Diagnostic Approaches to Glioblastoma Subtypes and Histologic Patterns

How have we changed our thinking?

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Disclosures

- I have no relevant financial relationships to disclose

Learning Objectives

- Name glioblastoma subtypes and histologic patterns according to the current World Health Organization Classification
- Compare the histopathological and molecular features of epithelioid glioblastoma, glioblastoma with a primitive neuronal component, glioblastoma with oligodendrocyte-like cells, gliosarcoma, giant cell glioblastoma, and small cell glioblastoma
- Identify additional testing for patient management following the diagnosis of giant cell glioblastoma and glioblastoma with primitive neuronal component

Overview

- Some of the history of glioblastoma
- Six case-based examples of subtypes and histologic patterns
  - Origin and underpinning of the subtype/pattern
  - Ancillary testing
  - Differential considerations
  - Clinical implications
- Summary and Q&A/discussion

What is *not* in this talk

- A precise and unassailable definition of glioblastoma
- A strict definition of a “subtype” vs. “pattern” vs. “variant”
- A clear line for “how much is enough?” in diagnostic practice
- A comprehensive review of all the relevant literature

AANP

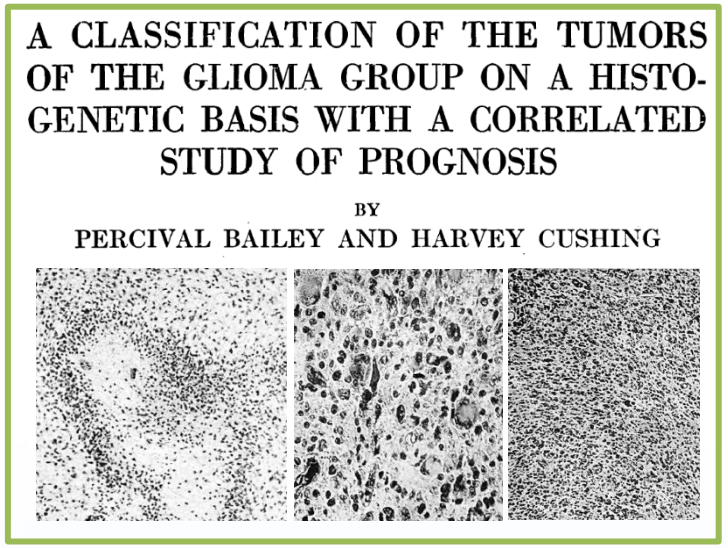
1864 — Virchow identifies “glioma” and hard/soft CNS “sarcoma”

