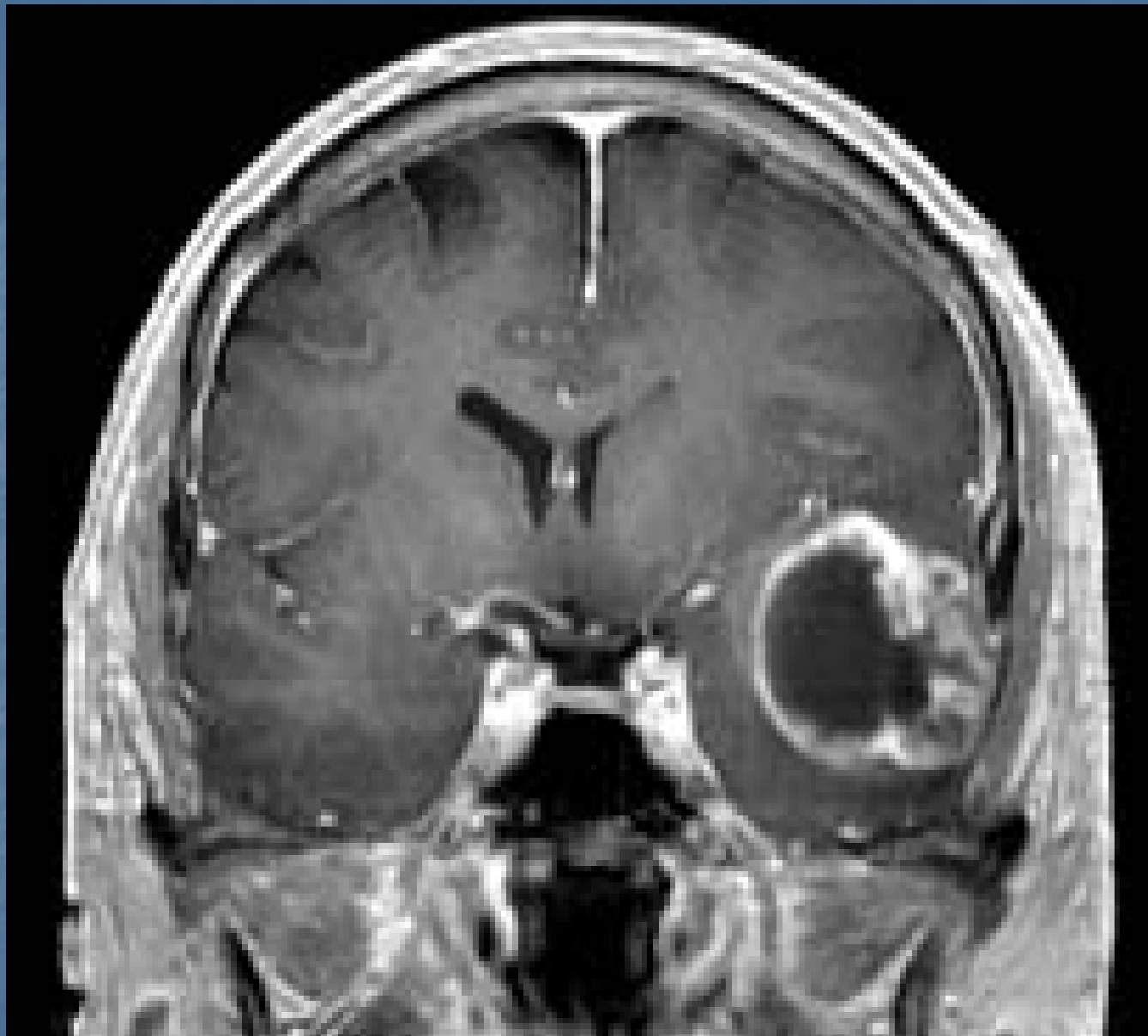


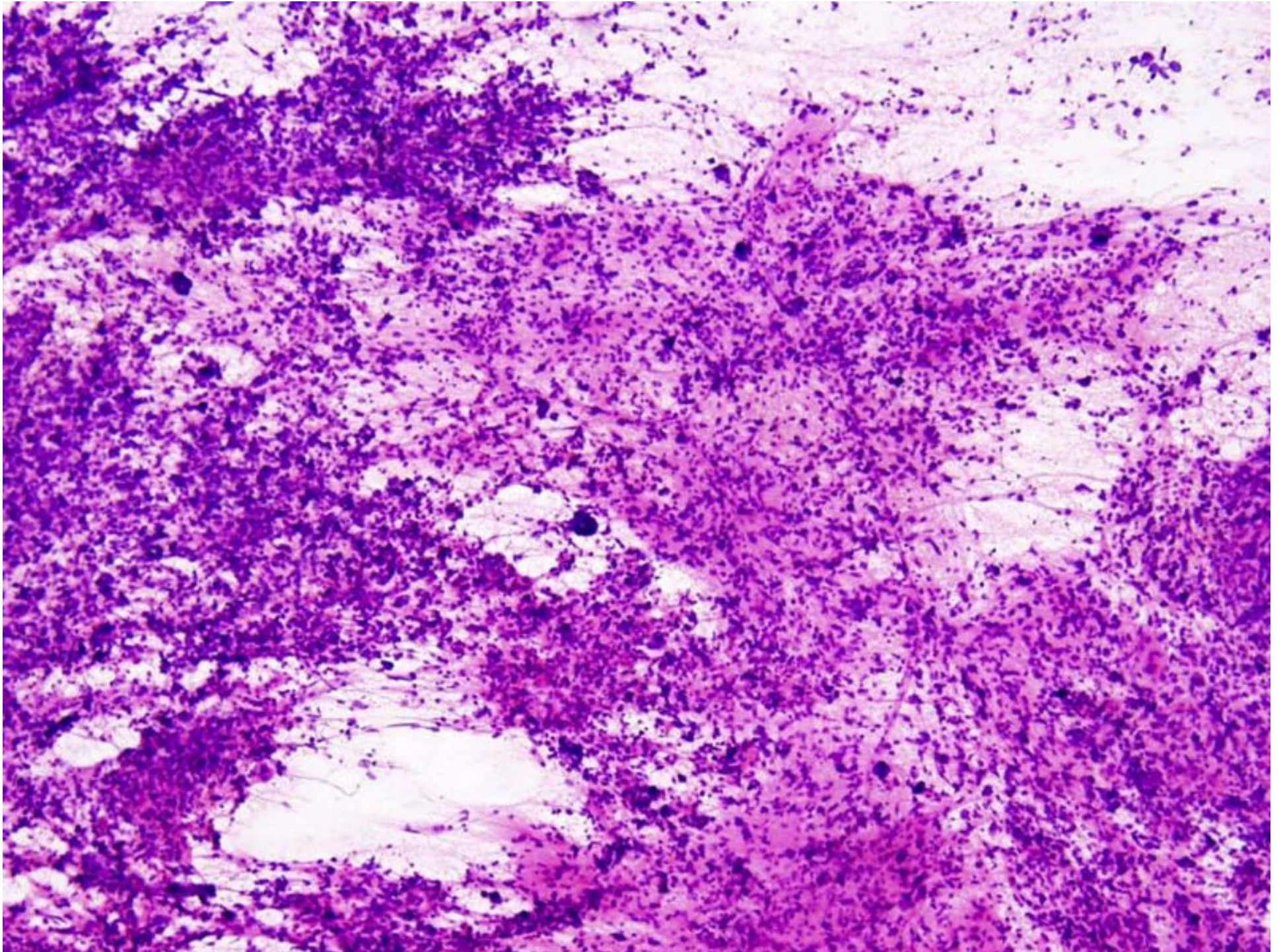
