# CLINICAL, RADIOLOGICAL, AND PATHOLOGIC PATTERNS IN SURGICAL NEUROPATHOLOGY

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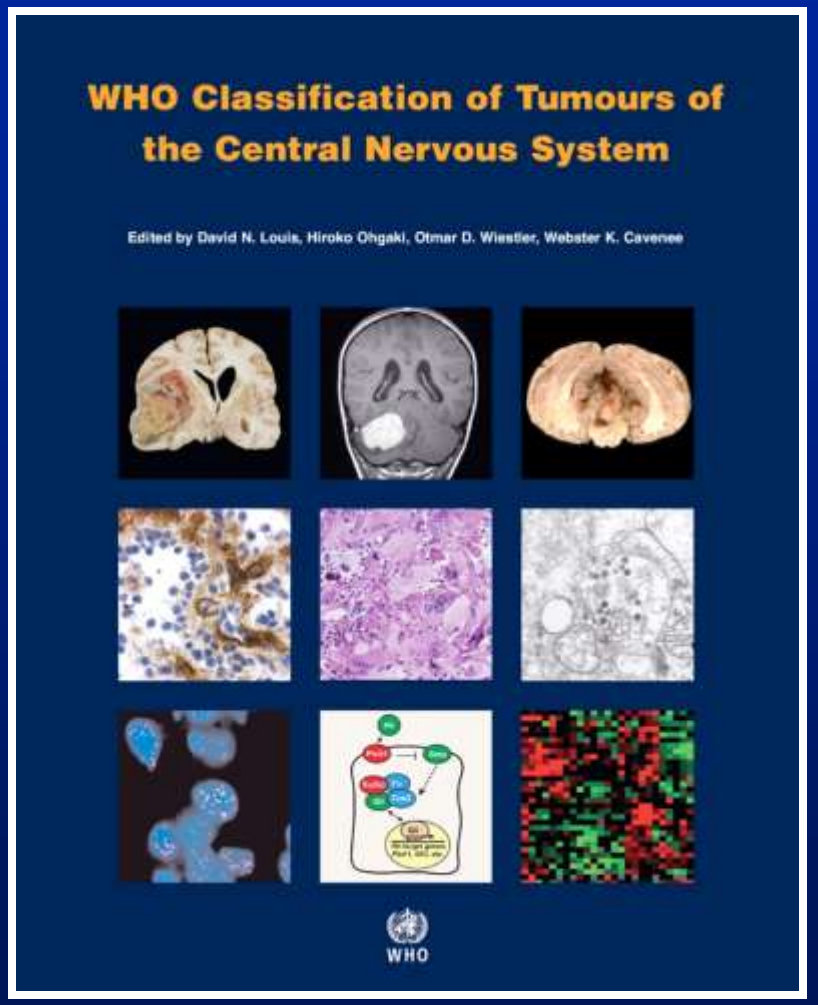
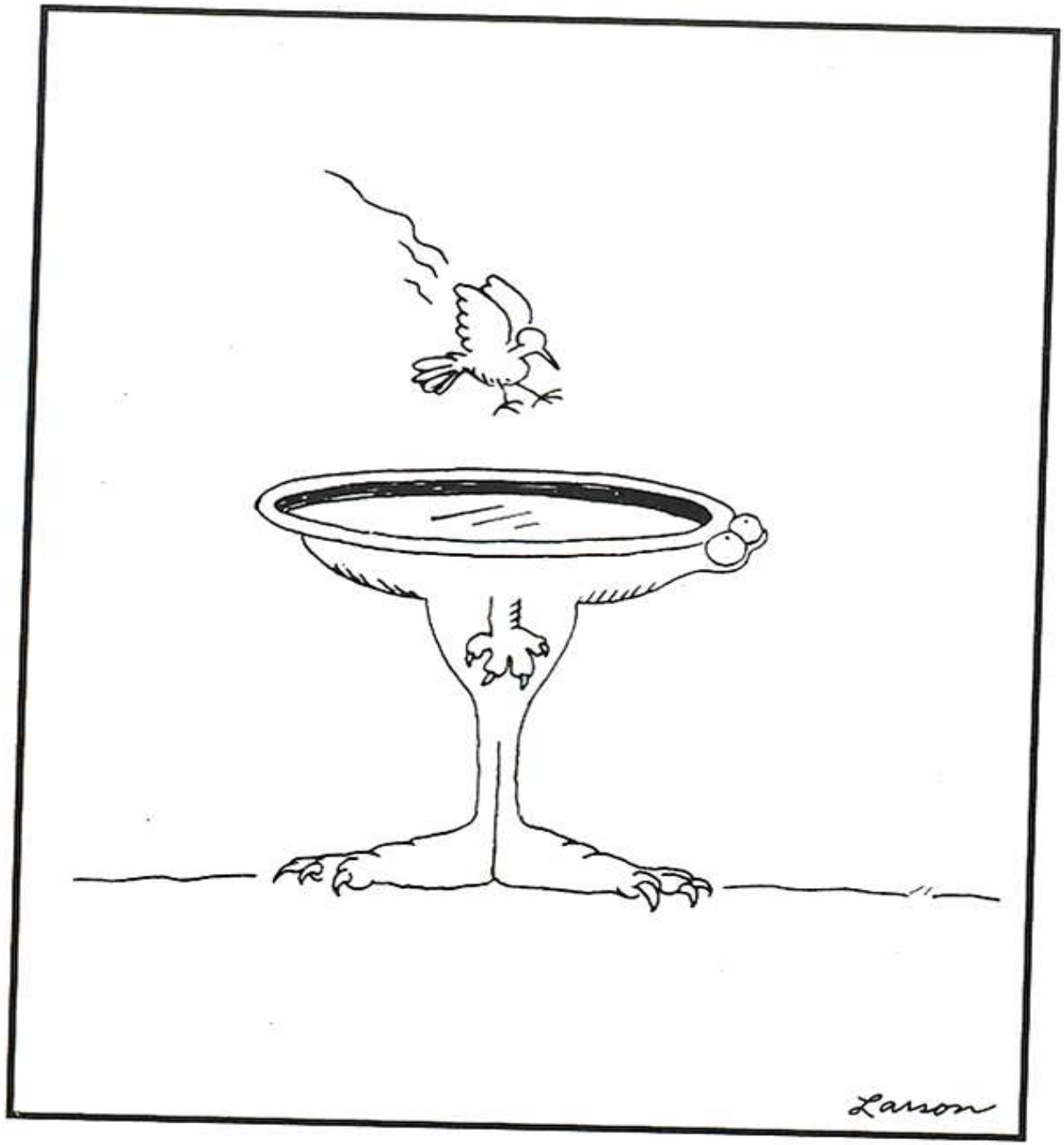
# WHO 2007 CNS TUMOR SCHEME

- Grade I = Benign
- Grade II = Low-grade
- Grade III = Anaplastic
- Grade IV = Poorly diff. malignancy



# PATTERN RECOGNITION

# IMPERSONATORS




# Beware: Look-alikes and Mimics

PATTERN RECOGNITION SERIES
SERIES EDITORS: KEVIN O. LESLIE AND MARK WICK

Practical Surgical Neuropathology

# Practical Surgical Neuropathology

## A Diagnostic Approach

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# DIAGNOSTIC PATTERNS

- 8 major histological patterns
- 20 minor histological patterns
- Clinical patterns
- Radiological patterns
- Musical patterns

| Pattern | Diseases to Be Considered |
|---|---|
| **Parenchymal infiltrate with hypercellularity** | Diffuse glioma<br>CNS lymphoma<br>Infections<br>Active demyelinating disease<br>Cerebral infarct<br>Reactive gliosis |
| **Solid mass (pure)** | Metastasis<br>Ependymoma<br>Subependymoma<br>Subependymal giant-cell astrocytoma (SEGA)<br>Central or extraventricular neurocytoma<br>Pineocytoma<br>Embryonal tumor (e.g., AT/RT)<br>Choroid plexus papilloma<br>Hemangioblastoma<br>Paraganglioma<br>Pituitary adenoma |
| **Solid and infiltrative process** | Pilocytic astrocytoma<br>Pleomorphic xanthoastrocytoma<br>Glioblastoma/gliosarcoma (and other high grade gliomas)<br>Ganglioglioma<br>Dysembryoplastic neuroepithelial tumor (DNT)<br>Embryonal tumor (e.g., medulloblastoma/CNS PNET)<br>Choroid plexus carcinoma<br>Germ cell tumors<br>Craniopharyngioma<br>CNS lymphoma<br>Sarcoma<br>Histiocytic disorders<br>Abscess and other forms of infection |
| **Vasculocentric process** | CNS lymphoma<br>Intravascular lymphoma<br>Angiocentric glioma<br>Ependymoma<br>Vasculitis<br>Meningioangiomatosis<br>Active demyelinating disease<br>Amyloid angiopathy<br>Arteriolosclerosis<br>Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)<br>Vascular malformations<br>Infections (e.g., aspergillosis)<br>Neurosarcoidosis<br>Thromboembolic disease |

| Pattern | Diseases to Be Considered |
|---|---|
| **Extra-axial mass** | Meningioma<br>Hemangiopericytoma<br>Solitary fibrous tumor<br>Hemangioblastoma<br>Sarcomas<br>Schwannoma and other nerve sheath tumors<br>Metastasis<br>Melanoma or melanocytoma<br>Secondary lymphoma or leukemia<br>Paraganglioma<br>Pituitary adenoma<br>Neurosarcoidosis<br>Granulomatous infections<br>Inflammatory pseudotumors<br>Calcifying pseudotumor of the neuraxis<br>Primary bone tumors (e.g., chordoma)<br>Histiocytic disorders (e.g., Rosai-Dorfman disease) |
| **Meningeal infiltrate** | Meningeal carcinomatosis, gliomatosis, melanosis, melanomatosis, sarcomatosis, or hemangioblastomatosis<br>Metastatic medulloblastoma/CNS PNET<br>Secondary lymphoma or leukemia<br>Histiocytic disorders<br>Meningitis<br>Neurosarcoidosis<br>Infectious granulomatous diseases<br>Collagen vascular disorders<br>Sturge-Weber syndrome |
| **Destructive/necrotic process** | Cerebral infarct<br>Radiation necrosis or treatment effects<br>Infections<br>Vasculitis<br>CNS lymphoma in an immunosuppressed patient<br>Intravascular lymphoma<br>CADASIL<br>Severe demyelinating disease<br>Metabolic/toxic disease |
| **Subtle pathology or near-normal biopsy** | Nonrepresentative biopsy specimen<br>Subtle diffuse glioma (WHO grade II)<br>Hypothalamic hamartoma<br>Cortical dysplasia or tuber<br>Mesial temporal sclerosis<br>Intravascular lymphoma<br>Meningioangiomatosis<br>Mild encephalitis<br>Cerebral malaria<br>Ischemic disease<br>Neurodegenerative diseases<br>Benign cysts<br>Metabolic or toxic disorder<br>Reactive gliosis or "glial scar" |

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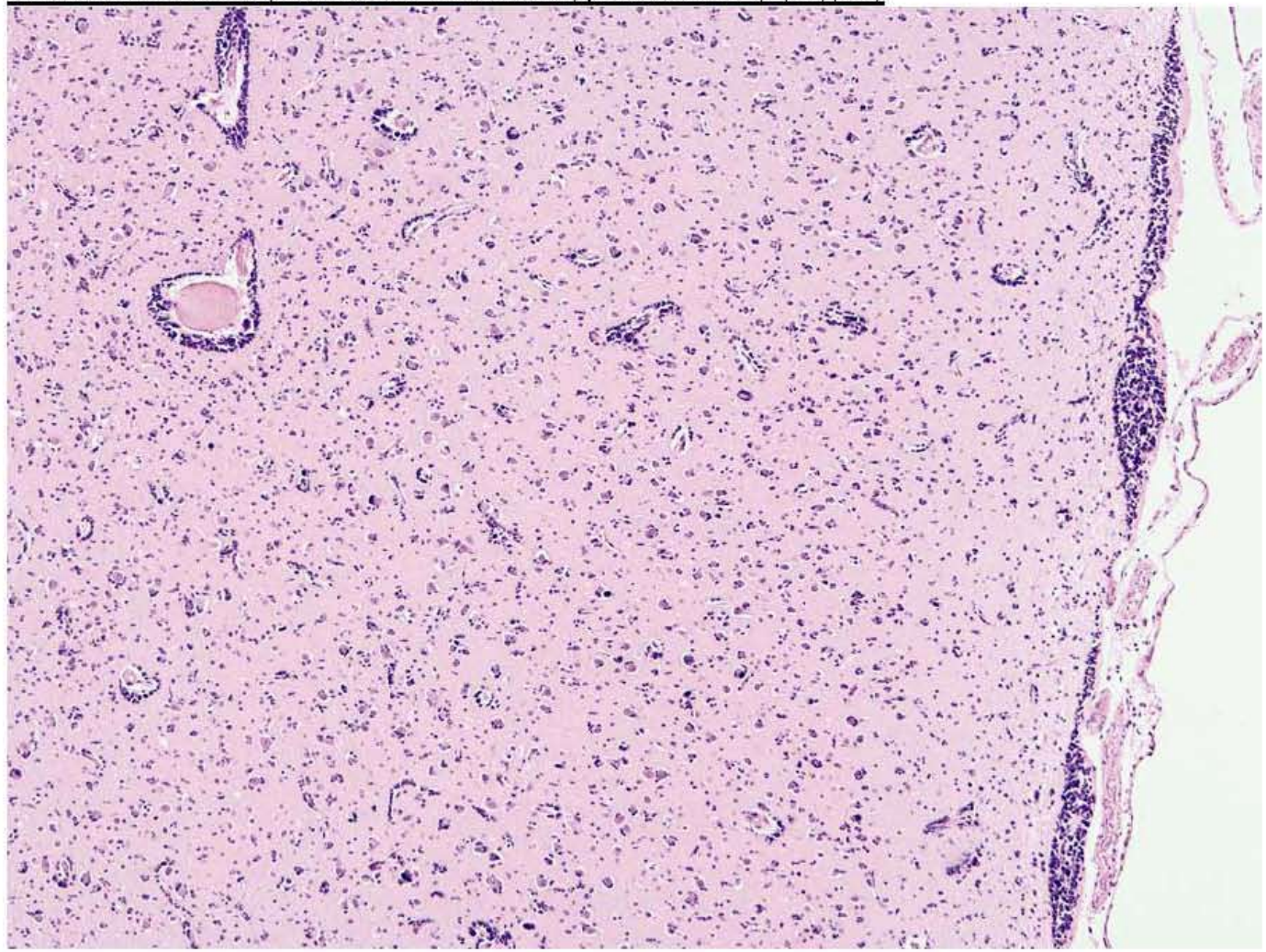
# Neuropathology Patterns and Introduction

Arie Perry and Daniel J. Brat



characteristics is a critical way to narrow the differential diagnosis, often to a few fairly common entities. In fact, the combination of *patient age* and *neuroimaging features* (including tumor location) provides some of the most powerful diagnostic clues before any tissue is even sampled or examined under the microscope. For example, the differential varies considerably for supratentorial versus infratentorial, pediatric versus adult, and enhancing versus nonenhancing tumors. The most common diagnostic considerations are summarized by age, location, and imaging features in Table 1-1, with each specific entity discussed in greater detail in subsequent chapters. Also, for a much more detailed background on the use of neuroimaging, the reader is referred to Chapter 4. This is a particularly critical topic in surgical neuropathology, since brain and spinal

Pattern 1: Parenchymal Infiltrate with Hypercellularity (Fig. 1)

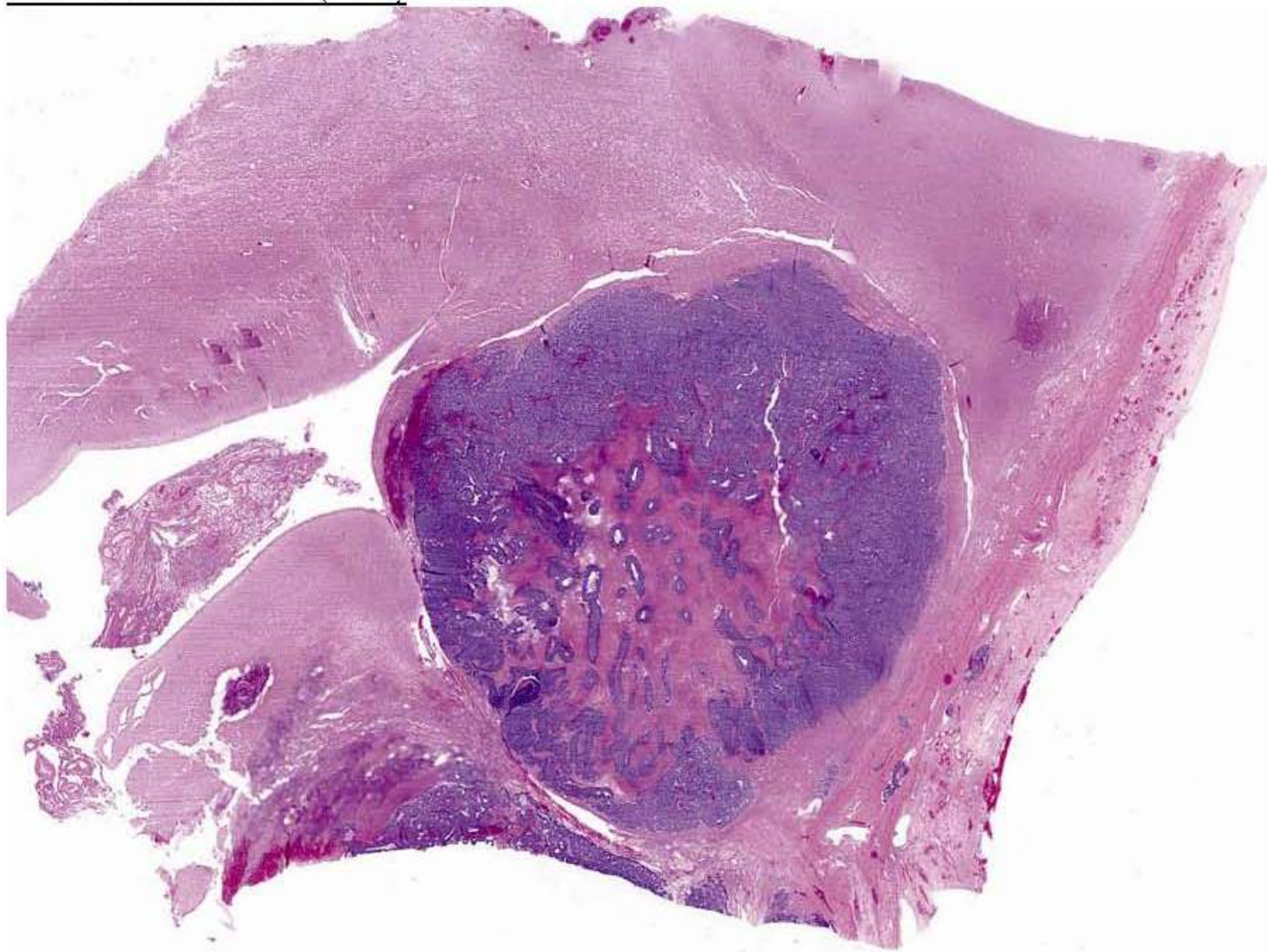


**Elements of the pattern:** The brain biopsy shows intact cortical architecture, but a hypercellular infiltrate is evident at scanning magnification. In this particular example, an additional finding is *secondary structure* formation, with subpial condensation, perivascular aggregates, and perineuronal satellitosis. This growth pattern is most common in diffuse gliomas.

## Pattern 1: Parenchymal Infiltrate with Hypercellularity

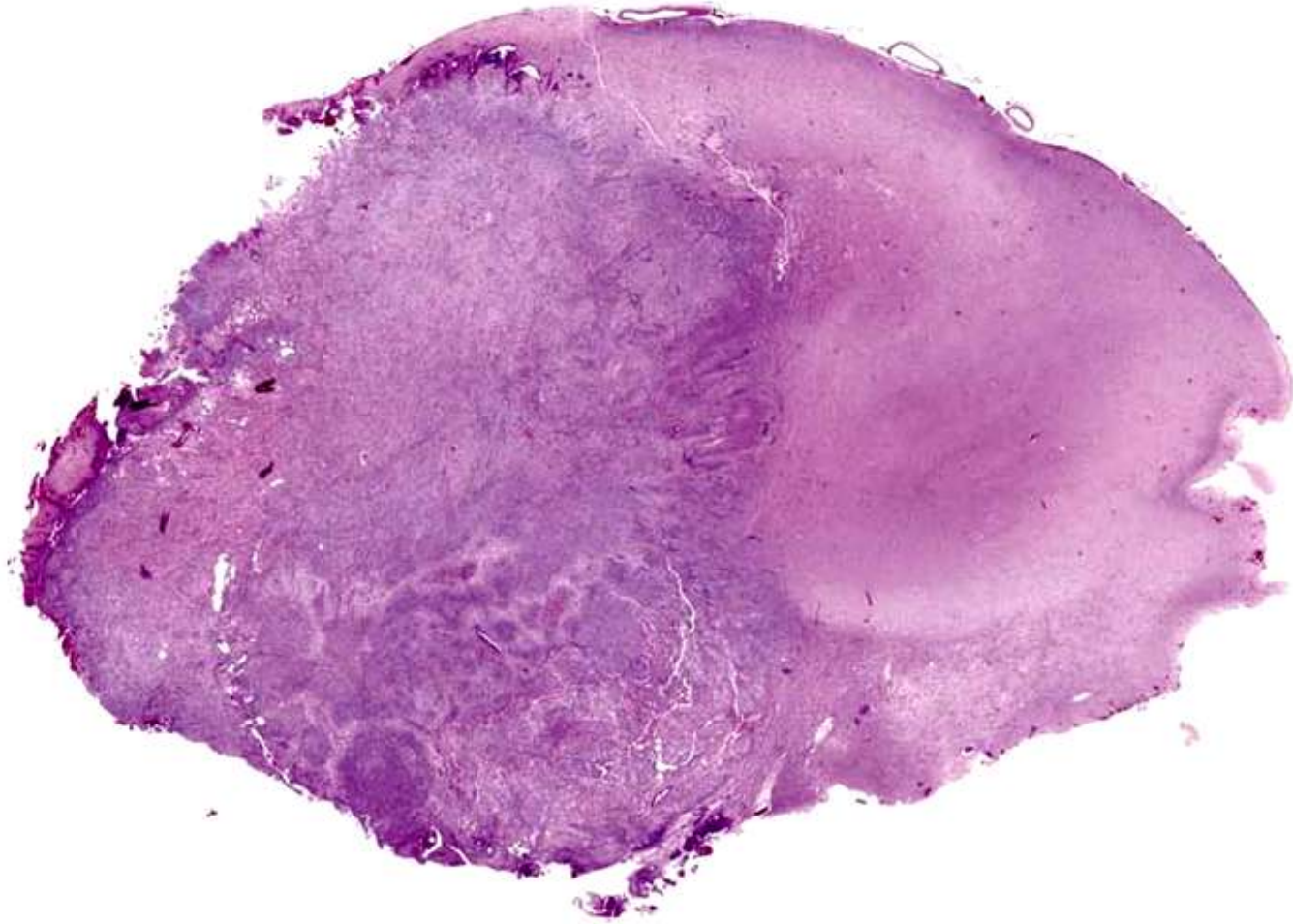
| Additional Findings | Diagnostic Considerations | Chapter/page |
|---|---|---|
| Secondary structures of Scherer | Diffuse gliomas | (Ch. 5) |
| Extensive bilateral cerebral involvement | Gliomatosis cerebri<br>Lymphomatosis cerebri | (Ch. 5)<br>(Ch. 14) |
| Angiocentric pattern | CNS lymphoma<br>Angiocentric glioma<br>Meningoencephalitis/Infections<br>Active demyelinating disease | (Ch. 14)<br>(Ch. 17)<br>(Ch. 21)<br>(Ch. 22) |
| Microcystic pattern | Diffuse gliomas | (Ch. 5) |
| Pleomorphism | Astrocytoma/glioblastoma<br>Infections, especially PML | (Ch. 5)<br>(Ch. 21) |
| Monomorphism | Oligodendroglioma<br>Some lymphomas | (Ch. 5)<br>(Ch. 14) |
| Lymphocytic infiltrate | Gemistocytic astrocytoma<br>CNS lymphoma<br>Meningoencephalitis/Infections<br>Active demyelinating disease | (Ch. 5)<br>(Ch. 14)<br>(Ch. 21)<br>(Ch. 22) |
| Foamy histiocytes | CNS lymphoma<br>Active demyelinating disease<br>Cerebral infarct | (Ch. 14)<br>(Ch. 22)<br>(Ch. 24) |
| Cytologic atypia or anaplasia | Diffuse gliomas<br>CNS lymphoma | (Ch. 5)<br>(Ch. 14) |
| Viral inclusions or organisms | Meningoencephalitis/Infections | (Ch. 21) |
| None | Reactive gliosis | (Chs. 1, 5) |

Pattern 2: Solid Mass (Pure)



**Elements of the pattern:** The biopsy shows a very sharply demarcated intracerebral mass. The increased cellularity imparts a blue color to the tumor, whereas foci of central necrosis appear pink. An additional finding was gland formation, consistent with metastatic adenocarcinoma.

