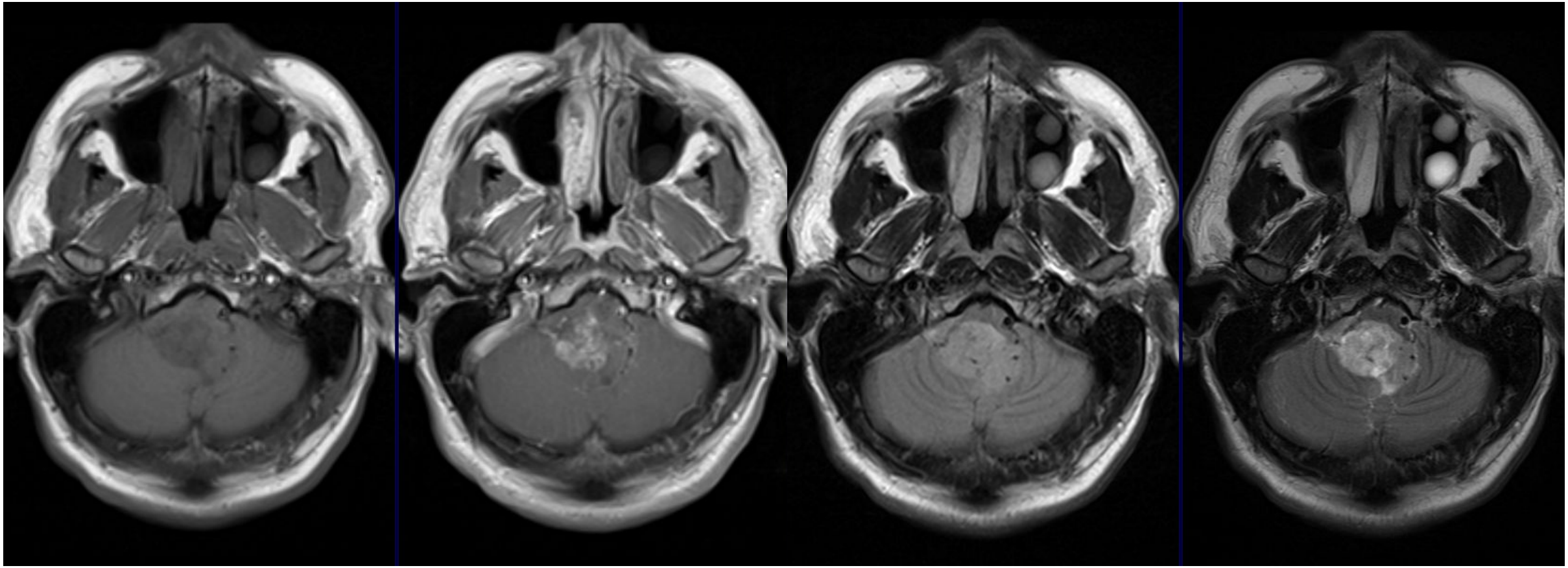
# Ependymoma-PFB

# Presentation

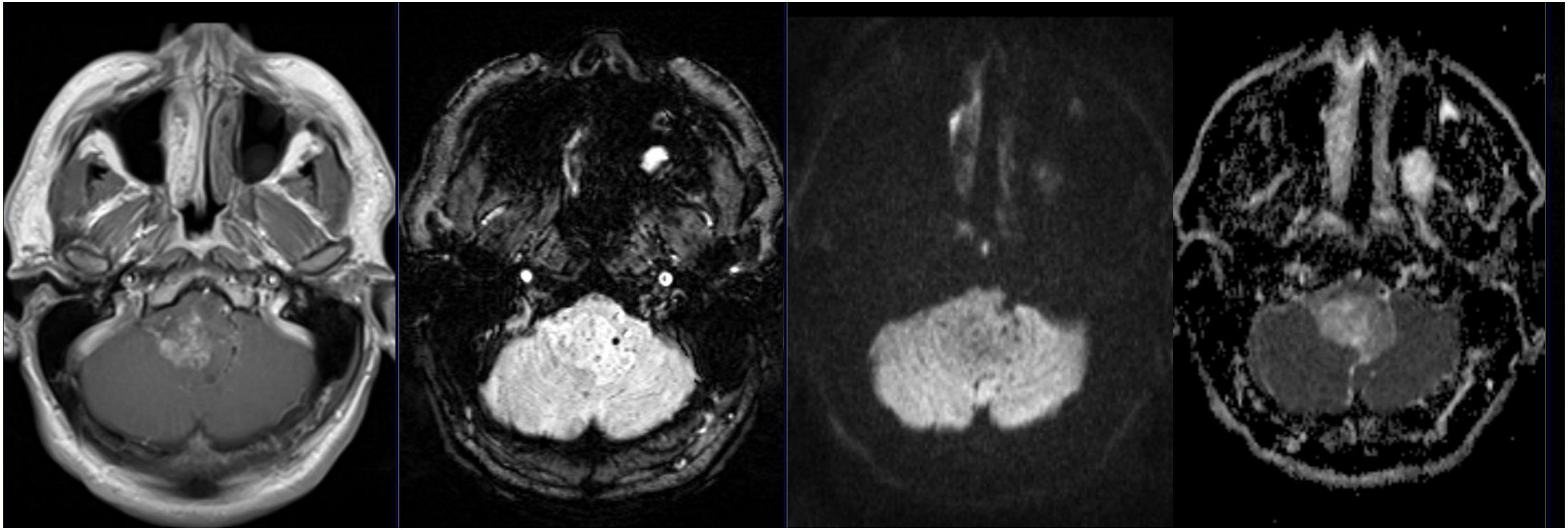
- Male in their 30s presented with several year history of progressively worsening HAs
- Neuroimaging revealed $4^{th}$ ventricular mass with hydrocephalus
- Right frontal ventriculostomy followed by suboccipital craniectomy with resection of tumor

