CASE OF THE MONTH- AUGUST 2019

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HISTORY

- 34Y/M
- Presenting complaints:
  - Headache
  - Clumsiness
  - Difficulty in walking
  - Change in handwriting
  - Stammering

6-7 months

- No significant past medical history

On examination..

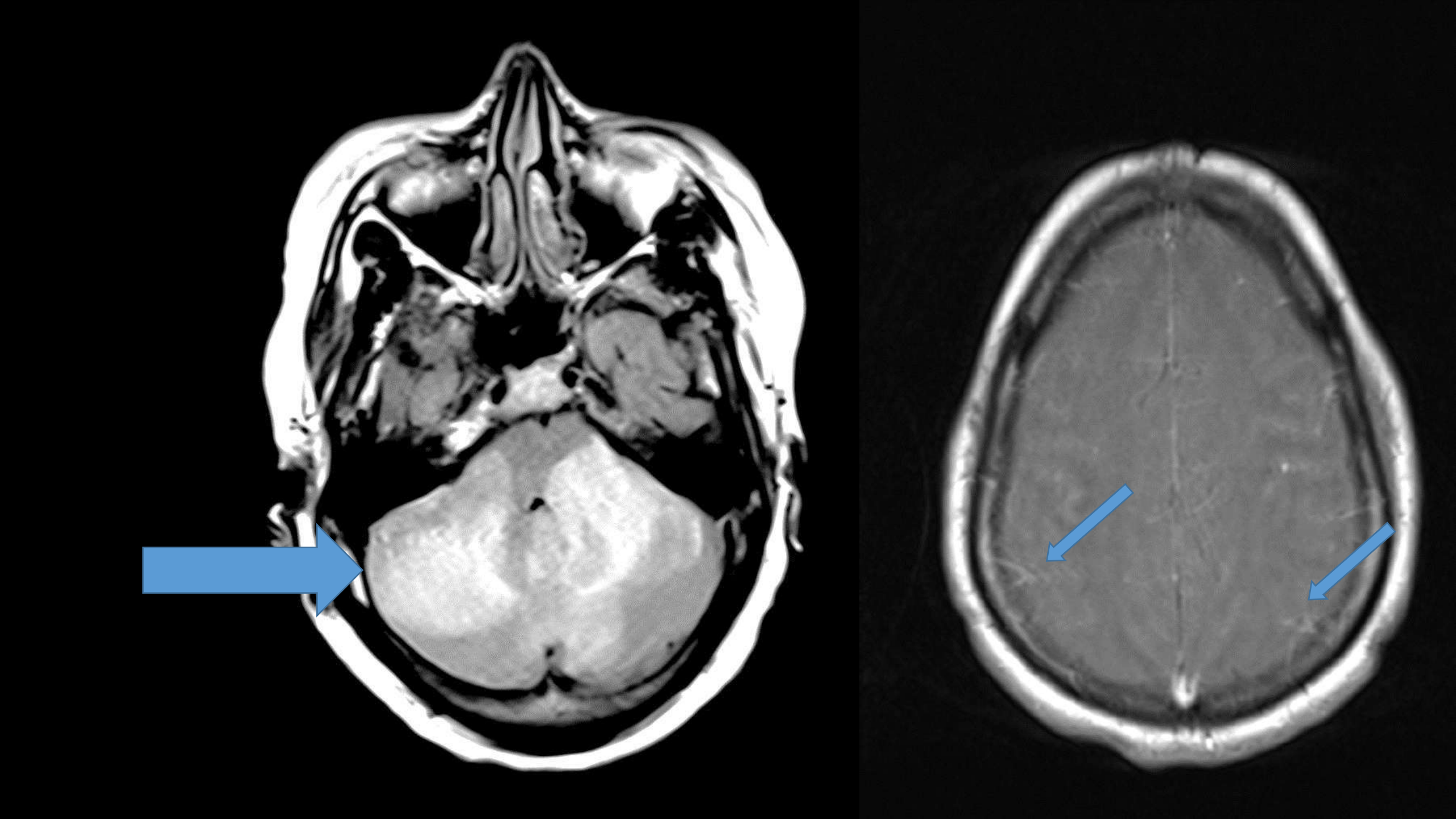
- Conscious, dull, drowsy & disoriented
- Cerebellar signs + (L>R)
- Left side swaying of body
- Ataxia +
- Incoordination+

Investigations..

- Routine blood & biochemical profile: WNL
- MRI brain: infiltrative SOL in cerebellum

MRI Brain

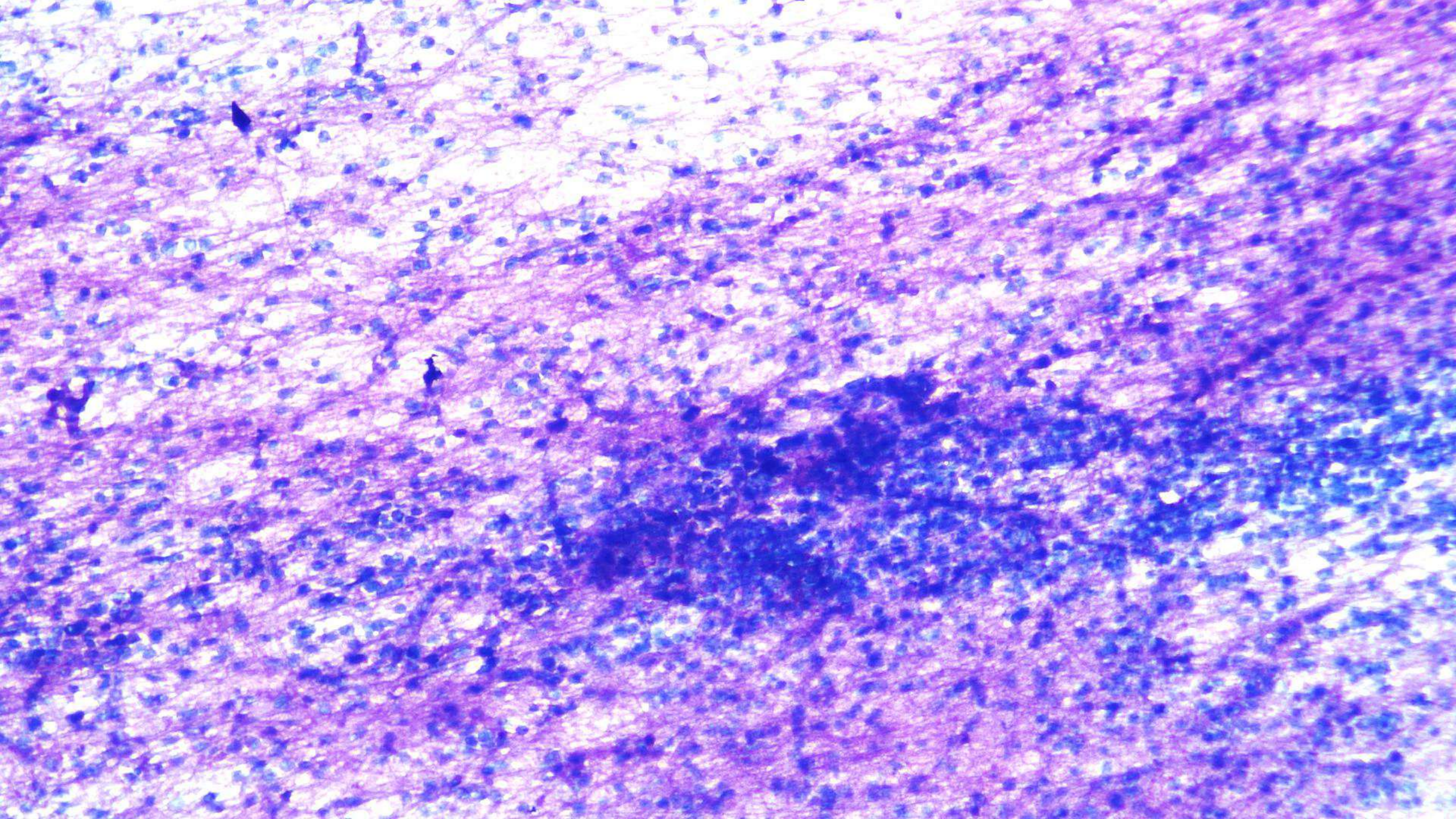
- Bilateral cerebellum shows an infiltrative lesion with necrotic areas involving vermis, bilateral cerebellar peduncles, extending to left pons and midbrain, causing effacement of 4th ventricle with lateral and 3rd ventricle dilatation
- Fine leptomeningeal enhancement along bilateral cerebral sulca

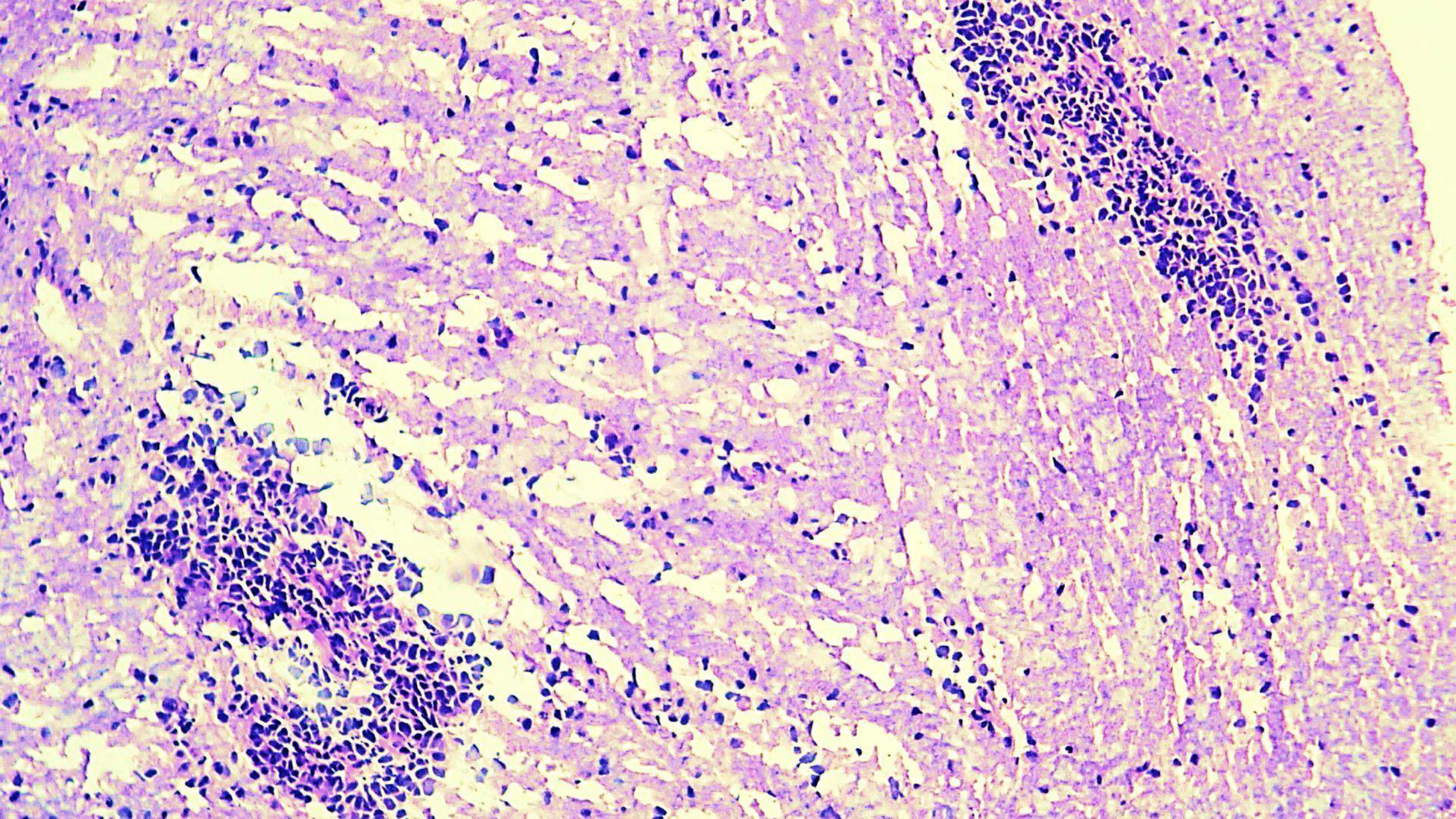


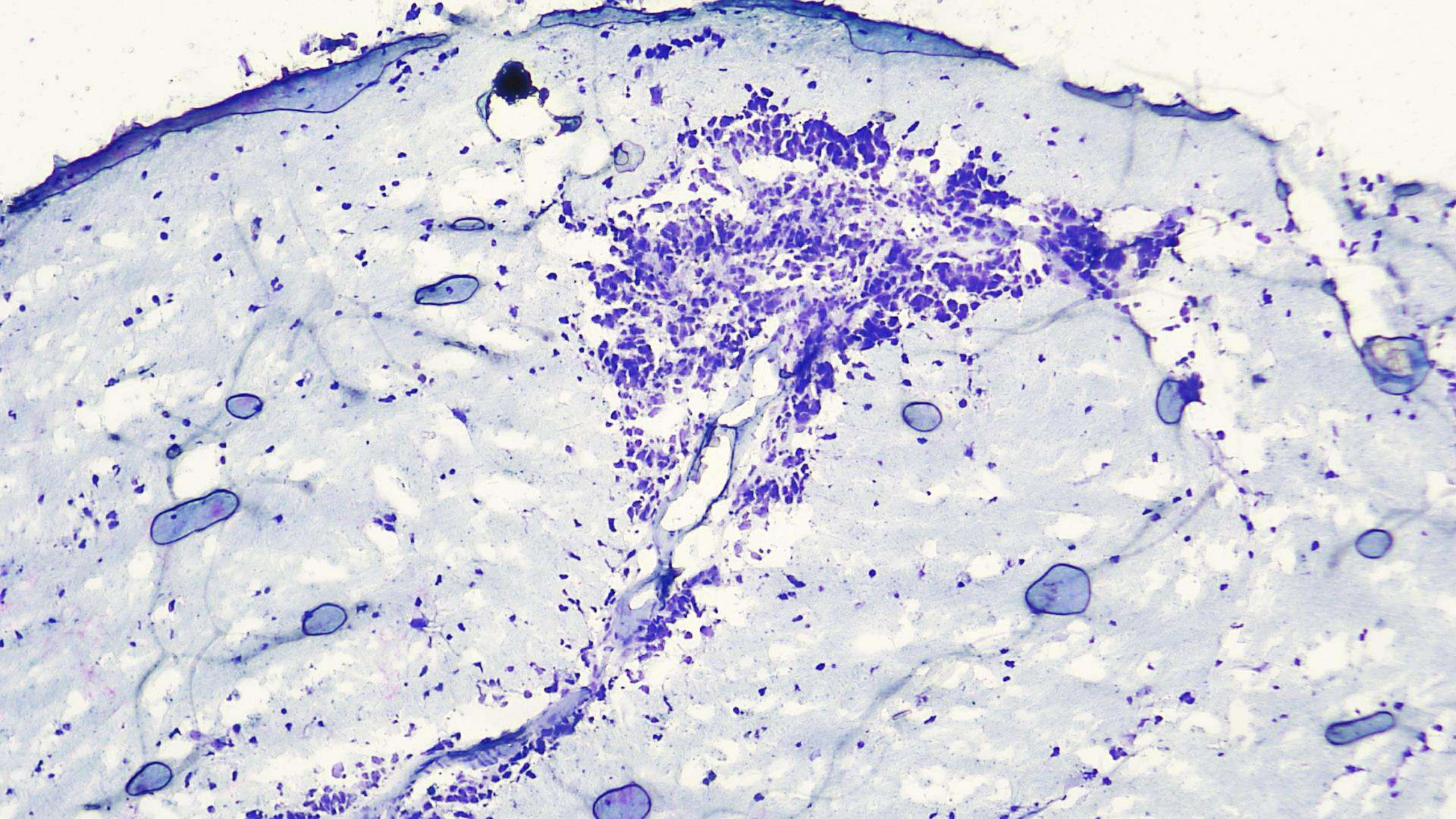
Clinical diagnosis: Posterior fossa SOL with hydrocephalus

