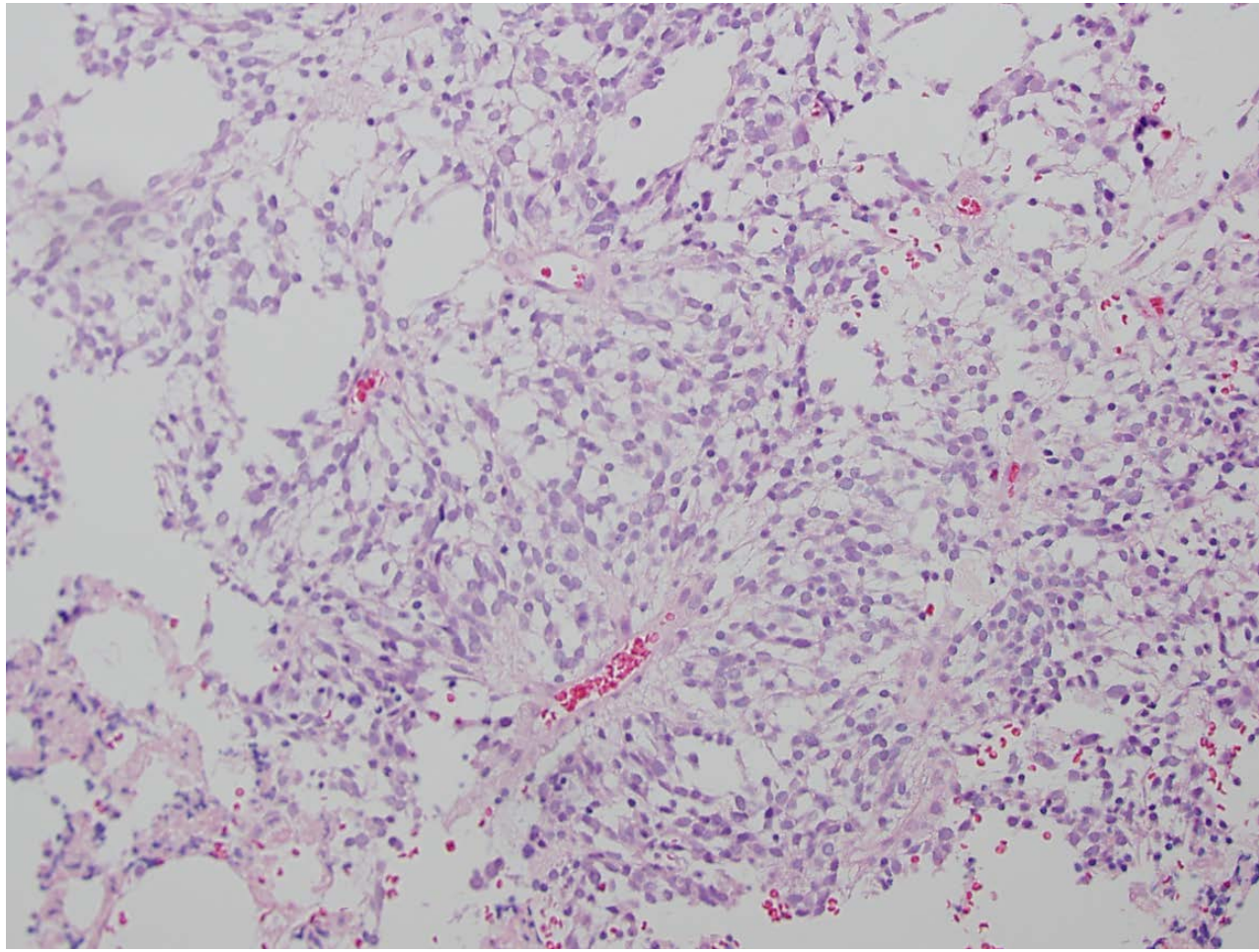




# Permanent sections

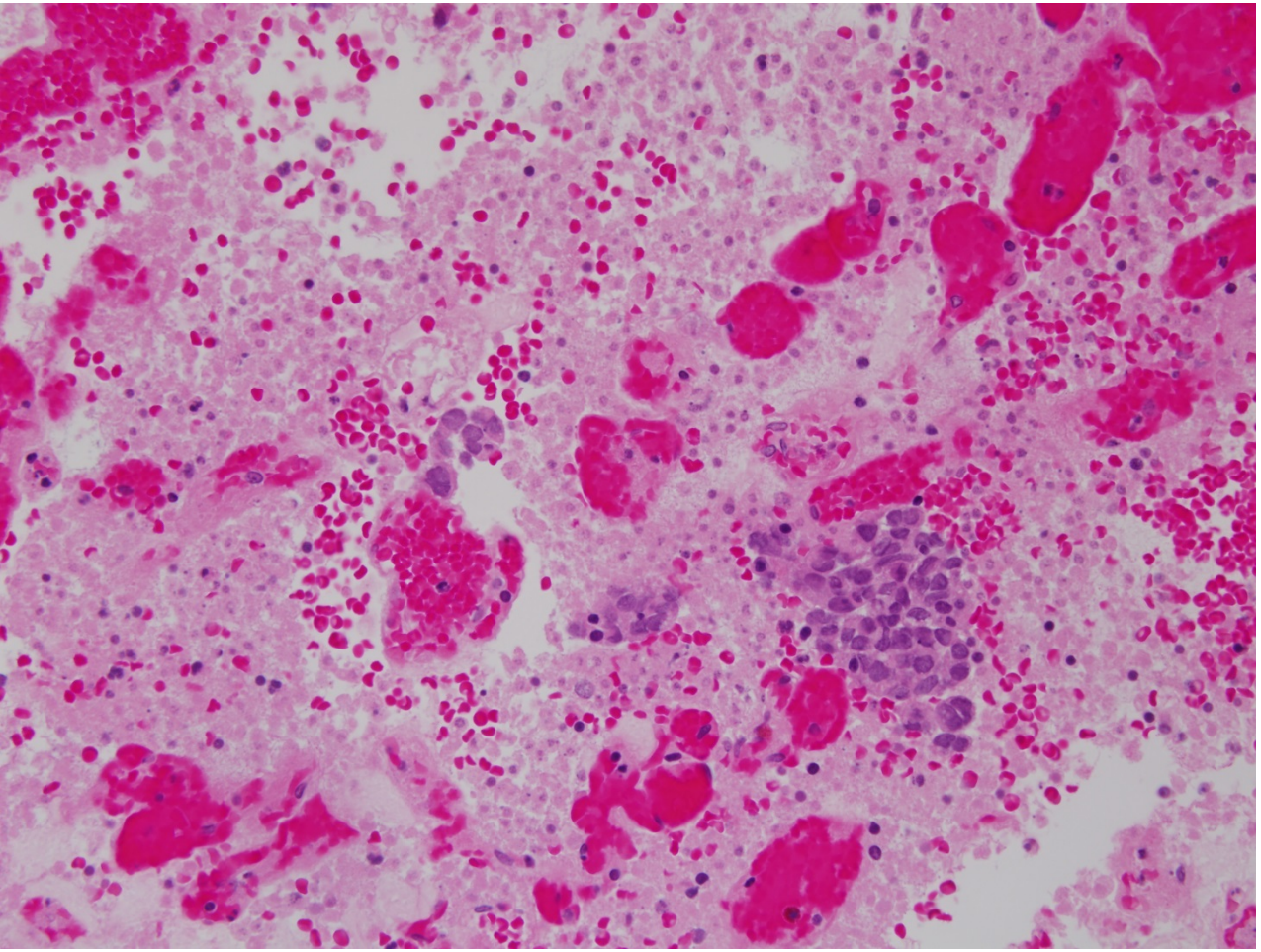
## Pseudorosettes

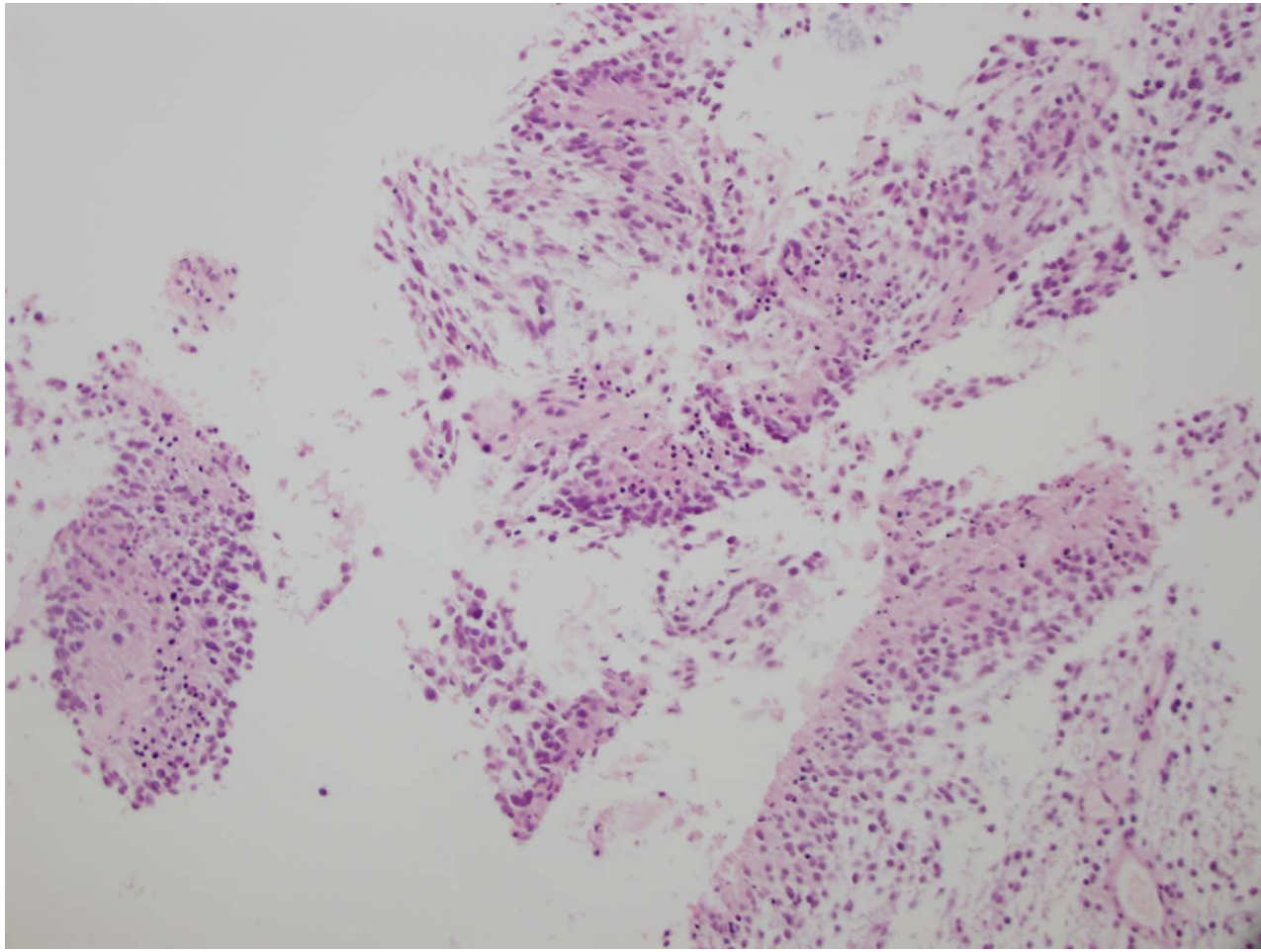




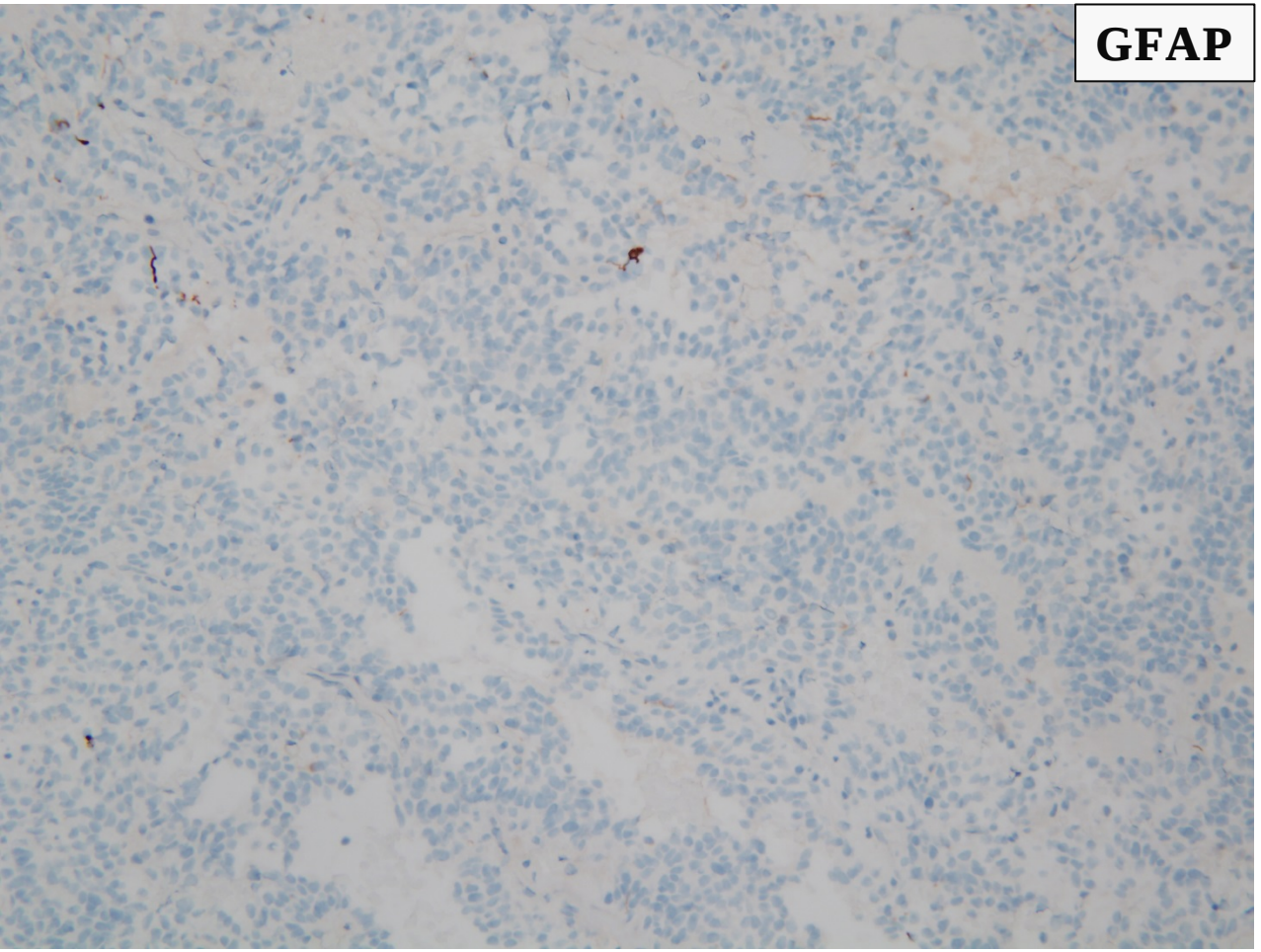