# MRI on presentation

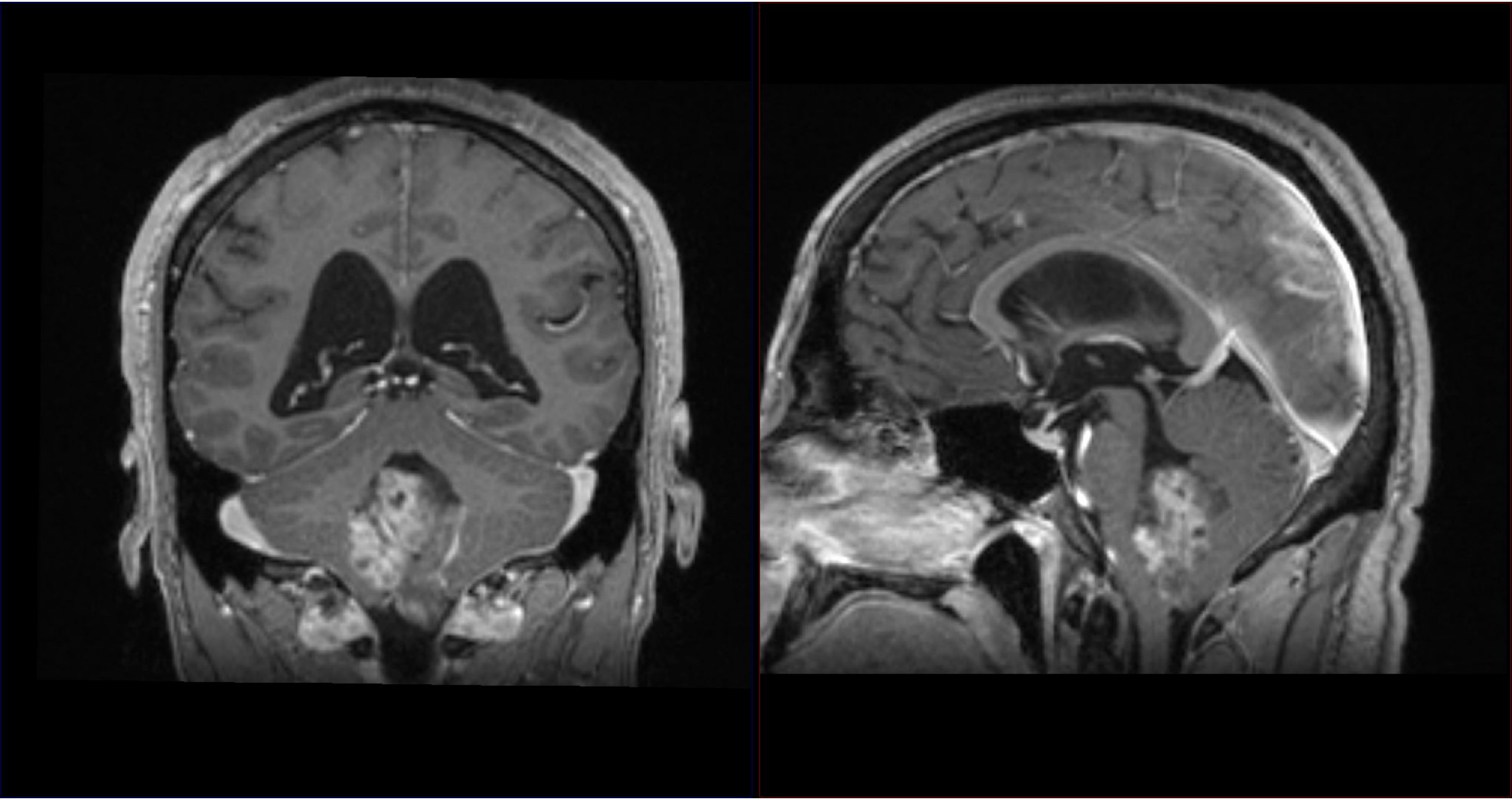


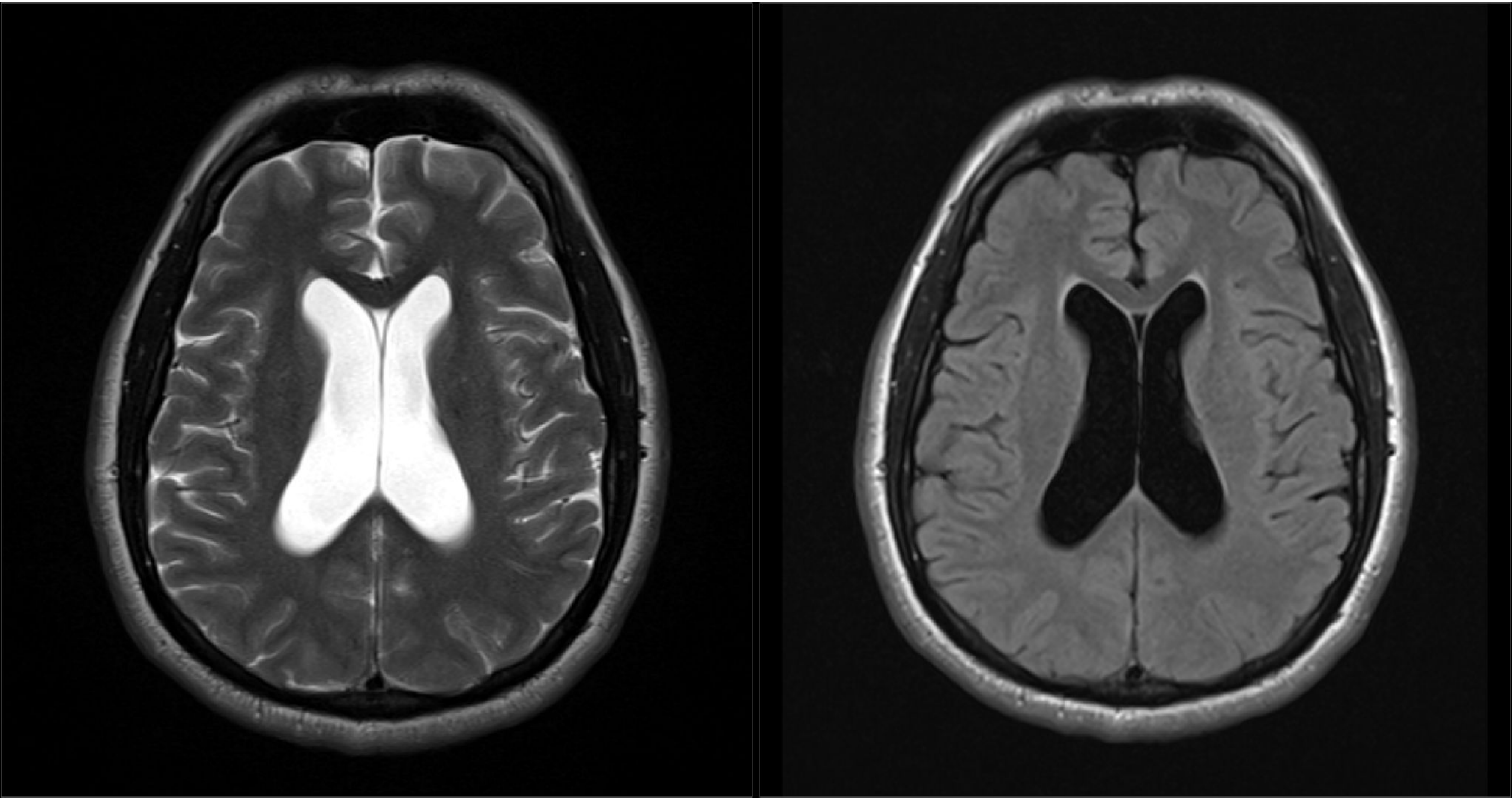