Pattern 3: Solid and Infiltrative Process



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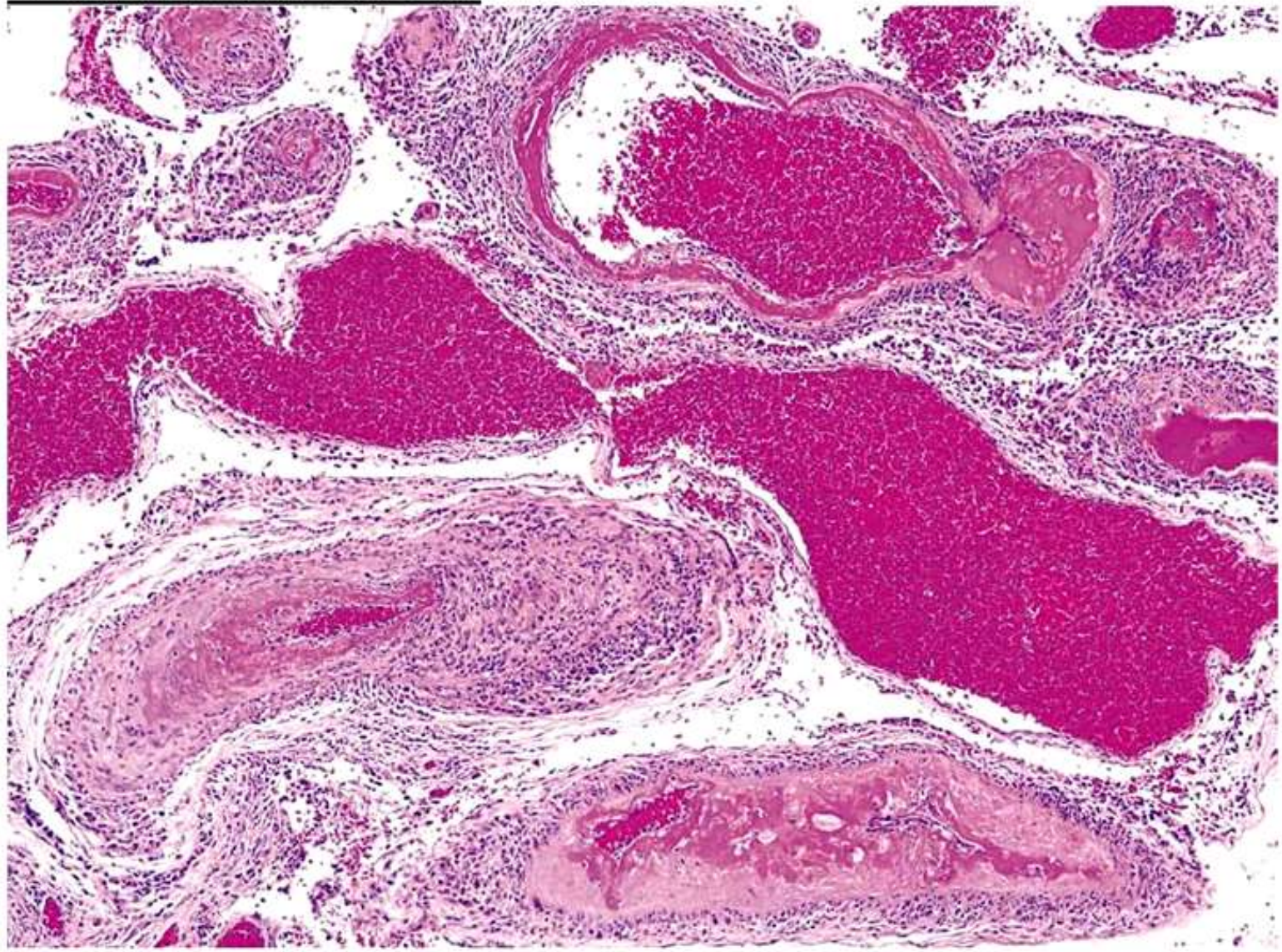
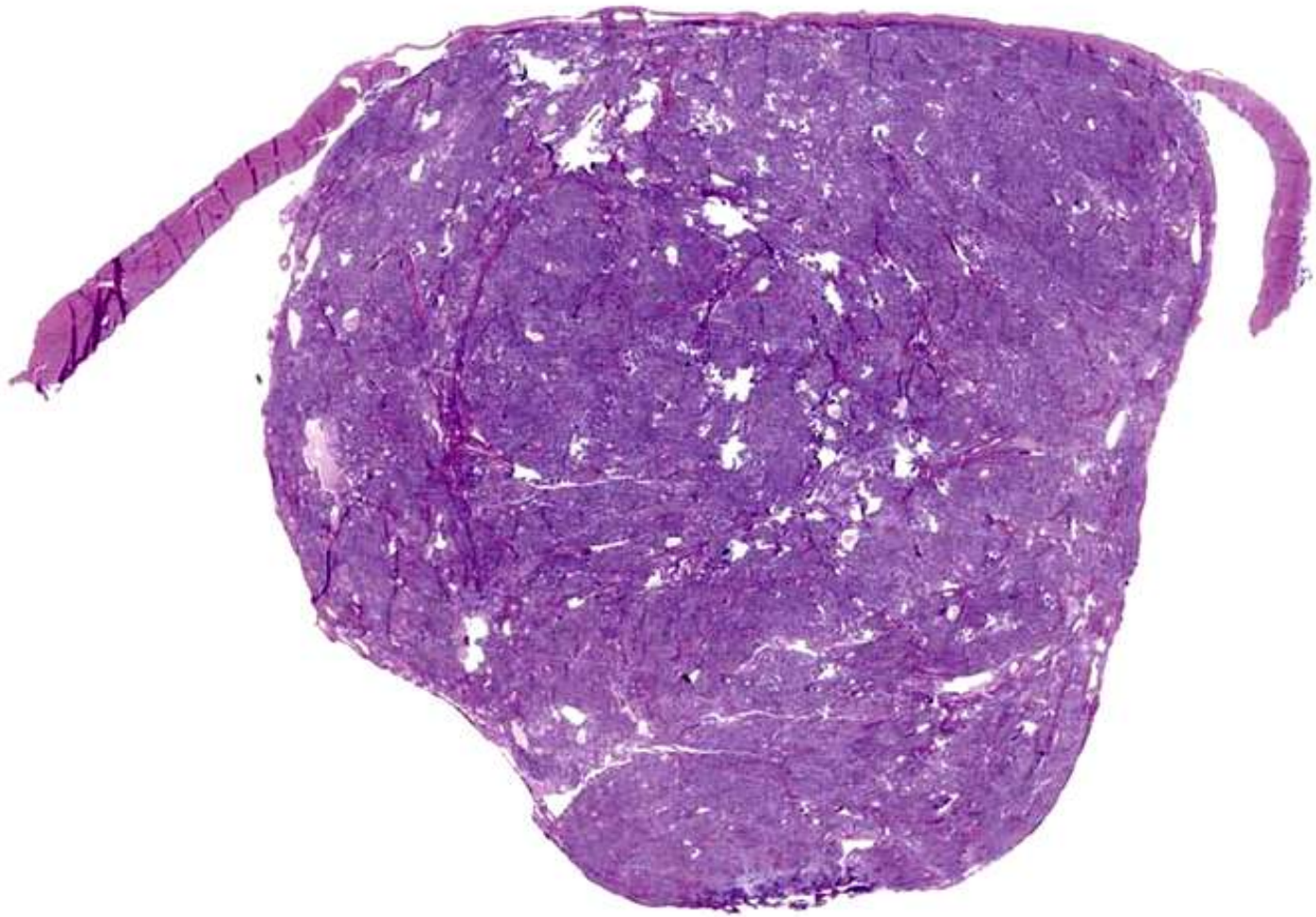
**Elements of the pattern:** The biopsy shows a mostly solid appearing neoplasm (left half), but has fuzzy or ill-defined margins with the adjacent brain parenchyma, consistent with at least a partially infiltrative component as well (right half, especially in white matter). Additional findings in this case were reticulin-rich spindled elements, GFAP-positive glial elements, and pseudopalisading necrosis, consistent with gliosarcoma.

Pattern 4: Vasculocentric Process



**Elements of the pattern:** The biopsy shows a disease process that is clearly centered on blood vessels. Additional findings in this case were foci of angionecrosis and vascular/perivascular inflammation, consistent with vasculitis.

Pattern 5: Extra-axial Mass

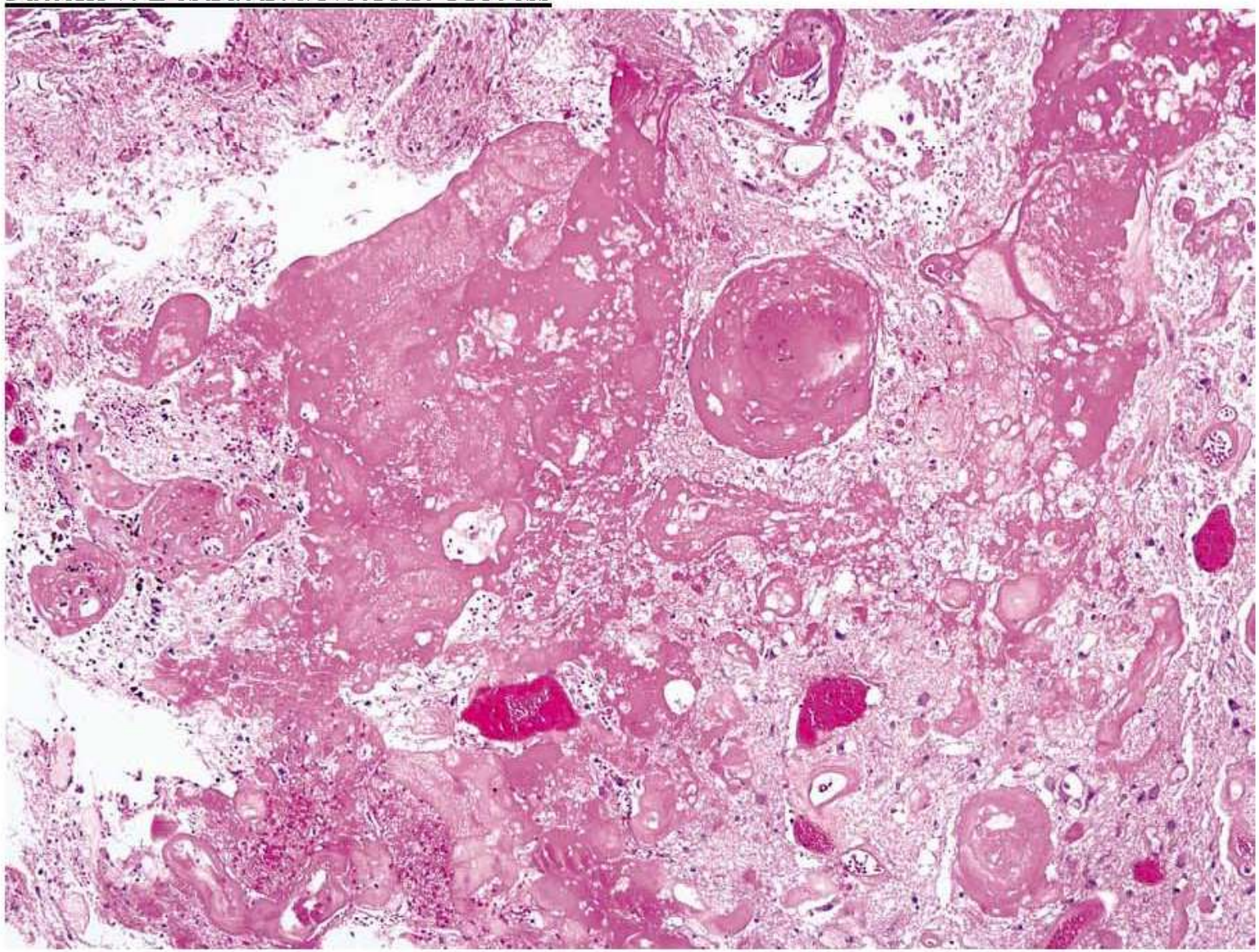


**Elements of the pattern:** The biopsy shows a solid mass attached to a strip of dura in the upper portion of the image. Additional findings in this case were whorls of epithelioid cells and scattered psammoma bodies, consistent with meningioma.

Pattern 6: Meningeal Infiltrate

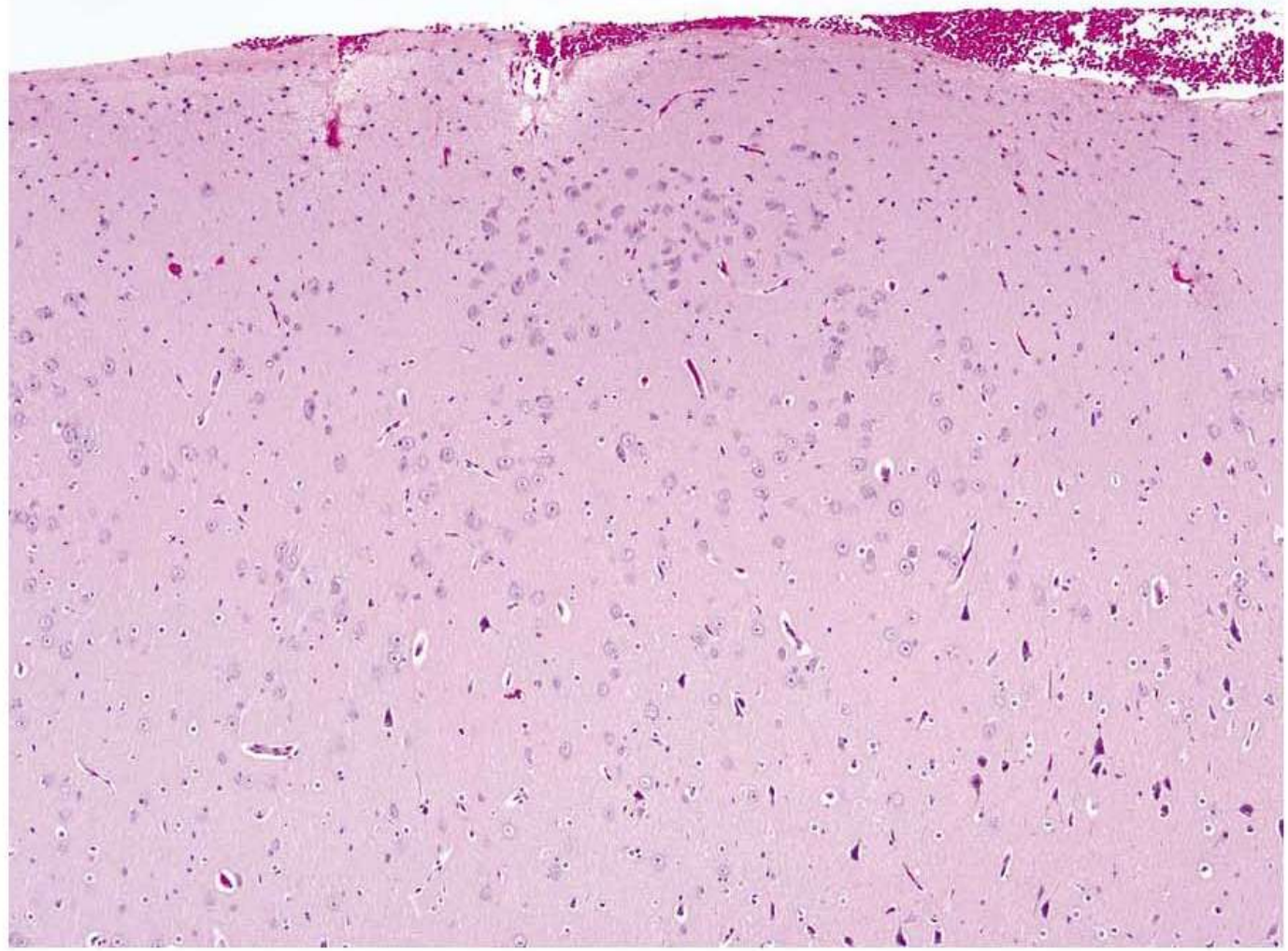
**Elements of the pattern:** The brain section shows a markedly expanded subarachnoid space filled with blue cells. At higher magnification, the infiltrate consisted predominantly of neutrophils, consistent with acute meningitis.

Pattern 7: Destructive/Necrotic Process

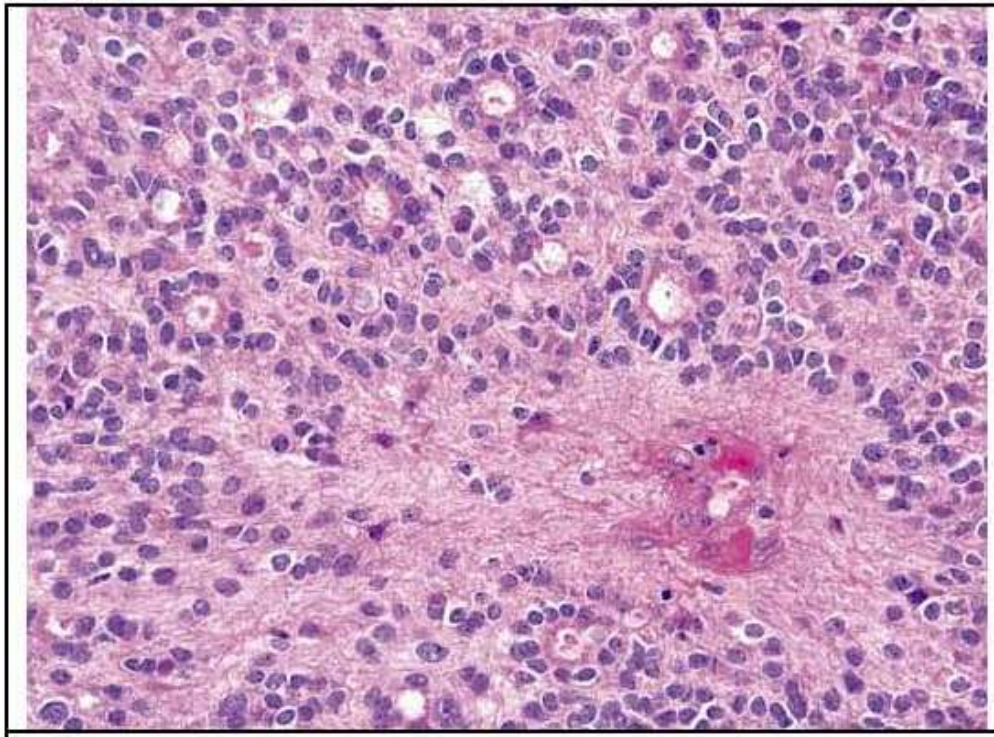


**Elements of the pattern:** The brain biopsy from a patient with known glioma shows extensive fibrinoid parenchymal and vascular necrosis, consistent with radiation necrosis.

Pattern 8: Subtle Pathology or Near Normal Biopsy

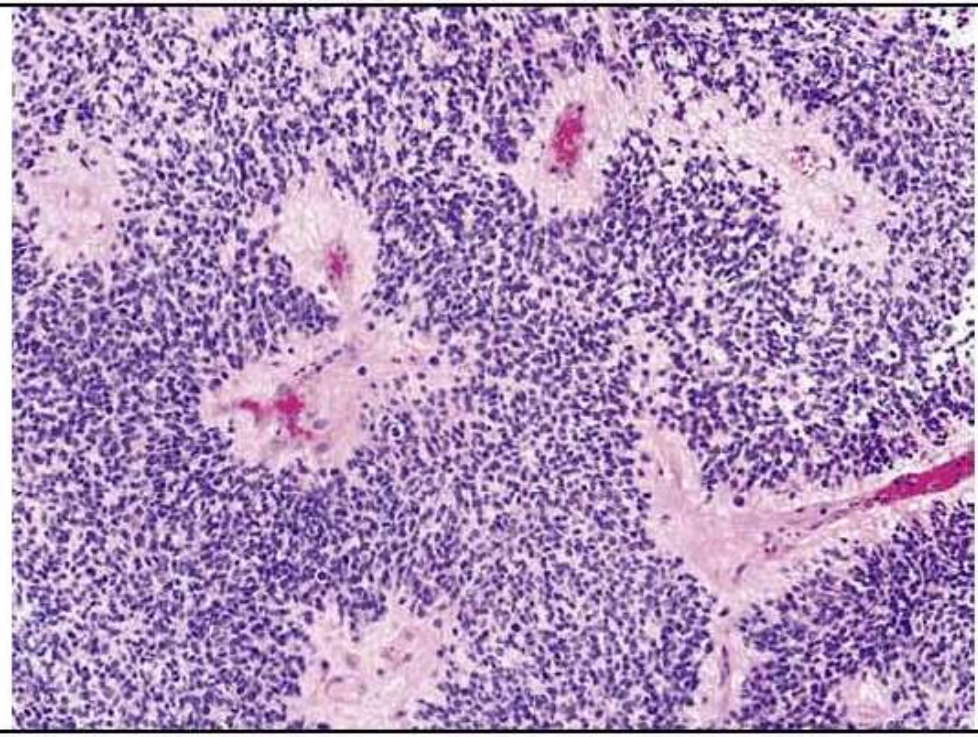


**Elements of the pattern:** The brain biopsy from a patient with chronic seizure disorder shows a nearly normal cortex. However, there is a subtle disarray of the laminar architecture and clustering of large superficial neurons in the center. Leptomeningeal gray matter heterotopia was also seen in other regions of the biopsy. This constellation of findings is consistent with a malformation of cortical development (i.e., cortical dysplasia).