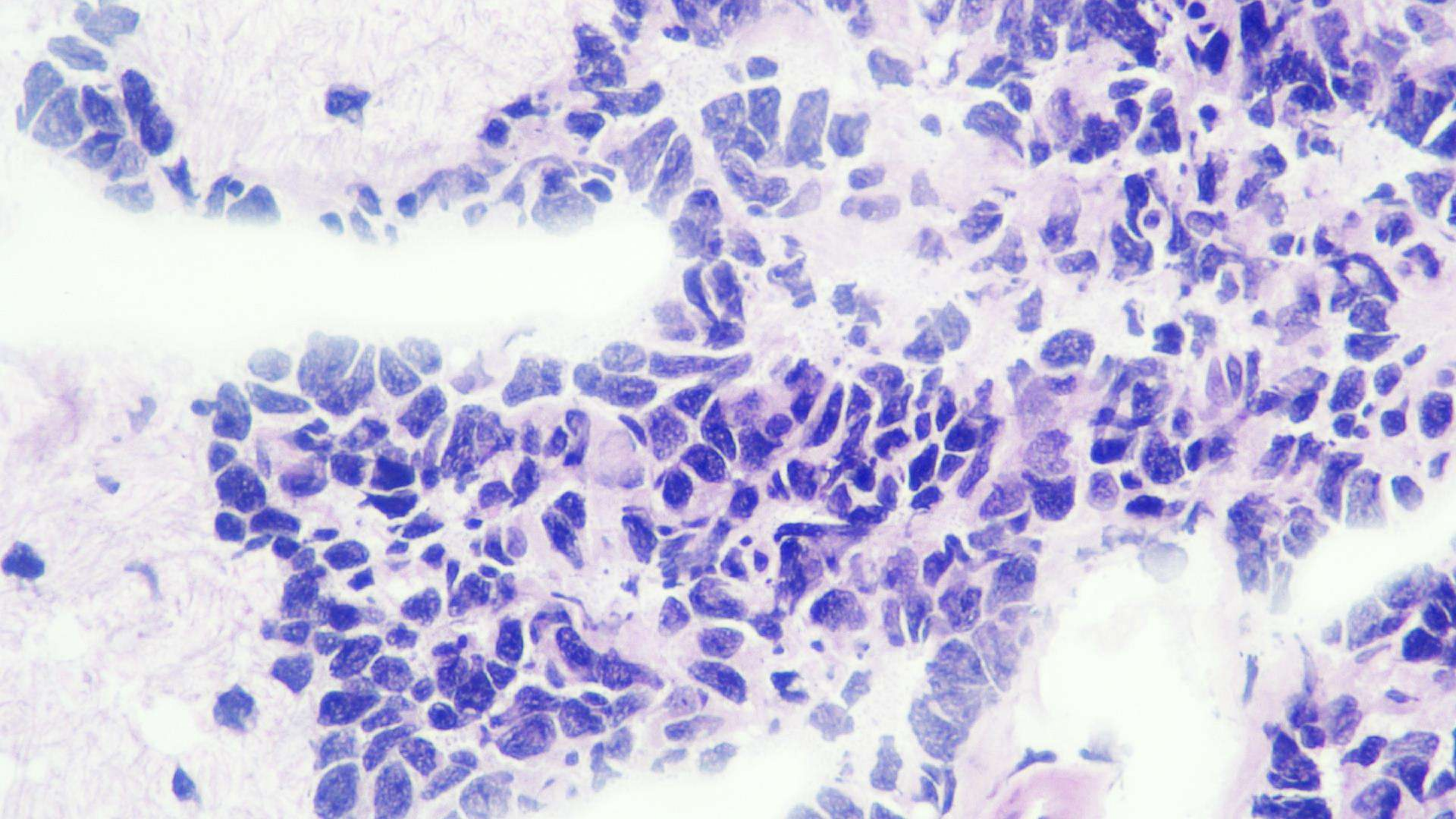
- MRI Spine: No focal vertebral lesion or evidence of spinal drop metastasis
- Emergent VP Shunt performed
- CSF cytology: negative for any atypical cells
- Stereotactic biopsy