# Case #3

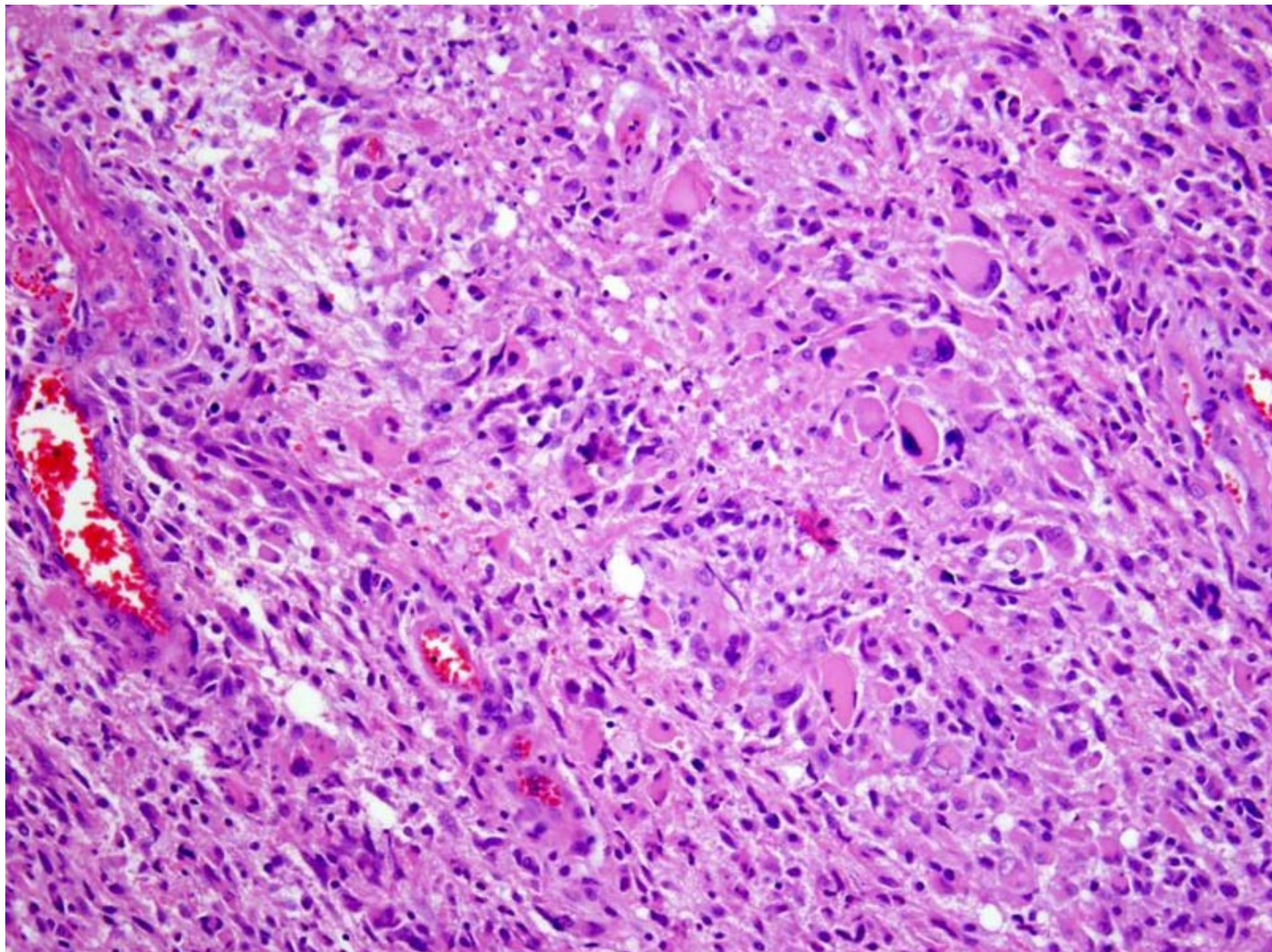
USCAP Neuropathology Evening  
Seminar/Companion Meeting