**Rosette forming**

- Ependymoma (true ependymal)
- Medulloblastoma (Homer Wright)
- CNS PNET (Homer Wright, ependymoblastic)
- Neurocytomas (neurocytic)
- Pineocytoma (pineocytic)
- Pineoblastoma (pineoblastic)
- Embryonal tumor with abundant neuropil and true rosettes (ependymoblastic)
- Pituitary adenoma (rosette-like pattern)



**Perivascular pseudorosettes**

- Ependymoma
- Astroblastoma
- Angiocentric glioma
- Papillary glioneuronal tumor
- Central/extraventricular neurocytomas
- Medulloblastomas/PNETs (occasionally)
- Glioblastoma (occasionally)
- Papillary meningioma
- Pituitary adenoma

# CLINICAL AND RADIOLOGICAL PATTERNS

- Location
- Location
- Location

Real estate analogy

- Patient Age
- Radiology
- Histologic Patterns

**Table 1-1.** Common Central Nervous System Tumor Diagnoses by Location, Age, and Imaging Characteristics

| Location | Child/Young Adult | Older Adult |
|---|---|---|
| Cerebral/supratentorial | Ganglioglioma (TL, cyst-MEN, E)<br>DNT (TL, intracortical nodules)<br>PNET (solid, E)<br>AT/RT (infant, E) | Grade II-III diffuse glioma (NE, focal E)<br>GBM (E or rim E, "butterfly" mass)<br>Metastases (grey-white junctions, E or rim E)<br>Lymphoma (periventricular, E) |
| Cerebellar/infratentorial/4th v. | PA (cyst-MEN)<br>Medulloblastoma (vermis, E)<br>Ependymoma (4th v., E)<br>Choroid plexus papilloma (4th v., E)<br>AT/RT (infant, E) | Metastases (multiple, E or rim E)<br>Hemangioblastoma (cyst-MEN)<br>Choroid plexus papilloma (4th v., E) |
| Brainstem | "Brainstem glioma" (pons, ± E)<br>PA (dorsal, exophytic, cyst-MEN) | Gliomatosis cerebri (multifocal, ± E) |
| Spinal cord (intra-medullary) | Ependymoma (E, ± syrinx)<br>PA (cystic, E)<br>Drop metastases (cauda equina, E)<br>MPE (filum terminale, E) | Ependymoma (E, ± syrinx)<br>Diffuse astrocytoma (ill-defined, ± E)<br>MPE (filum terminale, E)<br>Paraganglioma (filum terminale, E) |
| Spinal cord (intradural, extramedullary) | Clear cell meningioma (± dural tail, E)<br>Schwannoma (NF2, nerve origin, dumbbell shape, E)<br>Drop metastases (leptomeningeal, E) | Schwannoma (nerve origin, dumbbell shape, E)<br>Meningioma (± dural tail, E) |
| Spinal cord (extradural) | Bone tumor spread (EWS/PNET, usually E)<br>Meningioma (± dural tail, E)<br>Abscess (E)<br>Vascular malformations (dilated vessels on imaging, ± E) | Herniated disc (T1-spin echo MRI, NE)<br>Postoperative scar (E)<br>Secondary lymphoma (E)<br>Metastases (E)<br>Abscess (E) |
| Extra-axial/dural | Secondary lymphoma/leukemia (E) | Meningioma (E with dural tail)<br>Metastases (E)<br>Secondary lymphoma/leukemia (E) |
| Intrasellar | Pituitary adenoma (solid, E)<br>Craniopharyngioma (cystic, E) | Pituitary adenoma (solid, E)<br>Craniopharyngioma (cystic, E) |

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# COMMON CLINICAL PATTERNS

- Infant with cerebral tumor
- Child/young adult with cerebral tumor
- Child/young adult with posterior fossa tumor
- Older adult with cerebral tumor
- Older adult with dural-based tumor

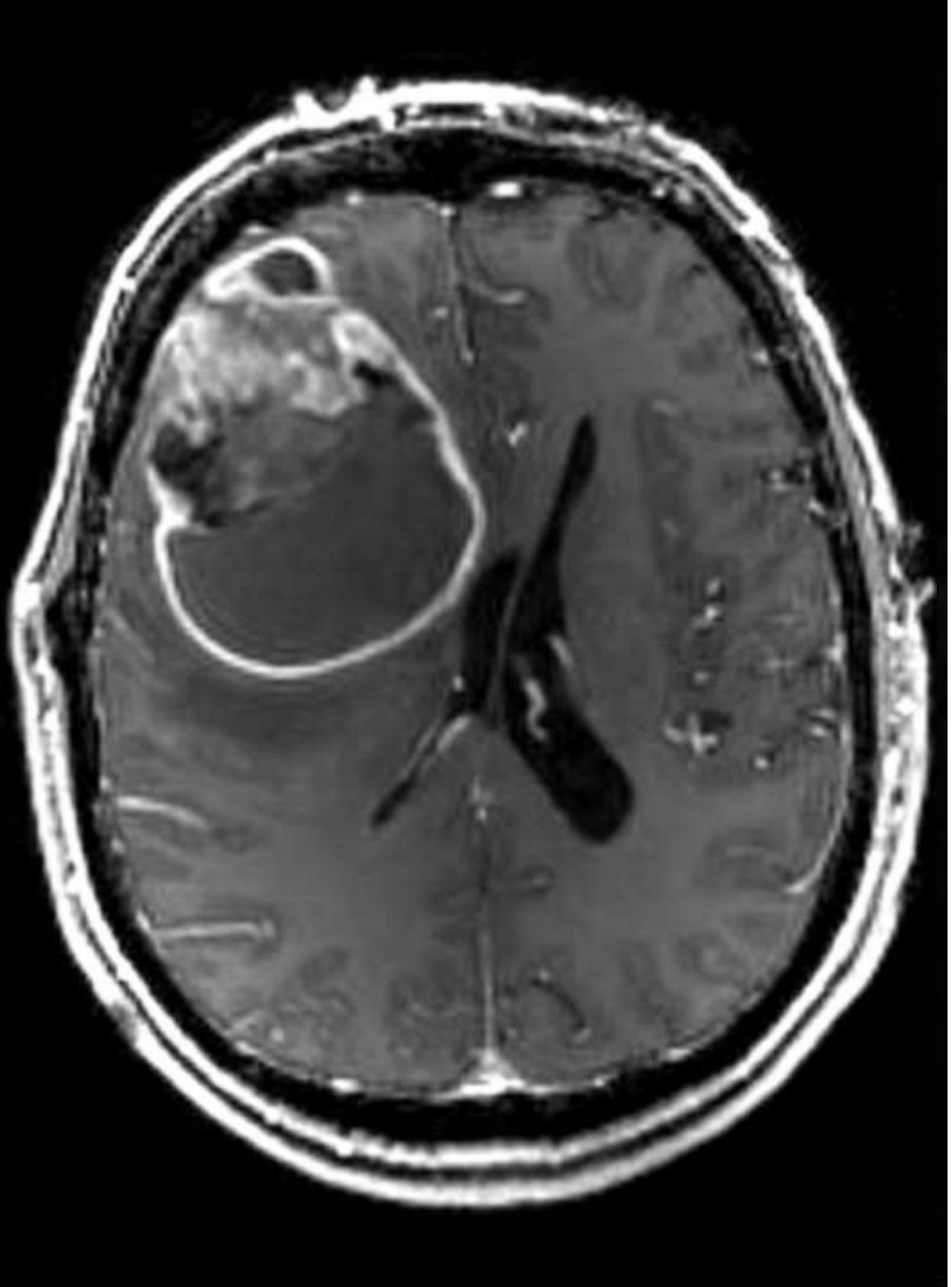
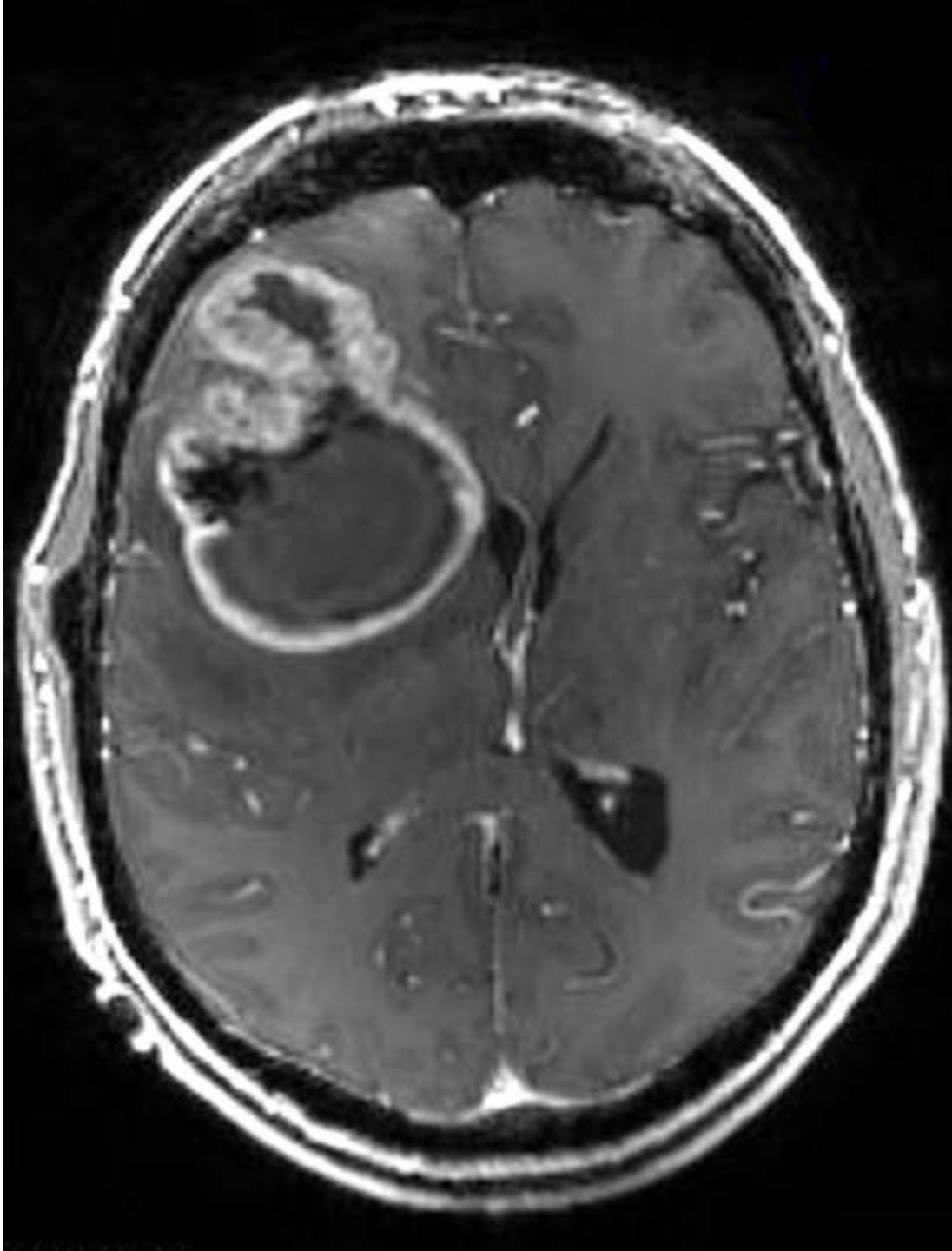
4

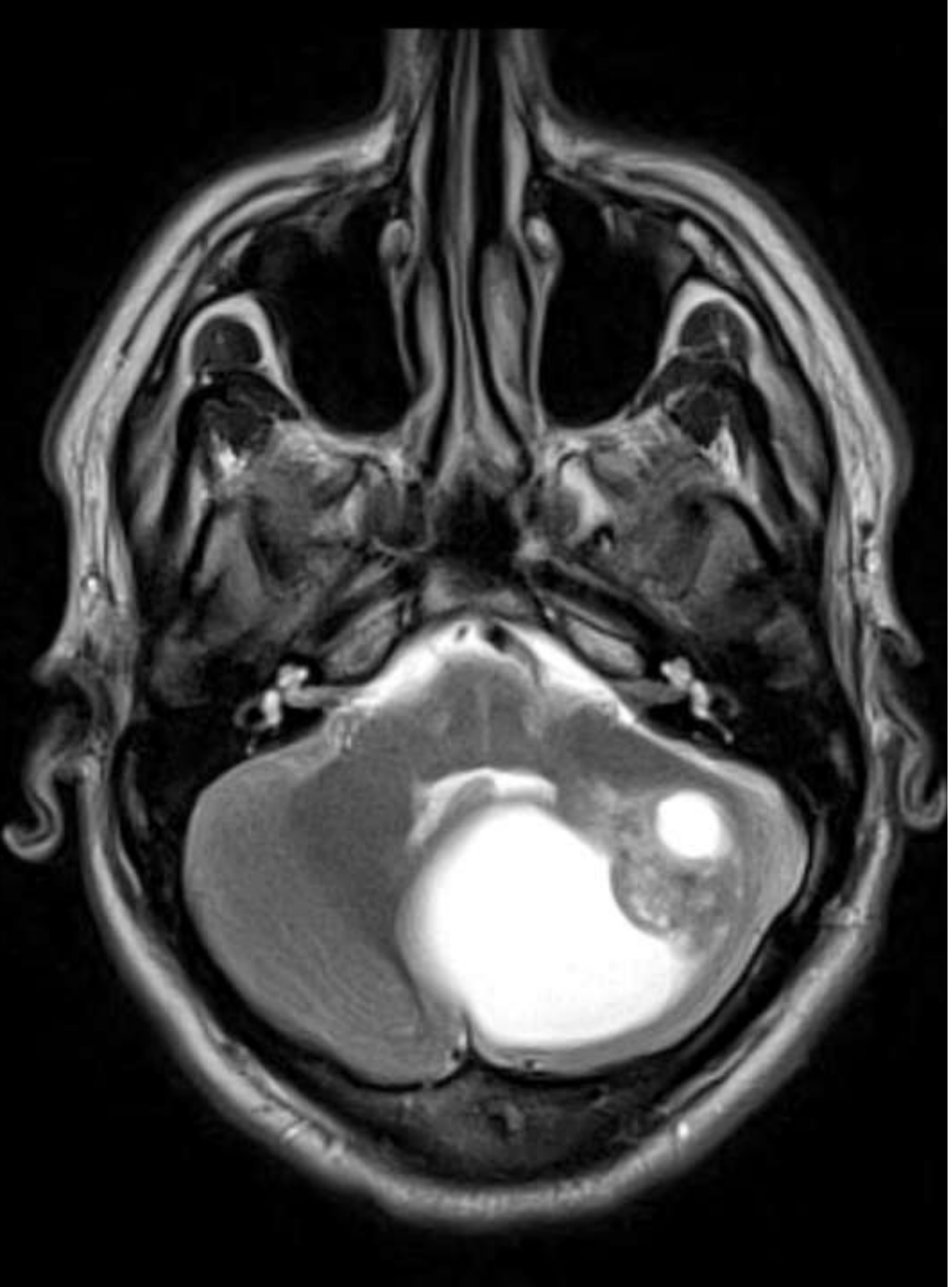
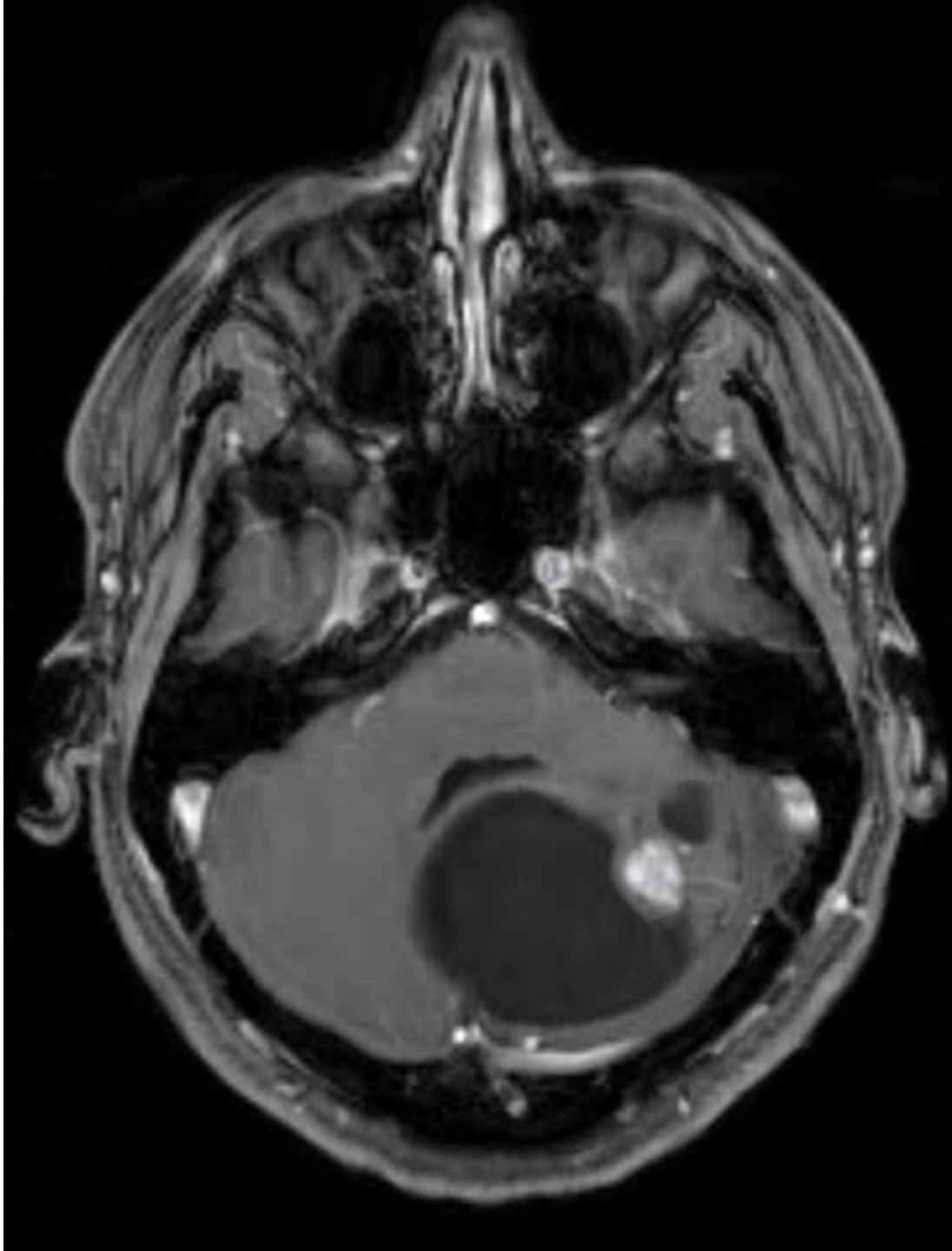
# Neuroradiology: The Surrogate of Gross Neuropathology