# Permanent sections

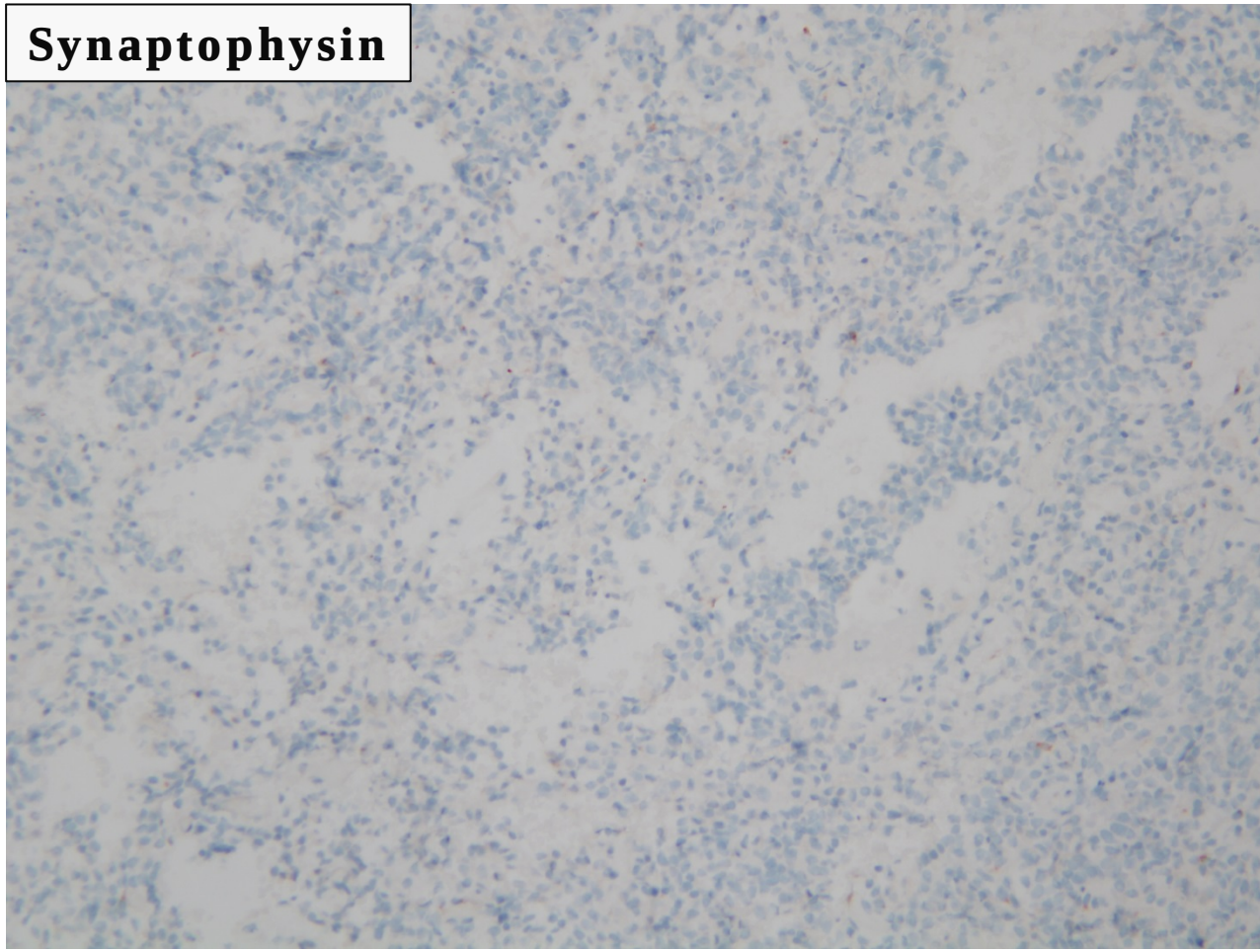
## Necrosis





# Immunohistochemistry

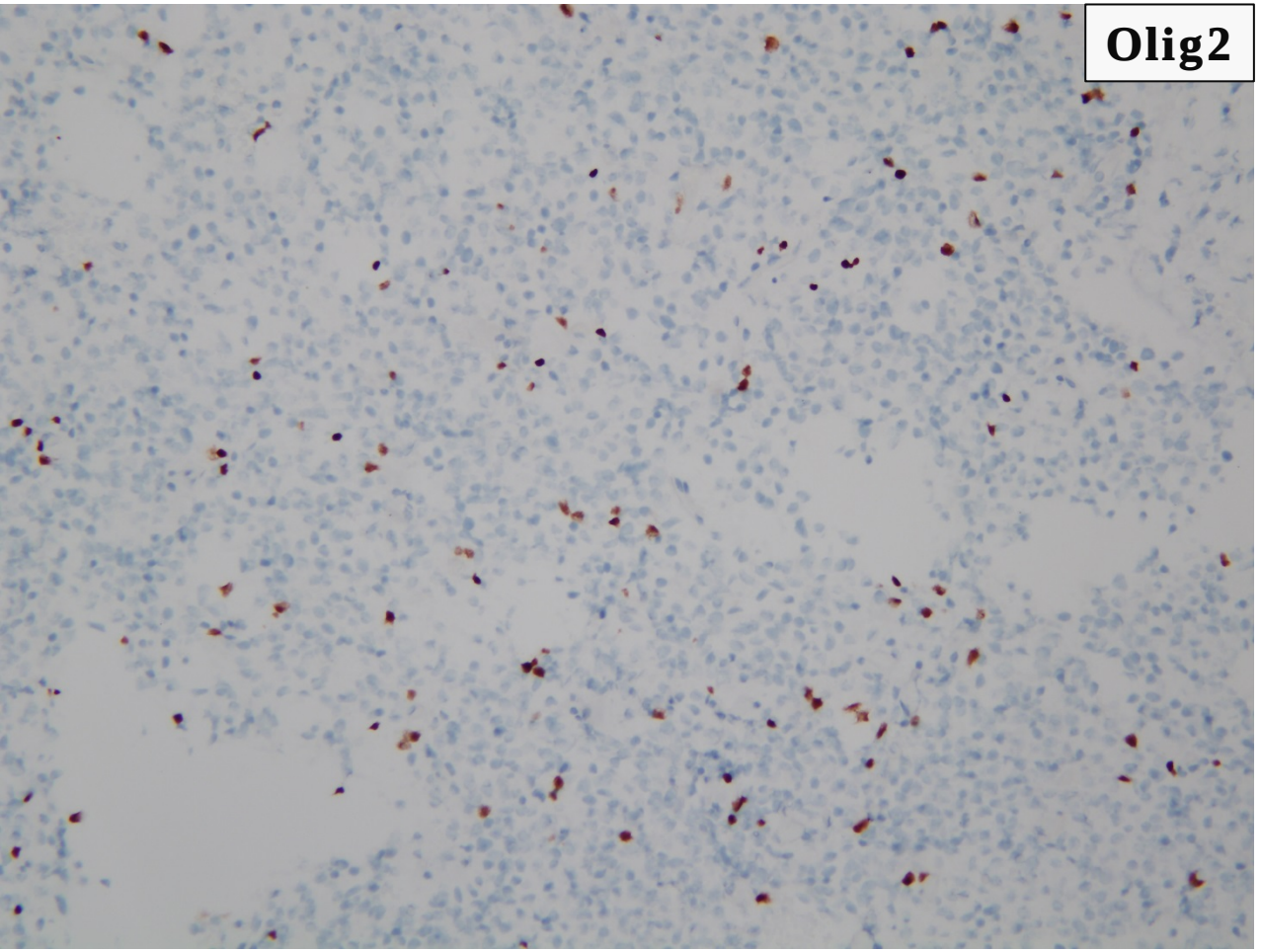


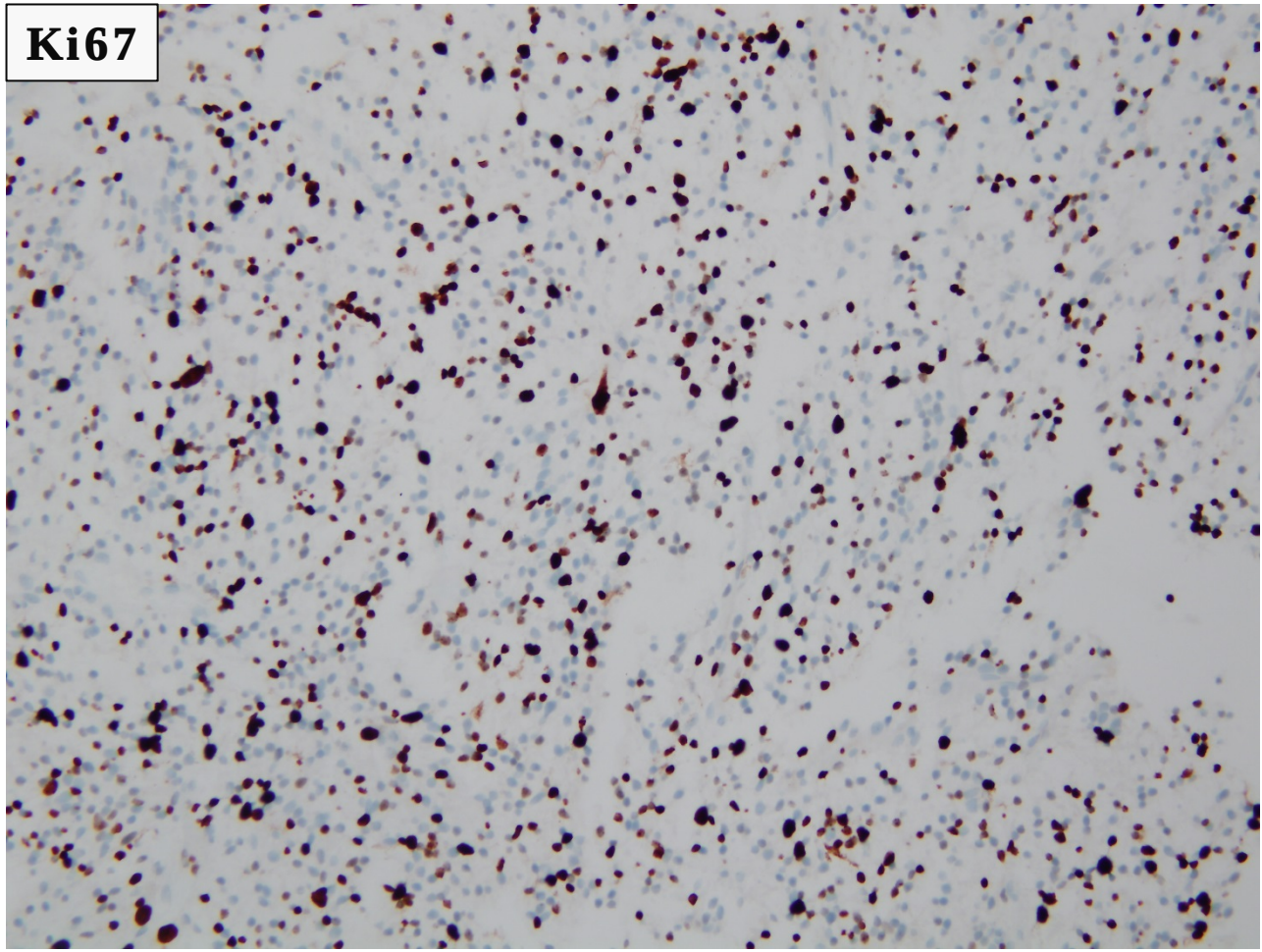