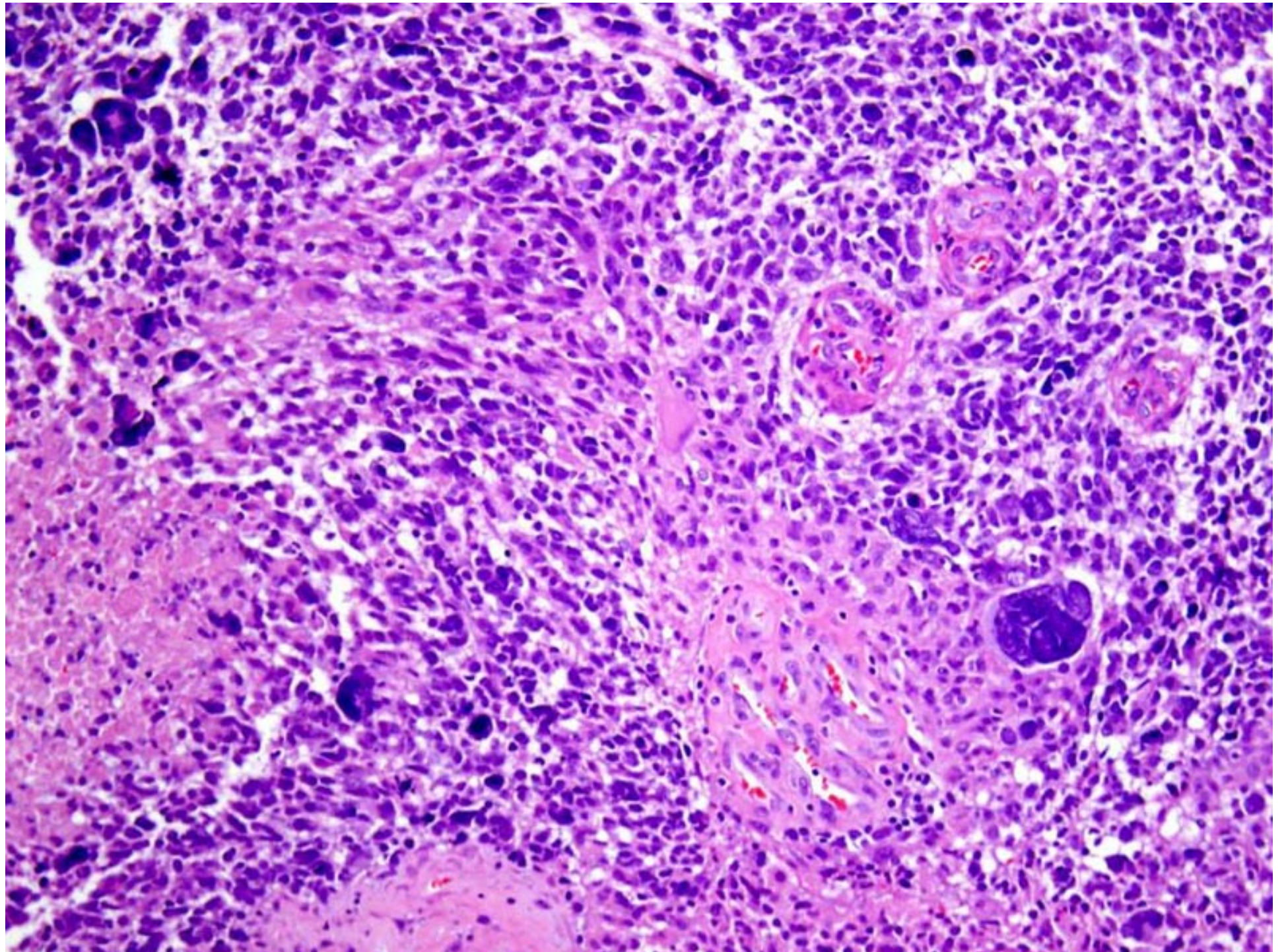
# Clinical History

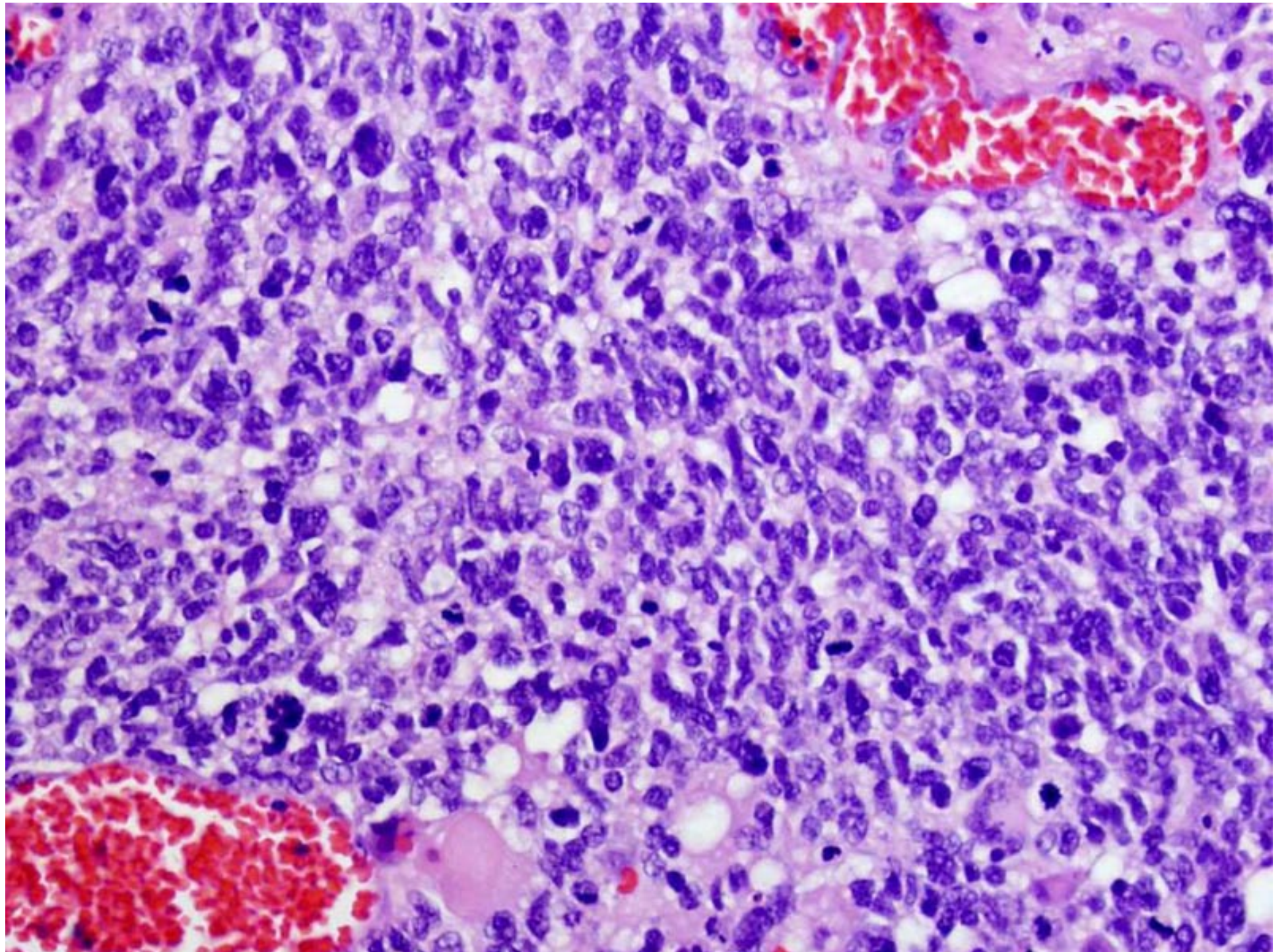
A 71-year-old man presented with a 4-week history of word finding difficulty. An initial screening head CT followed by an MRI scan revealed a large ring-enhancing mass of the left temporal lobe that abutted the dura. The patient was referred to a tertiary care hospital where craniotomy and surgical resection of the mass were performed.