Frozen section examination



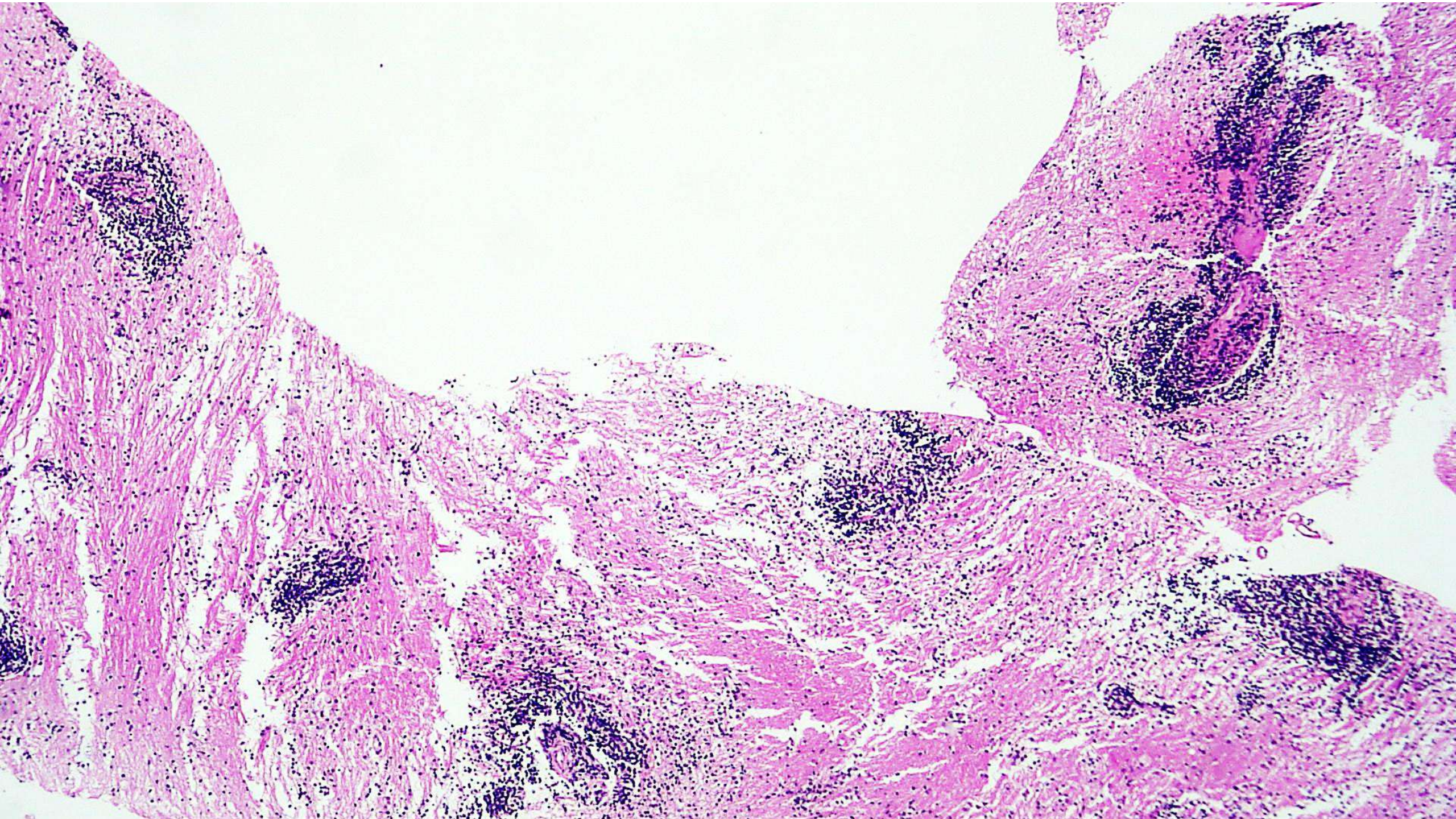


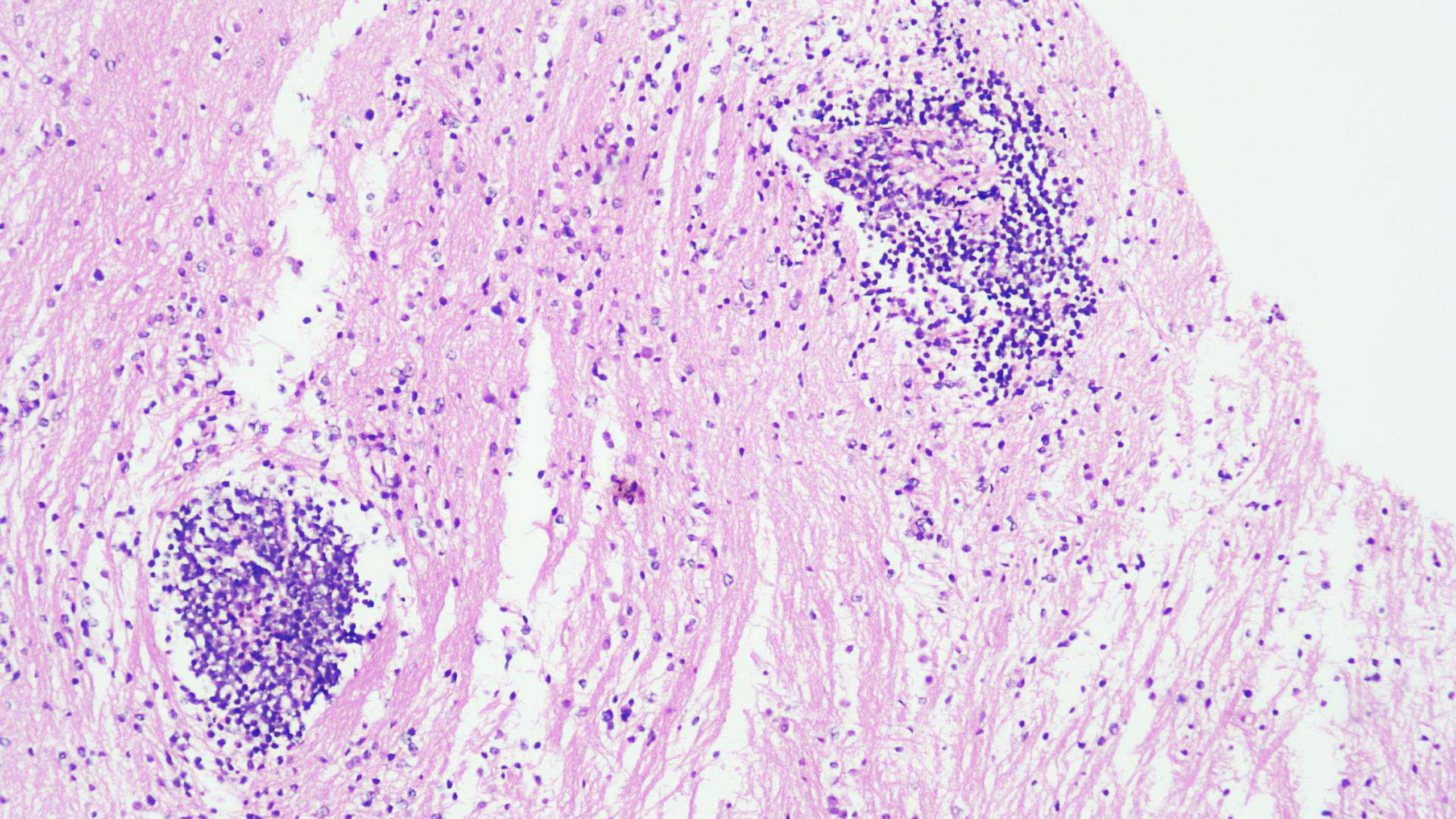


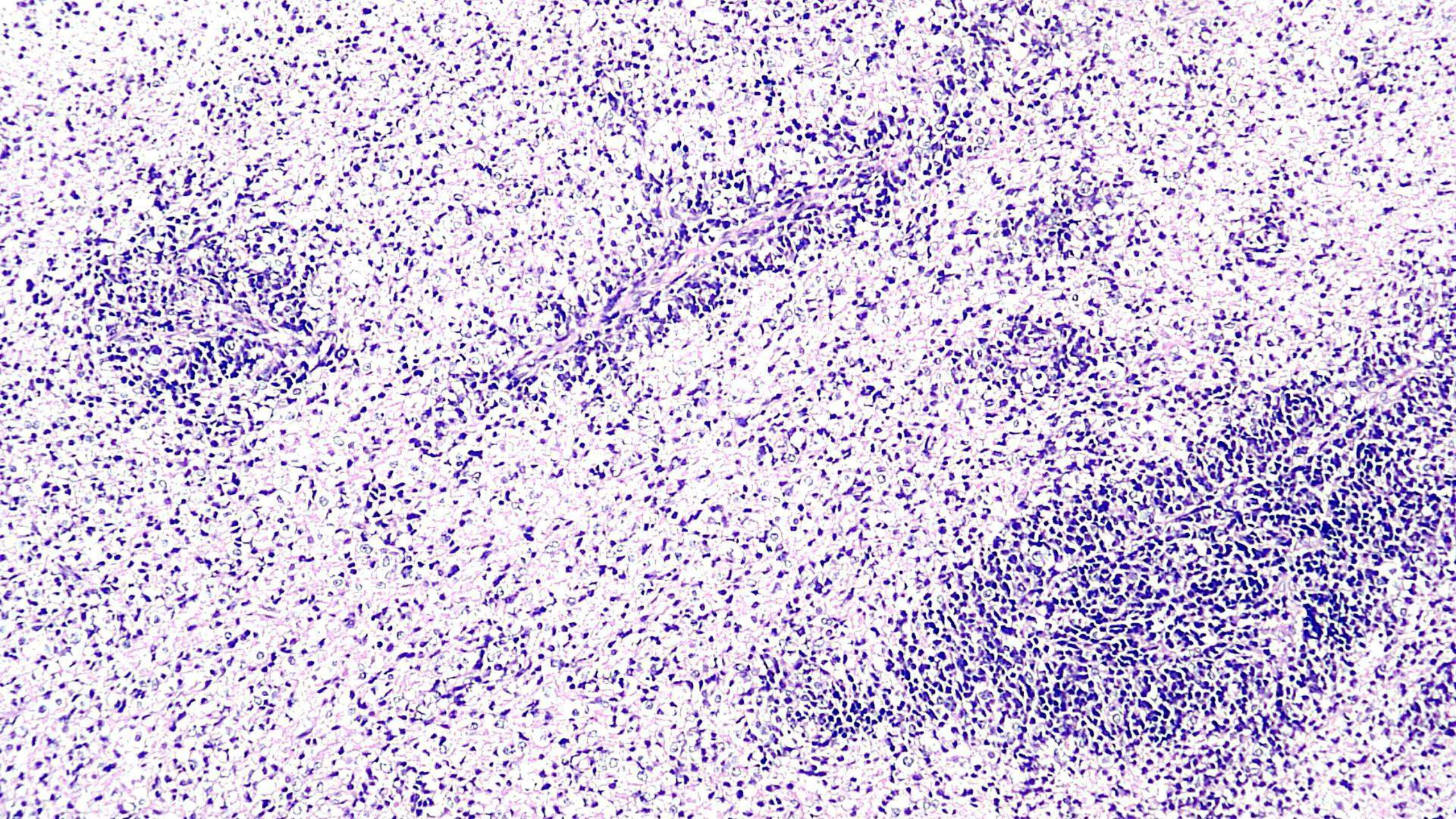


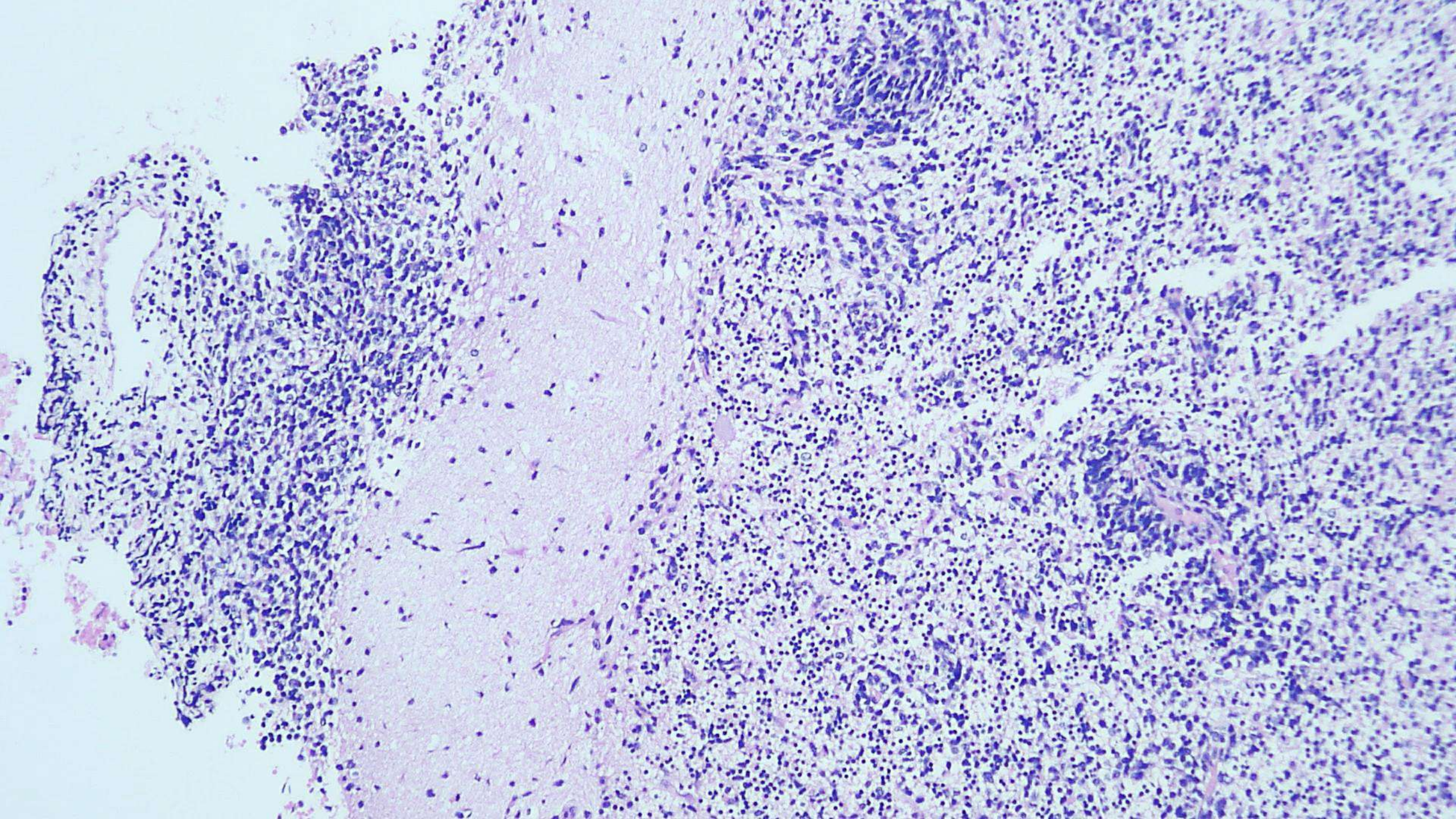
INTRAOPERATIVE DIAGNOSIS

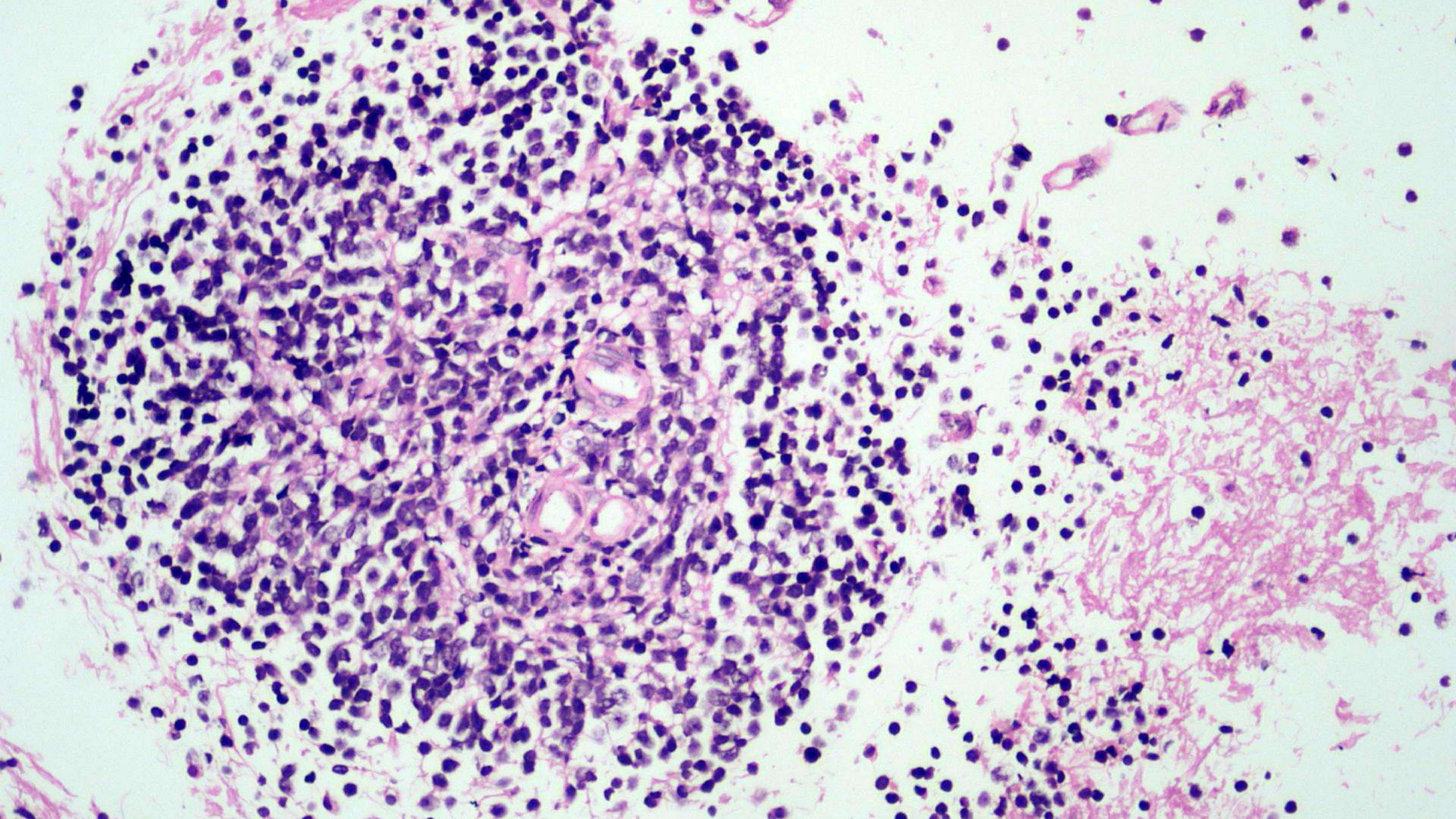
MALIGNANT: SMALL ROUND CELL BLUE TUMOR

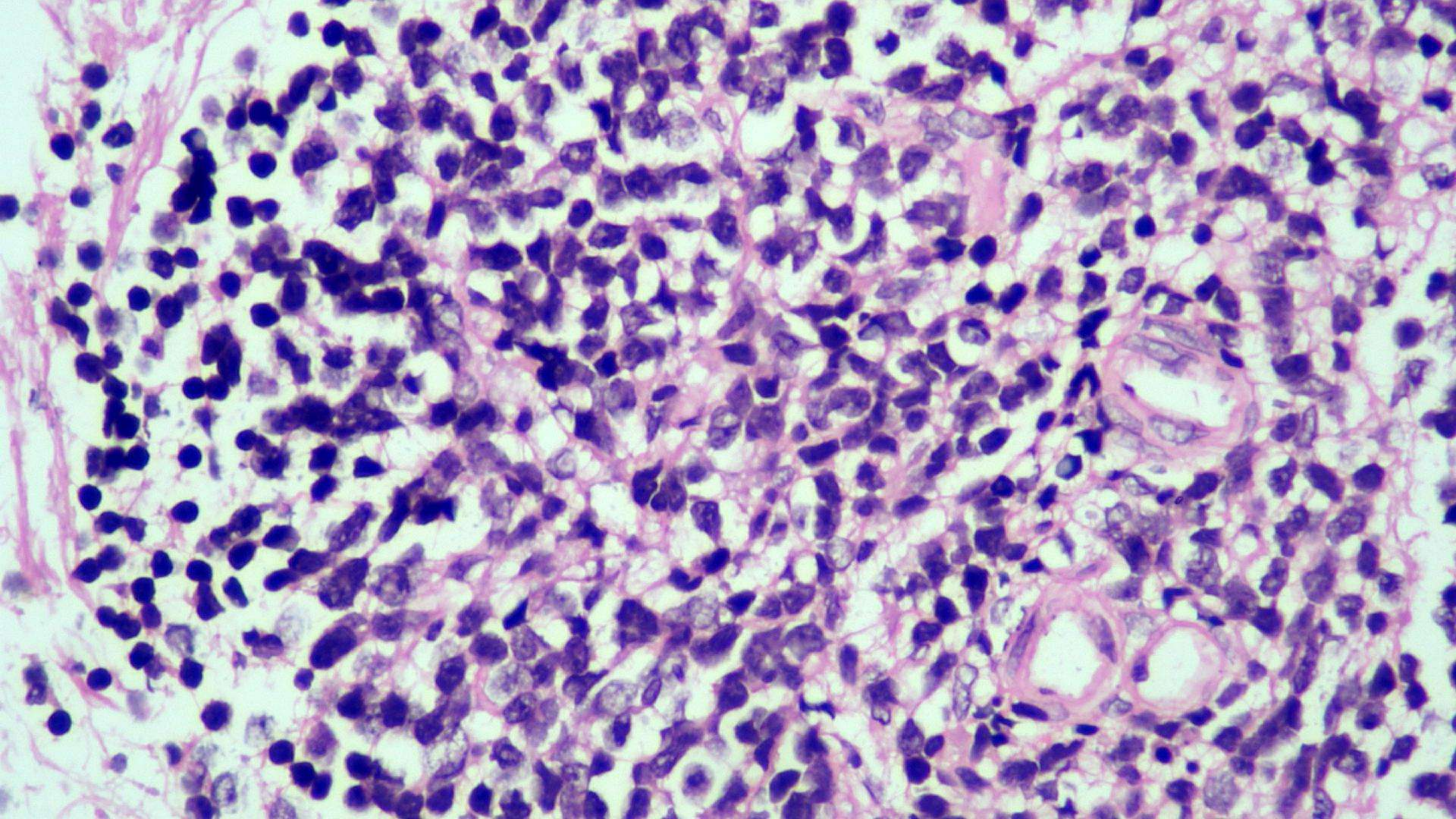


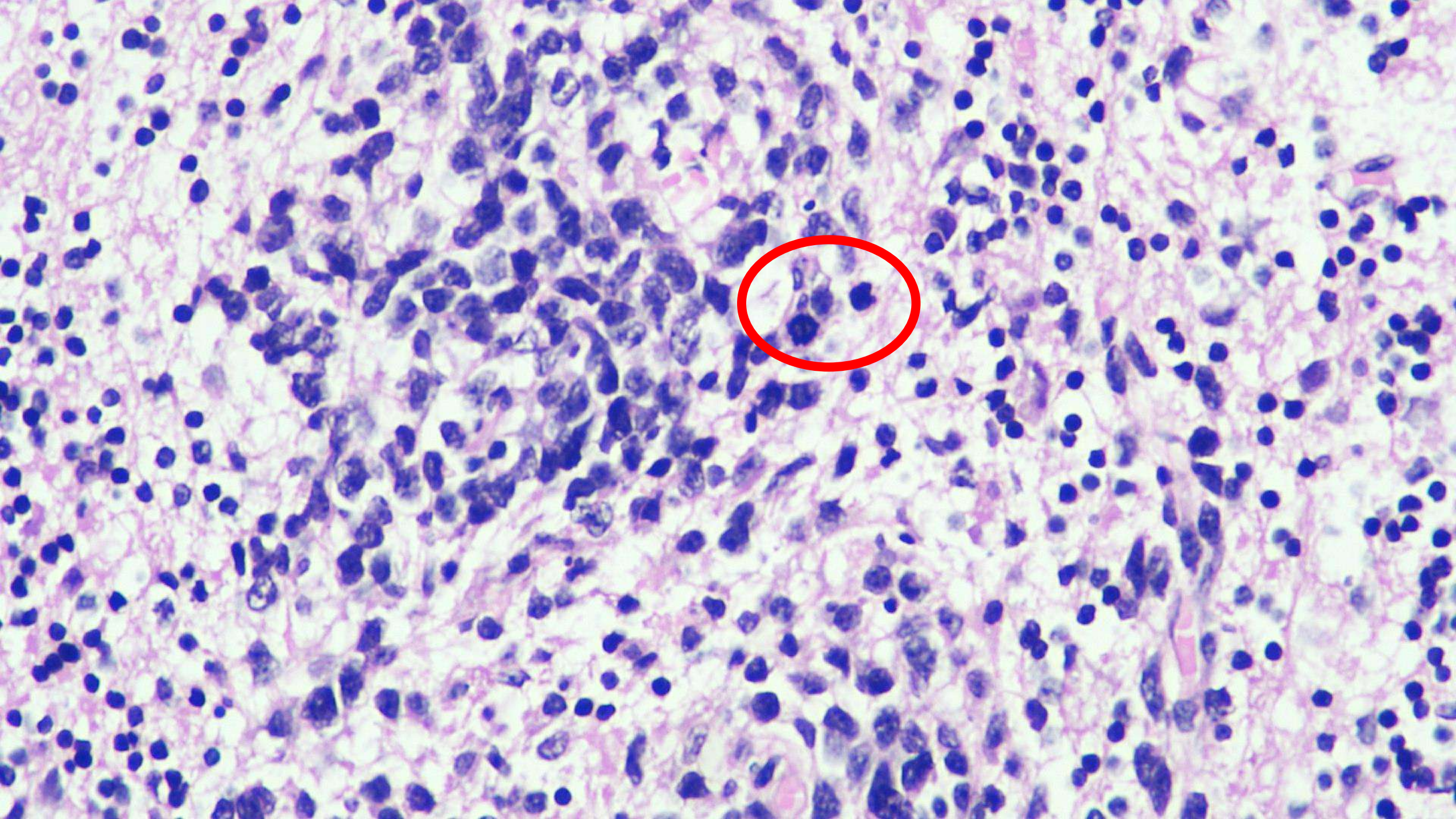