Franz J. Wippold II



Additionally, injectable radioisotope pharmaceuticals reveal nuances of brain metabolism in the technique known as *positron emission tomography* (PET). *Molecular imaging* uses biomarker probes coupled with imaging tools, such as PET, to explore various molecular pathways in the brain implicated in preclinical and disease states. *Optical imaging*, still in its infancy, uses the absorption and scattering of visible or infrared light to analyze the chemical composition and physiologic processes of the brain. Despite advances in digital cross-sectional and functional imaging, older techniques remain essential. For example, invasive *catheter angiography* portrays the vascular anatomy in great detail and remains a prime method of nonsurgical treatment of vascular conditions such as aneurysms. Interestingly, both noninvasive CT and MR vascular imaging have advanced sufficiently to replace catheter angiography in many diagnostic applications. All of these methods complement and supplement the traditional physical examination and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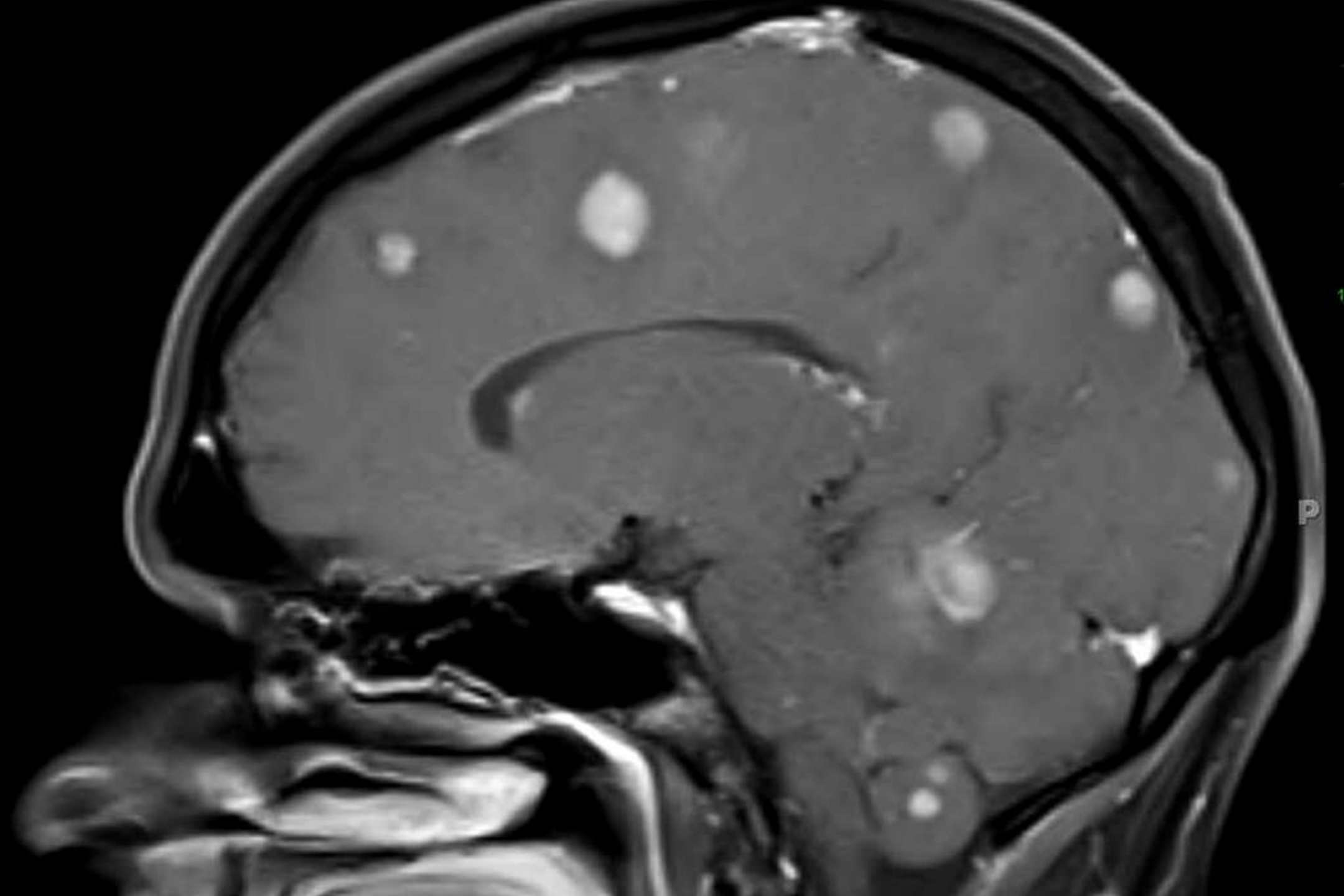
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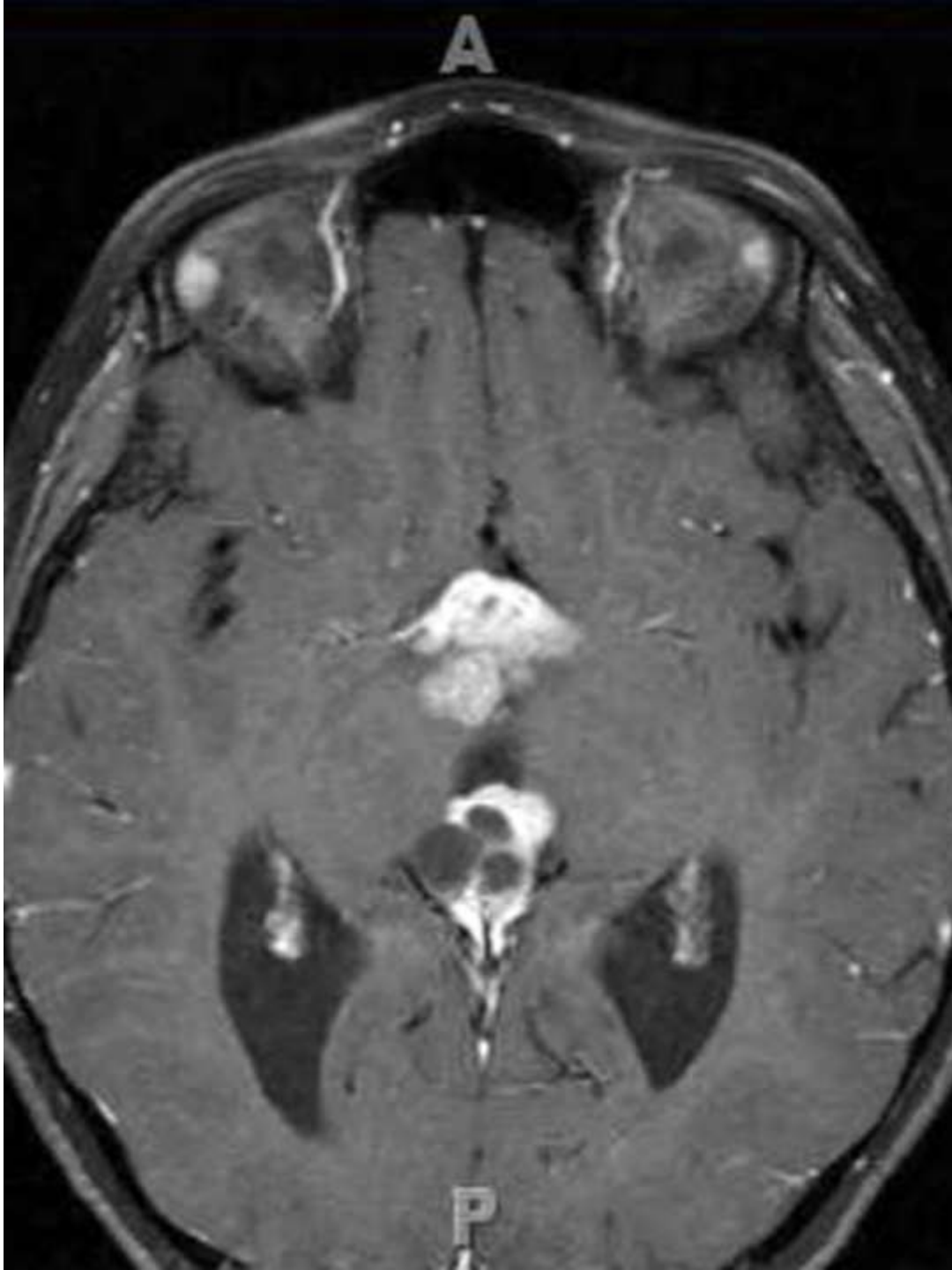
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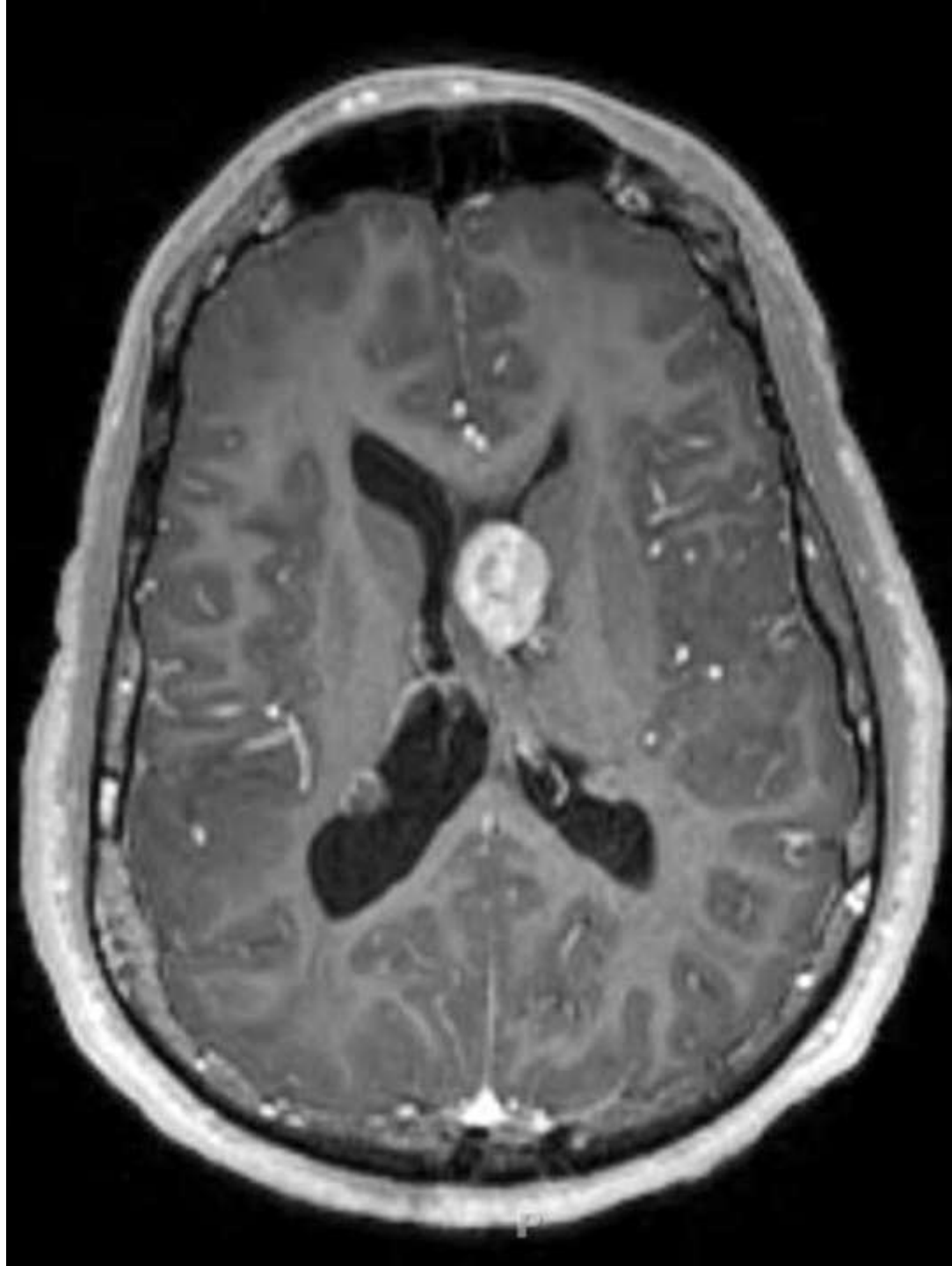
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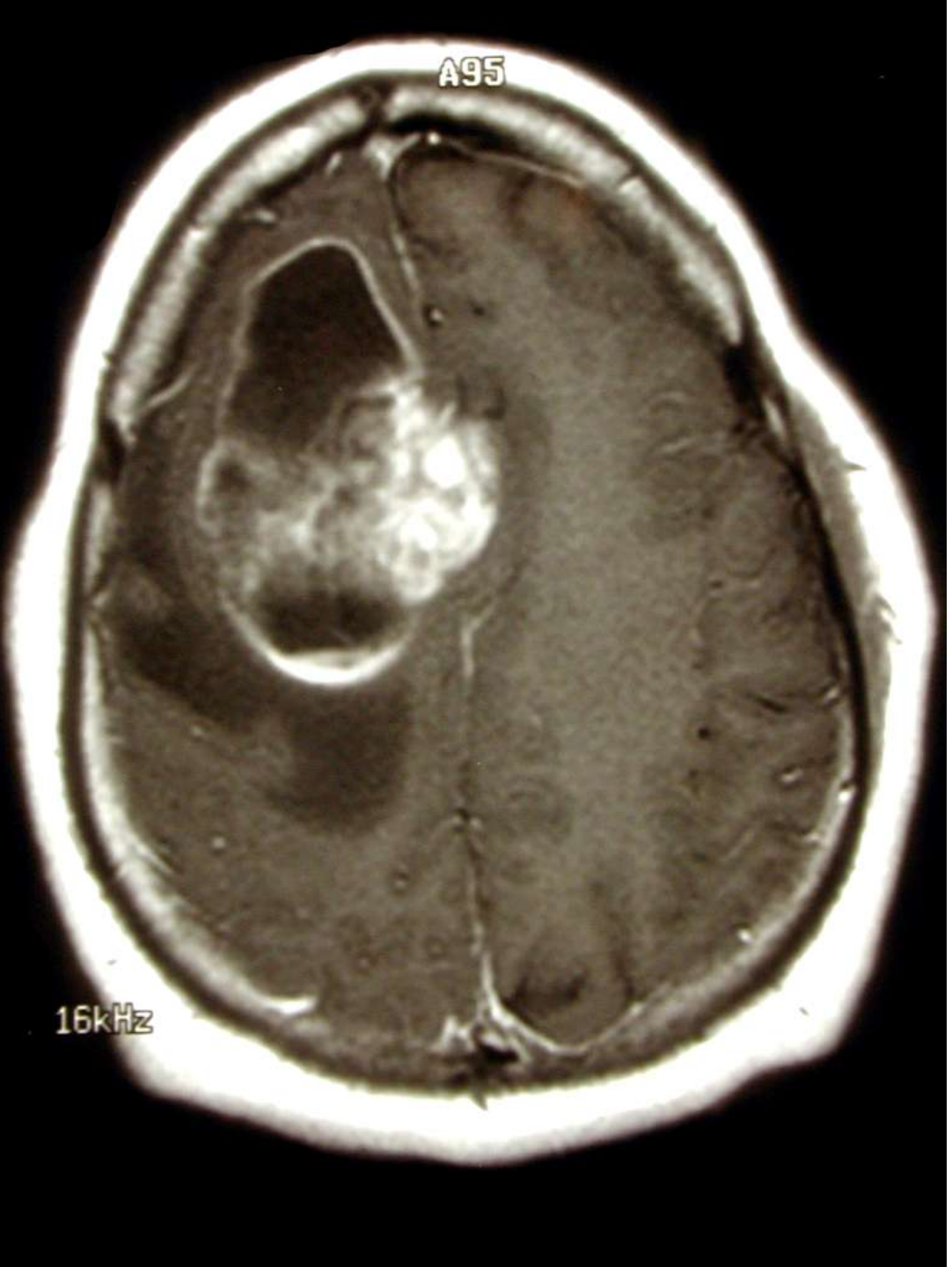
# NP CASE 1

- This 36-yo man presented with headaches and left sided weakness
- A gross total resection of a R parietal mass was performed
- He was treated with radiation and PCV chemotherapy
- After 5 years of followup, he was free of disease and a review of his pathology was requested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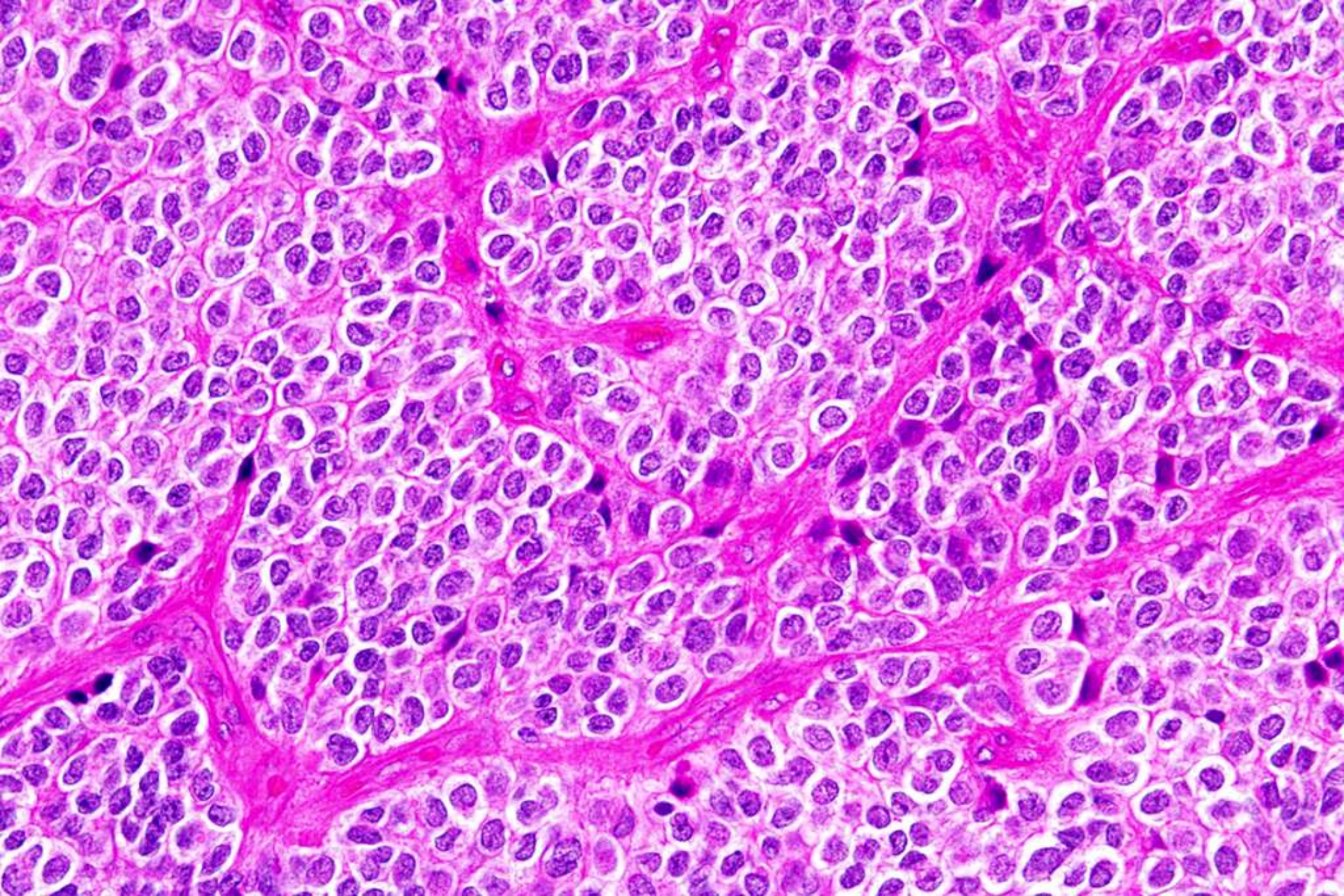
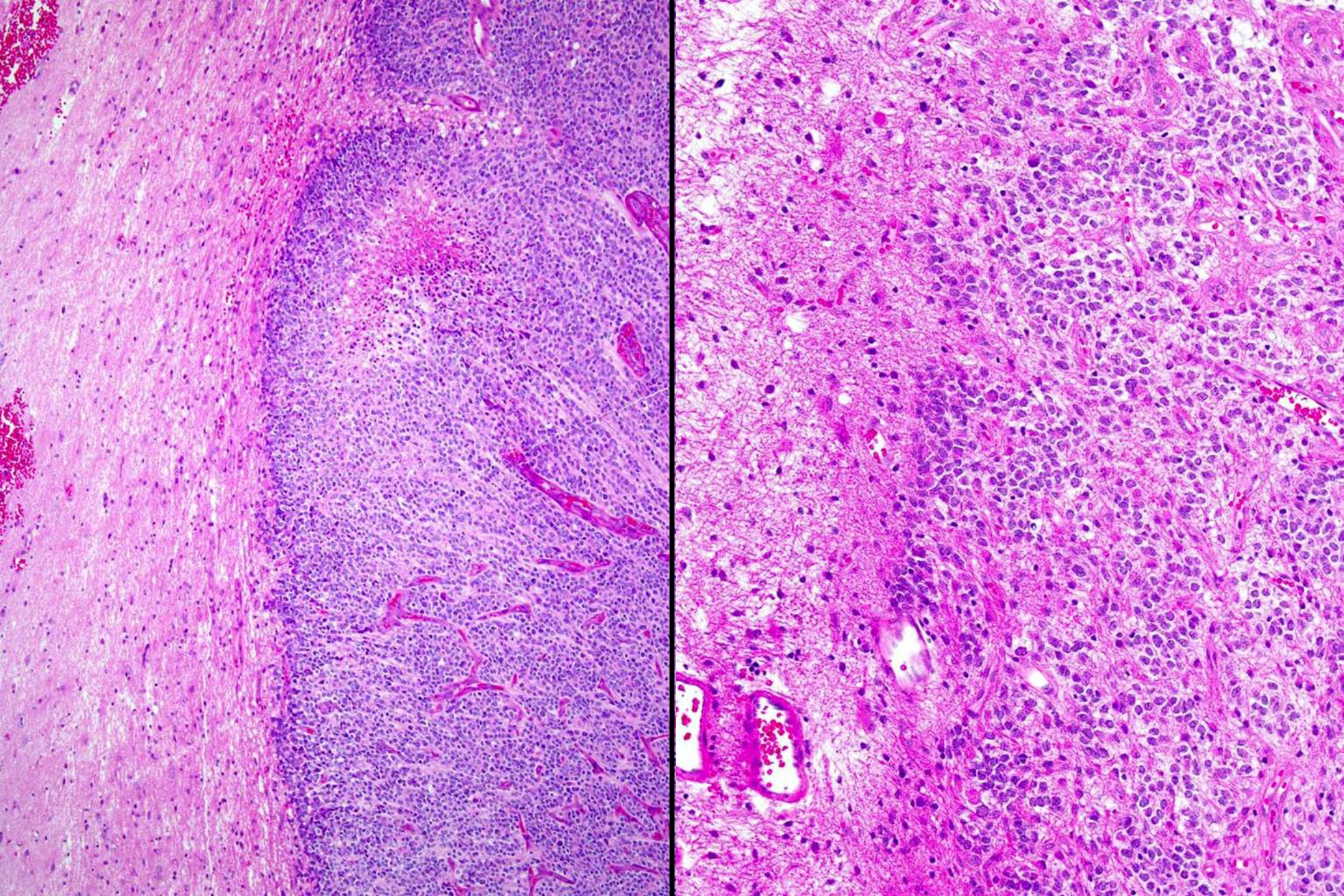
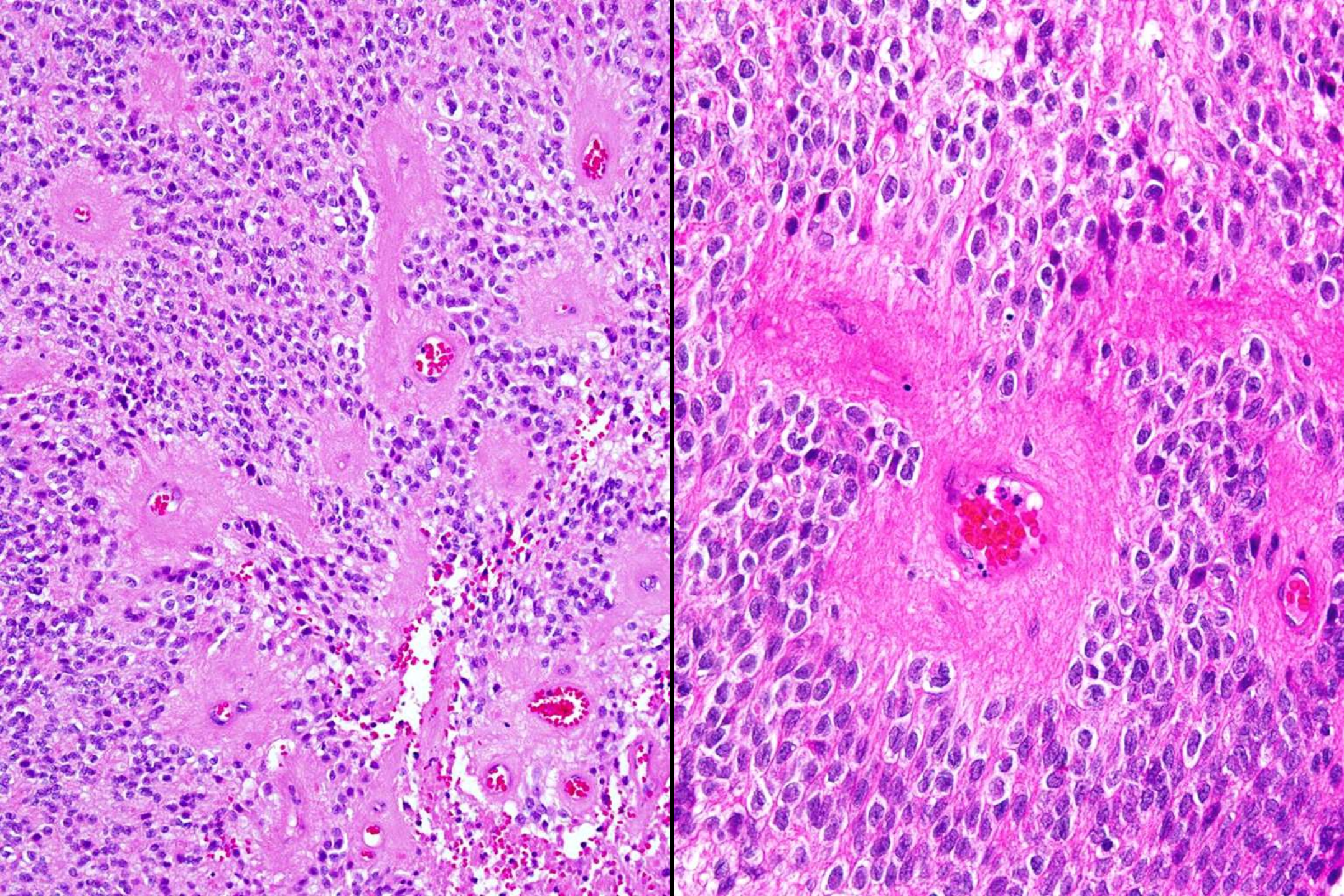
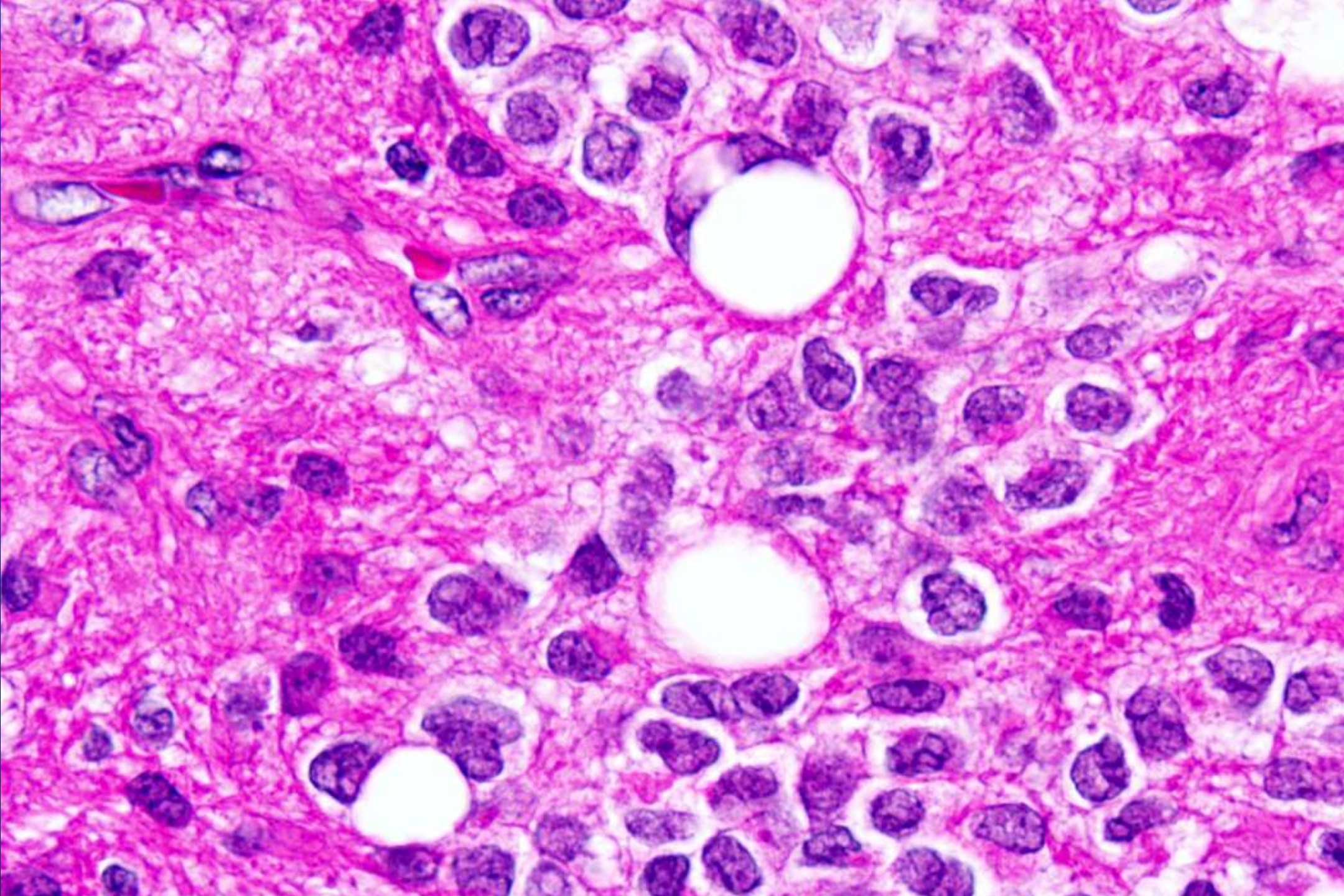
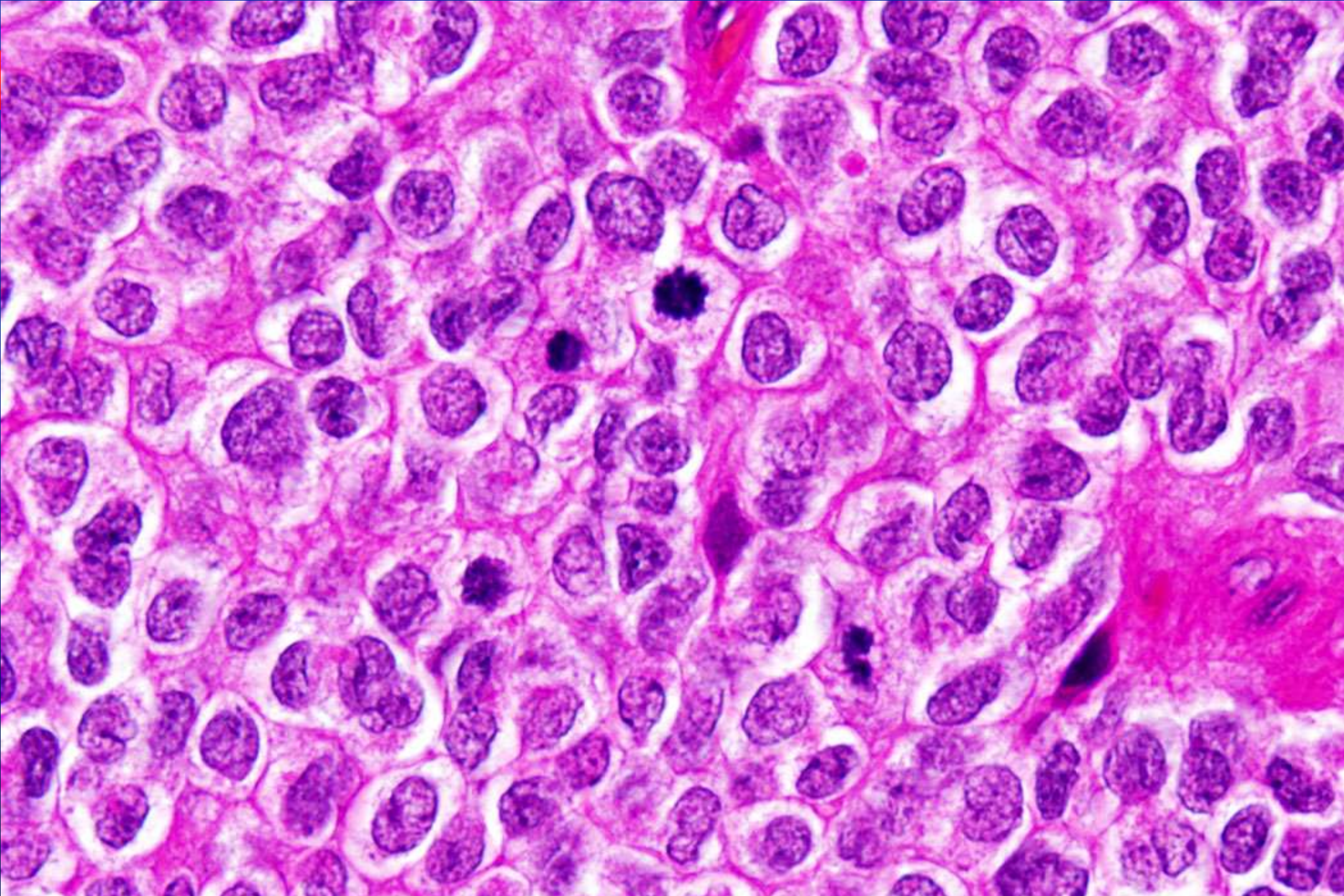
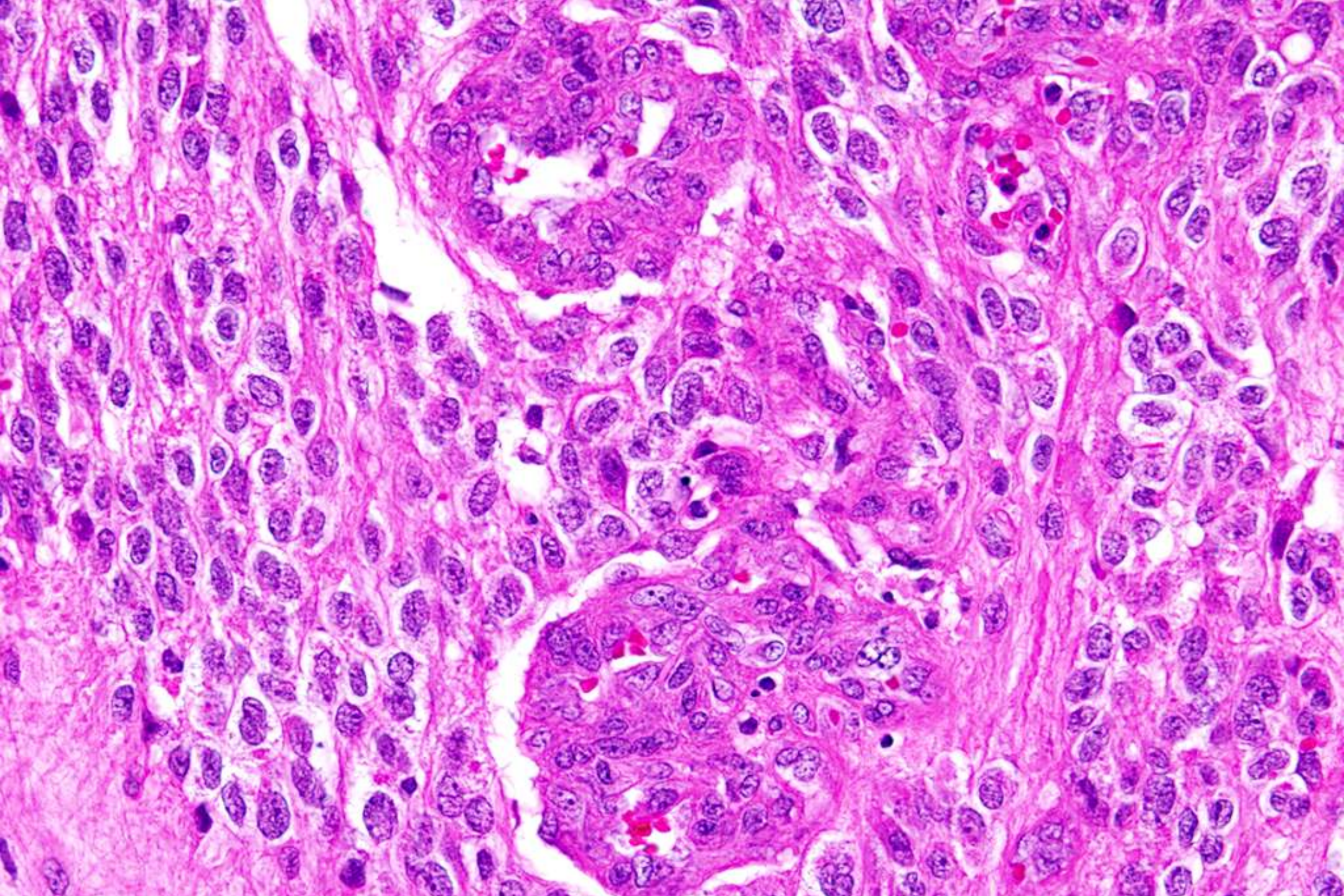