T1 pre T1 post T2 FLAIR T2

# MRI on presentation

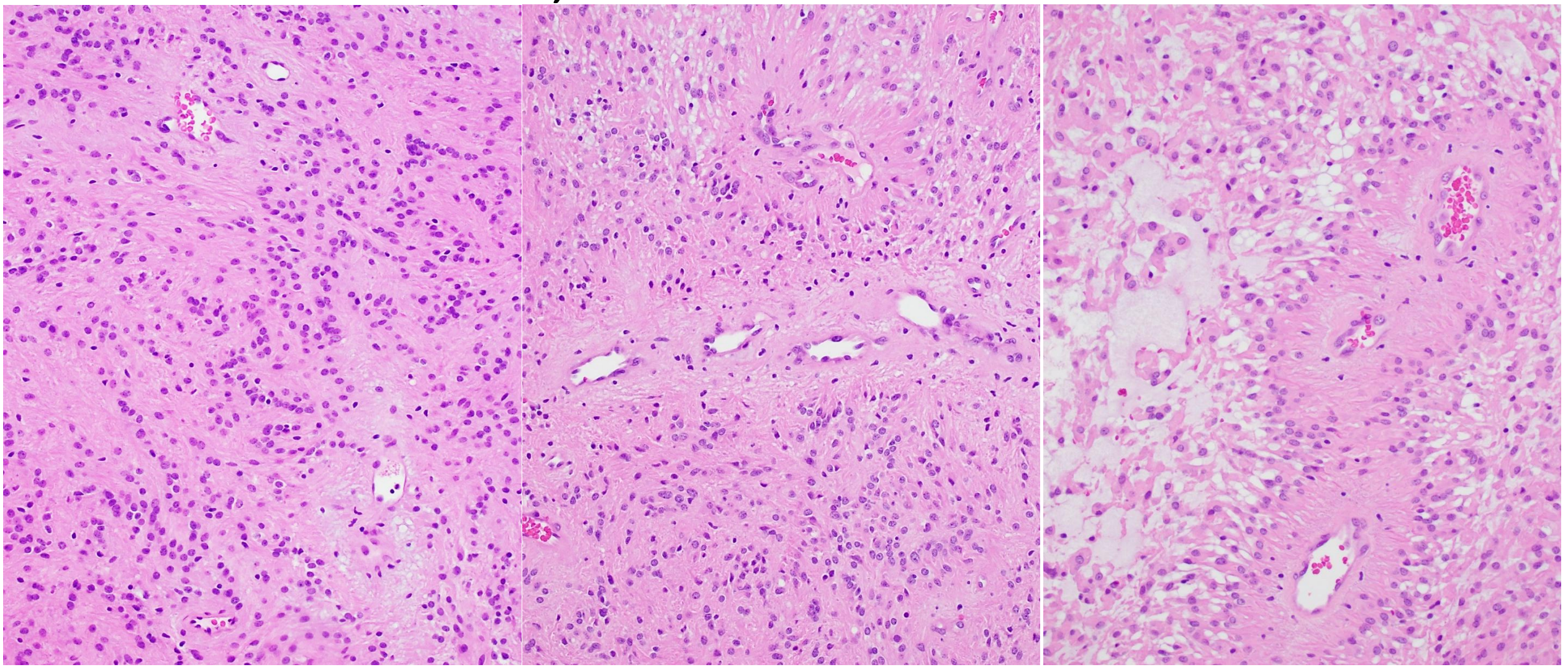