# Immunohistochemistry

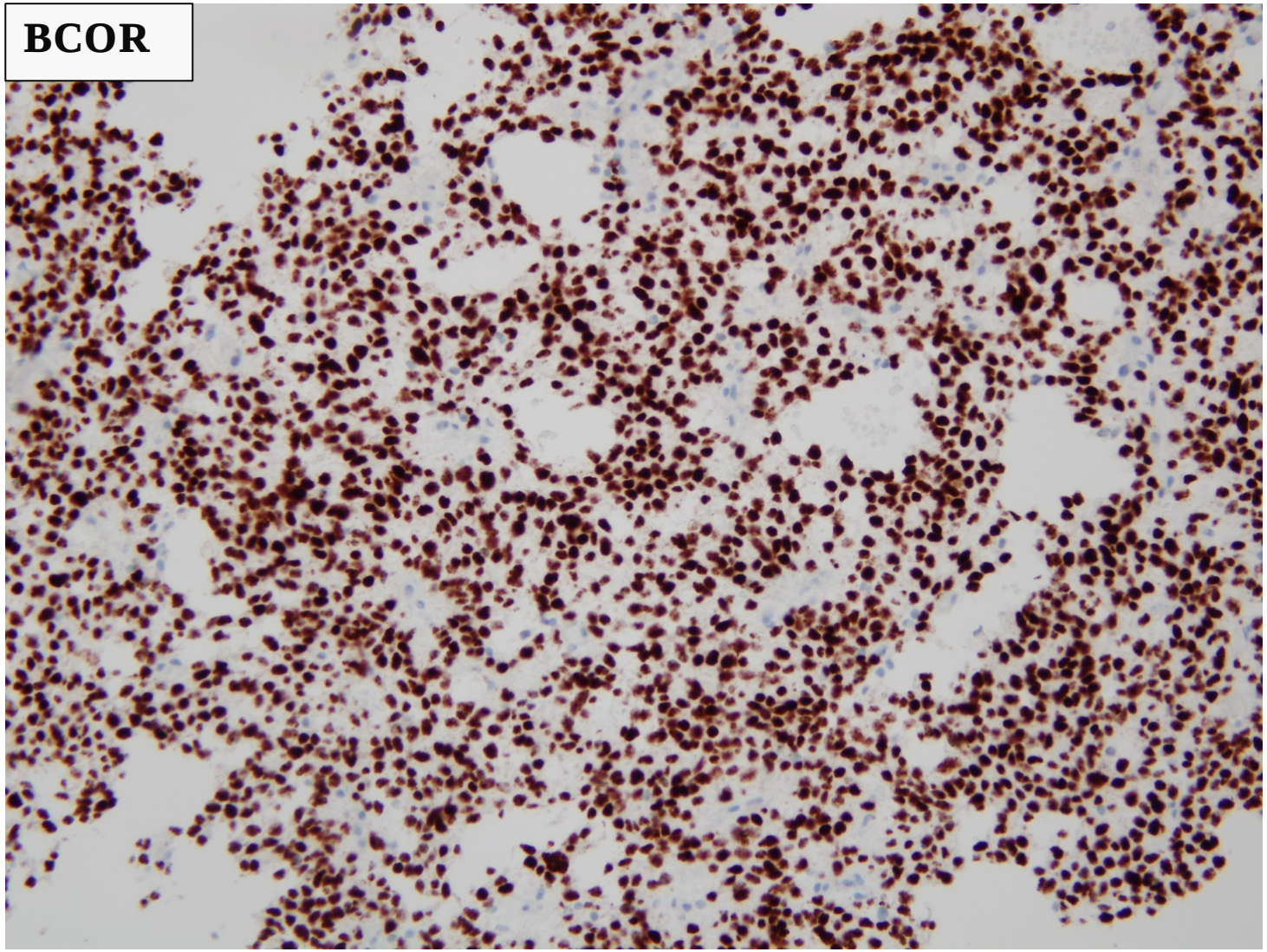
- Positive stains
  - Vimentin
  - CD99
  - D2-40 (membranous pattern)
  - FLI-1
  - S-100 (occasional)
  - LIN28A (patchy)
  - GLUT-1 (focal)
  - Olig2 (patchy)
  - Ki67 (~40%)