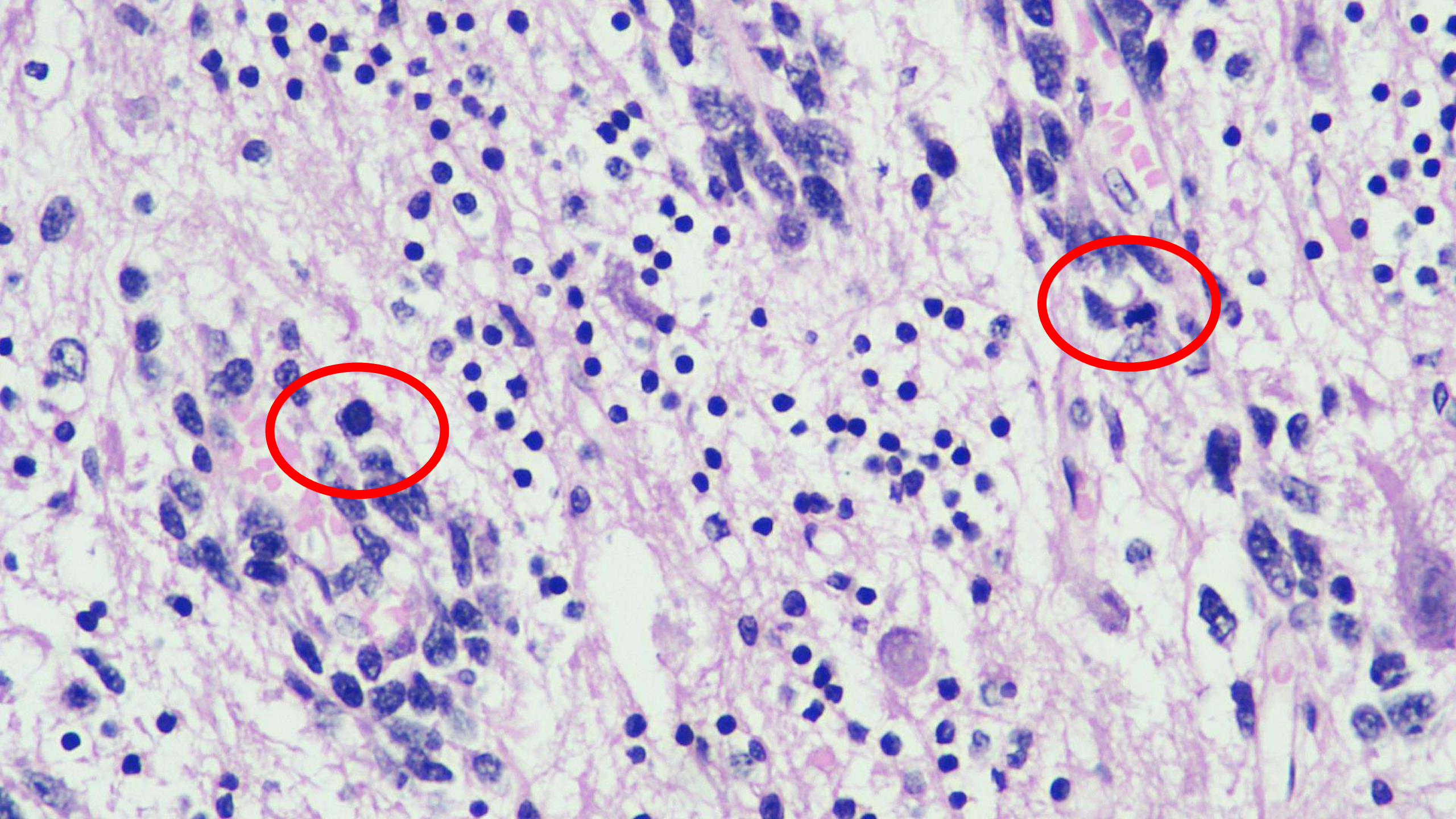












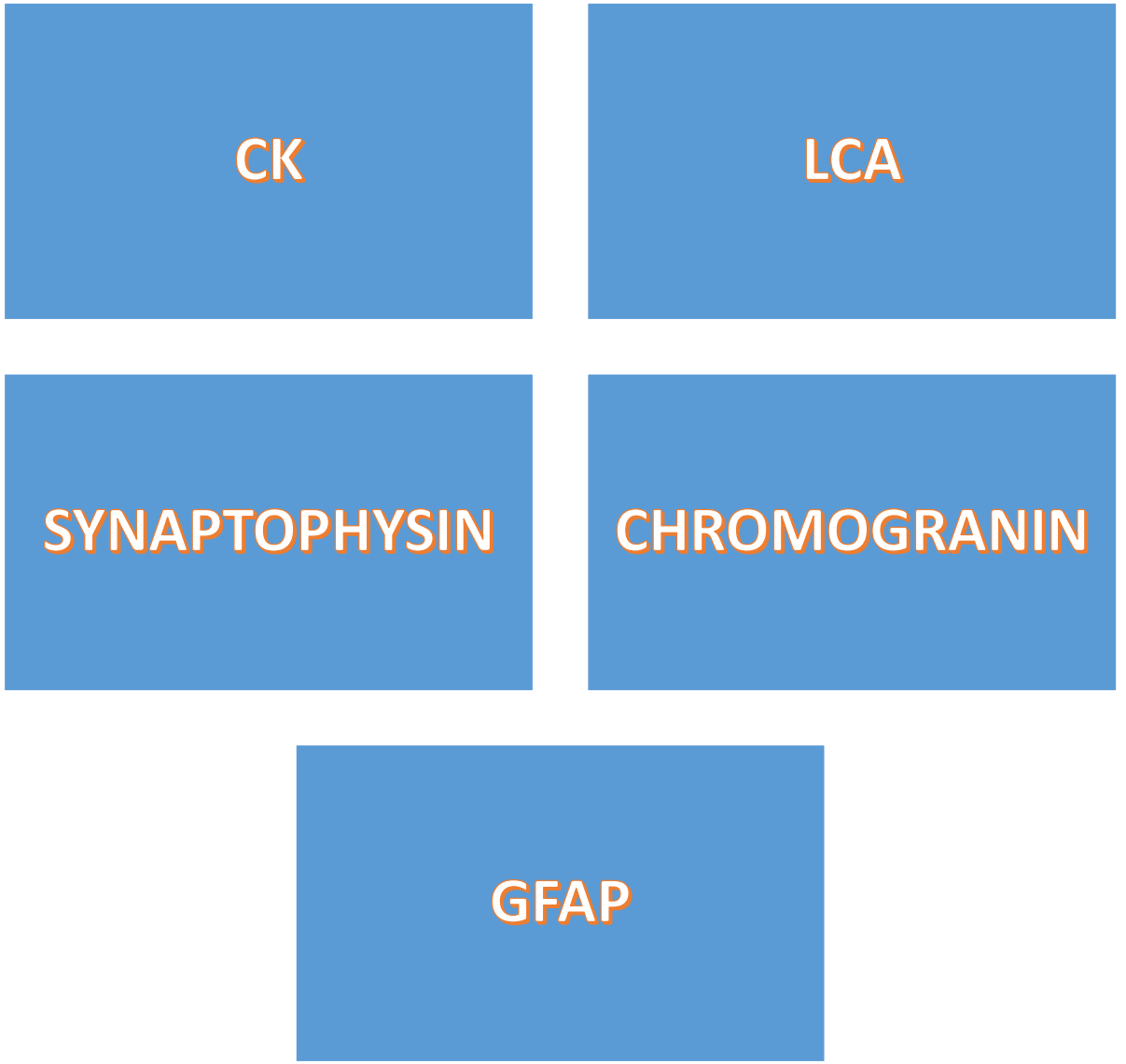
MORPHOLOGICAL FEATURES

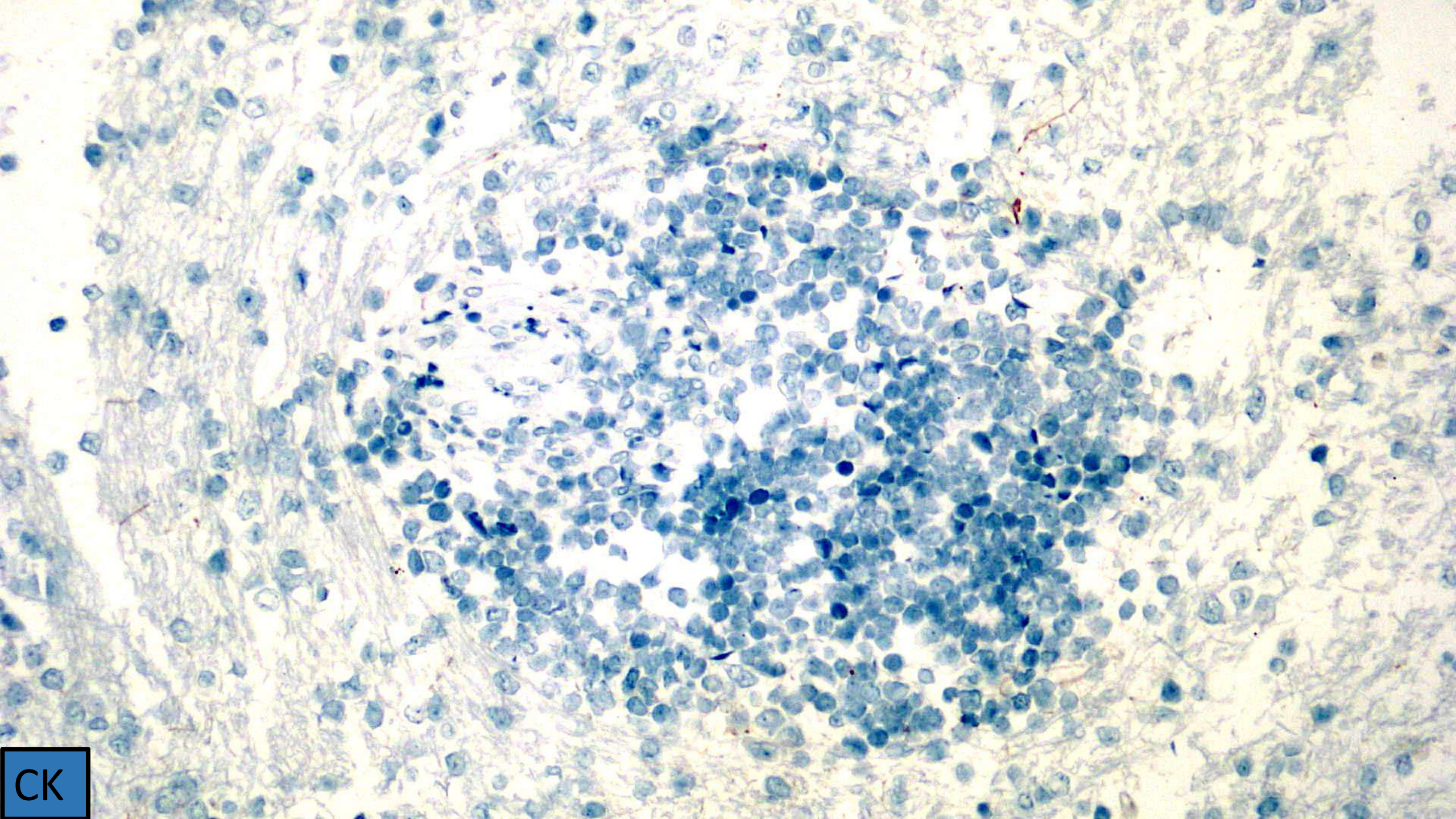
- Cellular undifferentiated tumor; infiltration into cortex, white matter & subarachnoid space
- Prominent angiocentric arrangement
- Tumor cells showed high N:C ratio, round to oval hyperchromatic nuclei with inconspicuous nucleoli
- Frequent mitosis
- No necrosis