T1 post SWI DWI (B1000) ADC



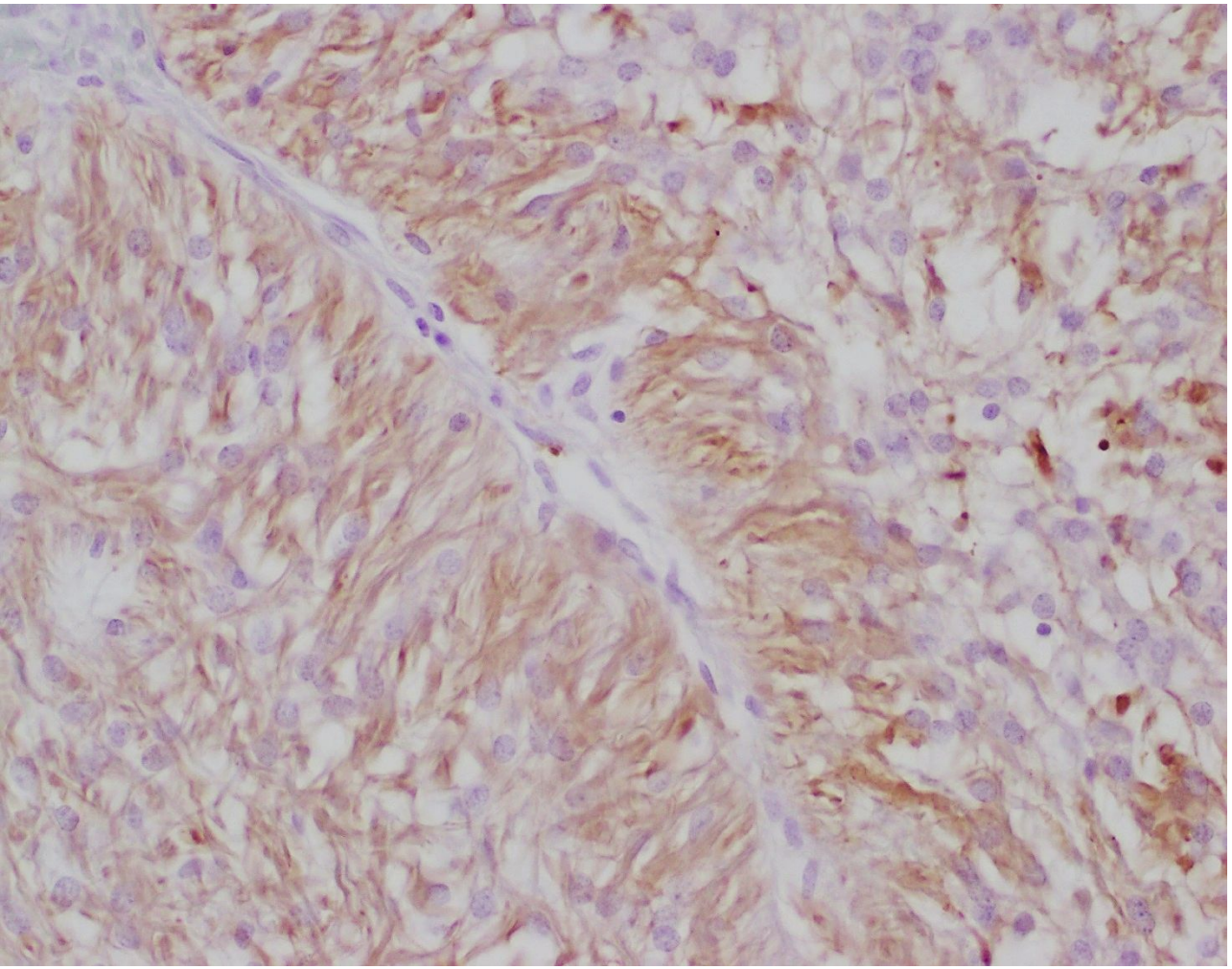


# Formalin-fixed, H&E-stained sections.