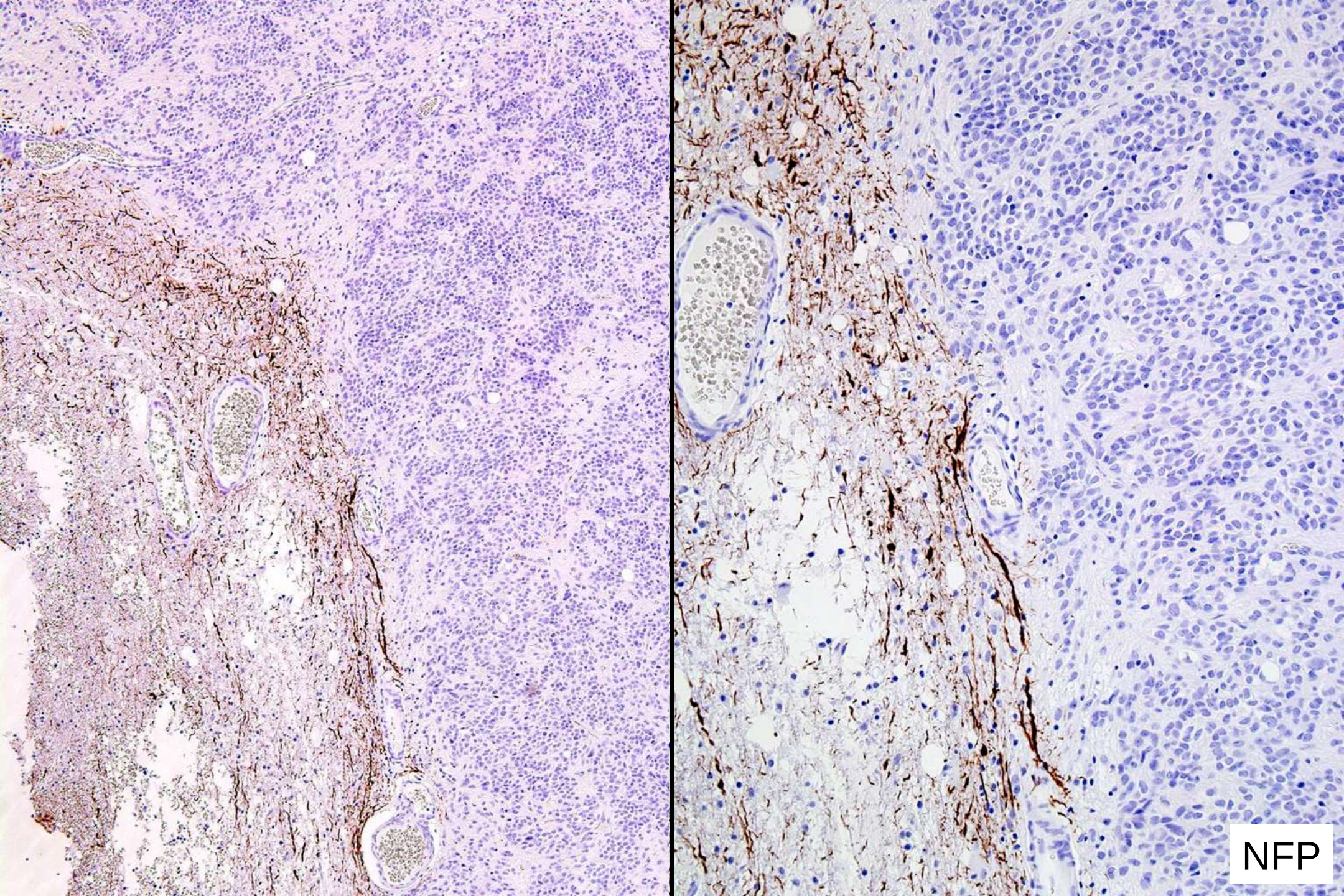


# WHICH PATTERN(S)?

- Parenchymal Infiltrate with Hypercellularity
- Solid Mass (Pure)
- Solid and Infiltrative Process
- Vasculocentric Process
- Extra-axial Mass
- Meningeal Infiltrate
- Destructive/Necrotic Process
- Subtle Pathology or Near Normal Biopsy

# WHAT IS YOUR FAVORED DIAGNOSIS?

- Anaplastic oligodendroglioma, WHO grade III
- Anaplastic ependymoma, WHO grade III
- Metastatic clear cell carcinoma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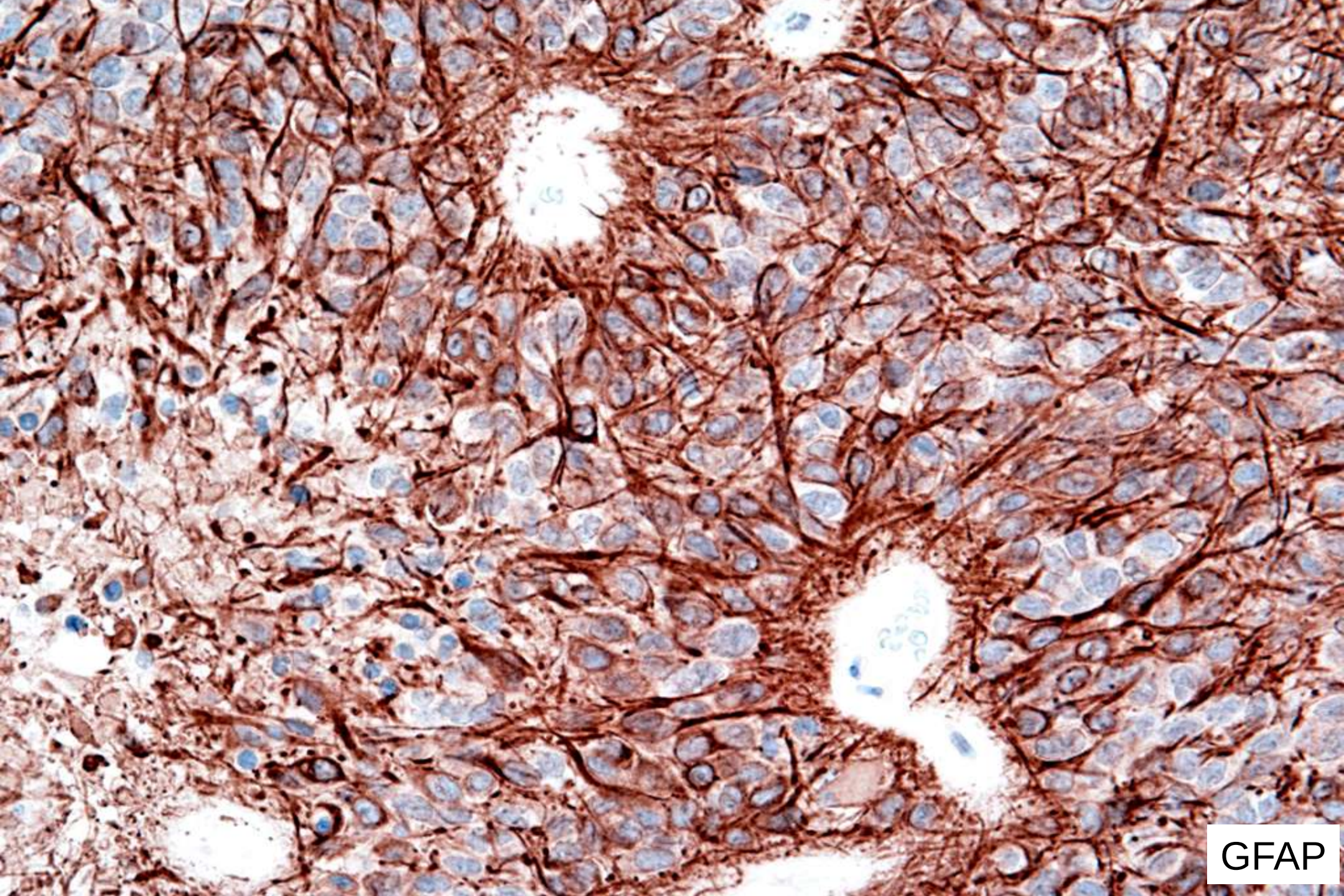
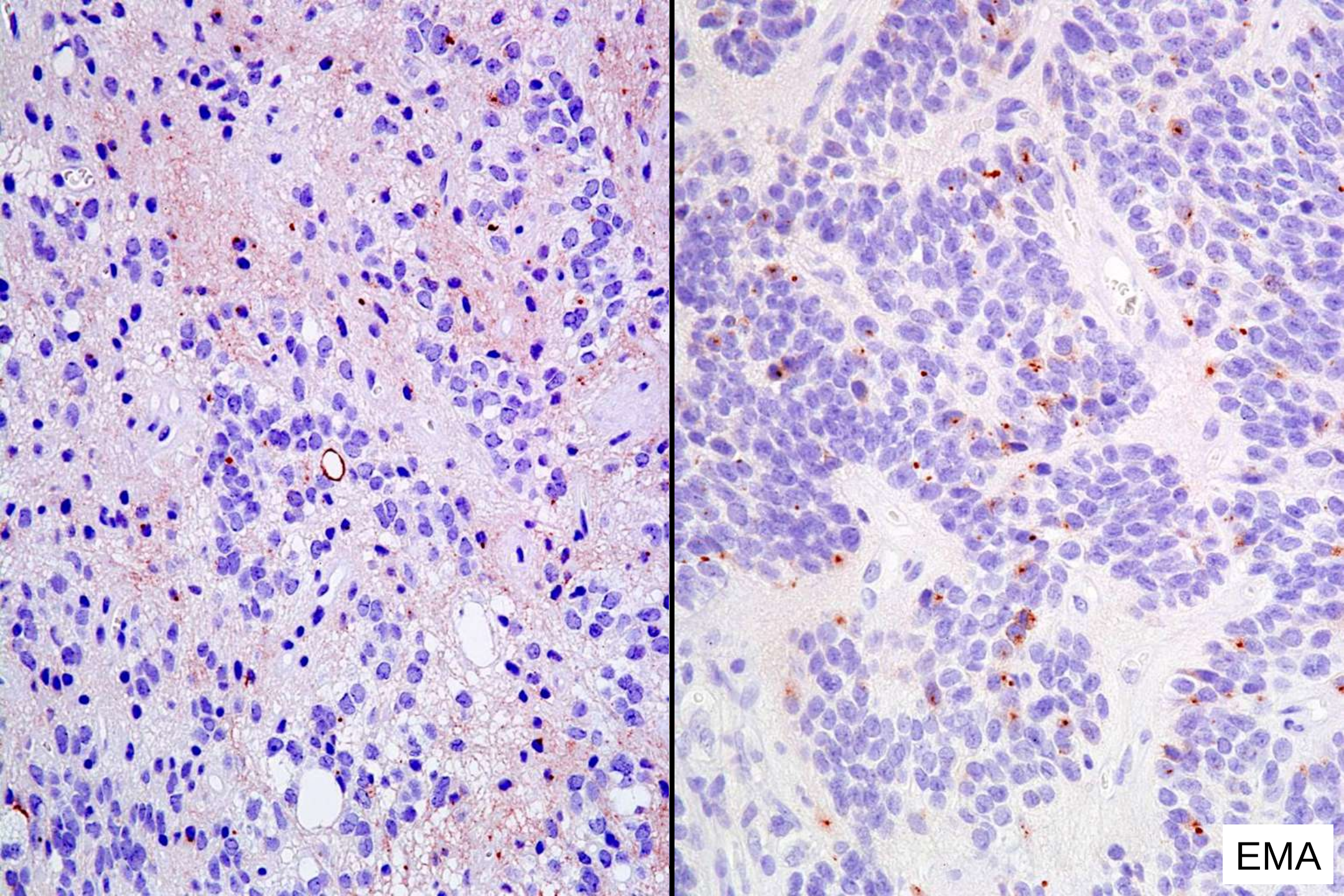