- Negative stains
  - GFAP
  - Synaptophysin
  - Neurofilament
  - NeuN
  - WT-1
  - SMA
  - Desmin
  - CD34
  - EMA
  - Inhibin
  - HMB-45
  - BRAF V600E
- Negative FISH
  - EWSR1 and C19MC

# Immunohistochemistry



# CNS Tumor with BCOR-ITD




## Genomic Findings

*For a complete list of the genes assayed, please refer to the Appendix.*

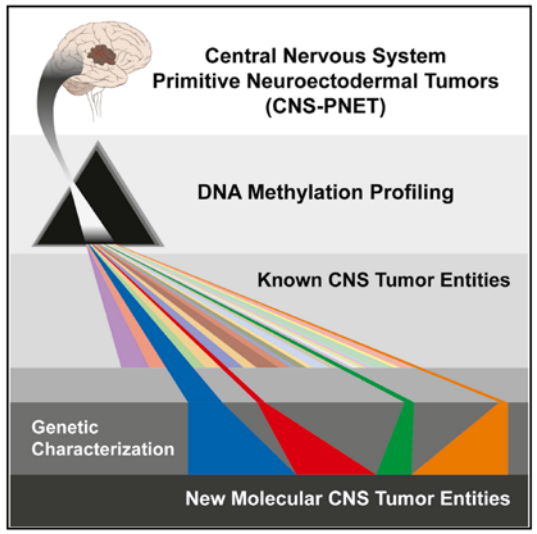
***BCOR*** BCOR-ITD (V1707_E1708ins30)