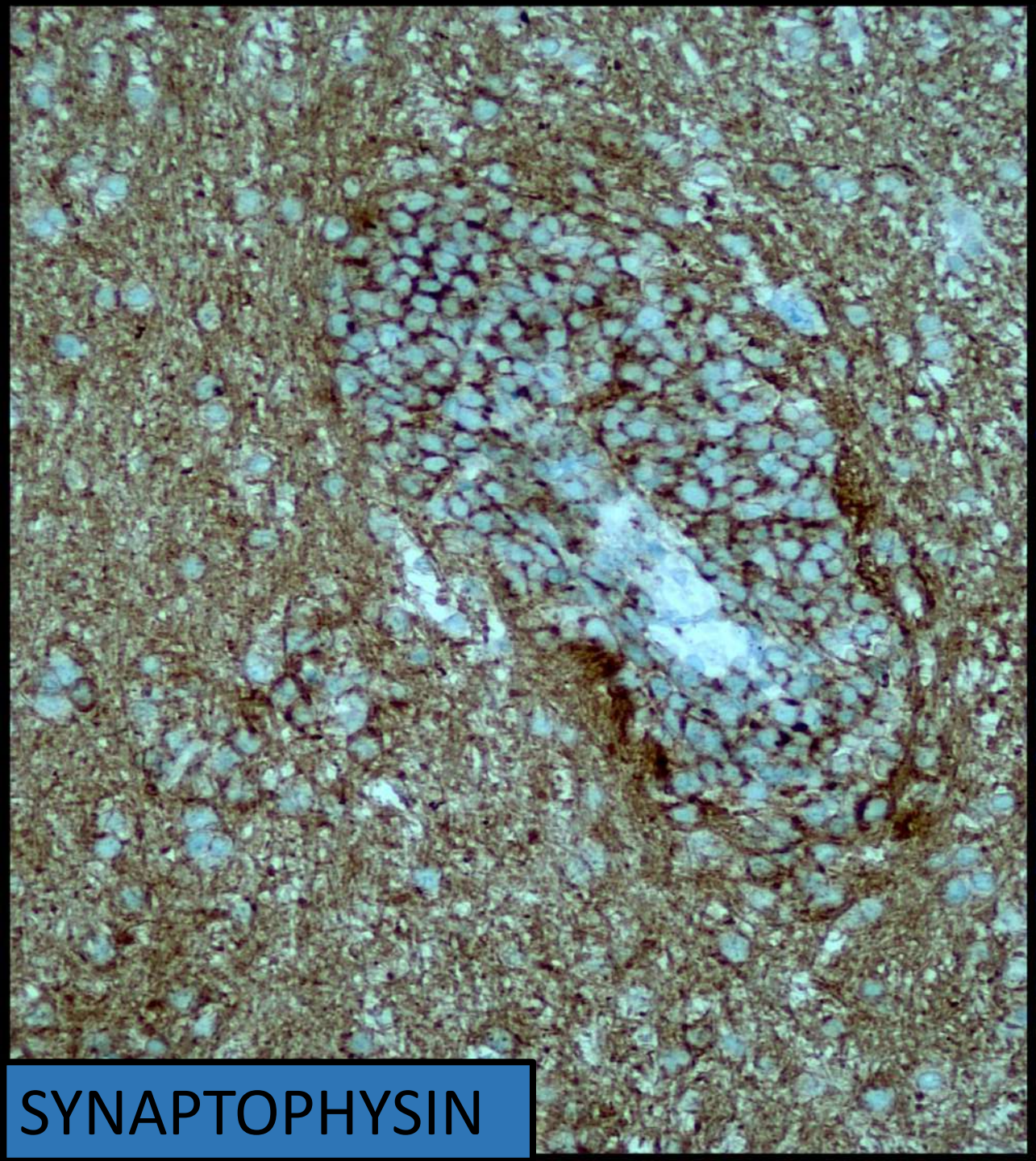
MORPHOLOGICAL DIFFERENTIALS

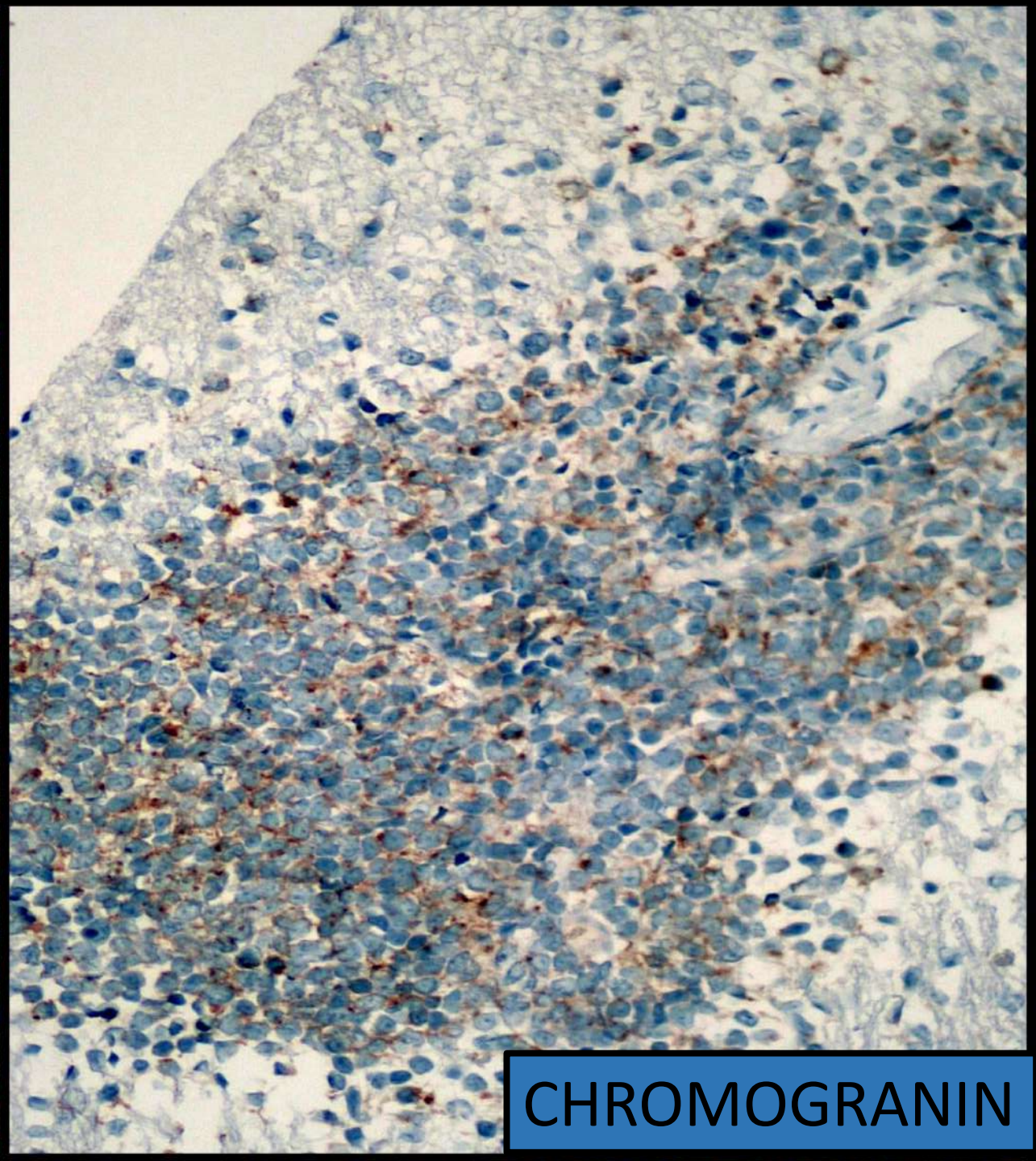
- NON HODGKINS LYMPHOMA
- PRIMARY BRAIN TUMOR (EMBRYONAL TUMOR/GBM)
- METASTATIC NEUROENDOCRINE CARCINOMA