GFAP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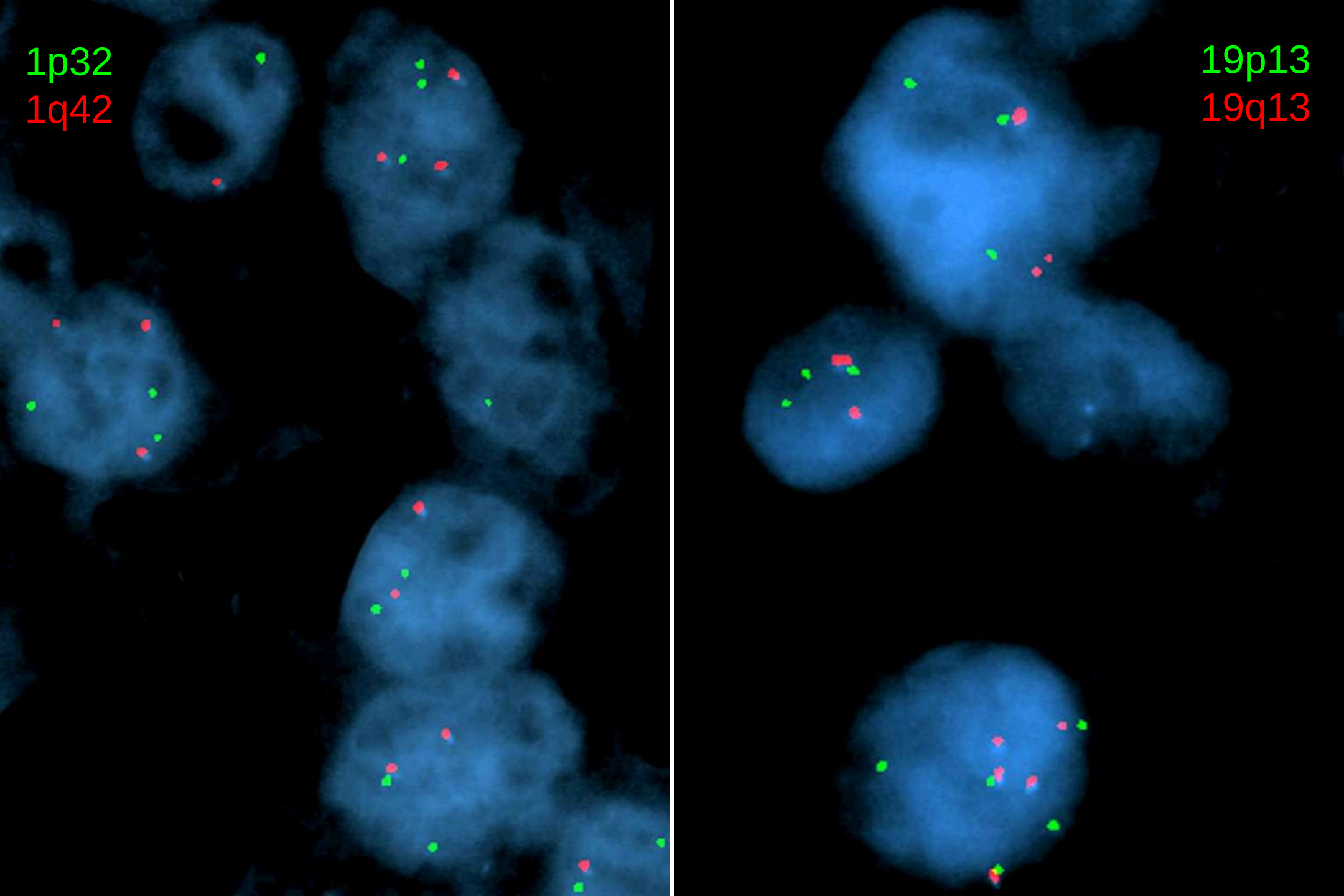
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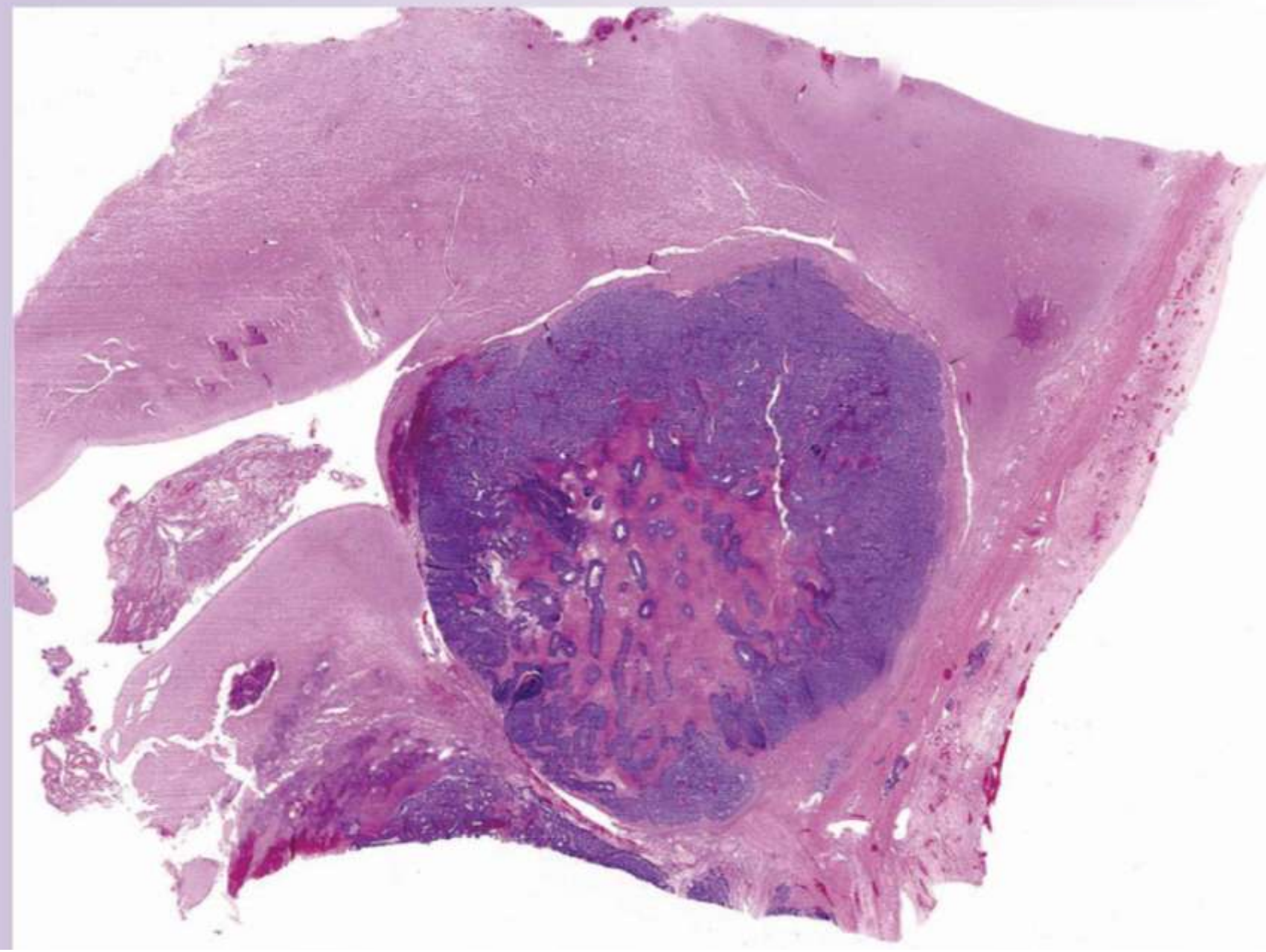
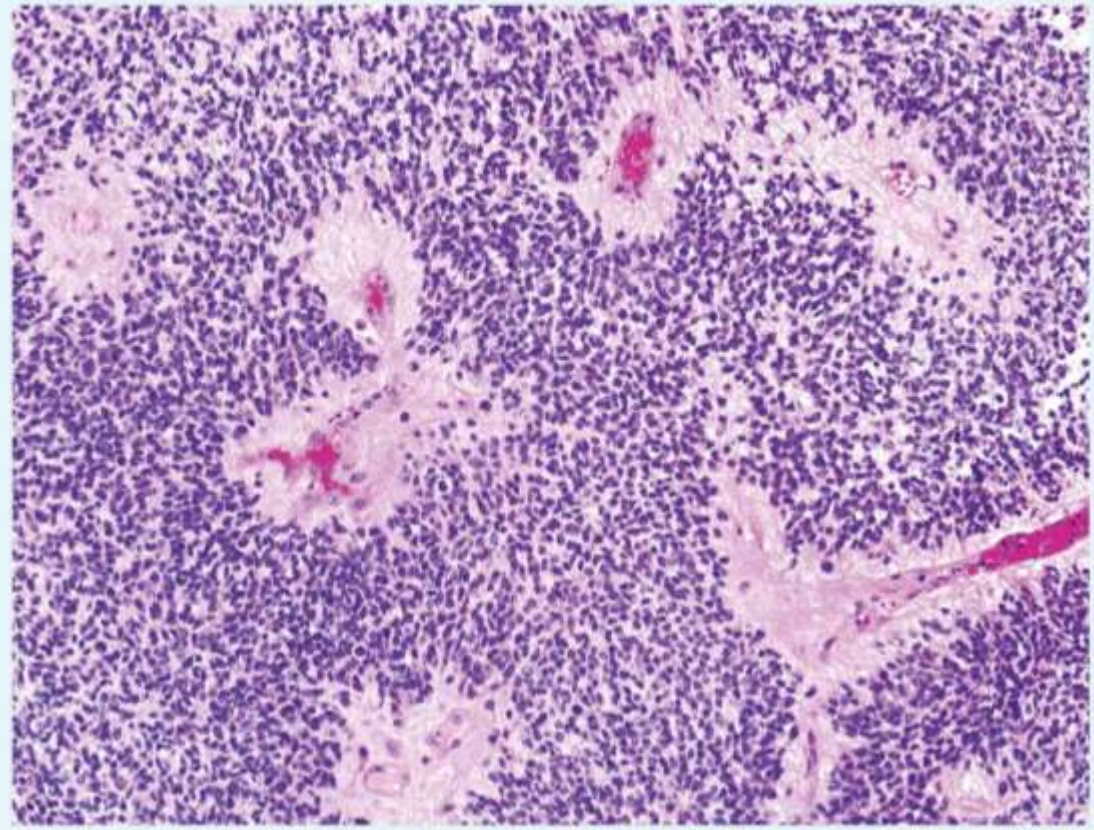
# DX: ANAPLASTIC EPENDYMOMA, CLEAR CELL VARIANT, WHO GRADE III

## Pattern 2: Solid Mass (Pure)



| Additional Findings | Diagnostic Considerations | Chapter/page |
|---|---|---|
| Mucin-filled glands | Metastatic adenocarcinoma | (Ch. 13) |
| Perivascular pseudorosettes | Subependymal giant-cell astrocytoma | (Ch. 5) |
| | → Ependymoma | (Ch. 6) |
| | Central or extraventricular neurocytoma | (Ch. 7) |
| | Pineocytoma | (Ch. 8) |
| | Metastasis (neuroendocrine) | (Ch. 13) |
| | Paraganglioma | (Ch. 13) |
| | Pituitary adenoma | (Ch. 18) |
| Nodularity | Subependymoma | (Ch. 6) |
| | Metastasis (neuroendocrine) | (Ch. 13) |
| | Paraganglioma | (Ch. 13) |
| | Pituitary adenoma | (Ch. 18) |
| Gliofibrillary processes | Subependymal giant-cell astrocytoma | (Ch. 5) |
| | → Ependymoma | (Ch. 6) |
| | Subependymoma | (Ch. 6) |
| Papillary pattern | Choroid plexus papilloma | (Ch. 6) |
| | Papillary ependymoma | (Ch. 6) |
| | Metastatic carcinoma | (Ch. 13) |
| | Pituitary adenoma | (Ch. 18) |
| Hypervascularity | Choroid plexus papilloma | (Ch. 6) |
| | Hemangioblastoma | (Ch. 10) |
| Neuropil/neuronal rosettes | Central or extraventricular neurocytoma | (Ch. 7) |
| | Pineocytoma | (Ch. 8) |

| | | |
|---|---|---|
| | Pituitary adenoma | **(Ch. 18)** |
| Gliofibrillary processes | Subependymal giant-cell astrocytoma | **(Ch. 5)** |
| | Ependymoma | **(Ch. 6)** |
| | Subependymoma | **(Ch. 6)** |
| Papillary pattern | Choroid plexus papilloma | **(Ch. 6)** |
| | Papillary ependymoma | **(Ch. 6)** |
| | Metastatic carcinoma | **(Ch. 13)** |
| | Pituitary adenoma | **(Ch. 18)** |
| Hypervascularity | Choroid plexus papilloma | **(Ch. 6)** |
| | Hemangioblastoma | **(Ch. 10)** |
| Neuropil/neuronal rosettes | Central or extraventricular neurocytoma | **(Ch. 7)** |
| | Pineocytoma | **(Ch. 8)** |
| Adjacent piloid gliosis | Craniopharyngioma | **(Ch. 18)** |
| | Hemangioblastoma | **(Ch. 20)** |
| Epithelioid cytology | Choroid plexus papilloma | **(Ch. 6)** |
| | Metastatic carcinoma | **(Ch. 13)** |
| Small primitive cells | Embryonal tumor (AT/RT) | **(Ch. 9)** |
| | Metastatic carcinoma (small cell) | **(Ch. 13)** |
| Melanin pigment | Melanoma (usually metastatic) | **(Chs. 13, 16)** |
| Clear cells | → Clear cell ependymoma | **(Ch. 6)** |
| | Central/extraventricular neurocytoma | **(Ch. 7)** |
| | Pineocytoma | **(Ch. 8)** |
| | Hemangioblastoma | **(Ch. 20)** |
| | Metastatic carcinoma | **(Ch. 13)** |



**Perivascular Pseudorosettes**

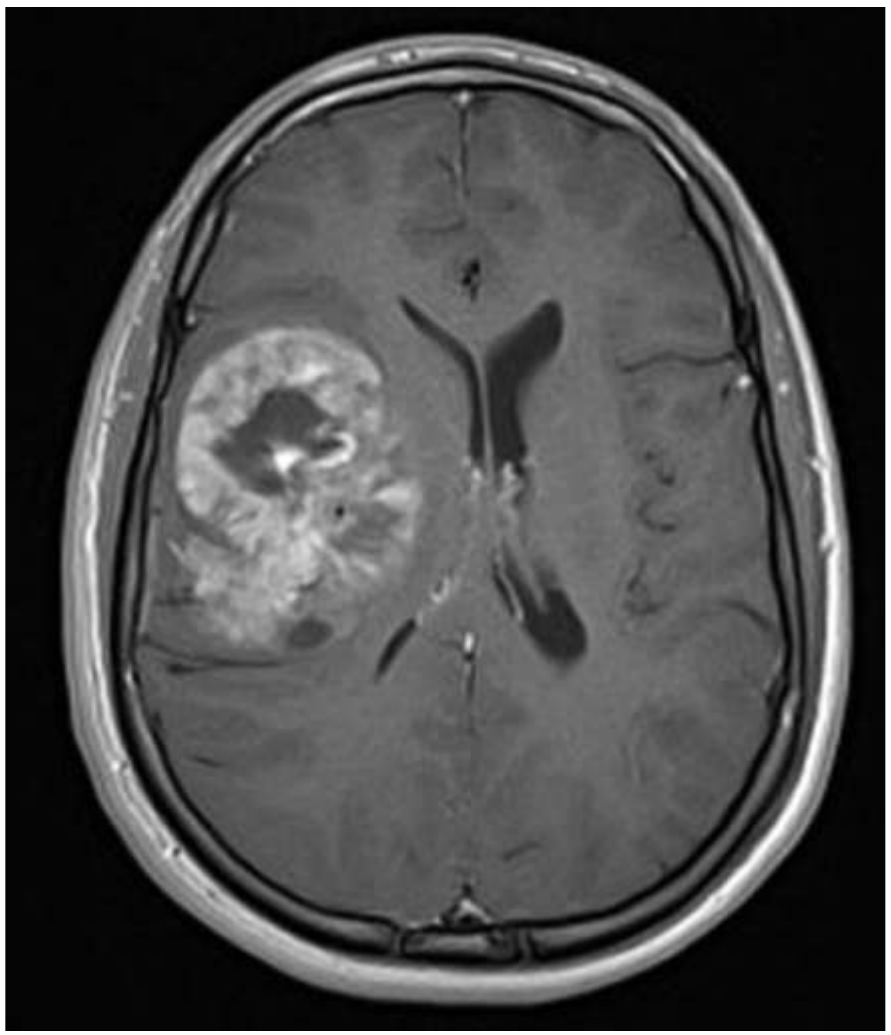
- Ependymoma
- Astroblastoma
- Angiocentric glioma
- Papillary glioneuronal tumor
- Central/extraventricular neurocytomas
- Medulloblastomas/PNETs (occasionally)
- Glioblastoma (occasionally)
- Papillary meningioma
- Pituitary adenoma

| Oligodendroglioma vs. → Clear Cell Ependymoma | |
|---|---|
| • Ill-defined margins<br>• Perineuronal satellitosis<br>• GFAP+ minigemistocytes and gliofibrillary oligodendrocytes<br>• Entrapped NFP+ axons<br>• Chromosome 1p/19q codeletion | • Sharp demarcation<br>• Vague perivascular pseudorosettes, highlighted on GFAP stain<br>• Nuclear grooves/folds<br>• Dot-like cytoplasmic EMA+ CD99+, D2-40+<br>• NFP+ axons pushed to periphery of tumor<br>• Ependymal features on EM |
| **Ependymoma vs.** | **Diffuse Astrocytoma** |
| • Sharp demarcation<br>• Perivascular pseudorosettes, highlighted on GFAP stain<br>• Dot-like cytoplasmically EMA+<br>• NFP+ axons pushed to periphery of tumor<br>• Ependymal features on EM | • Infiltrative growth pattern<br>• Secondary structures<br>• "Naked nuclei"<br>• Numerous intratumoral NFP+ axons |
| **Cellular Ependymoma vs.** | **Medulloblastoma/PNET** |
| • Solid growth pattern<br>• Low mitotic/proliferative<br>• Perivascular pseudorosettes with fibrillar processes, highlighted with GFAP<br>• Dot-like cytoplasmically EMA+<br>• NFP+ axons pushed to the periphery | • Solid and infiltrative growth patterns<br>• High mitotic/proliferative index<br>• Homer Wright rosettes and occasional pseudorosettes with deli<br>• Synaptophysin positive<br>• Ki-67 high |
| **Medulloblastoma/PNET vs.** | **Atypical Teratoid/Rhabdoid Tumor** |
| • Mostly children/young adults<br>• Solid and infiltrative growth patterns<br>• Homer Wright rosettes<br>• Retained INI1 expression<br>• Synaptophysin+, GFAP focal+, most other markers negative | • Mostly infants (<3 years)<br>• Mostly solid growth pattern<br>• Variable PNET-like, carcinoma-like, and sarcoma-like foci<br>• Rhabdoid cells present, but may be rare<br>• Loss of INI1 expression |

# EPENDYMOMAS

- Kids: 4th ventricle, supratentorial
- Adults: spinal cord
- Prognostic Variables
  - Extent of resection / location
  - Patient age (poor if <3 years old)
  - Histologic grade
  - CSF dissemination (<5%)

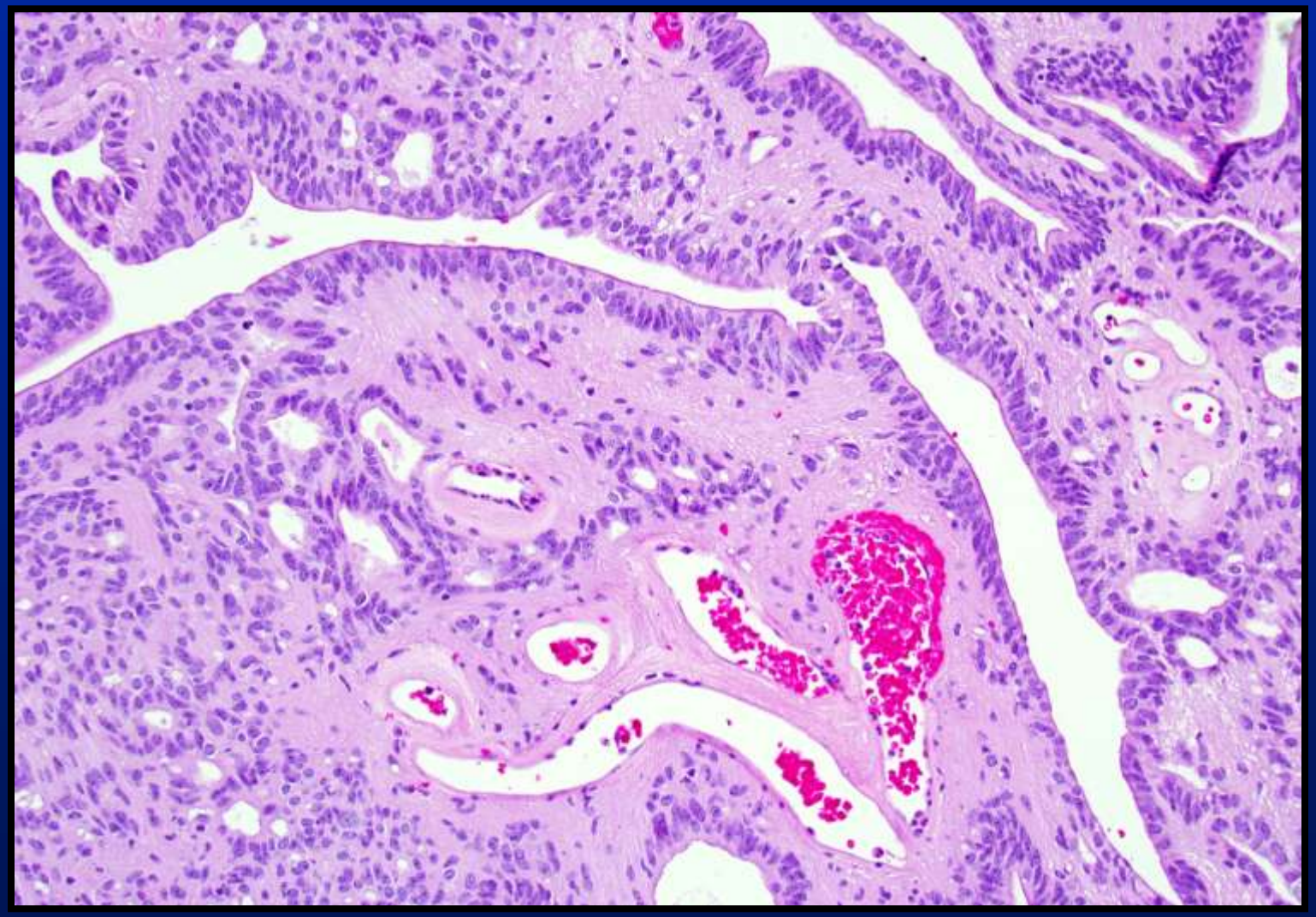
# EPENDYMOMA (II or III)