Resource

Cell

# New Brain Tumor Entities Emerge from Molecular Classification of CNS-PNETs

## Graphical Abstract

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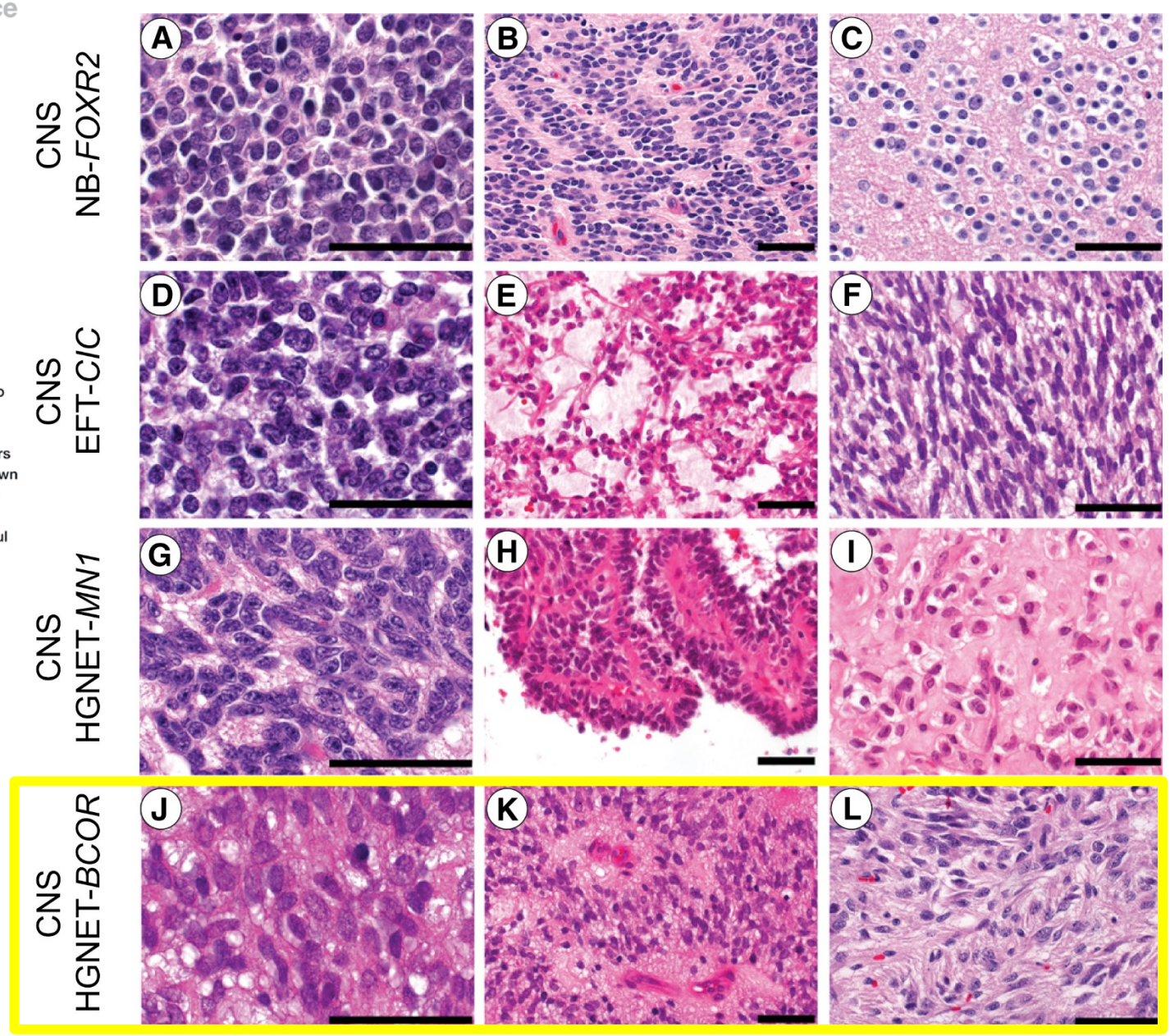
## In Brief

Highly malignant primitive neuroectodermal tumors of the CNS (CNS-PNETs) have been challenging to diagnose and distinguish from other kinds of brain tumors, but molecular profiling now reveals that these cancers can be readily classified into some known tumor types and four new entities with distinct histopathological and clinical features, paving the way for meaningful clinical trials.