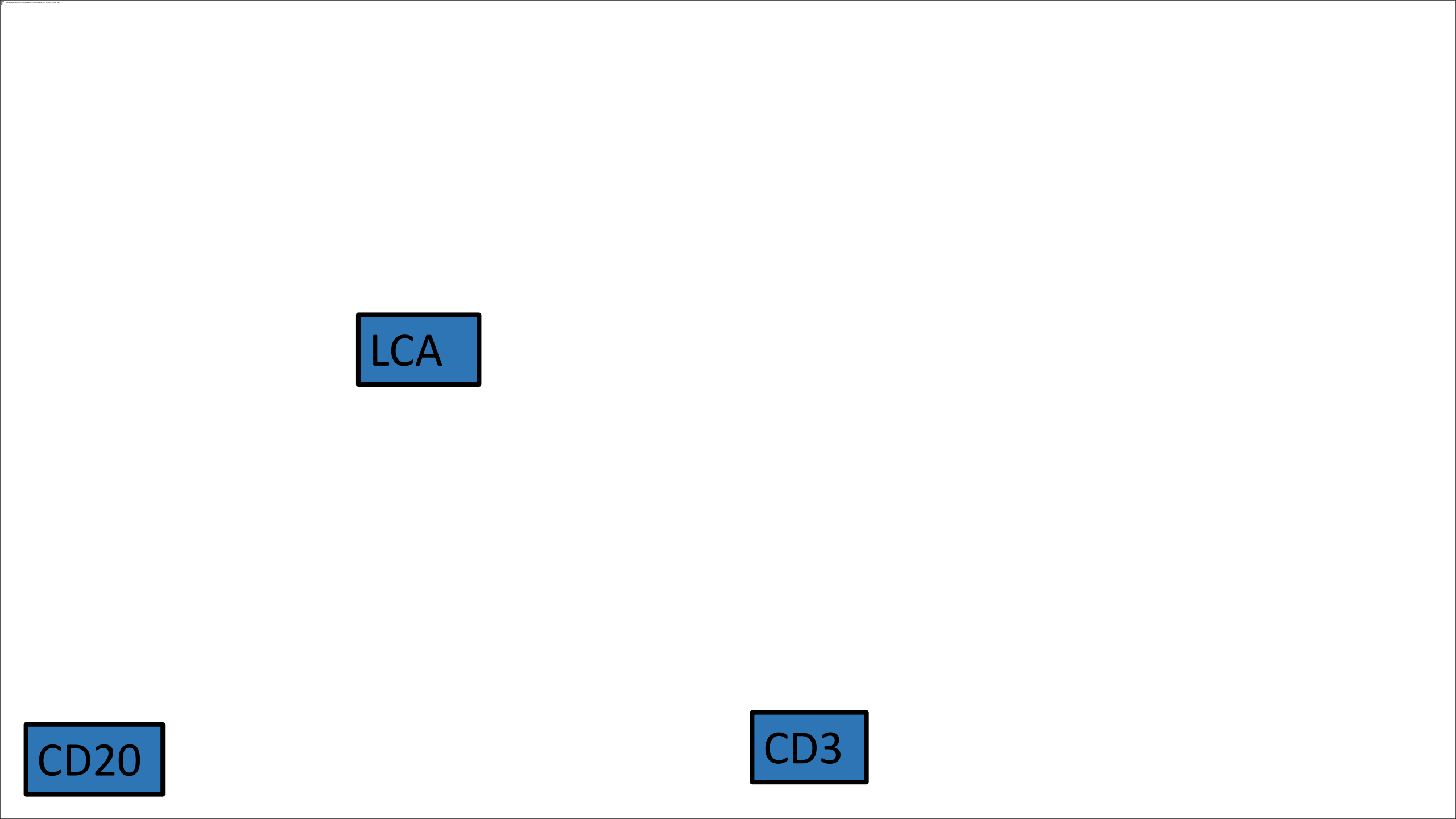
INITIAL IHC PANEL

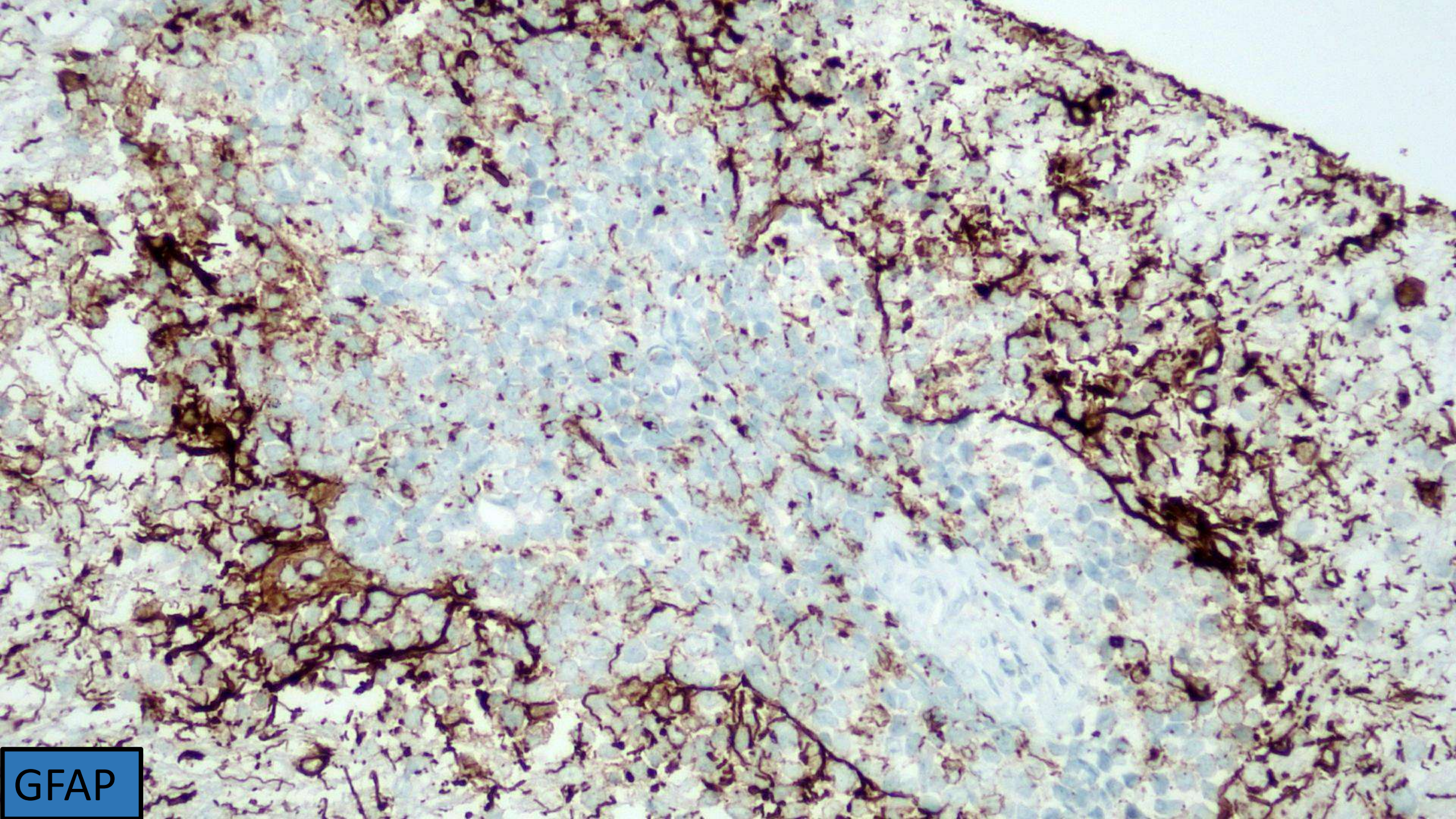


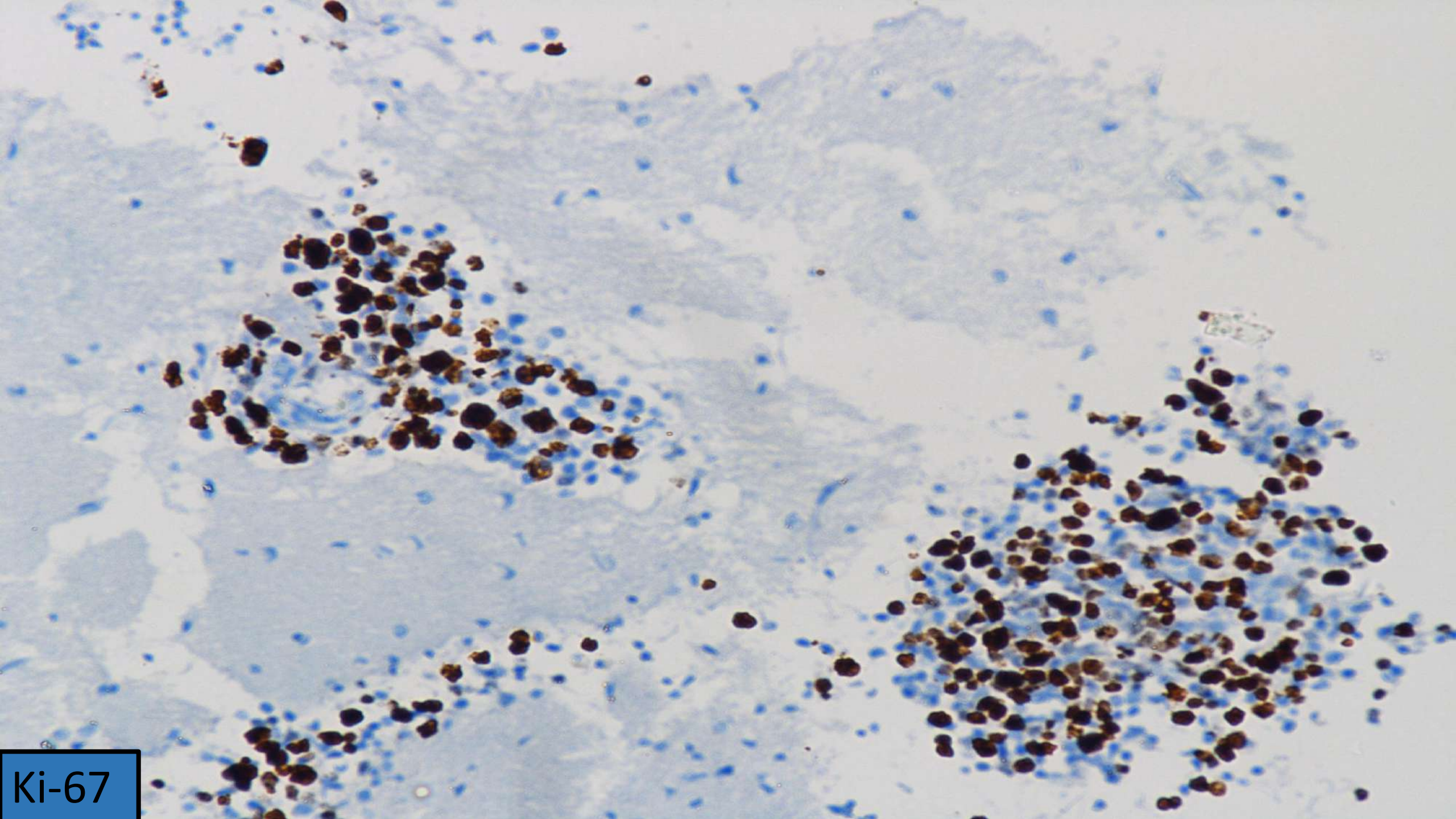

CK


SYNAPTOPHYSIN

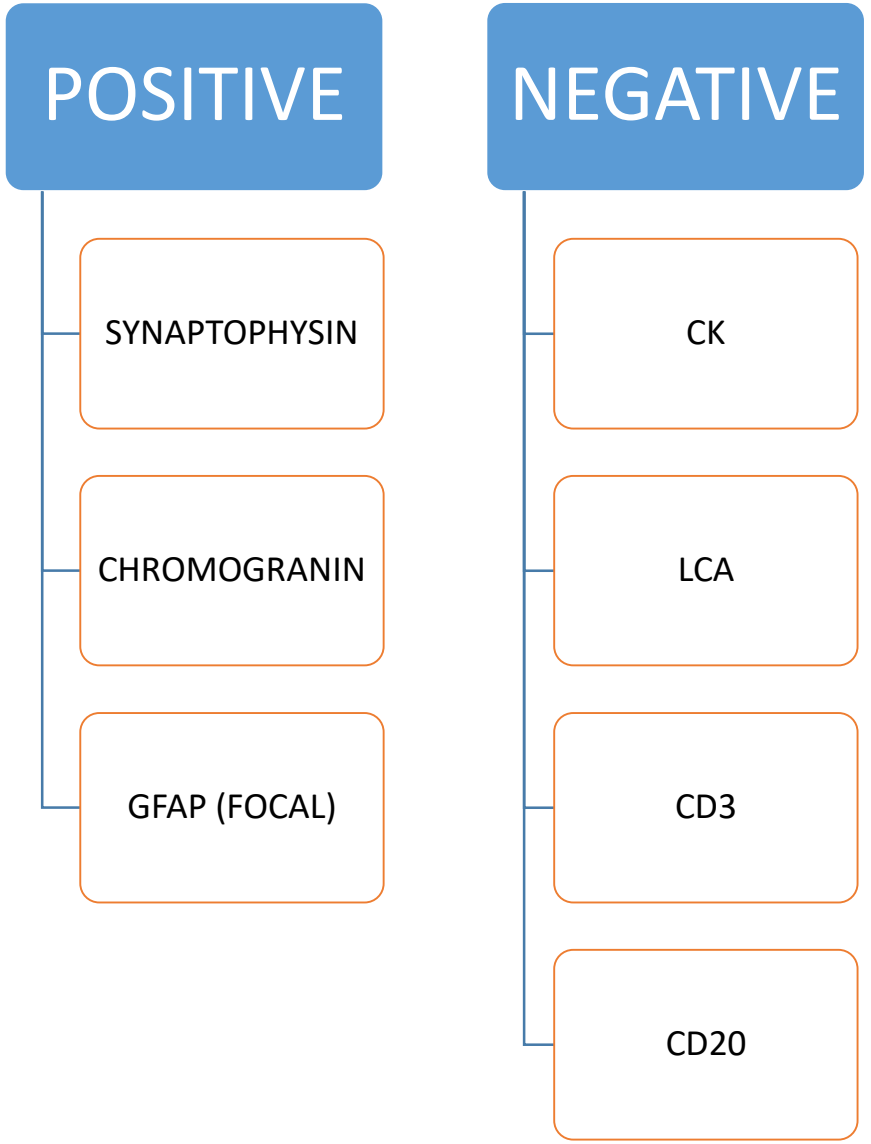

CHROMOGRANIN


LCA
CD20
CD3


GFAP