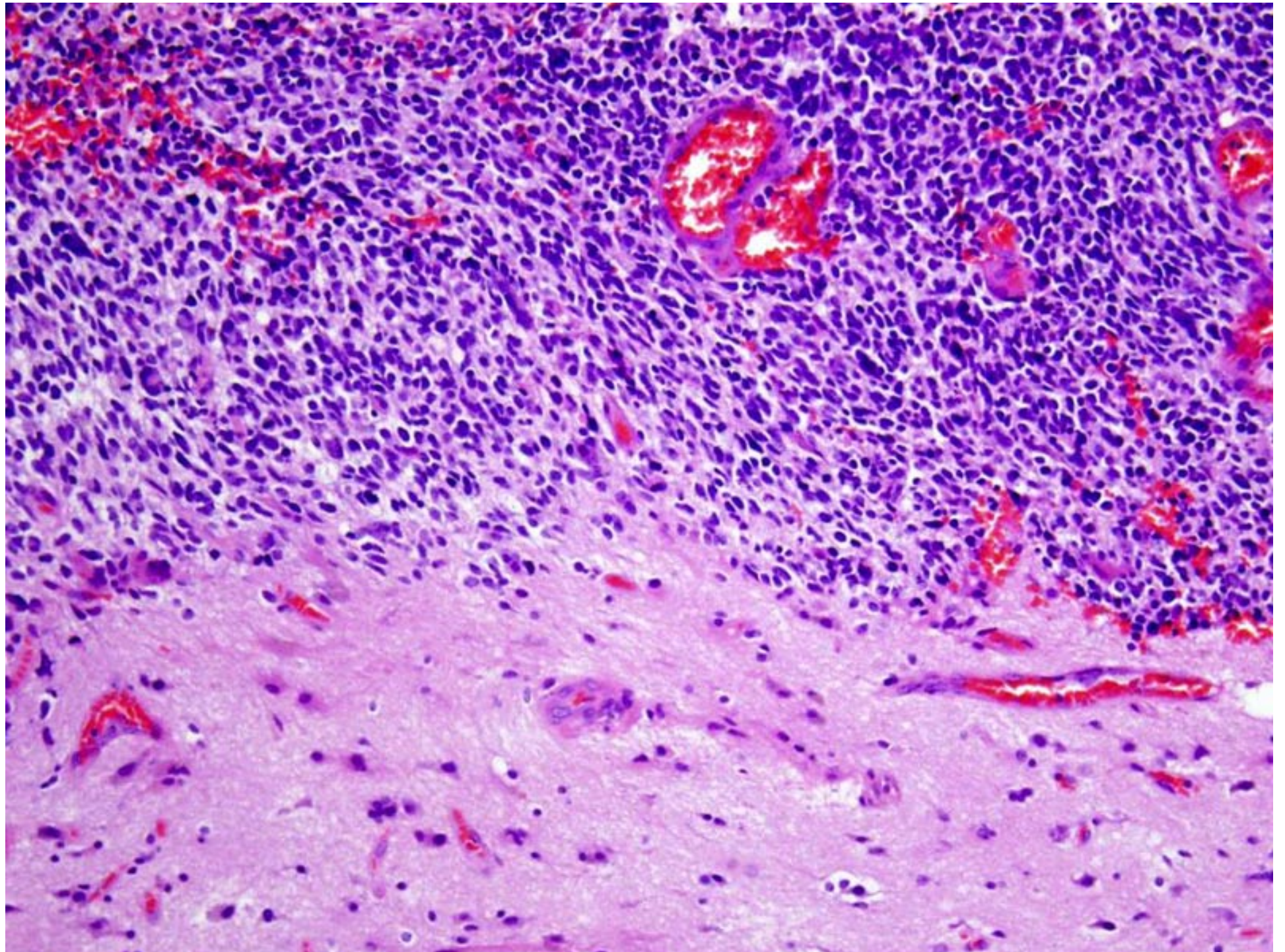




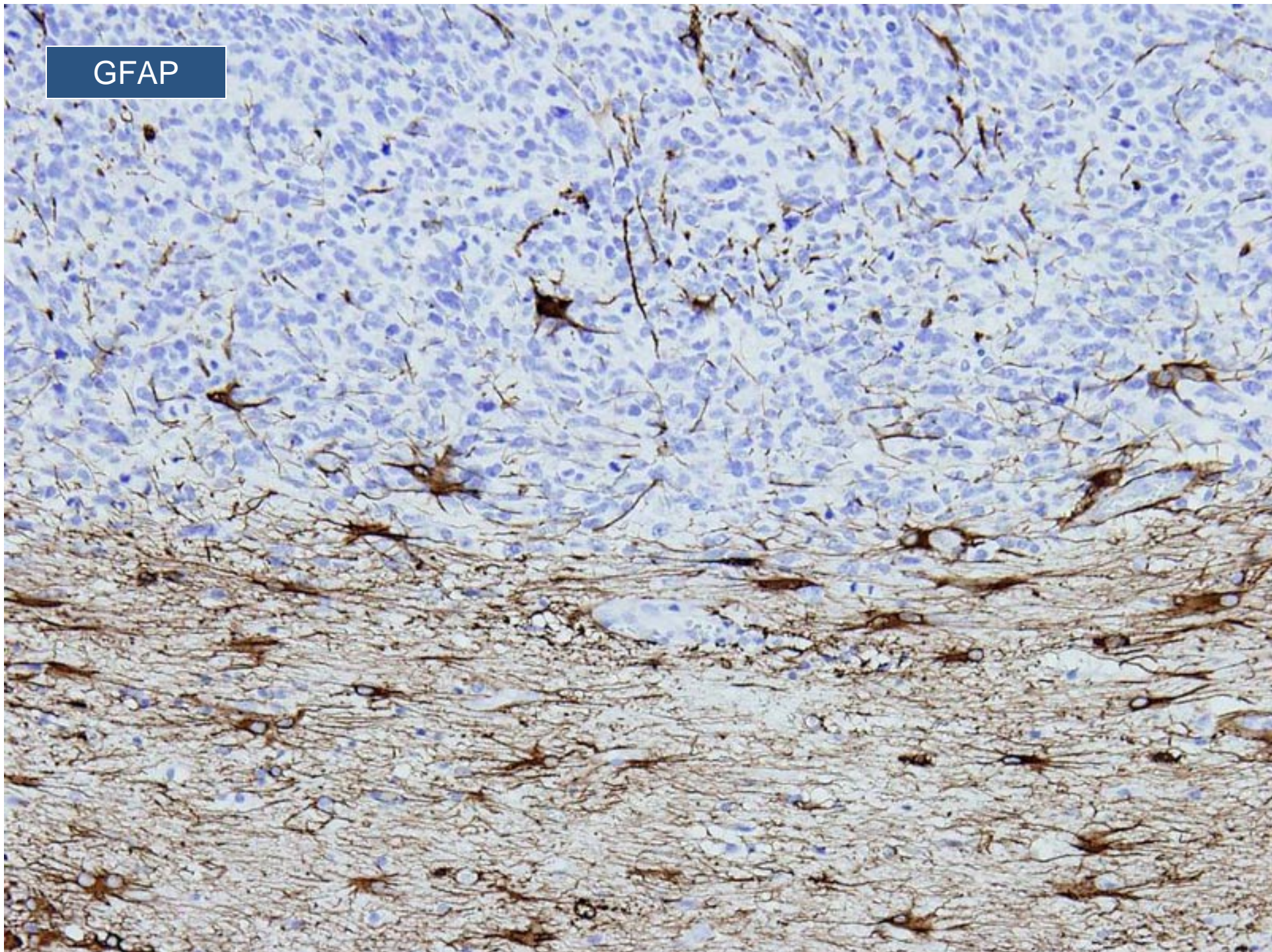




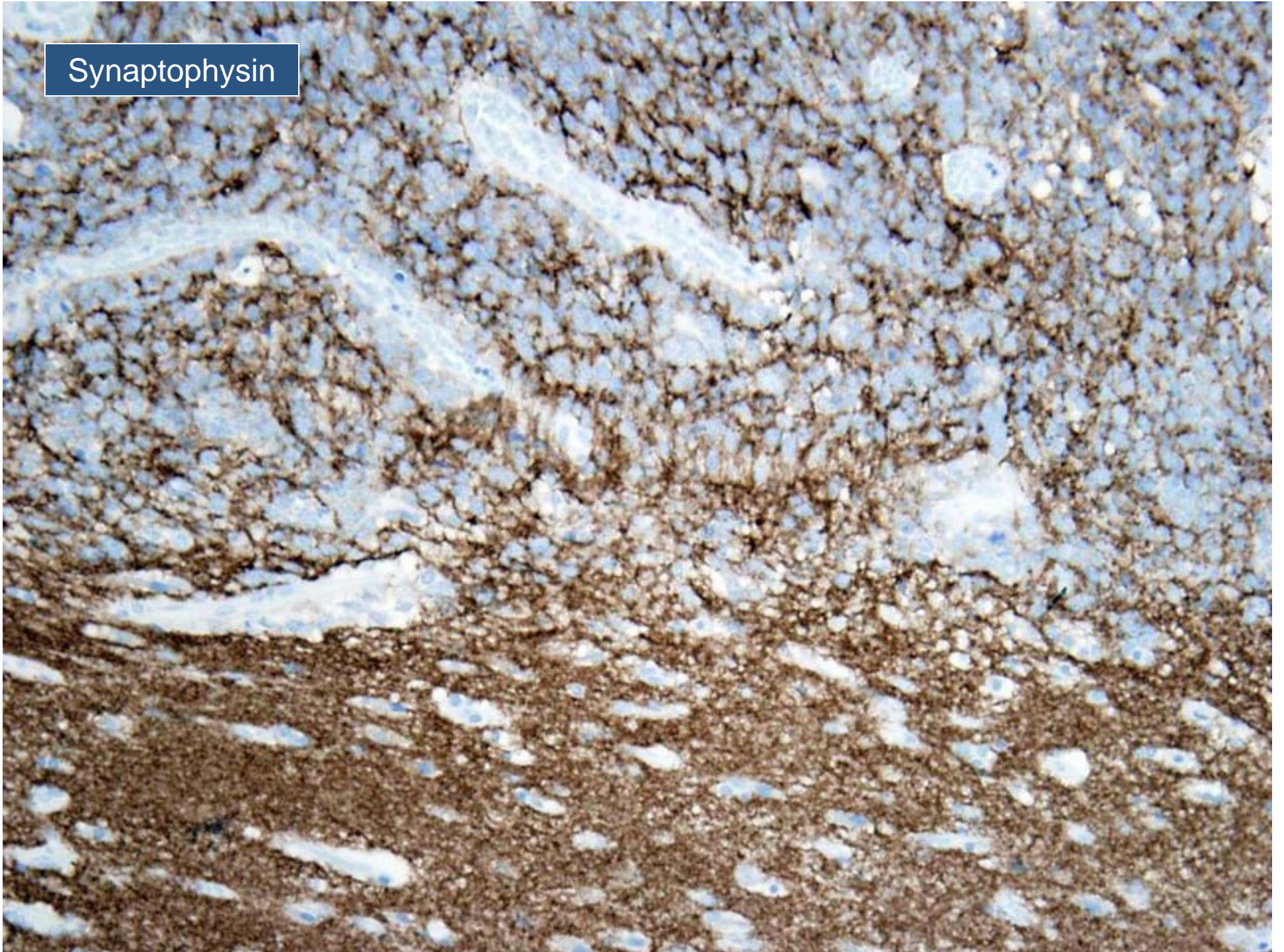


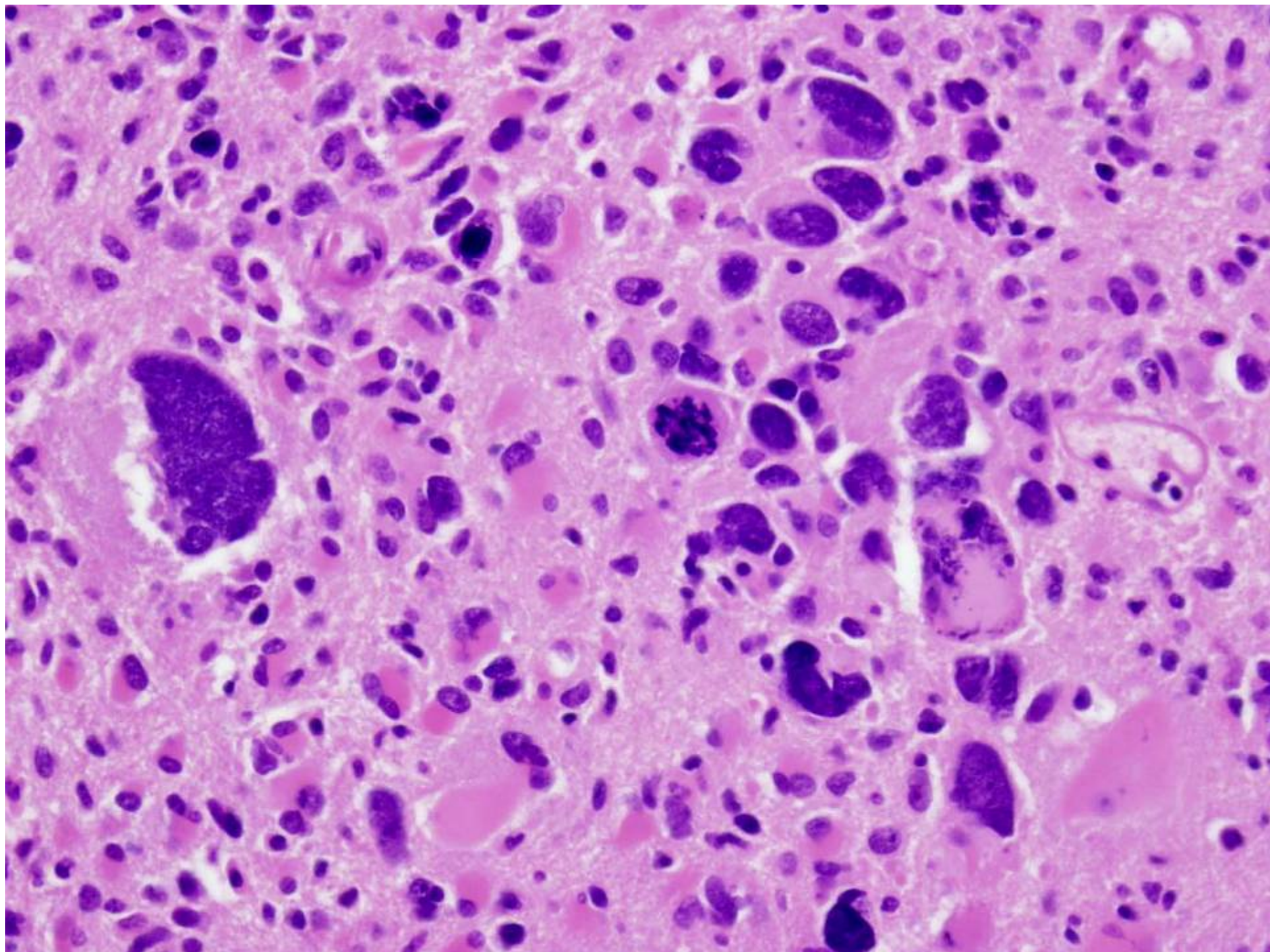


GFAP

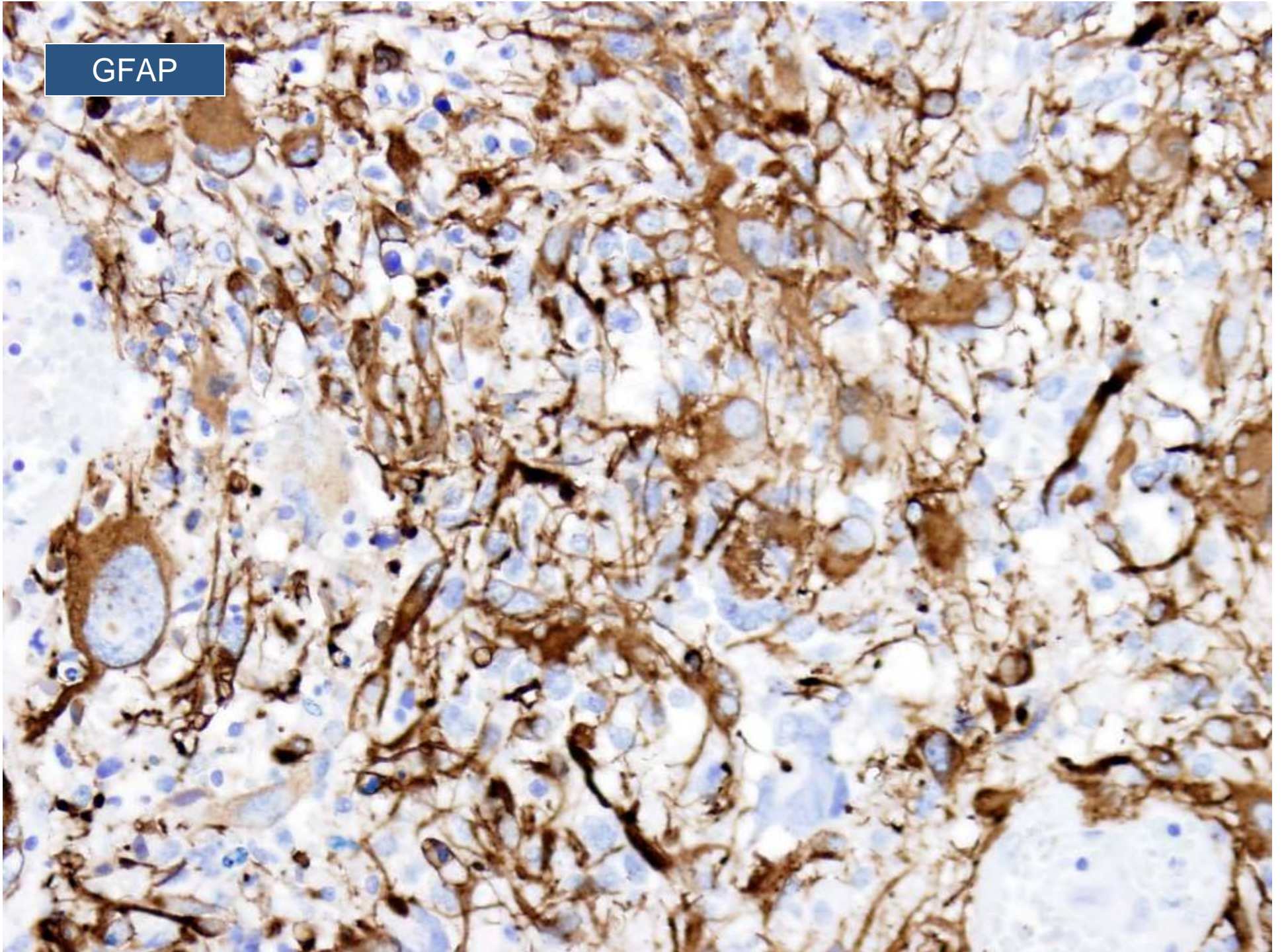


Synaptophysin

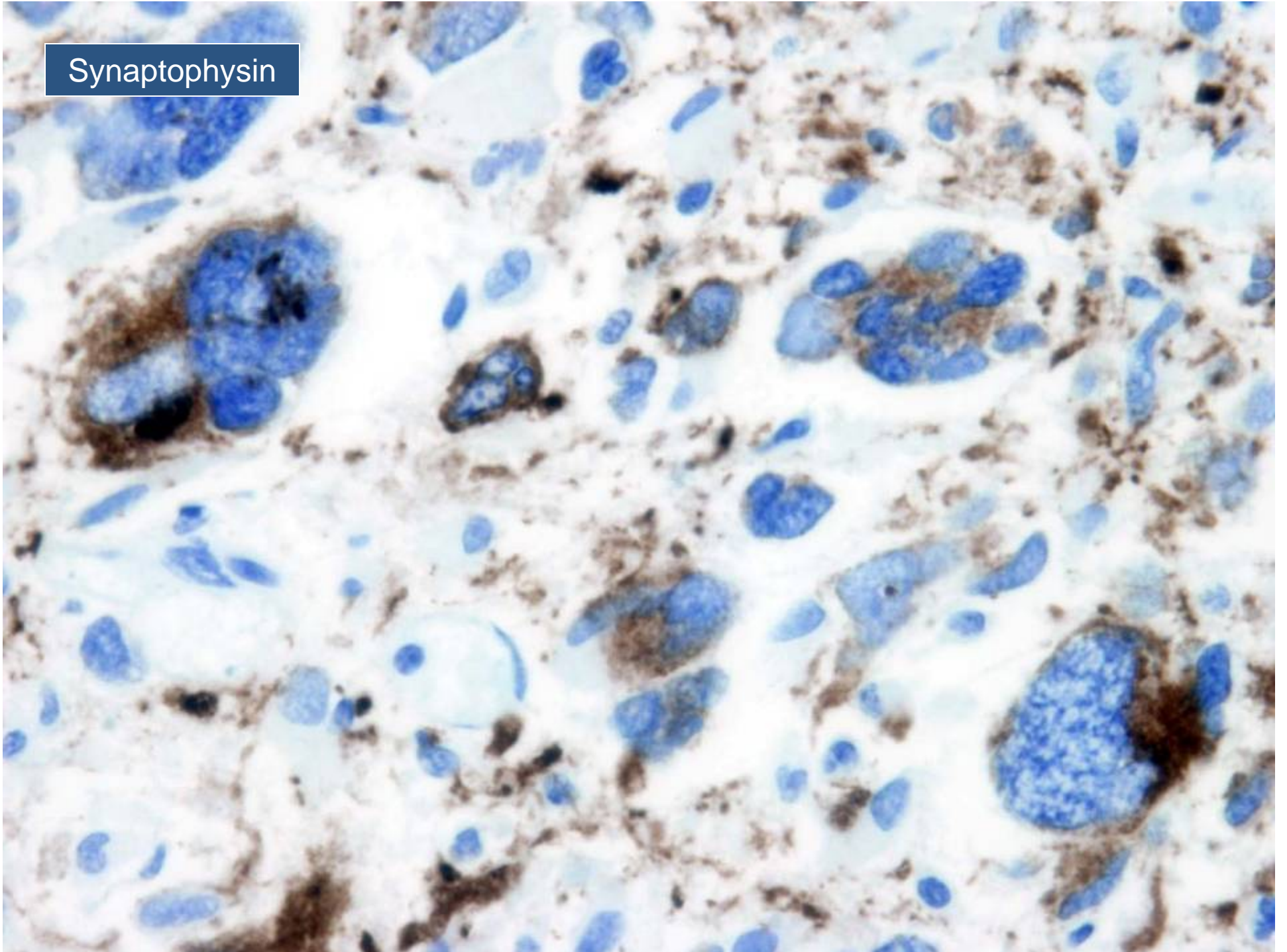




GFAP



Synaptophysin



# Diagnosis?

- Malignant glioneuronal tumor

# Histologic Features

- Features of a high grade malignant neoplasm with nuclear pleomorphism, mitotic activity, vascular proliferation and necrosis
- Both glial and neuronal differentiation as characterized by GFAP and synaptophysin immunoreactivity

# Glioneuronal Tumors

- “New entities”
  - Rosette-forming glioneuronal tumor
  - Glioneuronal tumor with neuropil-like islands
  - Papillary glioneuronal tumor
- “Traditional”
  - Dysplastic gangliocytoma of the cerebellum (Lhermitte-Duclos)
  - Desmoplastic infantile astrocytoma and ganglioglioma
  - Dysembryoplastic neuroepithelial tumor (DNET)
  - Gangliocytoma/ganglioglioma
  - Central neurocytoma and extraventricular neurocytoma
  - Cerebellar liponeurocytoma