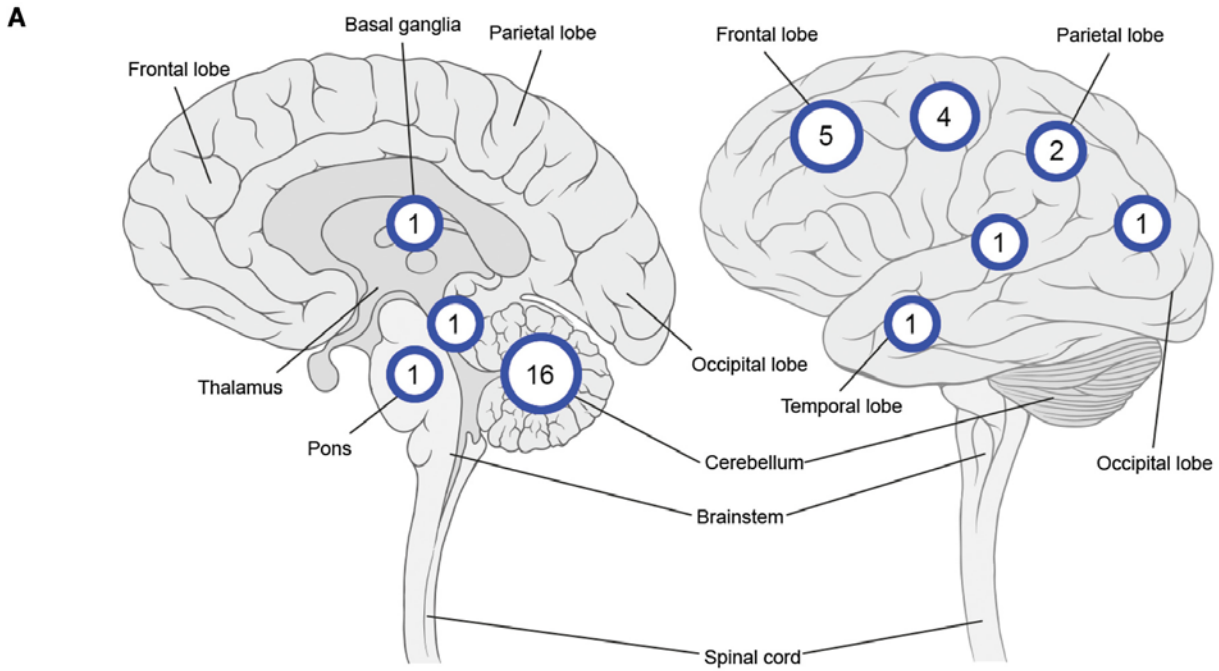


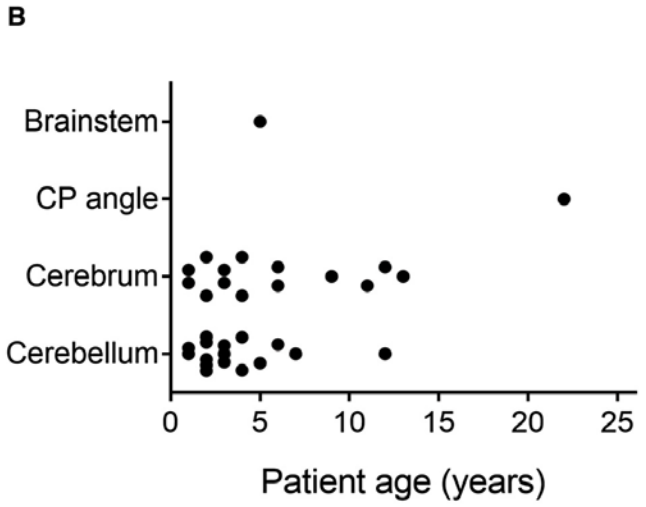
Brain Pathology ISSN 1015-6305

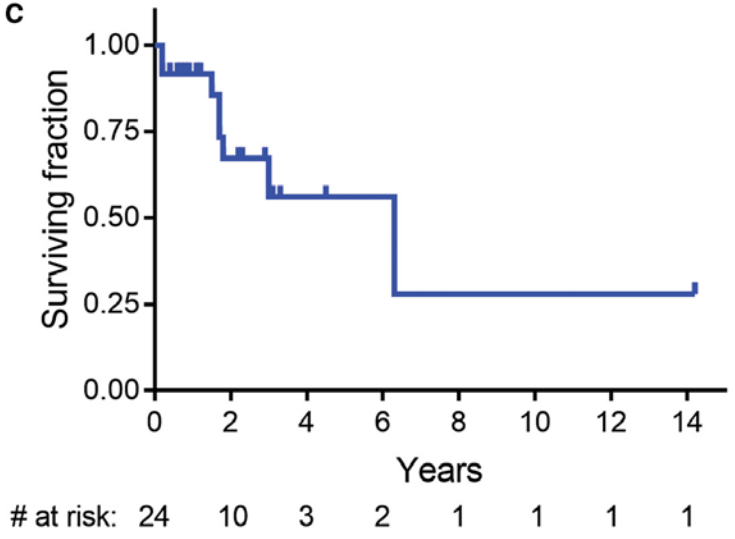
RESEARCH ARTICLE

# High-grade neuroepithelial tumor with *BCOR* exon 15 internal tandem duplication—a comprehensive clinical, radiographic, pathologic, and genomic analysis

Sean P. Ferris[1]; Jose Velazquez Vega[2]; Mariam Aboian[3]; Julieann C. Lee[1]; Jessica Van Ziffle[1,4]; Courtney Onodera[1,4]; James P. Grenert[1,4]; Tara Saunders[1]; Yunn-Yi Chen[1]; Anu Banerjee[5]; Cassie N. Kline[5,6]; Nalin Gupta[7]; Corey Raffel[7]; David Samuel[8]; Irune Ruiz-Diaz[9]; Shino Magaki[10]; Dianne Wilson[11]; Janna Neltner[11]; Zahra Al-Hajri[12]; Joanna J. Phillips[1,7]; Melike Pekmezci[1]; Andrew W. Bollen[1]; Tarik Tihan[1]; Matthew Schniederjan[2]; Soonmee Cha[3]; Arie Perry[1,7]; David A. Solomon[1,4]