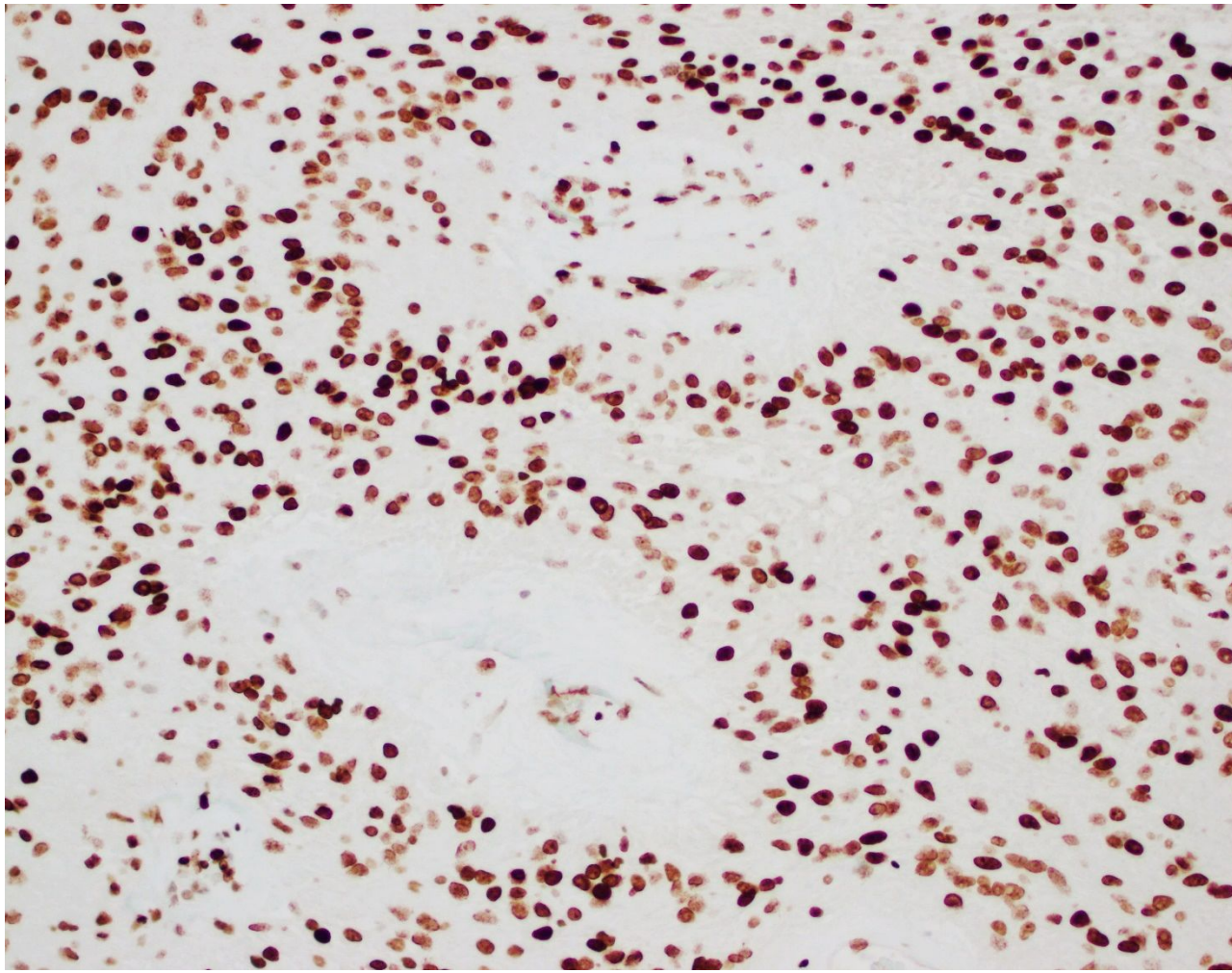
Monomorphic cells with perivascular pseudorosettes.