# “Malignancy” in neuronal/gangliocytic tumors

- Most often seen in tumors with both glial and neuronal/gangliocytic differentiation
- “Malignant” cells are often felt to be of glial origin
- However, mixed glioneuronal phenotypic expression in this category is increasingly recognized and under intense investigation.

# Differential Diagnosis and Pitfalls

- The clinical differential diagnosis of a solitary contrast-enhancing mass in an older adult patient is broad, but the most common etiologies are **metastatic carcinoma**, **glioblastoma**, and **primary central nervous system large B-cell lymphoma**; other entities to keep in mind are **demyelinating pseudotumor** and **cerebral abscess**.
- The **misdiagnosis of demyelinating pseudotumor as diffuse glioma** is one of the most common serious **diagnostic errors in surgical neuropathology**, which can lead to the inappropriate administration of CNS irradiation and/or chemotherapeutic intervention, both of which can have deleterious side effects.

# Varlet et al - New Variants of Malignant Glioneuronal Tumors: A study of 40 cases

- All tumors coexpressed glial fibrillary acidic protein and NFP
- Other neuronal markers tested were inconstantly expressed
- No recurrence was observed at the primary site in 36.4% of patients who underwent gross total resection
- Twelve patients (33.3%) developed intra-axial and/or systemic metastases, and 4 were free of disease at 39 to 184 months.
- Gross total surgical resection ( $P = 0.001$ ) and a long duration of symptoms (symptoms  $> 1$  yr;  $P = 0.013$ ) proved to be independent and statistically significant prognostic factors in the multivariate analysis.
- CONCLUSIONS: NFP immunostaining is required to identify MGNTs accurately
- Their distinction from malignant gliomas is of paramount clinical importance, particularly for neurosurgeons, because gross total surgical resection may be curative in some cases.
- MGNTs may account for the long-term survival and/or occurrence of metastases demonstrated in a subset of malignant gliomas.

## Vajtai et al - Malignant glioneuronal tumor of the adult cerebrum with neuropil-like islands involving “proliferating nodules”: confirmatory report of unusual variant

- Left frontal lobe mass in 59 year old woman
- 70% was conventional GBM