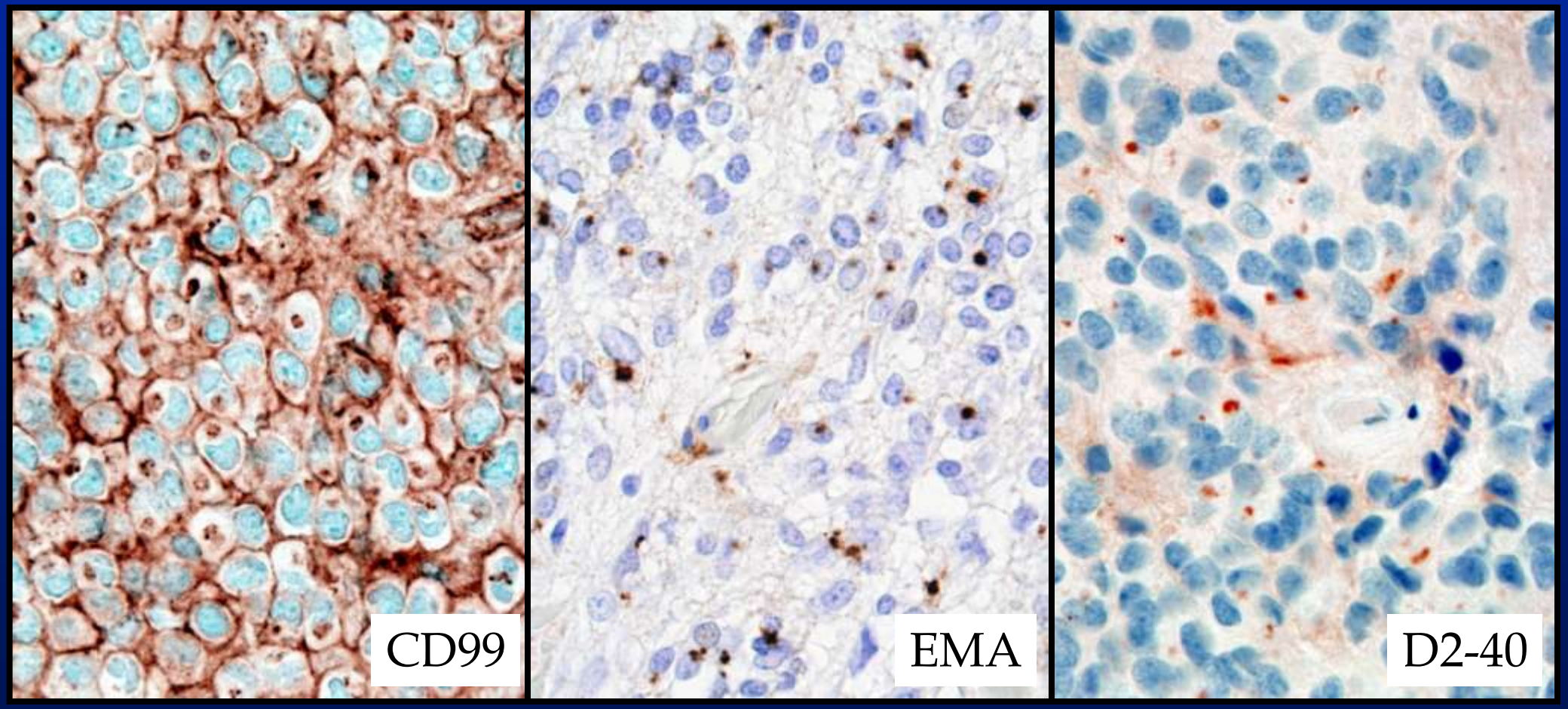
# EPENDYMOMA



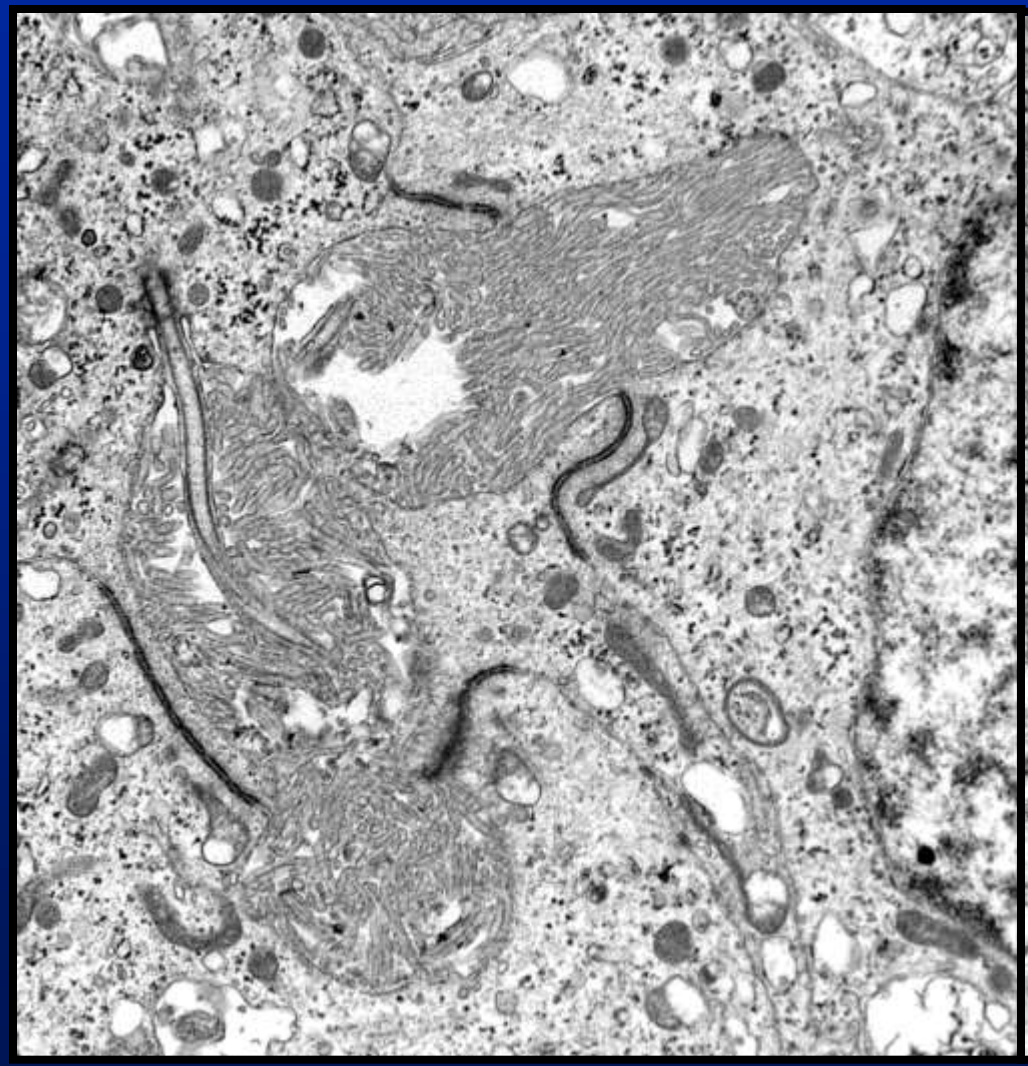

# EPENDYMOMA

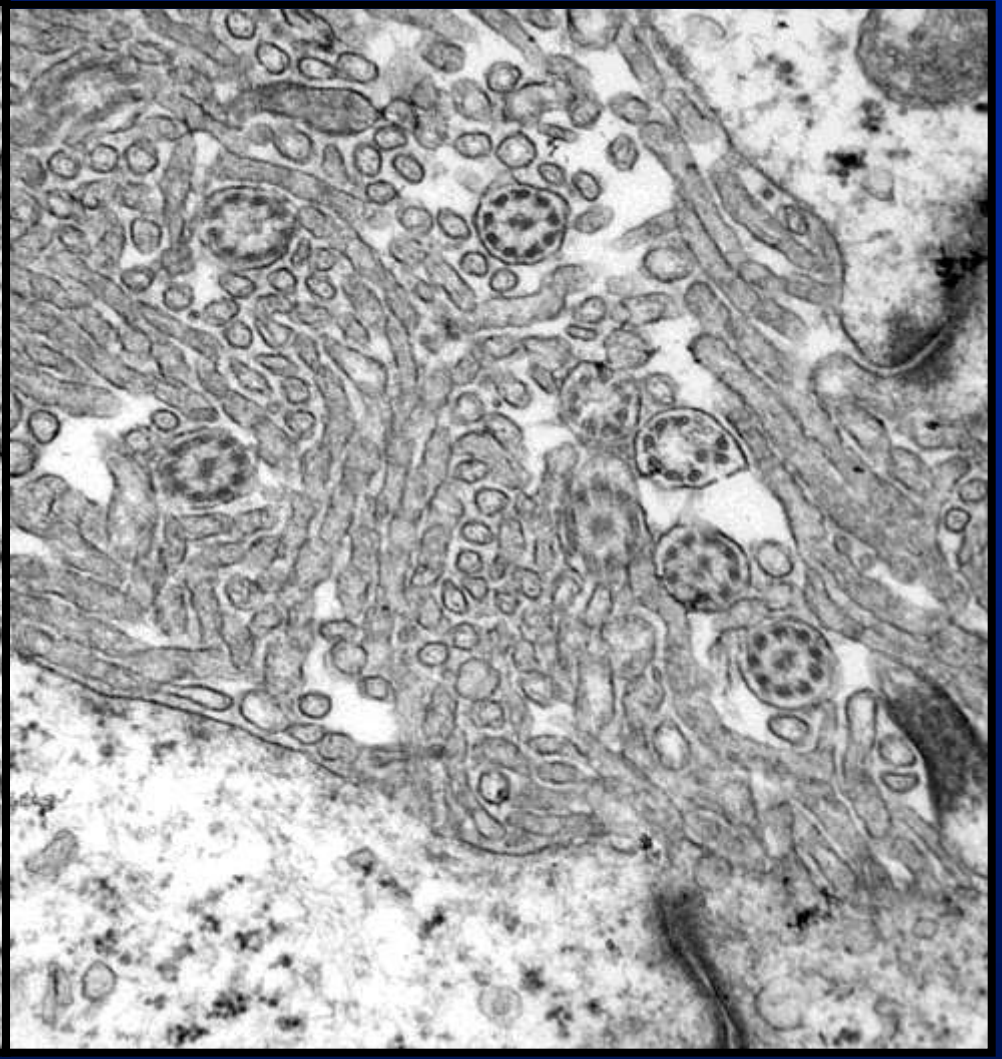


# EPENDYMOMA: IHC

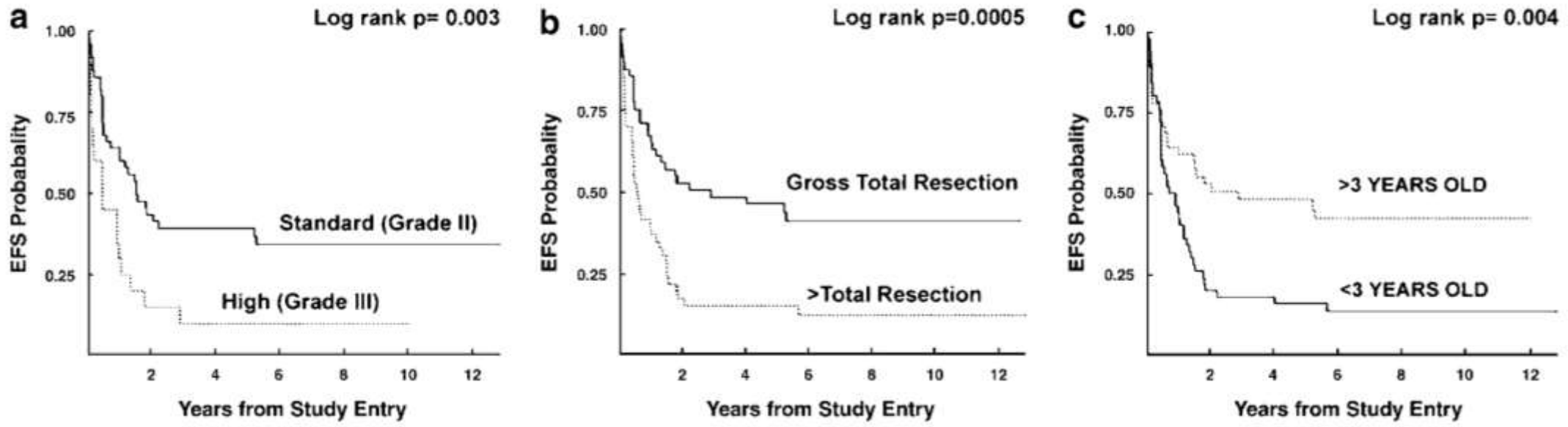


# EPENDYMOMA: EM





# PROGNOSIS




Tihan T, et al., Mod Pathol 2008: 21, 165–177

# HISTOLOGIC GRADING

Univariate Histologic Features Associated with Poor Outcome

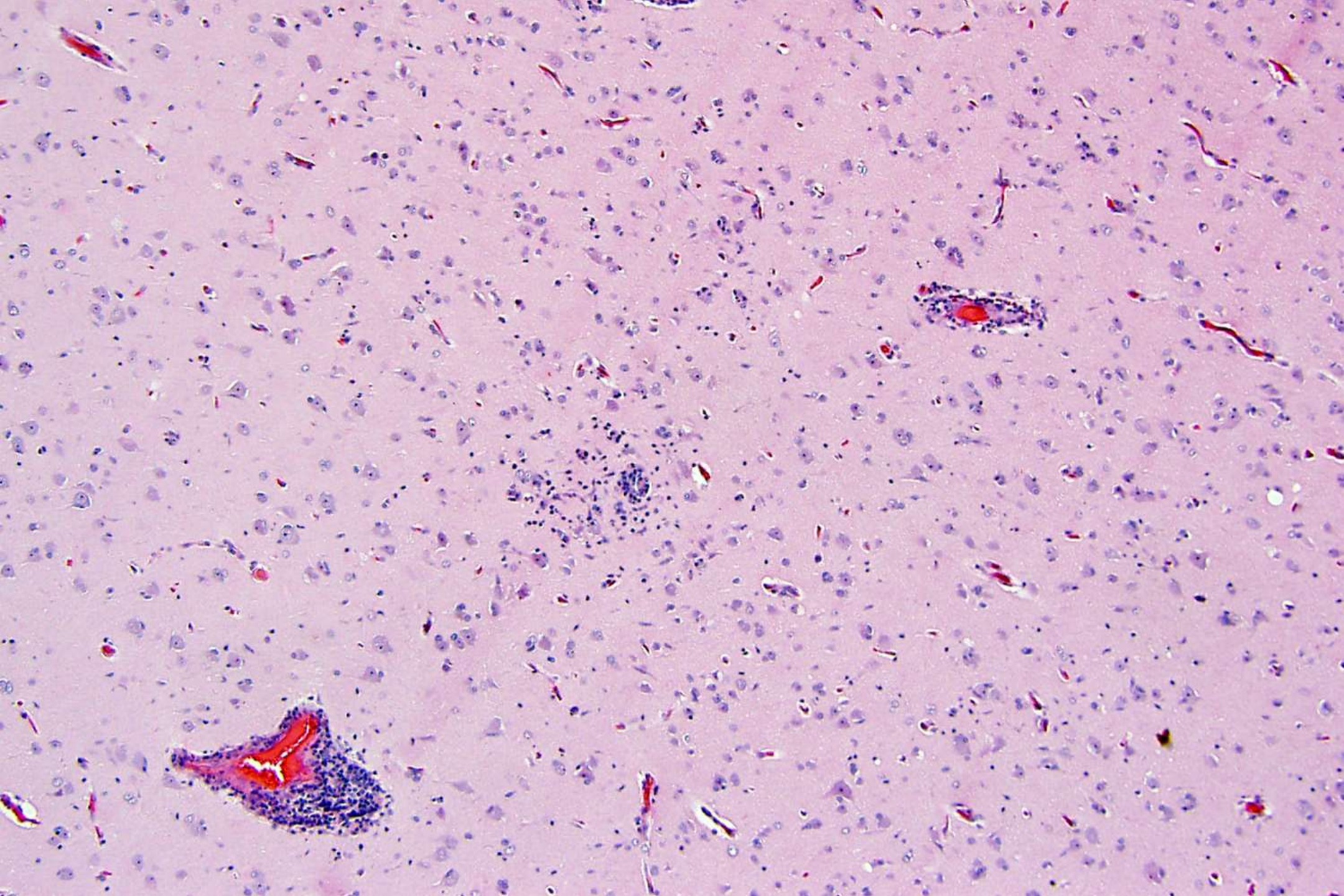
1) Hypercellularity
2) Vascular Proliferation
3) Mitoses > 4/10 HPF
4) Necrosis (pseudopalisading)

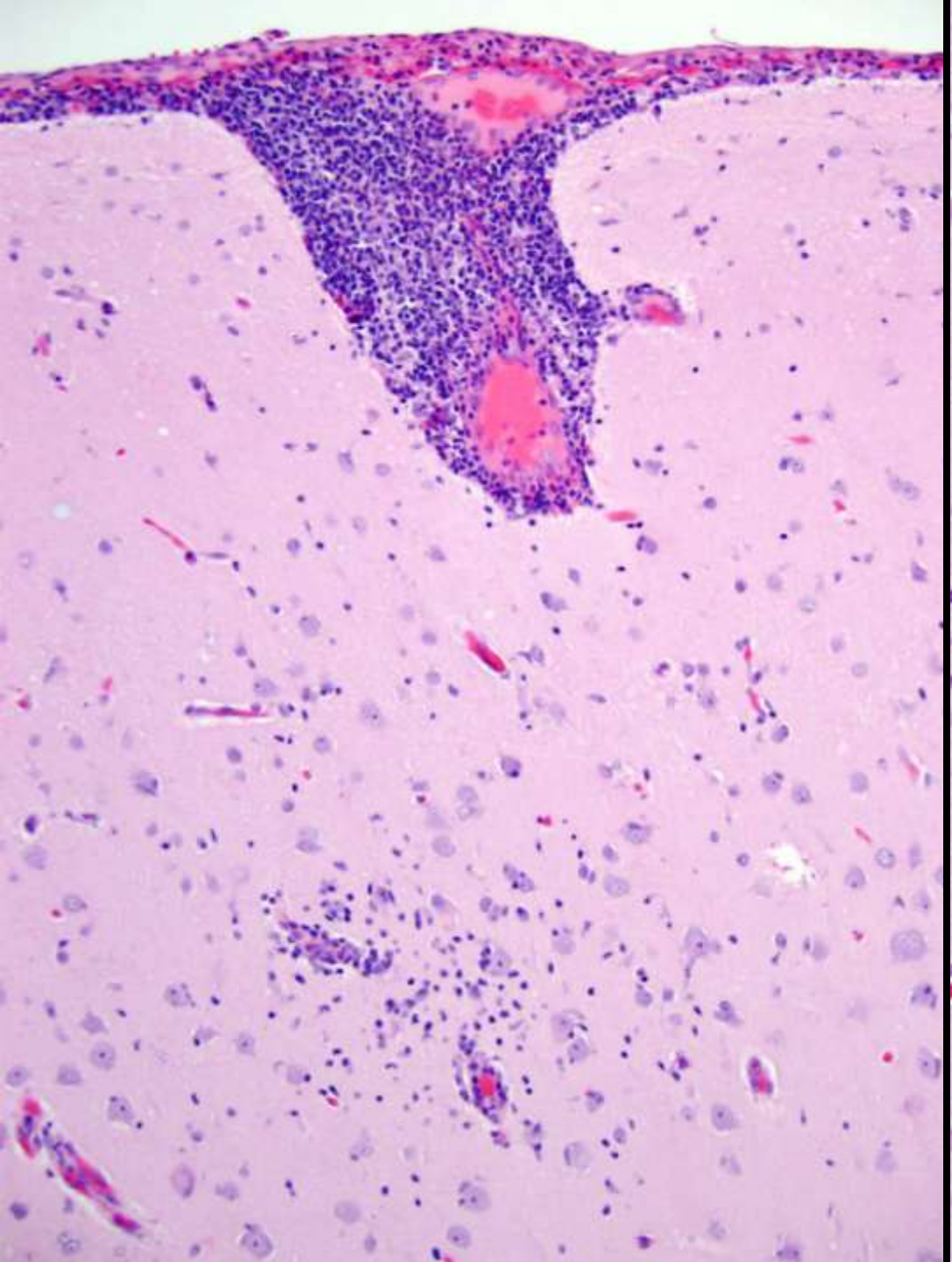
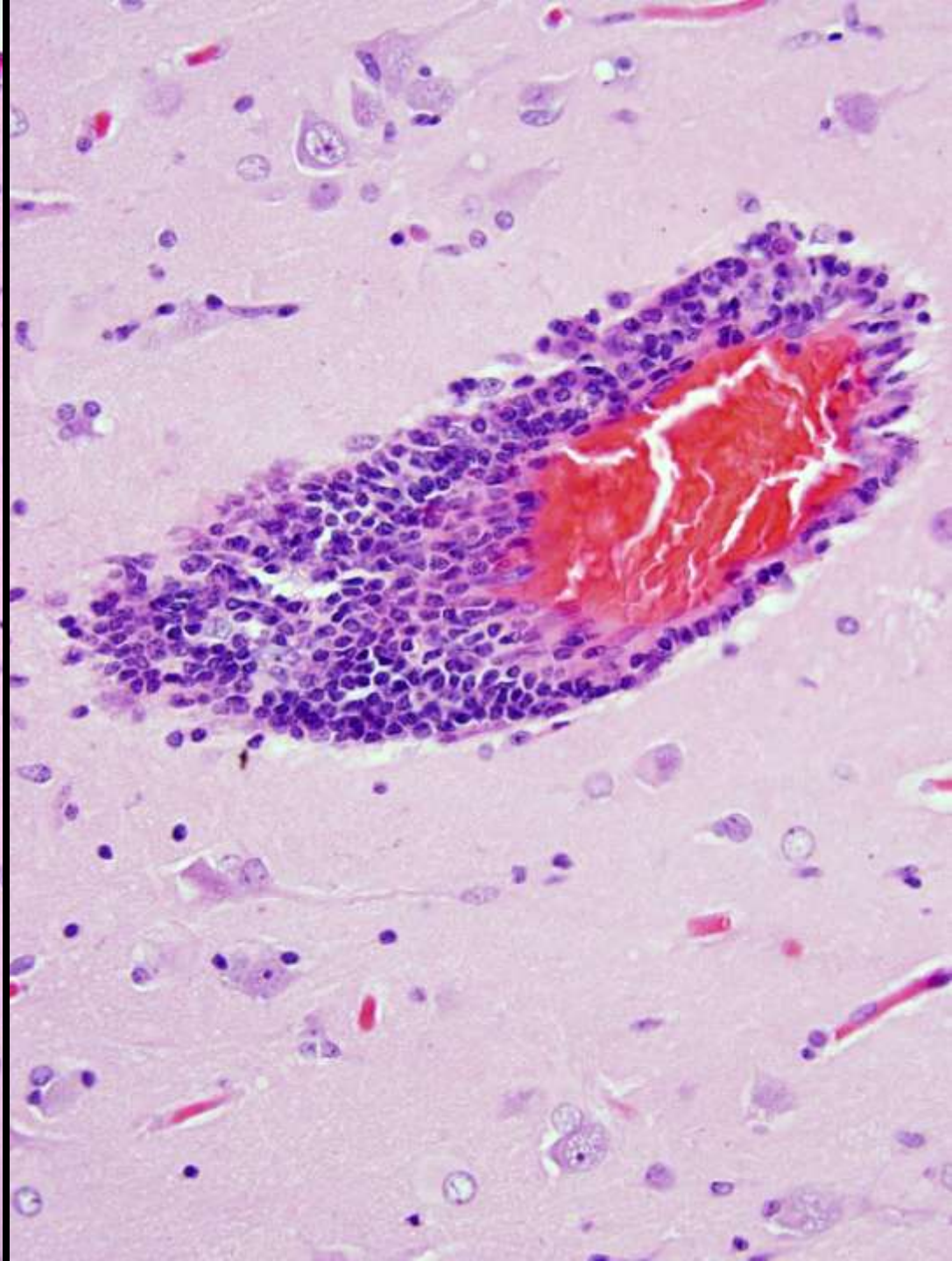
The presence of 2 of these features has been suggested as criteria for the diagnosis of Anaplastic Ependymoma, grade III.

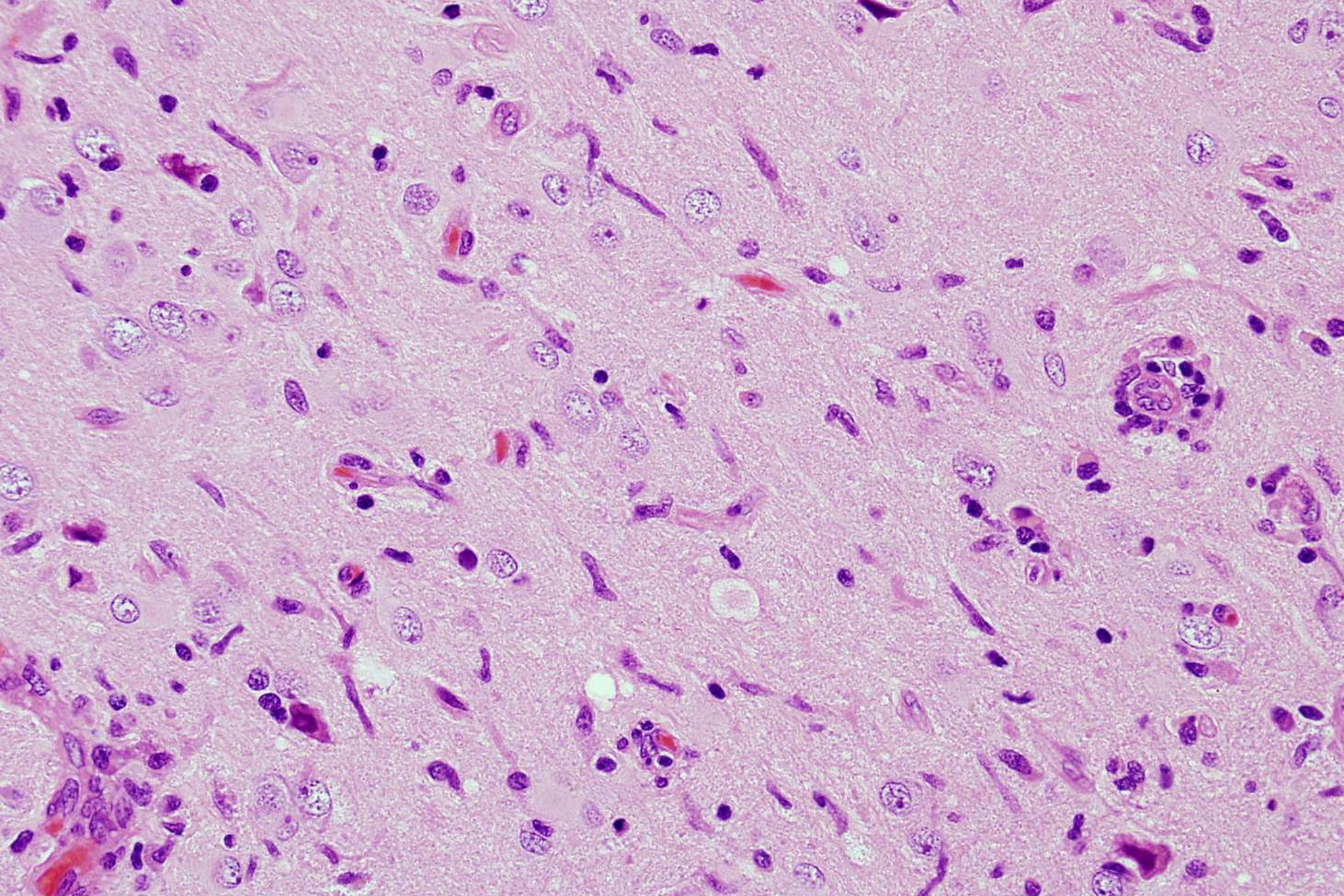
(Ho, et al J. Neuro-Oncol 2001, 55:77)