1916 — Globus & Strauss report an aggressive *spongioblastoma*

1925 — Globus, Strauss, Bailey, and Cushing hash out the naming

1926 — Bailey and Cushing glioma classification monograph

2026 — You are here



A CLASSIFICATION OF THE TUMORS OF THE GLIOMA GROUP ON A HISTOGENETIC BASIS WITH A CORRELATED STUDY OF PROGNOSIS

BY

PERCIVAL BAILEY AND HARVEY CUSHING

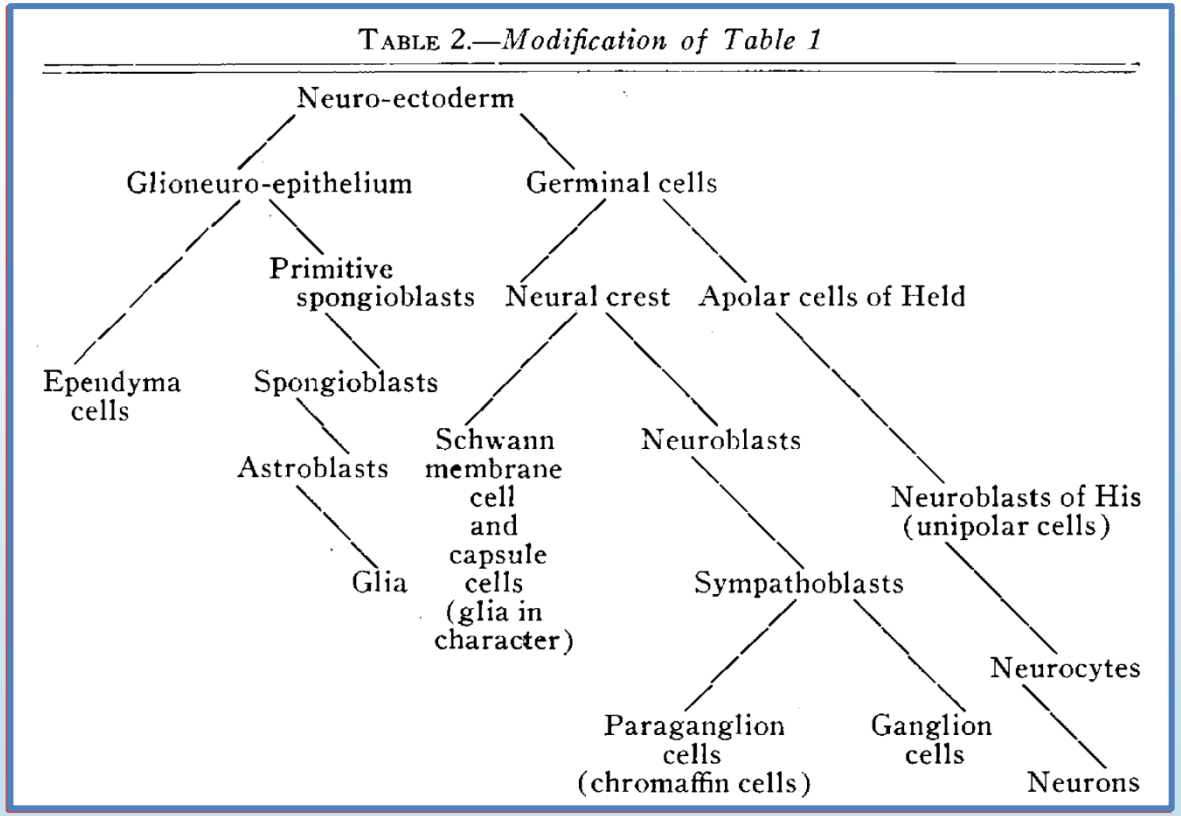


TABLE 2.—*Modification of Table 1*

- Neuro-ectoderm
  - Glioneuro-epithelium
    - Ependyma cells
    - Primitive spongioblasts
      - Spongioblasts
        - Astroblasts
          - Glia
        - Schwann membrane cell and capsule cells (glia in character)
  - Germinal cells
    - Neural crest
      - Neuroblasts
        - Sympathoblasts
          - Paraganglion cells (chromaffin cells)
          - Ganglion cells
        - Neurocytes
          - Neurons
    - Apolar cells of Held
      - Neuroblasts of His (unipolar cells)

1864 Virchow identifies “glioma” and hard/soft CNS “sarcoma”

1916 Globus & Strauss report an aggressive *spongioblastoma*

1925 Globus, Strauss, Bailey, and Cushing hash out the naming

1926 Bailey and Cushing glioma classification monograph

1949 Kernohan 4-tiered glioma grading system

1952 AFIP Fascicle – Kernohan and Sayre, eds.

1979 **WHO Histological Typing of Tumours of the CNS (1st ed.)**
K.J. Zulch, head

1993 **WHO CNS (2nd ed.)**
Kleihues, Burger, Scheithauer, eds.