- Several discrete aggregates of non-descript round cells with a primitive appearance were present with smudged contours
- Within individual clusters there were delicate processes but the round cells stained strongly for synaptophysin and were surrounded by GFAP positive astrocytes
- MIB-1 staining positive 9-11% in astrocytic component, the round cell nodules stained positively in approximately 40%

## Rodriguez et al - Unusual malignant glioneuronal tumors of the cerebrum of adults: a clinicopathologic study of three cases

- 2 men and 1 woman, ages ranging from 35 – 83
- Epithelioid cells in 3, spindle cells in 1 and undifferentiated small cells in 1
- Necrosis, non-pallisading was present in all 3 with brisk mitotic activity
- All immunoreactive for GFAP, S-100, synaptophysin, chromogranin and 2 were positive for Neu-N and neurofilament proteins
- EM showed convincing neurosecretory granules in one case, and some in filament containing cells were immunogold labeled for GFAP

# Shibahara et al – Secondary glioblastoma with advanced neuronal phenotype

- 35 year old man with a partially resected astrocytoma (immunoreactive for GFAP with a MIB-1 labeling index of approximately 2%) and treated with post-op radiation and chemotherapy
- Residual/regrowth resected 5 months and then again 8 months later with death at 11 months with subarachnoid and intraventricular dissemination
- Recurrences showed a small blue cell tumor with occasional large multinucleated giant cells
- Recurrences showed high MIB-1 labeling index (80%) and extensive positivity for both synaptophysin and NeuN but NOT for GFAP
- Although initially diagnosed as GBM, may be better classified as a malignant glioneuronal tumor

# Summary

- A wide range of diverse morphologies can be seen in high-grade diffuse glioma, and mixed glioneuronal phenotypic expression in this category is increasingly recognized and under investigation.
- The evaluation of CNS neoplasms increasingly relies on the interpretation and integration of panels comprised of several phenotypic markers rather than on single antibodies.
- Oncologic neuropathology remains a dynamic, evolving field in which novel tumor types and subtypes of clinical importance continue to be recognized and characterized.

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