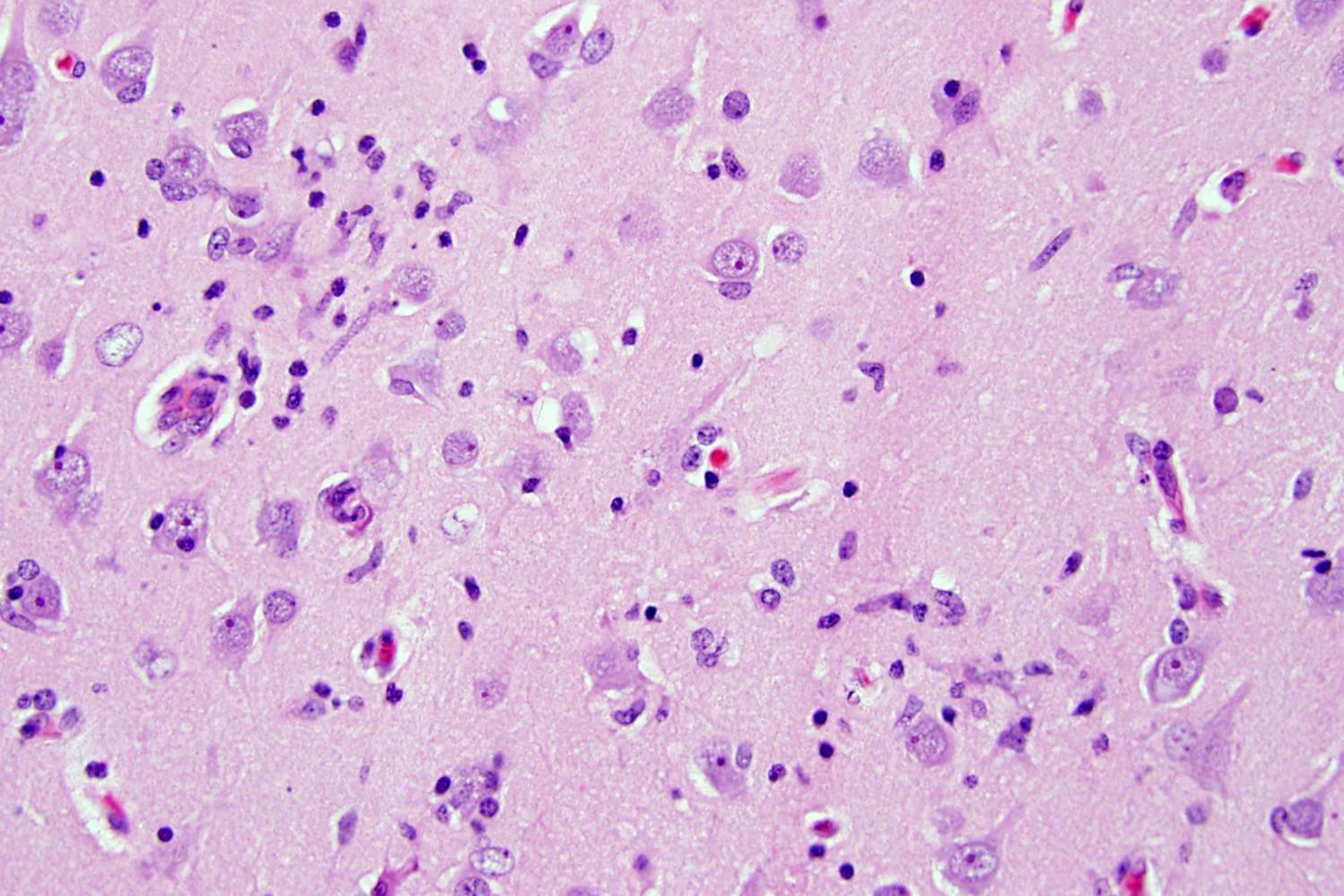
# NP CASE 2

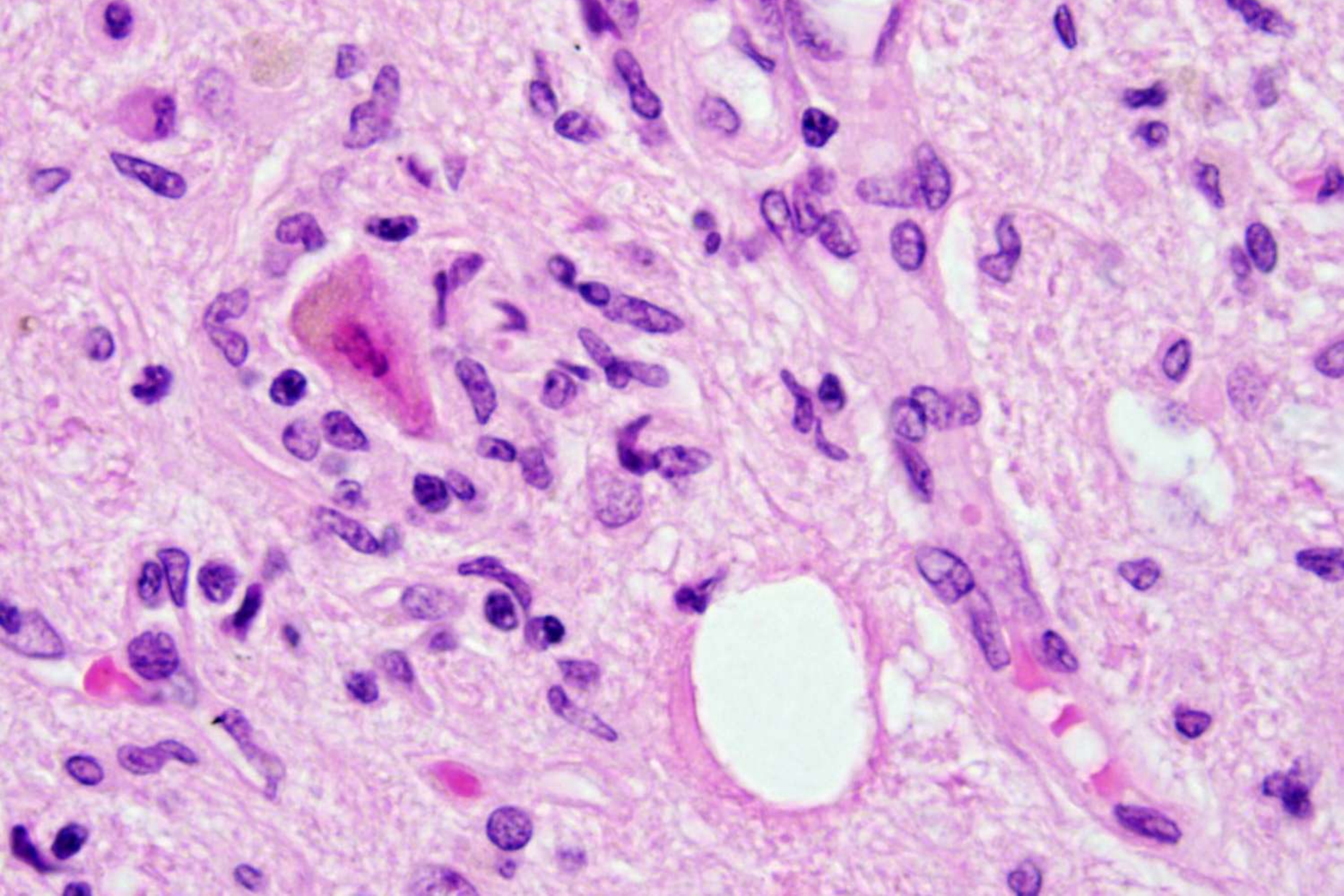
- 75-yo man with 2 week history of headaches and malaise
- Lethargy progressed to confusion, behavioral changes, and eventually stupor
- Imaging showed non-specific T2- and FLAIR-MRI abnormalities involving cortex and deep gray matter
- A frontal lobe biopsy was obtained









# HISTOLOGIC PATTERNS

(8 Major and 20 minor patterns in book)

- Parenchymal Infiltrate with Hypercellularity
- Solid Mass (Pure)
- Solid and Infiltrative Process
- Vasculocentric Process
- Extra-axial Mass
- Meningeal Infiltrate
- Destructive/Necrotic Process
- Subtle Pathology or Near Normal Biopsy

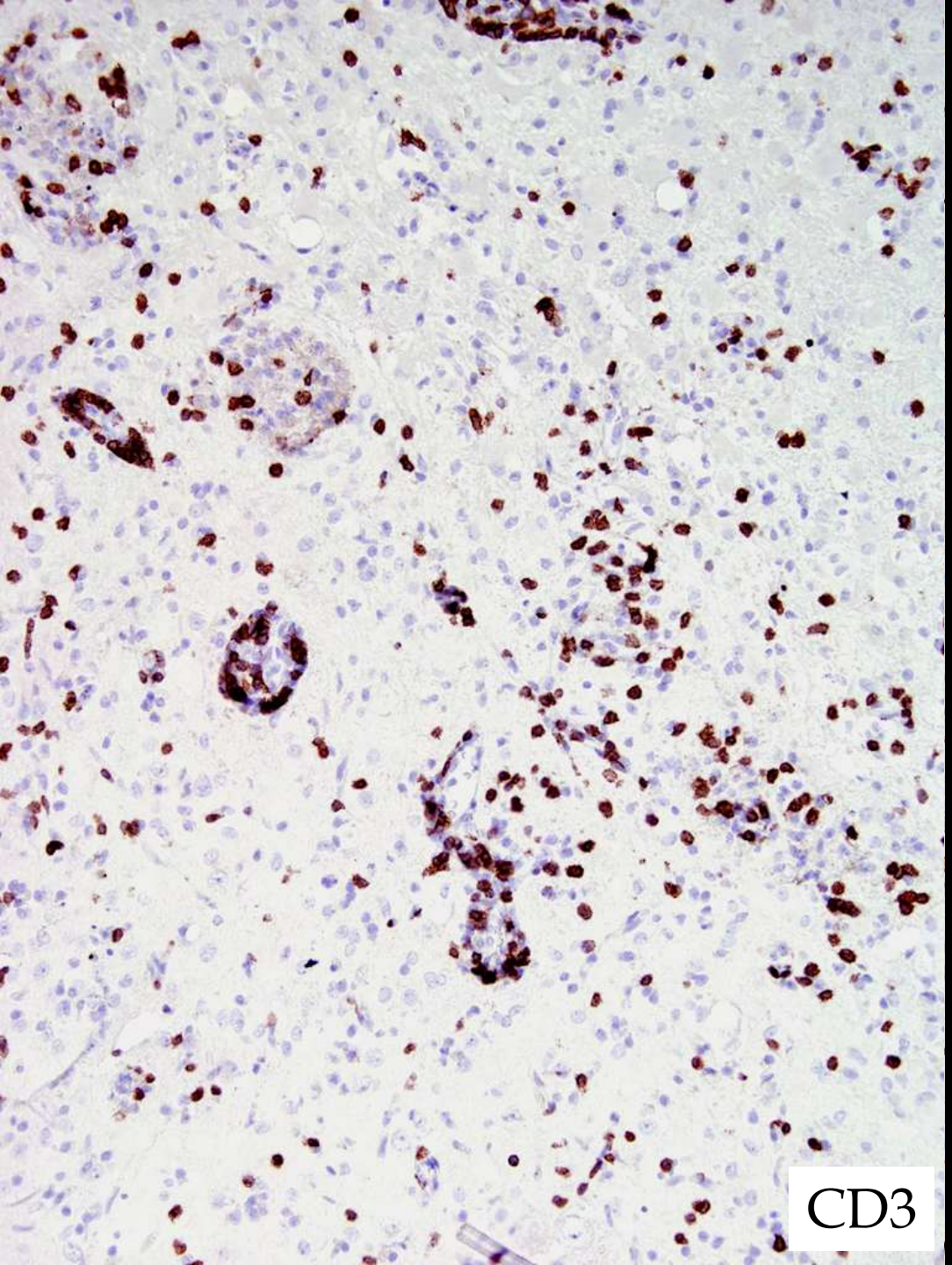
| | |
|---|---|
| **Parenchymal infiltrate with hypercellularity** | Diffuse glioma<br>CNS lymphoma<br>Infections<br>Active demyelinating disease<br>Cerebral infarct<br>Reactive gliosis |
| **Solid mass (pure)** | Metastasis<br>Ependymoma<br>Subependymoma<br>Subependymal giant-cell astrocytoma (SEGA)<br>Central or extraventricular neurocytoma<br>Pineocytoma<br>Embryonal tumor (e.g., AT/RT)<br>Choroid plexus papilloma<br>Hemangioblastoma<br>Paraganglioma<br>Pituitary adenoma |
| **Solid and infiltrative process** | Pilocytic astrocytoma<br>Pleomorphic xanthoastrocytoma<br>Glioblastoma/gliosarcoma (and other high grade gliomas)<br>Ganglioglioma<br>Dysembryoplastic neuroepithelial tumor (DNT)<br>Embryonal tumor (e.g., medulloblastoma/CNS PNET)<br>Choroid plexus carcinoma<br>Germ cell tumors<br>Craniopharyngioma<br>CNS lymphoma<br>Sarcoma<br>Histiocytic disorders<br>Abscess and other forms of infection |
| **Vasculocentric process** | CNS lymphoma<br>Intravascular lymphoma<br>Angiocentric glioma<br>Ependymoma<br>Vasculitis<br>Meningioangiomatosis<br>Active demyelinating disease<br>Amyloid angiopathy<br>Arteriolosclerosis<br>Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)<br>Vascular malformations<br>Infections (e.g., aspergillosis)<br>Neurosarcoidosis<br>Thromboembolic disease |

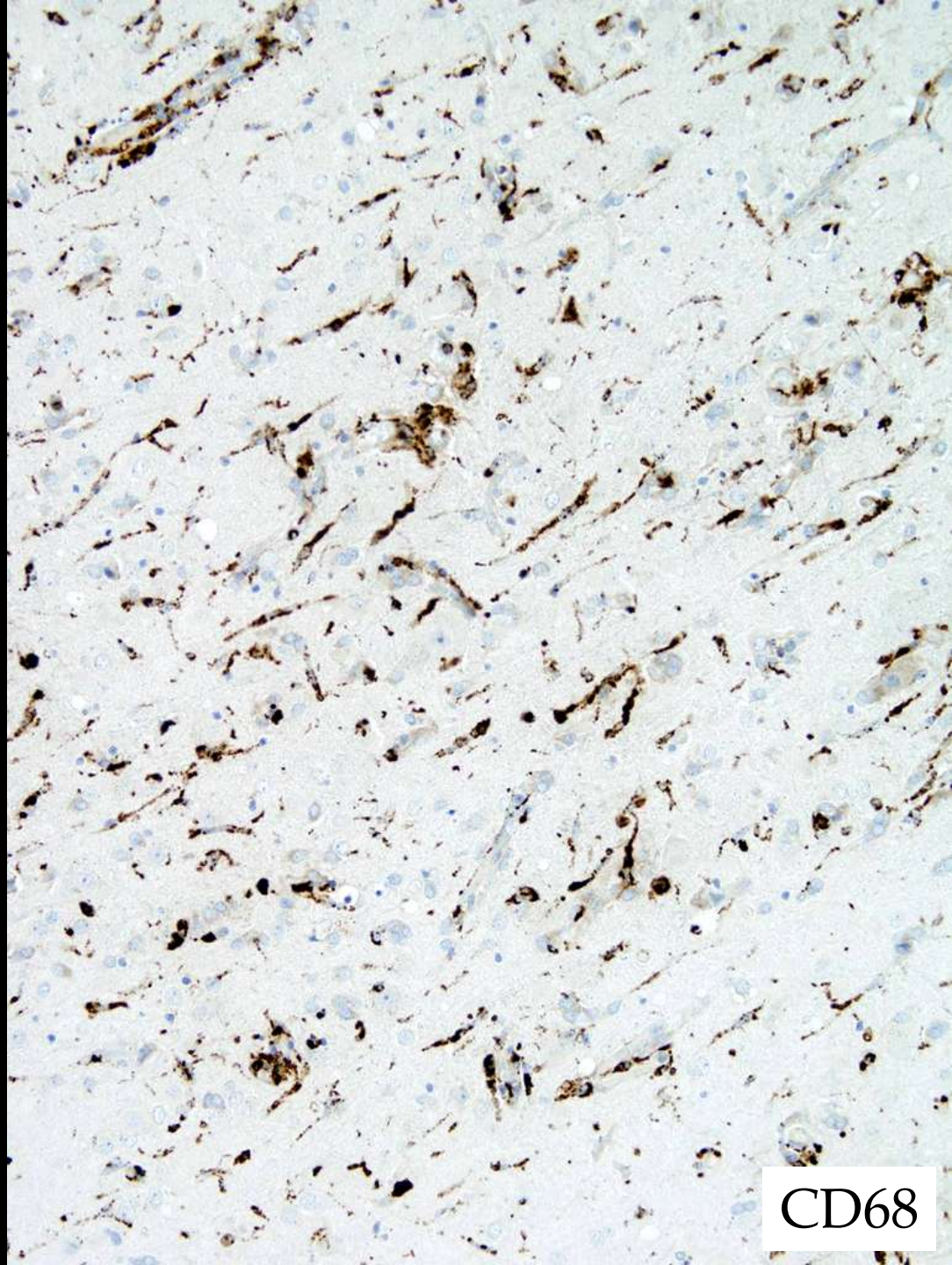
| | |
|---|---|
| **Extra-axial mass** | Meningioma<br>Hemangiopericytoma<br>Solitary fibrous tumor<br>Hemangioblastoma<br>Sarcomas<br>Schwannoma and other nerve sheath tumors<br>Metastasis<br>Melanoma or melanocytoma<br>Secondary lymphoma or leukemia<br>Paraganglioma<br>Pituitary adenoma<br>Neurosarcoidosis<br>Granulomatous infections<br>Inflammatory pseudotumors<br>Calcifying pseudotumor of the neuraxis<br>Primary bone tumors (e.g., chordoma)<br>Histiocytic disorders (e.g., Rosai-Dorfman disease) |
| **Meningeal infiltrate** | Meningeal carcinomatosis, gliomatosis, melanosis, melanomatosis, sarcomatosis, or hemangioblastomatosis<br>Metastatic medulloblastoma/CNS PNET<br>Secondary lymphoma or leukemia<br>Histiocytic disorders<br>Meningitis<br>Neurosarcoidosis<br>Infectious granulomatous diseases<br>Collagen vascular disorders<br>Sturge-Weber syndrome |
| **Destructive/necrotic process** | Cerebral infarct<br>Radiation necrosis or treatment effects<br>Infections<br>Vasculitis<br>CNS lymphoma in an immunosuppressed patient<br>Intravascular lymphoma<br>CADASIL<br>Severe demyelinating disease<br>Metabolic/toxic disease |
| **Subtle pathology or near-normal biopsy** | Nonrepresentative biopsy specimen<br>Subtle diffuse glioma (WHO grade II)<br>Hypothalamic hamartoma<br>Cortical dysplasia or tuber<br>Mesial temporal sclerosis<br>Intravascular lymphoma<br>Meningioangiomatosis<br>Mild encephalitis<br>Cerebral malaria<br>Ischemic disease<br>Neurodegenerative diseases<br>Benign cysts<br>Metabolic or toxic disorder<br>Reactive gliosis or "glial scar" |

| Additional Findings | Diagnostic Considerations | Chapter/page |
|---|---|---|
| Secondary structures of Scherer | Diffuse gliomas | (Ch. 5) |
| Extensive bilateral cerebral involvement | Gliomatosis cerebri<br>Lymphomatosis cerebri | (Ch. 5)<br>(Ch. 14) |
| Angiocentric pattern | CNS lymphoma<br>Angiocentric glioma<br>Meningoencephalitis/Infections<br>Active demyelinating disease | (Ch. 14)<br>(Ch. 17)<br>(Ch. 21)<br>(Ch. 22) |
| Microcystic pattern | Diffuse gliomas | (Ch. 5) |
| Pleomorphism | Astrocytoma/glioblastoma<br>Infections, especially PML | (Ch. 5)<br>(Ch. 21) |
| Monomorphism | Oligodendroglioma<br>Some lymphomas | (Ch. 5)<br>(Ch. 14) |
| Lymphocytic infiltrate | Gemistocytic astrocytoma<br>CNS lymphoma<br>Meningoencephalitis/Infections<br>Active demyelinating disease | (Ch. 5)<br>(Ch. 14)<br>(Ch. 21)<br>(Ch. 22) |
| Foamy histiocytes | CNS lymphoma<br>Active demyelinating disease<br>Cerebral infarct | (Ch. 14)<br>(Ch. 22)<br>(Ch. 24) |
| Cytologic atypia or anaplasia | Diffuse gliomas<br>CNS lymphoma | (Ch. 5)<br>(Ch. 14) |
| Viral inclusions or organisms | Meningoencephalitis/Infections | (Ch. 21) |
| None | Reactive gliosis | (Chs. 1, 5) |

| Additional Findings | Diagnostic Considerations | Chapter/page |
|---|---|---|
| Perivascular or intravascular infiltrate | CNS lymphoma | (Ch. 14) |
| | Meningoencephalitis/infection | (Ch. 21) |
| | Neurosarcoidosis | (Ch. 21) |
| | Active demyelinating disease | (Ch. 22) |
| | Vasculitis | (Ch. 24) |
| | Amyloid angiopathy with vasculitis | (Ch. 24) |
| Intraluminal atypical cells | Intravascular lymphoma | (Ch. 14) |
| Perivascular glial or spindled cells | Ependymoma | (Ch. 6) |
| | Angiocentric glioma | (Ch. 17) |
| | Meningioangiomatosis | (Ch. 20) |
| Angionecrosis | Infections (aspergillosis) | (Ch. 21) |
| | Vasculitis | (Ch. 24) |
| | Thromboembolic disease | (Ch. 24) |
| Vascular hyalinization | Meningioangiomatosis | (Ch. 20) |
| | Amyloid angiopathy | (Ch. 24) |
| | CADASIL | (Ch. 24) |
| | Arteriolosclerosis | (Ch. 24) |
| | Vasculitis | (Ch. 24) |
| | Vascular malformations | (Ch. 24) |
| Granular vascular deposits | CADASIL | (Ch. 24) |
| Granulomas or giant cells | Infections | (Ch. 21) |
| | Neurosarcoidosis | (Ch. 21) |
| | Vasculitis | (Ch. 24) |
| | Amyloid angiopathy with vasculitis | (Ch. 24) |
| Cerebral hemorrhage | Infections (aspergillosis) | (Ch. 21) |
| | Amyloid angiopathy | (Ch. 24) |
| | Vascular malformations | (Ch. 24) |
| Cerebral infarcts or microinfarcts | Intravascular lymphoma | (Ch. 14) |
| | Infections | (Ch. 21) |
| | Neurosarcoidosis | (Ch. 21) |
| | Vasculitis | (Ch. 24) |
| | Amyloid angiopahty | (Ch. 24) |
| | CADASIL | (Ch. 24) |
| | Arteriolosclerosis | (Ch. 24) |
| | Thromboembolic disease | (Ch. 24) |
| Disorganized, irregular blood vessels | Meningioangiomatosis | (Ch. 24) |
| | Vascular malformations | (Ch. 24) |

| Additional Findings | Diagnostic Considerations | Chapter/page |
|---|---|---|
| Neoplastic cells | Meningeal gliomatosis | (Ch. 5) |
| | Metastatic medulloblastoma/CNS PNET | (Ch. 9) |
| | Meningeal sarcomatosis | (Ch. 11) |
| | Meningeal carcinomatosis | (Ch. 13) |
| | Secondary lymphoma/leukemia | (Ch. 14) |
| | Meningeal melanosis/melanomatosis | (Ch. 16) |
| | Meningeal hemangioblastomatosis | (Ch. 20) |
| Venous malformation | Sturge-Weber syndrome | (Ch. 20) |
| Neutrophil-rich infiltrate | Acute bacterial meningitis | (Ch. 21) |
| Lymphoplasmacytic infiltrate | → Infectious meningitis | (Ch. 21) |
| | Chemical meningitis | (Ch. 21) |
| | Neurosarcoidosis | (Ch. 21) |
| | Collagen vascular disorder | (Ch. 21) |
| Granulomas/giant cells | Infectious meningitis (TB, fungal) | (Ch. 21) |
| | Neurosarcoidosis | (Ch. 21) |
| | Collagen vascular disorder | (Ch. 21) |
| Clear to foamy cells | Meningeal carcinomatosis | (Ch. 13) |
| | Histiocytic disorders | (Ch. 14) |


CD3


CD68

NOT SAME CASE

# DX: ENCEPHALITIS (MENINGO-ENCEPHALITIS)

- Viral Encephalitis
  - HSV: inclusions
  - Epidemic (e.g., WNV): no inclusions
- Other Infections
  - Toxoplasma
  - Syphilis
  - Rickettsia
- Paraneoplastic Disease

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- 2nd Year medical students
- Memorization aid
- Fun way to learn!

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# Full Arrangements: Chris Bergmann – RFJ Music


Encephalitis

# ENCEPHALITIS
## Music and Lyrics by Arie Perry, M.D.

Microglial activation and nodule formation,
Along with neuronophagia and perivascular lymphocytes
Meningoencephalitis or encephalomyelitis,
Depending on extent of disease, there's a range of liabilities

Ch: Viral encephalitis, there are two major kinds,
In the arthropod associated, no inclusions you'll find
But in herpes encephalitis, Cowdry A is the sign,
Red inclusion with a clear halo, is how it's defined

With herpes encephalitis, temporal lobe is the nidus,
Imaginary senses of smell is a common type of spell
It's often necrotizing, the damage is agonizing,
As you wait for CSF PCR, acyclovir will make you a star (chorus)

In AIDS dementia complex, with mental and motor deficits,
Multinucleated giant cells, a diagnostic feature that compels
CMV is a TORCH infection that inspires your recollection,
Of AIDS and perinatal disease, ependymitis brings them to their knees (chorus)