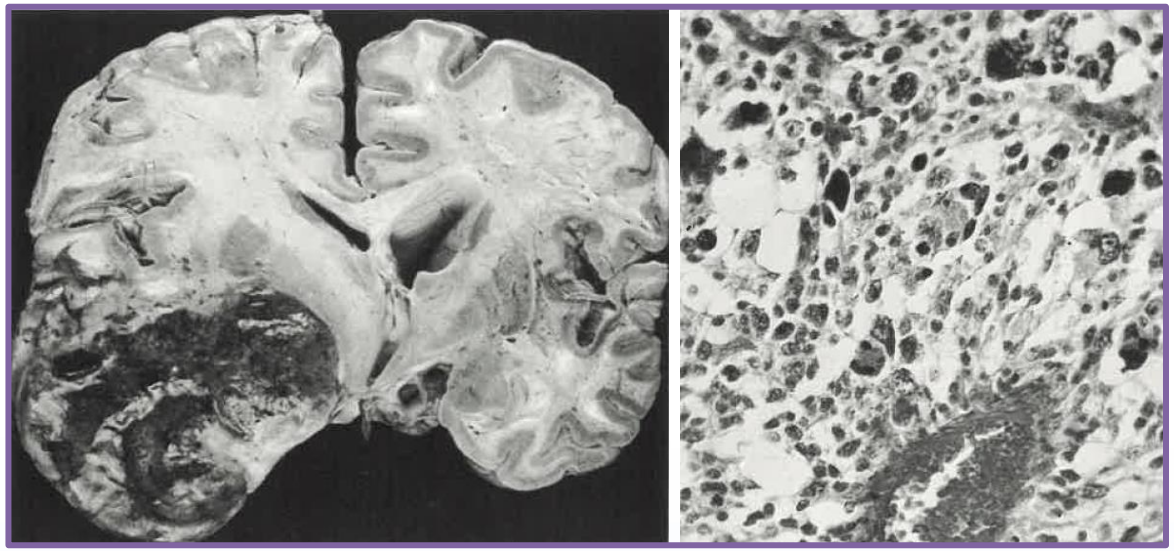
2000 **WHO CNS (3rd ed.)**
Kleihues & Cavenee, eds.

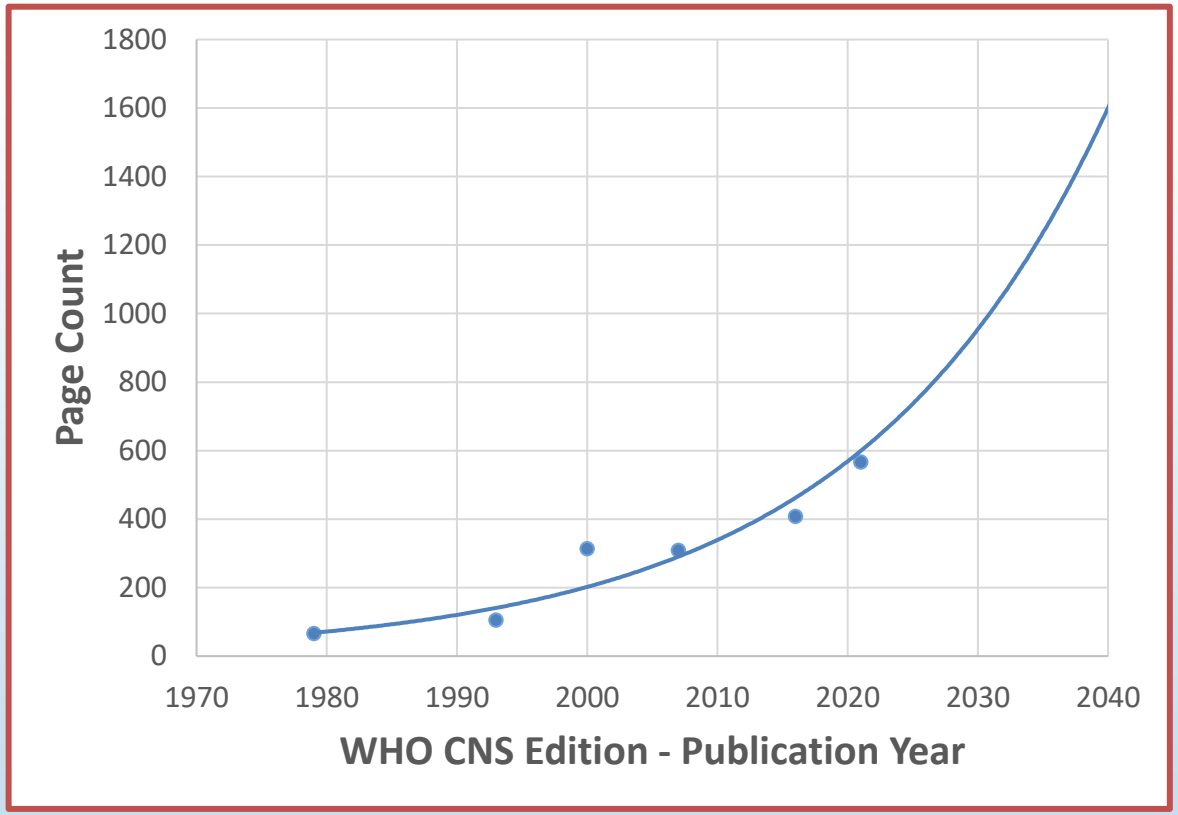
2007 **WHO CNS (4th ed.)**
Louis, Ohgaki, Wiestler, Cavenee, eds.