## GFAP



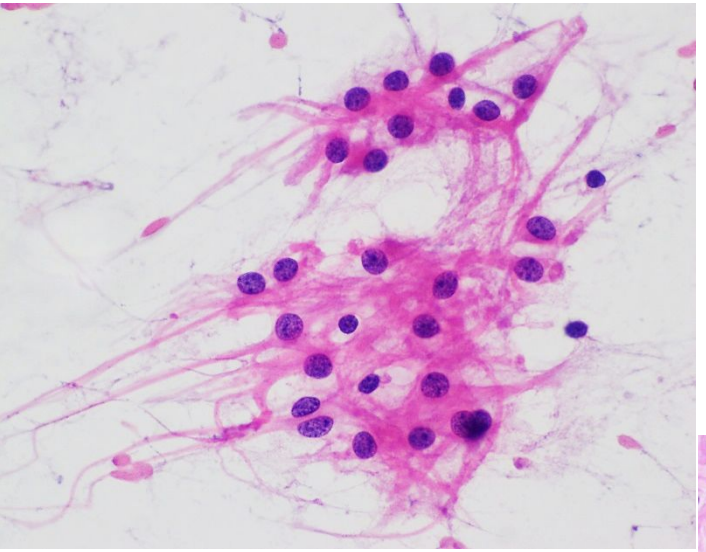
Tapering cell processes oriented towards blood vessels.