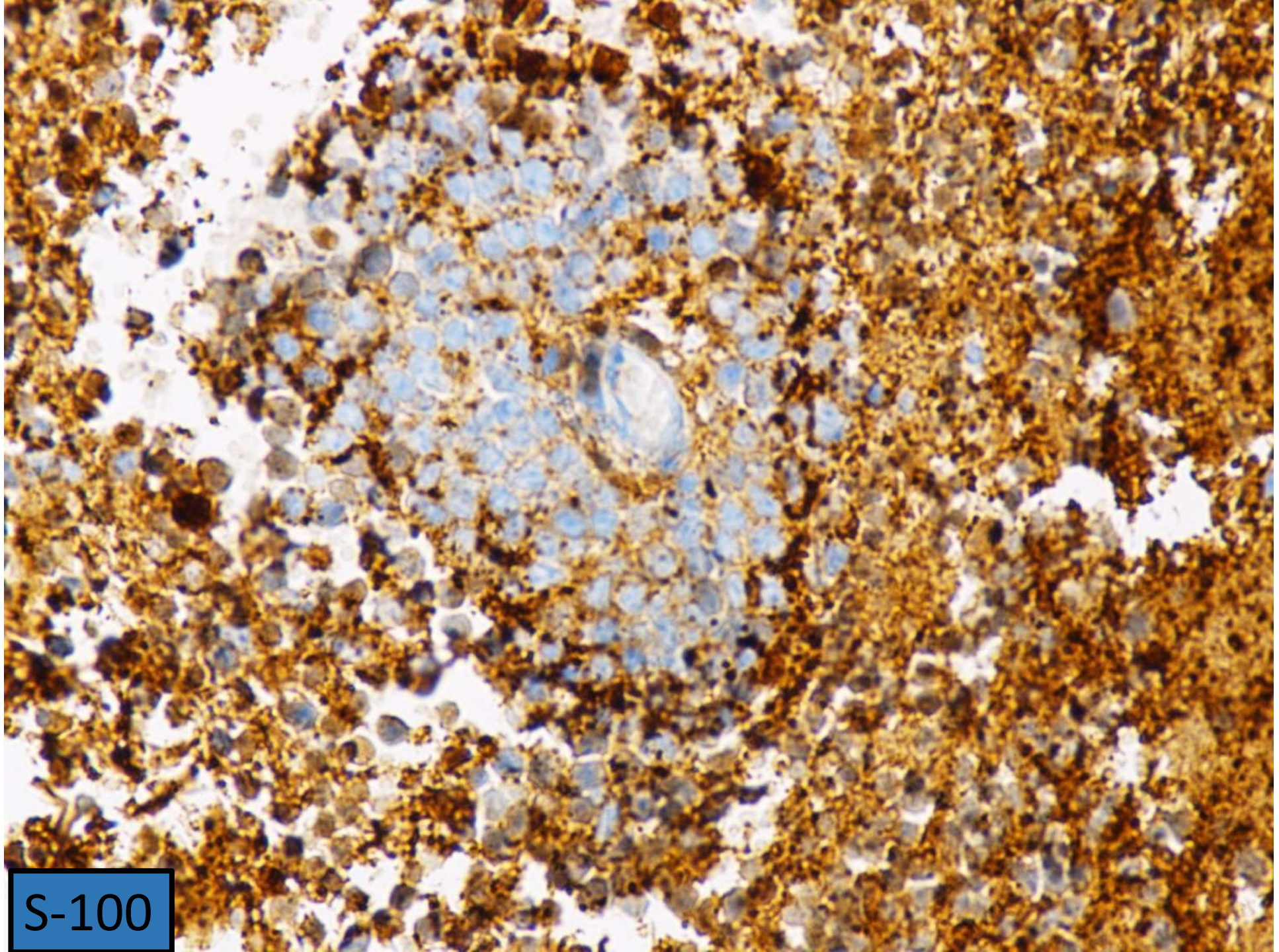

Ki-67

INITIAL IHC PANEL



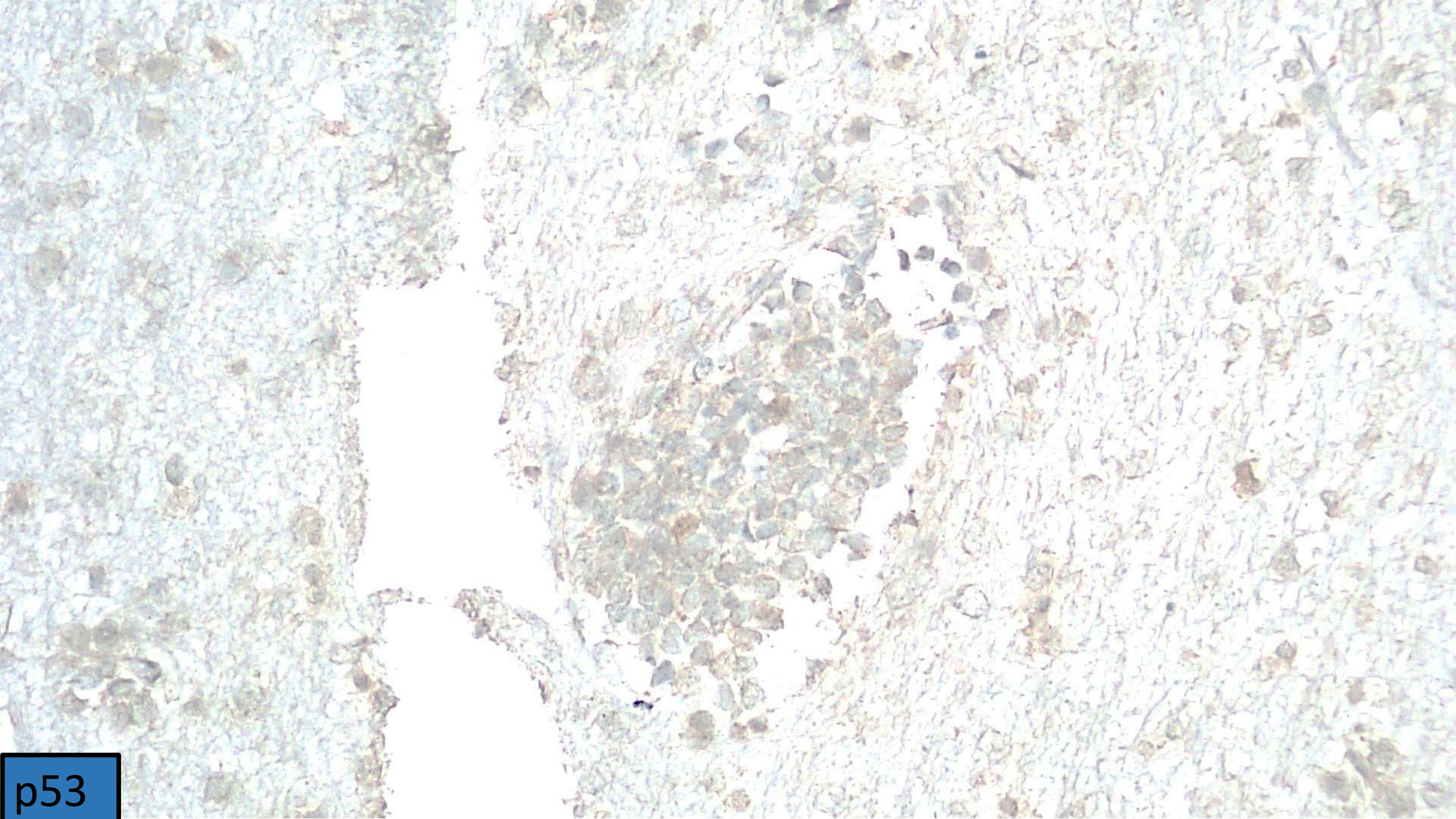
DIFFERENTIAL DIAGNOSIS

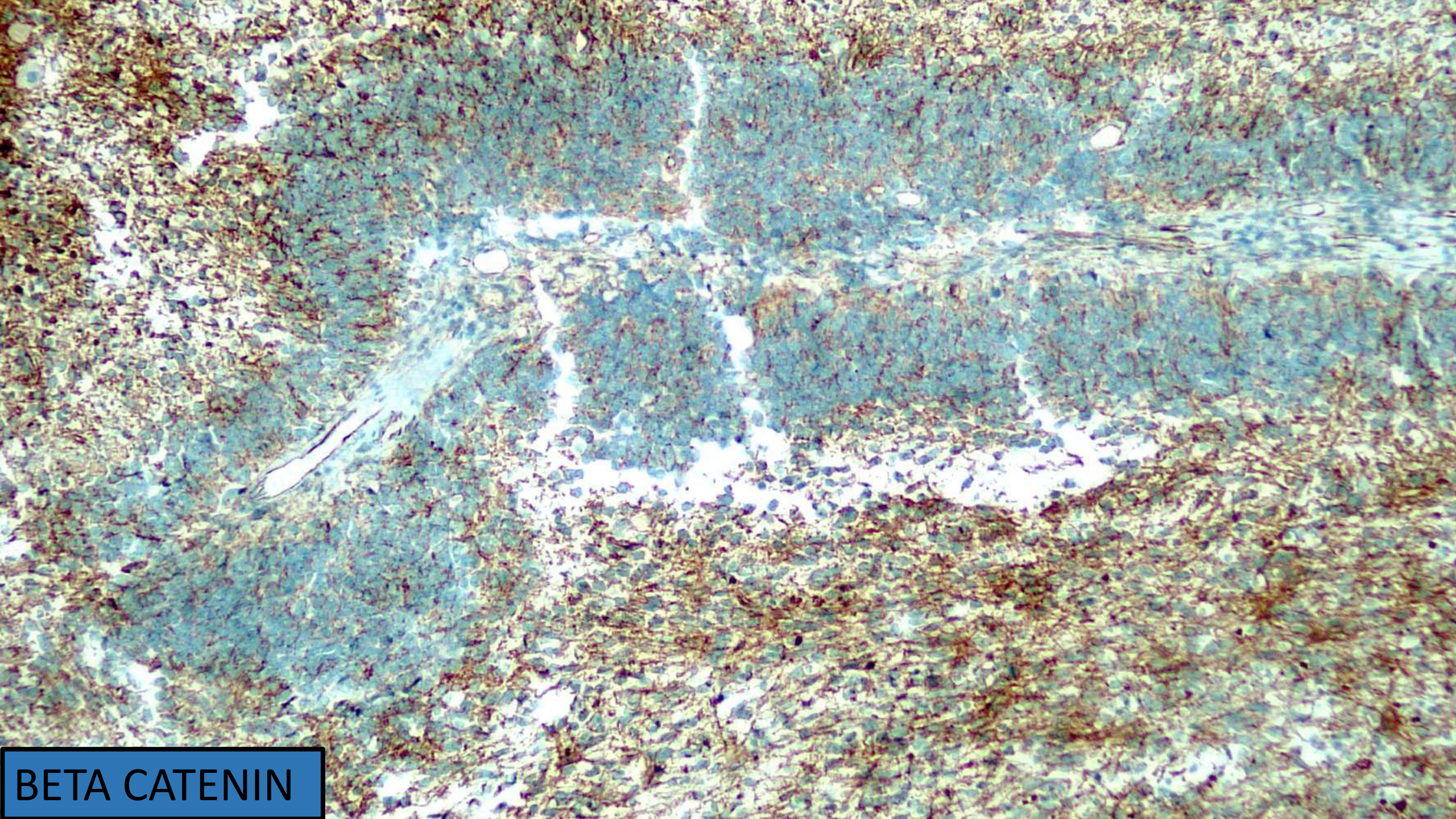
- NON HODGKINS LYMPHOMA
- EMBRYONAL TUMOR
- GBM
- METASTATIC NEUROENDOCRINE CARCINOMA