2016 **WHO CNS (4th ed. revised)**
Louis, Ohgaki, Wiestler, Cavenee, Ellison, Figarella-Branger, Perry, Reifenberger, von Diemling, eds.

2021 **WHO CNS (5th ed.)**
Brat, Ellison, Figarella-Branger, Hawkins, Louis, Ng, Perry, Pister, Reifenberger, Soffietti, von Deimling, Wesseling, eds.

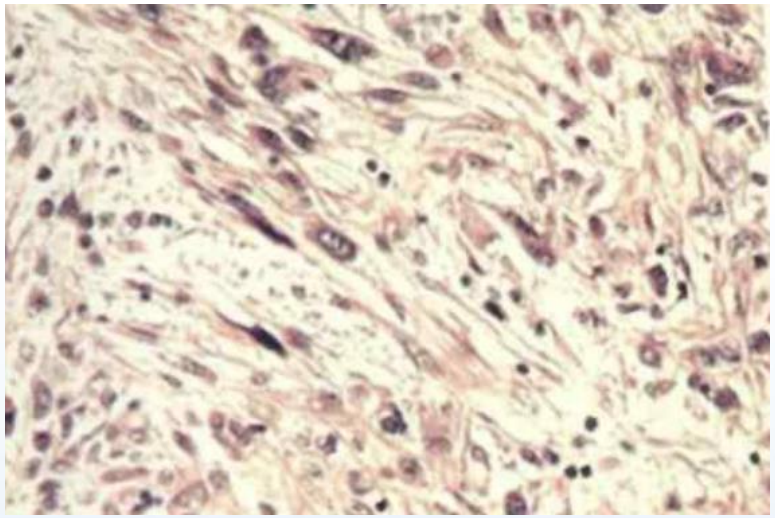
2026 You are here