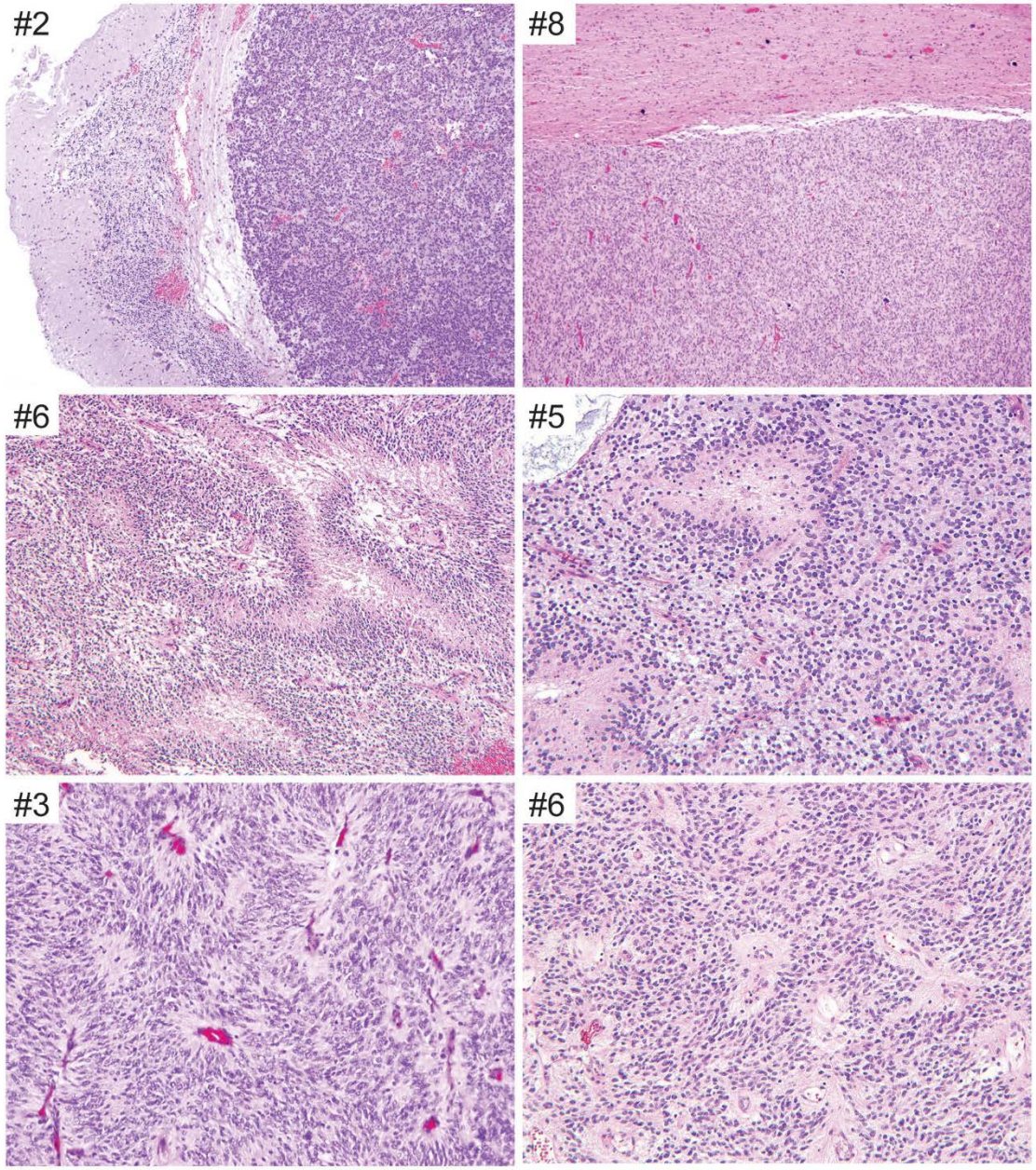



**Table 3.** Immunohistochemical features of the 10 CNS high-grade neuroepithelial tumors with *BCOR* exon 15 internal tandem duplication.

| Tumor ID | GFAP | OLIG2 | NeuN | Synaptophysin | Neurofilament | EMA | p53 | Ki-67 | BCOR |
|---|---|---|---|---|---|---|---|---|---|
| SF-BCOR-1 | Negative | – | – | Negative | Positive (10%) | – | 5% | 20% | Strongly positive |
| SF-BCOR-2 | Negative | Positive (20%) | Positive (10%) | Negative | Positive (10%) | Granular cytoplasmic positivity | 30% | – | – |
| SF-BCOR-3 | Negative | Positive (20%) | Negative | Negative | Positive (5%) | Granular cytoplasmic positivity | – | 40% | Strongly positive |
| SF-BCOR-4 | Negative | Positive (10%) | Positive | Negative | – | Negative | 15% | 20% | – |
| SF-BCOR-5 | Focally positive | – | Positive | Negative | Negative | Negative | 10% | 15% | Strongly positive |
| SF-BCOR-6 | Negative | – | Positive (40%) | Negative | Positive (1%) | Negative | 10% | 60% | Strongly positive |
| SF-BCOR-7 | Negative | Positive (30%) | Positive (80%) | – | Negative | Negative | – | – | Strongly positive |
| SF-BCOR-8 | – | Positive (40%) | Positive (70%) | Negative | Negative | – | – | – | Strongly positive |
| SF-BCOR-9 | Negative | Negative | Positive (20%) | Negative | Positive (10%) | Granular cytoplasmic positivity | – | – | Strongly positive |
| SF-BCOR-10 (LG) | Negative | Positive (20%) | Positive (80%) | Negative | Negative | Granular cytoplasmic positivity | 0% | 5% | Strongly positive |
| SF-BCOR-10 (HG) | Focally positive | Negative | Positive (20%) | Negative | Positive (1%) | Granular cytoplasmic positivity | 90% | 60% | Strongly positive |

HG = high-grade/anaplastic component; LG = low-grade appearing component.

# Other CNS tumors with BCOR protein expression

- Astroblastoma-like neuroepithelial tumor with *MN1* rearrangement[2]
- Pediatric gliomas with EP300-BCOR fusions[3]
- High-grade neuroepithelial tumor, NOS[4]

# cIMPACT-NOW update 6

**Table 1.** Summary of cIMPACT-Utrecht recommendations.

| | |
|---|---|
| A | Newly recognized type, subtype, diagnostic criteria, or family of tumors |
| | Specific genetic features sufficient for diagnosis of "glioblastoma, IDH-wildtype" |
| | Astrocytomas, IDH-mutant, grades 2 through 4 |
| | Pediatric-type glial/glioneuronal tumors (see Table 3) |
| | Diffuse glioma, H3.3 G34-mutant |
| | CNS neuroblastoma, *FOXR2*-activated |
| | CNS tumor with *BCOR* internal tandem duplication |
| | *CIC* sarcoma (aligned with the WHO classification of tumors of soft tissue and bone) |

LETTER TO THE EDITOR Open Access

# The *EP300:BCOR* fusion extends the genetic alteration spectrum defining the new tumoral entity of "CNS tumors with *BCOR* internal tandem duplication"

Tauziède-Espariat *et al.*
*acta neuropathol commun* (2020) 8:178

**Table 1 Comparison of clinical, histopathological and molecular data according to methylation classes and diagnoses**

| | HGNET-BCOR ITD (n = 29) | HGNET-BCOR EP300:BCOR/BCORL1 fusions (n = 3) | GLIOMAS EP300:BCOR fusion (n = 4) |
|---|---|---|---|
| Location | Infratentorial (52%) | Supratentorial (100%) | Supratentorial (100%) |
| Age | Median age = 3.5 YO (0;22) | Median age = 27 YO (13;72) | Median age = 12 YO (10;18) |
| Sex | Male (54%) | Male (100%) | Male (66%) |
| Radiology | Large, well-circumscribed, solid with meningeal attachment; T1 hypointense, T2 hyperintense, low ADC, heterogeneous enhancement | Large, well-circumscribed, solid with meningeal attachment; T1 hypointense, T2 hyperintense, low ADC, heterogeneous enhancement | Limited data: no meningeal attachment, not well circumscribed, T2 hyperintense, mild enhancement |
| Histopathology | High-grade solid tumor with perivascular pseudorosettes and microcysts | High-grade solid tumor with perivascular pseudorosettes and microcysts | Infiltrative tumor Variable grade (low in 2 cases, high in 2 cases) |
| Immunohistochemistry | GFAP-/Olig2+/EMA-/Neuronal markers+/BCOR+ | GFAP-/Olig2+/EMA-/Neuronal markers+/BCOR- | GFAP+/Olig2+/Neuronal markers-/BCOR+ |
| DNA-methylation class | HGNET-BCOR | HGNET-BCOR | LGG-MYB/MYBL1 |
| Outcome | 65% recurrences<br>Median PFS = 12.5 months 30% dead at the end of follow-up<br>Median OS = 26 months | 0% recurrences<br>0% dead at the end of follow-up<br>Median OS = 27 months | 100% recurrences<br>Median PFS = 4.0 months<br>0% dead at the end of follow-up<br>Median OS = 7 months |

*ADC* apparent diffusion coefficient, *ITD* internal tandem duplication, *OS* overall survival, *PFS* progression-free survival, *YO* years-old

# References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