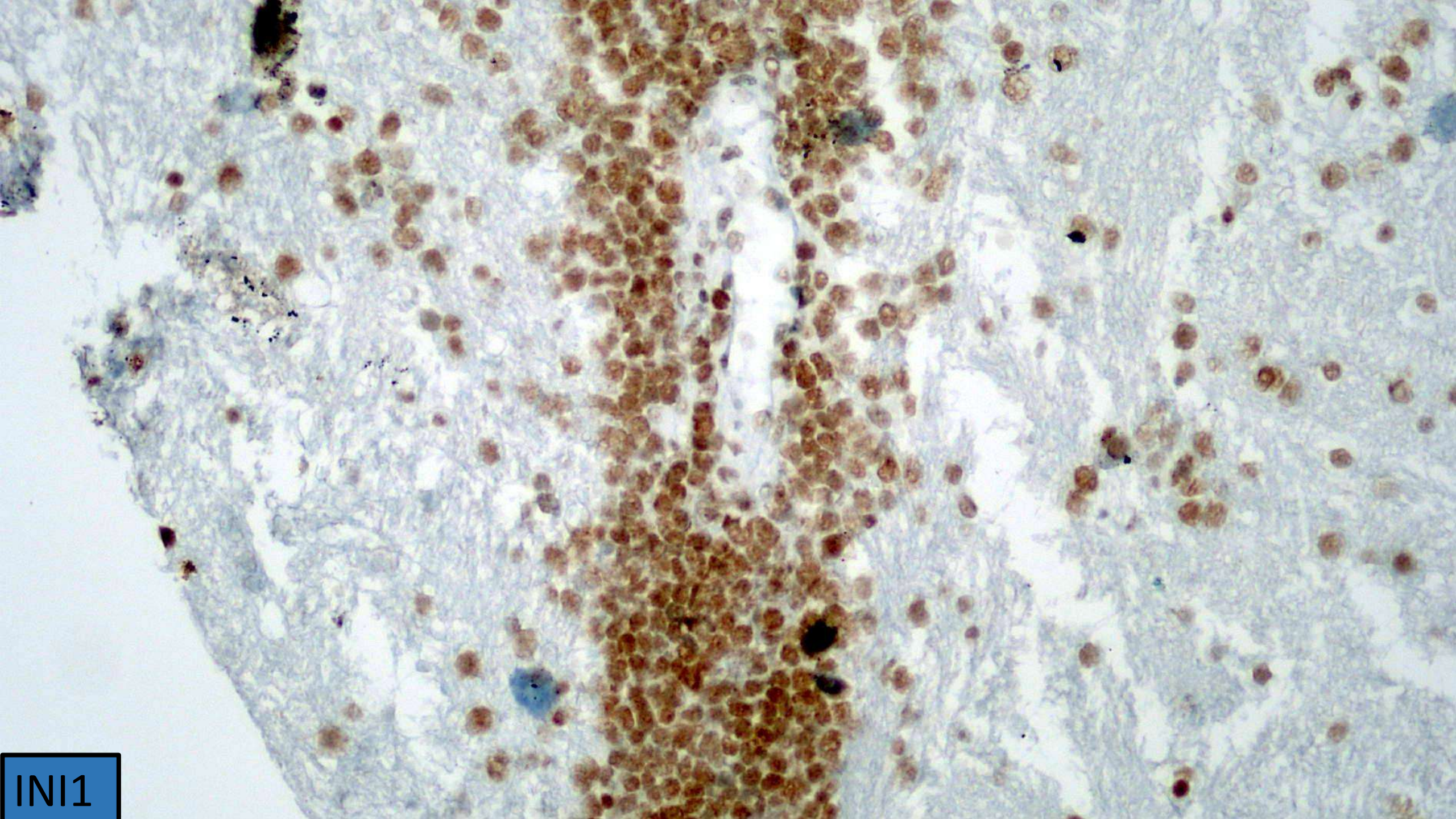

S-100

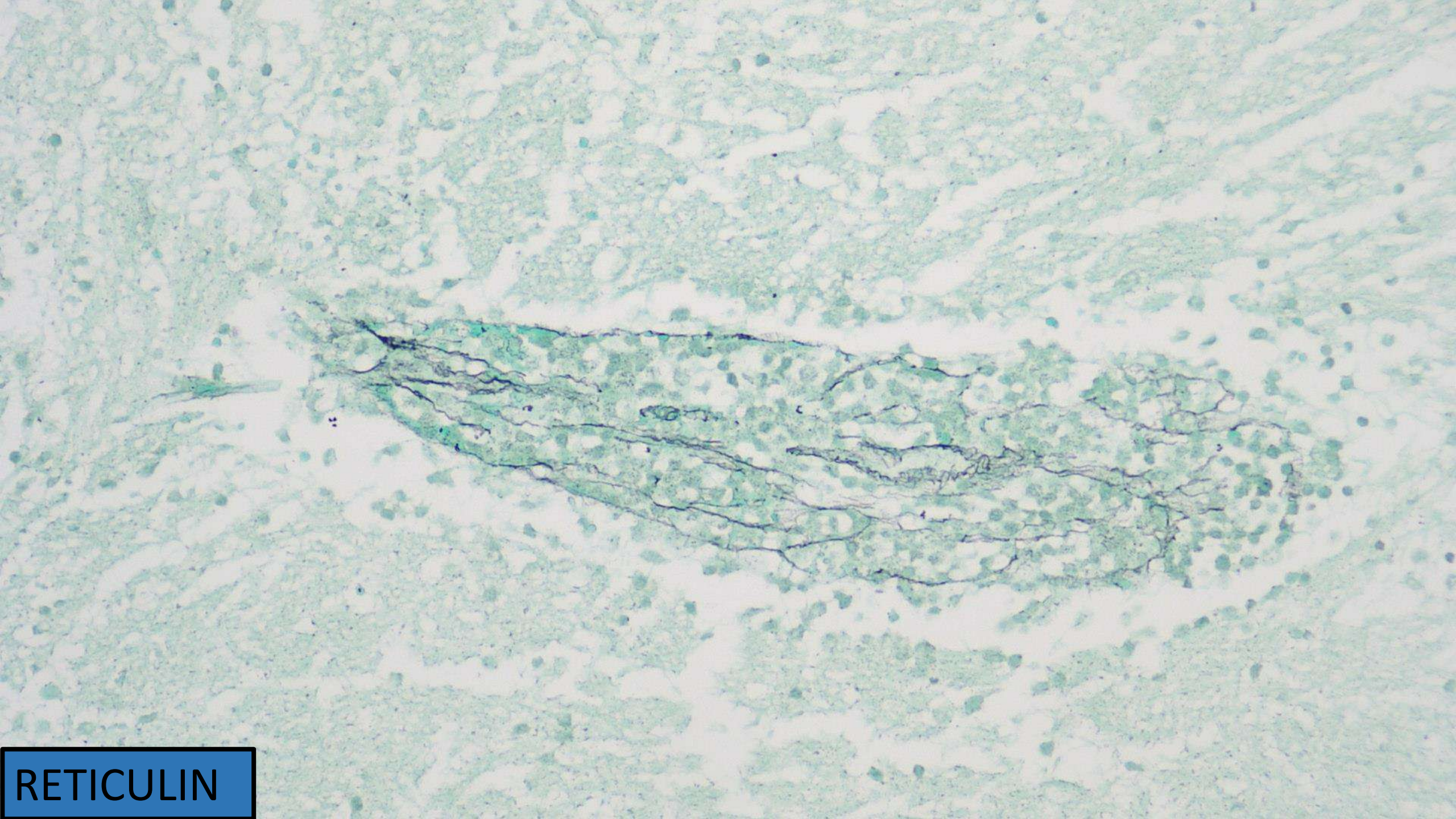
DIAGNOSIS

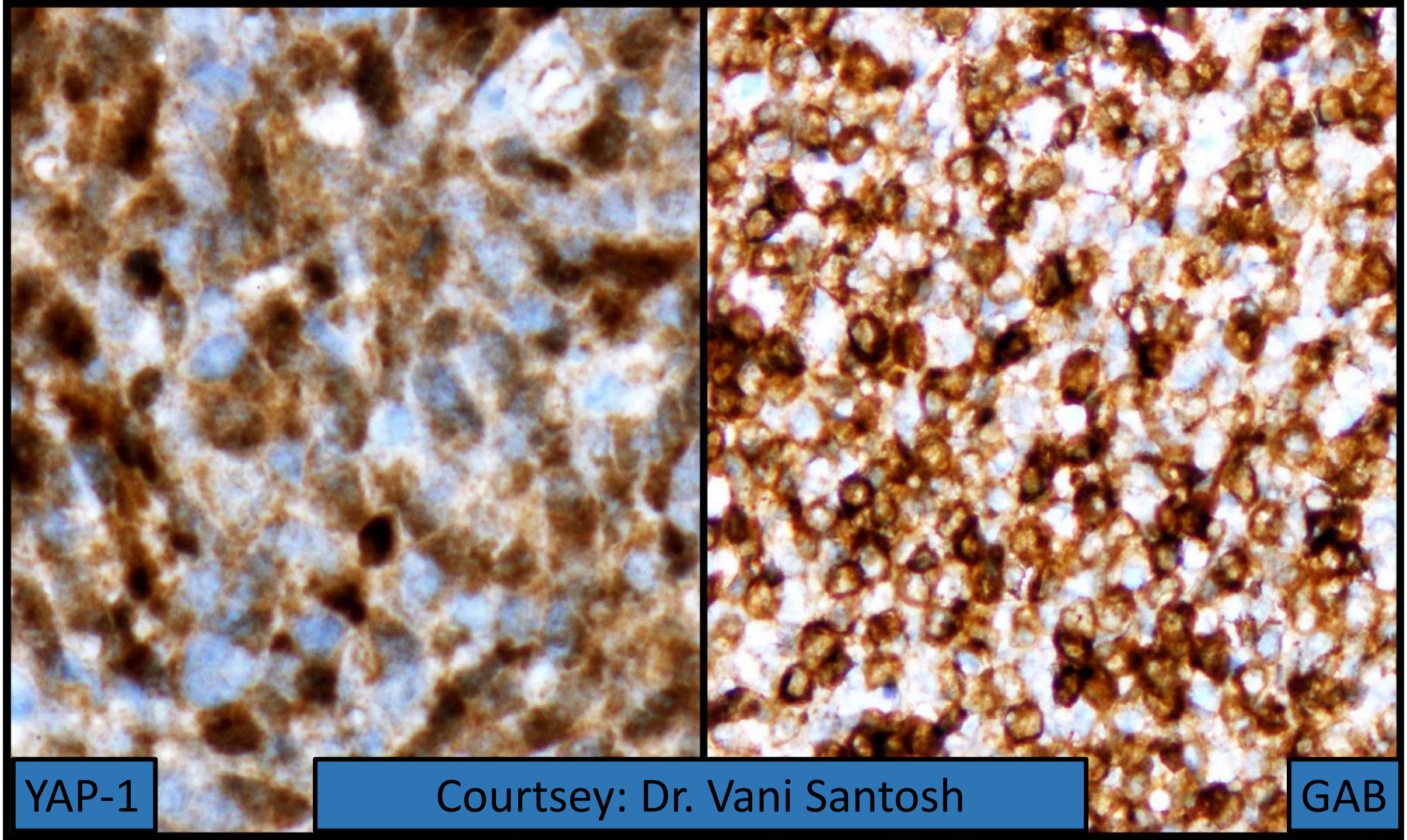
EMBRYONAL TUMOR: MEDULLOBLASTOMA


p53


BETA CATENIN

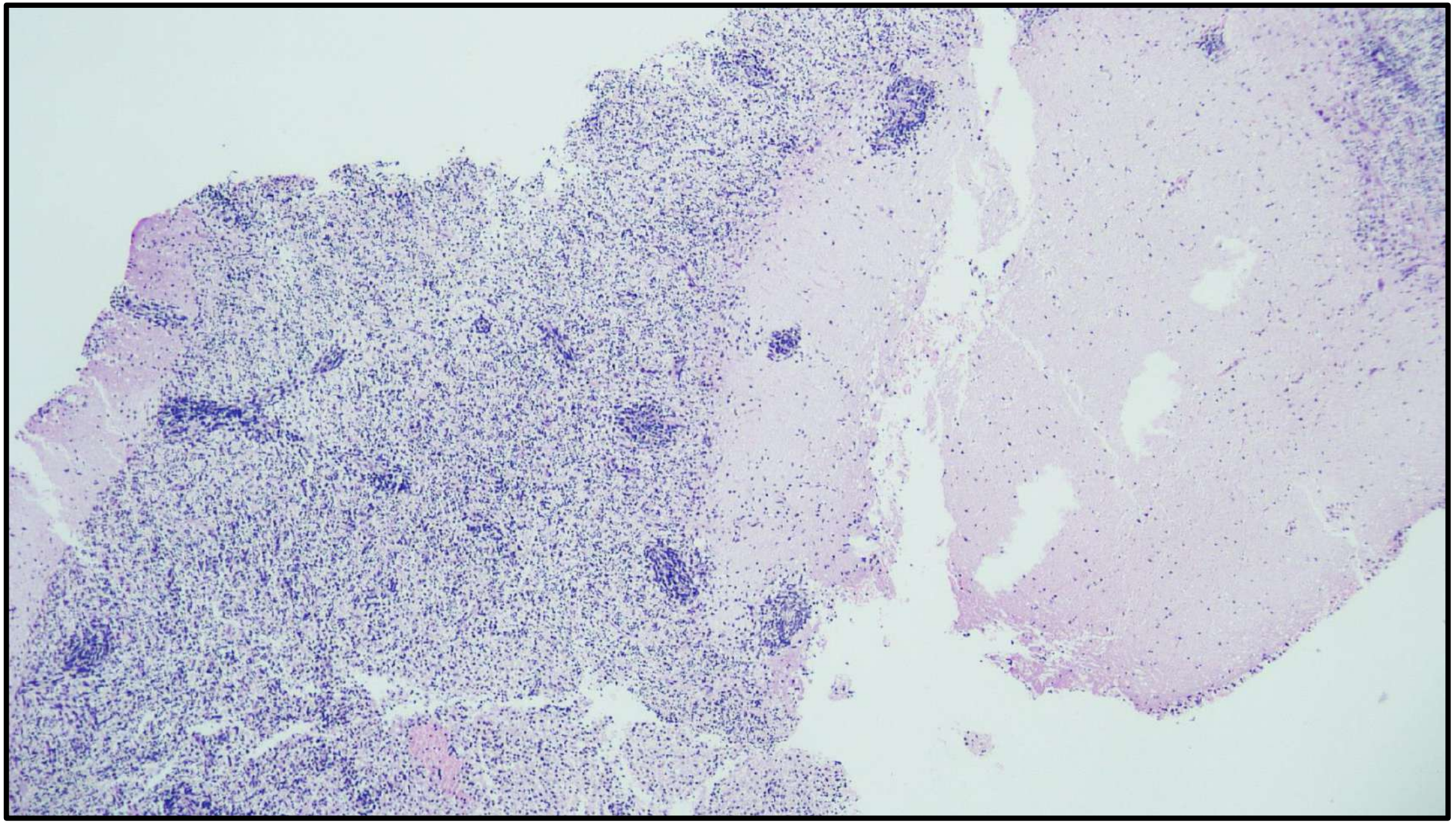

INI1


RETICULIN


YAP-1
Courtsey: Dr. Vani Santosh
GAB

Final Impression:
Medulloblastoma, SHH activated, p53 wild type, WHO grade-IV - cerebellum.

Tumor resection



DISCUSSION

- Medulloblastomas are embryonal **tumors of the posterior fossa**
- Fairly common in children, rare entity in adults (~0.5 per million)
- Rarely seen beyond the fifth decade, 80% occur in pts aged 21-40 years
- Analysis of 2037 medulloblastomas from NCI SEER database found a 5-year cumulative relative survival rate of 67% in adults, lower than adolescents (69%) and children (72%) and higher than infants (42%)
- Higher recurrence rate for medulloblastomas in adults: ~ 50-60%
- Late recurrences are more common in adults than in children
- Thus, long-term monitoring is important for adult medulloblastoma pts

- Most common subtype in adults: desmoplastic , SHH activated & TP53-wildtype
- @ mutations in PTCH1, SUFU & SMO
- Intermediate prognosis (depends on histology)
- SMO receptor inhibitors (Vismodegib, Sonidegib) have been shown to be effective in this category of tumors

- Four histological variants of medulloblastoma are recognized:
  - classic
  - desmoplastic/nodular
  - large cell-anaplastic
  - medulloblastoma with extensive nodularity
- The histological features seen in our case did not show the recognized architectural patterns of Medulloblastoma
- There was prominent angiocentric arrangement and peculiar perivascular accentuation
- The background cerebellar cortex was focally infiltrated by tumor cells, which also showed subpial accumulation and extension to the subarachnoid spaces.
- There was no e/o Homer-Wright rosettes, large cell/anaplastic change or features of neurocytic differentiation.

Thus our tumor had the appearance of an idiosyncratic perivascular niche phenotype which has been described rarely in medulloblastomas before

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Medulloblastoma: clinicopathological correlates of SHH, WNT, and non-SHH/WNT molecular subgroups

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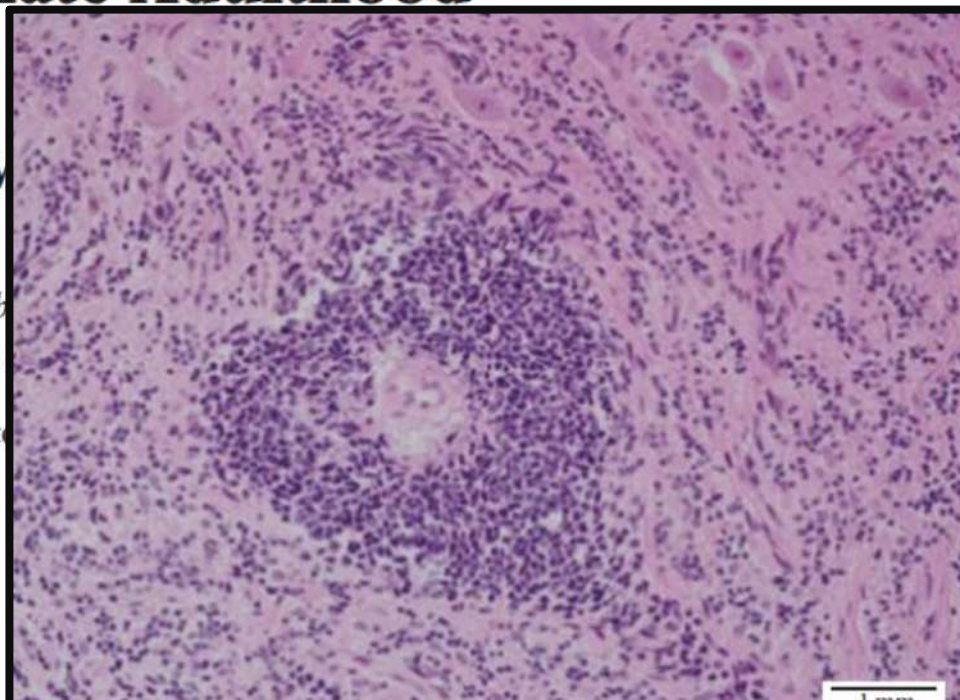
A single classic tumor in the cohort demonstrated an idiosyncratic morphology characterized by the perivascular accumulation of pleomorphic cells with an anaplastic phenotype (Supplementary Figure 4). Away from blood vessels, tumor cells had round nuclei, a neurocytic morphology, and a much lower nuclear:cytoplasmic ratio than perivascular cells. Ki-67 immunolabeling was higher among perivascular cells than among the neurocytic cells. The tumor did not contain ependymoblastic rosettes.

Medulloblastoma molecular subgroups: immunophenotypes

Hindawi
Case Reports in Pathology
Volume 2018, Article ID 5425398, 4 pages
https://doi.org/10.1155/2018/5425398

Case Report

Cerebellar Medulloblastoma in Middle-to-Late Adulthood



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- It is possible that because of their propensity to reach the subarachnoid space, medulloblastomas reenter the brain along perivascular spaces & display an angiocentric pattern as they follow the course of intraparenchymal vessels

Take home message

- Morphology is a pathologist's *fidus achates,* but insufficient in this era of precision medicine
- It guides in selection of a judicious & appurtenant IHC panel
- Molecular profiling is necessary in medulloblastoma to tailor therapy & predict response & prognosis
- Standard nomenclature should be used while reporting and all clinically relevant pathologic factors should be mentioned

FOLLOWUP…

- The patient has completed course of craniospinal irradiation followed by boost to post-op cavity & is doing well.
- Scheduled to receive lomustine (CCNU) and cisplatin chemotherapy


Thanks!