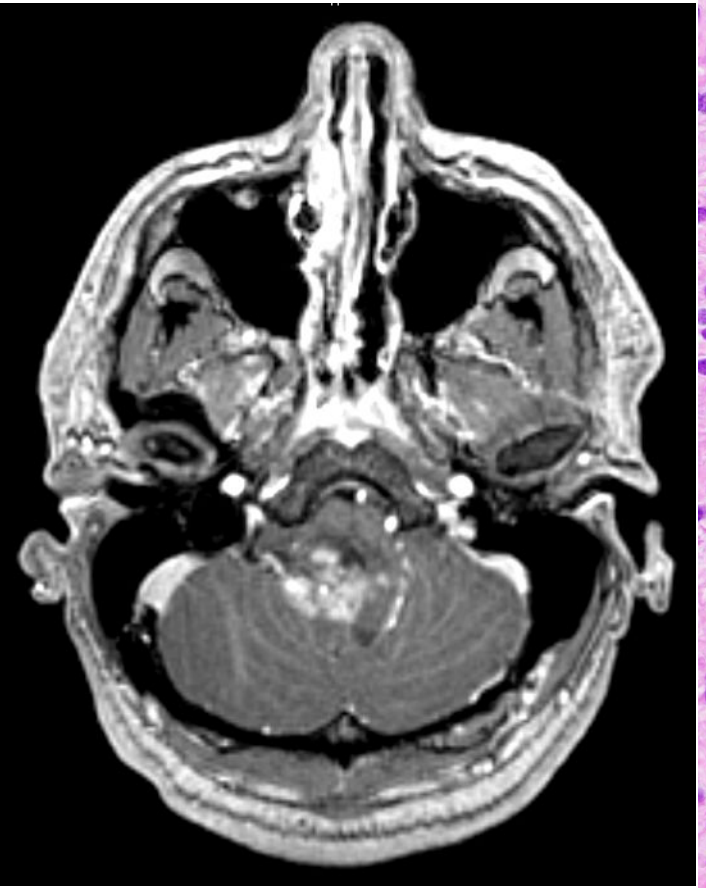
## H3 K27me3

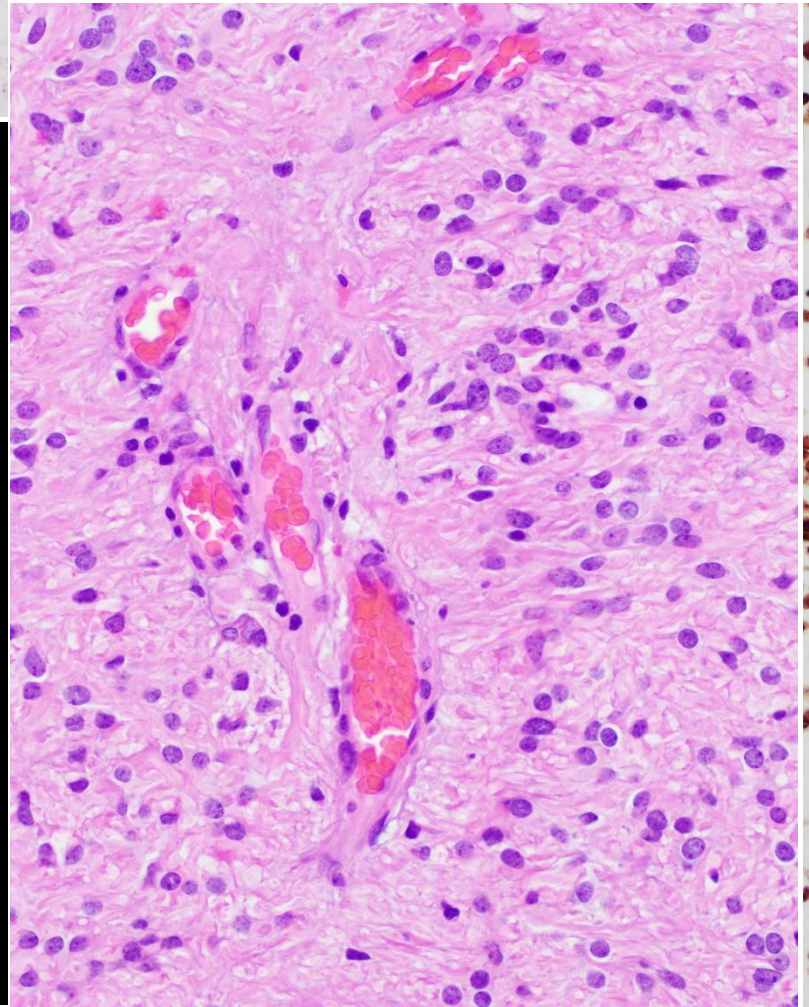


Retained nuclear reactivity.

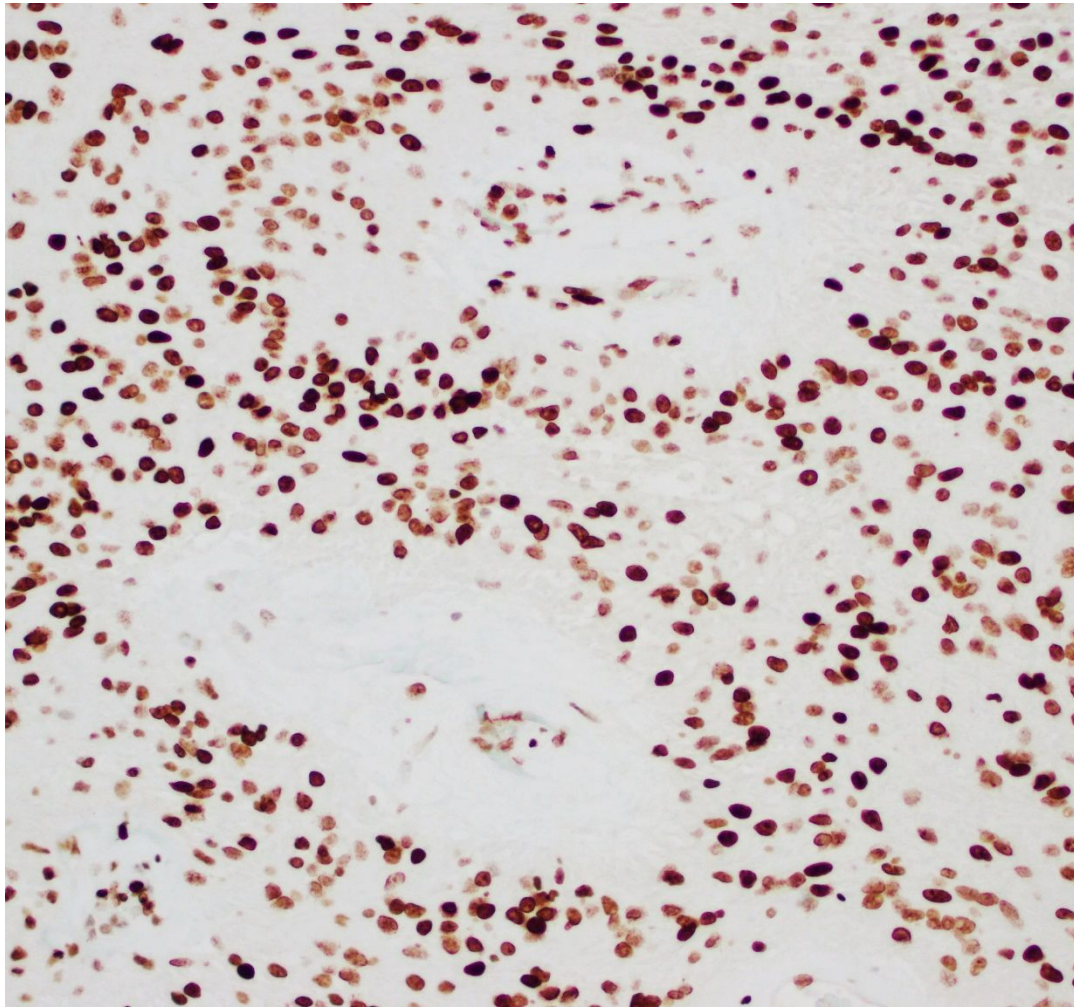
# Posterior fossa group B (PFB) Ependymoma







H3 K27me3 - retained



# FINAL DIAGNOSIS:

BRAIN, POSTERIOR FOSSA TUMOR

UPMC METHYLATION ARRAY FOR CENTRAL NERVOUS SYSTEM (CNS) TUMORS RESULTS:

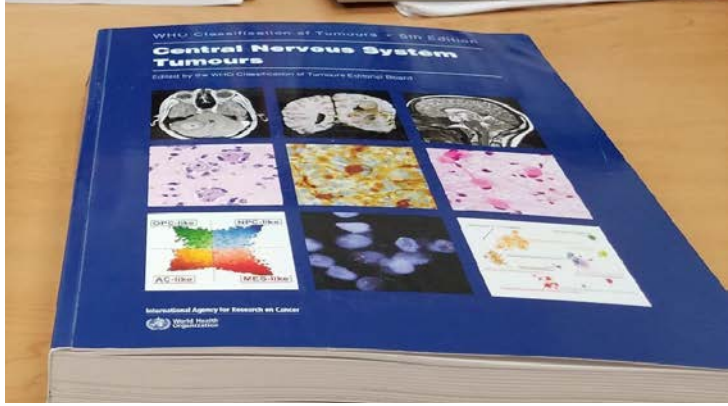
**Methylation Class (Calibrated Score): Posterior fossa group B (PFB) ependymoma (0.99)**

**Methylation Subclass (Calibrated Score): Posterior fossa group B (PFB) ependymoma, subclass 2 (0.53)**

**MGMT Promoter Methylation Status by Array: Unmethylated**
**Classifier version: Heidelberg Epignostix v12.8**

**INTERPRETATION:**
The methylation class "posterior fossa group B (PFB) ependymoma" comprises the molecular subclasses 1-5 and represents the molecularly rendered tumor type posterior fossa group B (PFB) ependymoma. Histologically, these tumors typically demonstrate pseudorosettes or ependymal rosettes and comprise uniform small cells with round nuclei embedded in a fibrillary matrix. Numeric whole chromosome changes are frequent in these tumors. Retention of nuclear H3 p.K28me3 (K27me3) expression is observed, but it is not specific for PFB ependymoma.

# Ependymomas, WHO - 2021




| Ependymal tumors | |
|---|---|
| Supratentorial ependymoma | |
| Supratentorial ependymoma, *ZFTA* fusion-positive | **Younger - Poor prognosis** |
| Supratentorial ependymoma, *YAP1* fusion-positive | |
| Posterior fossa ependymoma | |
| Posterior fossa ependymoma, group PFA | **H3K27me3 loss – Poor prognosis** |
| Posterior fossa ependymoma, group PFB | **H3K27me3 retained – better prognosis** |
| Spinal ependymoma | **Most have good prognosis** |
| Spinal ependymoma, *MYCN*-amplified | **Poor prognosis** |
| Myxopapillary ependymoma | **Now CNS WHO grade 2** |
| Subependymoma | **Remains CNS WHO grade 1** |

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RESEARCH LETTER

Brain Pathology

# cIMPACT-NOW update 11: Proposal on adaptation of diagnostic criteria for IDH- and H3-wildtype diffuse high-grade gliomas and for posterior fossa ependymal tumors

Pieter Wesseling[1,2] | David Capper[3,4] | Guido Reifenberger[5,6] |

TABLE 3 Suggested diagnostic criteria for *posterior fossa group A (PFA) ependymoma* (changes compared to WHO CNS5 in bold).

| **Essential** |
|---|
| Posterior fossa tumor with morphological and immunohistochemical features of ependymoma |
| AND |
| **Loss of H3 K27me3 expression**[a] in tumor cell nuclei |
| OR |
| DNA methylation profile aligned with PFA ependymoma |
| **Desirable** |
| i. Stable genome on genome-wide copy number analysis[b] |
| ii. **Strong and diffuse nuclear expression of EZHIP** |

[a]"Global reduction of H3 K27me3" replaced by "Loss of H3 K27me3 expression."
[b]Presence of chromosome 1q gain and/or chromosome 6q loss are associated with worse survival [60].

TABLE 4 Suggested diagnostic criteria for *posterior fossa group B (PFB) ependymoma* (changes compared to WHO CNS5 in bold).

| **Essential** |
|---|
| Posterior fossa tumor with morphological and immunohistochemical features of ependymoma |
| AND |
| DNA methylation profile aligned with PFB ependymoma. |
| **Desirable** |
| i. Chromosomal instability and aneuploidy on genome-wide copy number analysis |
| ii. Retained nuclear expression of H3 K27me3 |
| iii. **No EZHIP expression in tumor nuclei** |

# Ependymomas

- Classified using histology, molecular and anatomic features
- Subependymoma Grade 1 – Commonly slow-growing (Near ventricle)
- Myxopapillary ependymoma Grade 2 – Commonly slow-growing (lower part of spine)
- Ependymomas Grade 2-3 : Most common (spine and posterior fossa)
  - Histopathological – Papillary, Clear cell, Tancytic
  - Molecular features – ZFTA or YAP1 fusion positive, MYCN amplification
    - MYCN amplification associated with more aggressive course
  - Location – supratentorial, posterior fossa (group A or B), spine

# Treatment landscape for Ependymoma

- Surgery (depending on subtype, may be curative)
- When more aggressive, residual or recurrent
  - Clinical Trials if available
  - Radiation
  - Systemic treatment
    - Temozolomide, Temozolomide + Lapatinib, Bevacizumab
    - Emerging options – PARP inhibitors and Immune checkpoint inhibitors
- For Clinical Trials, access the Collaborative Ependymoma Research Network (CERN) – developed to translate bench research to clinical trials

# Plan

- Post operative imaging noted small nodule of residual tumor
- Fractionated RT recommended