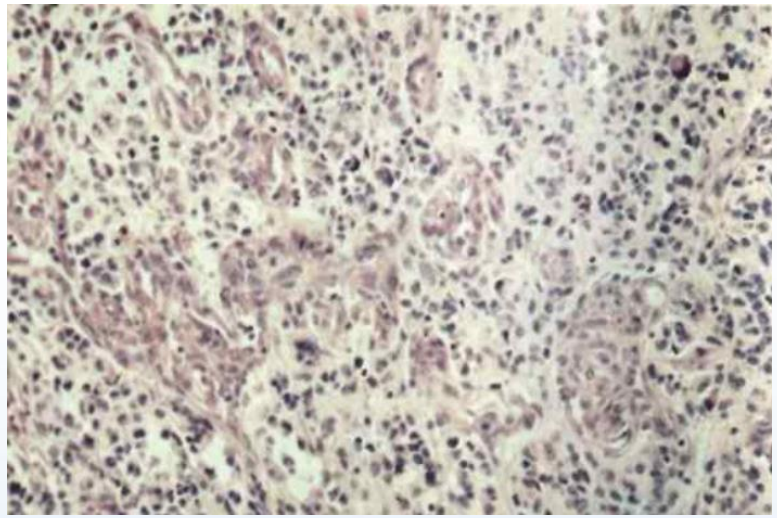


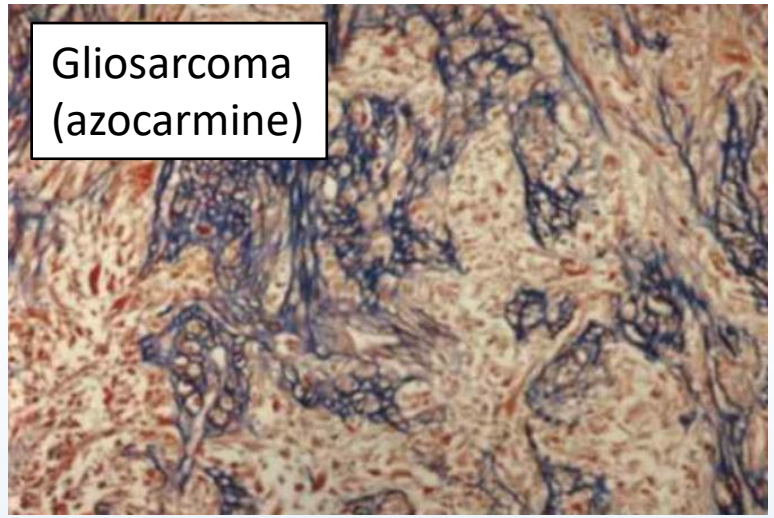


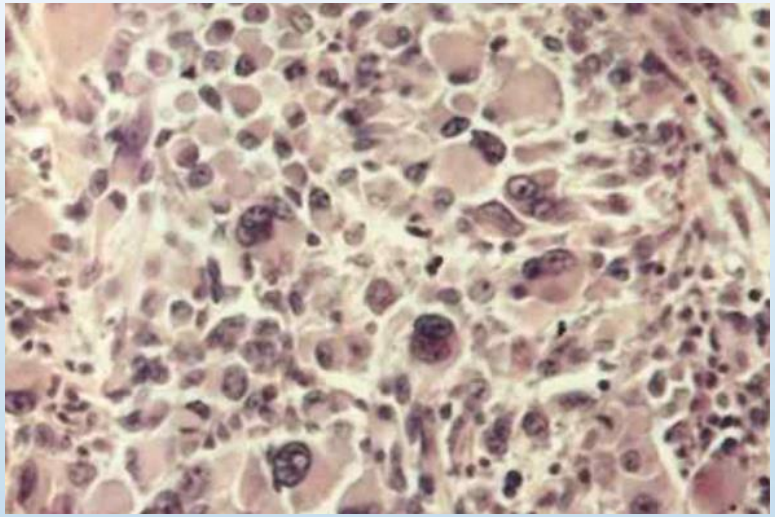
"Many subgroups have been distinguished … but there is no practical advantage in doing so, as the behavior of all these subgroups is identical" Bailey (1927)

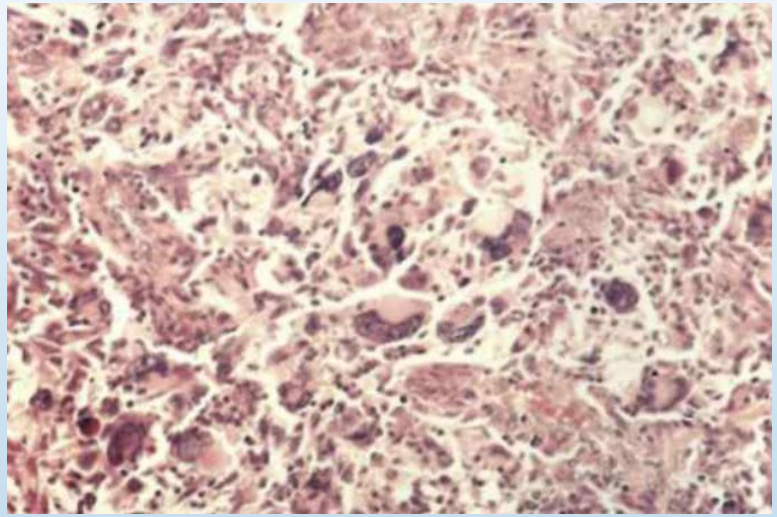
Glioblastoma in WHO CNS 1 (1979)

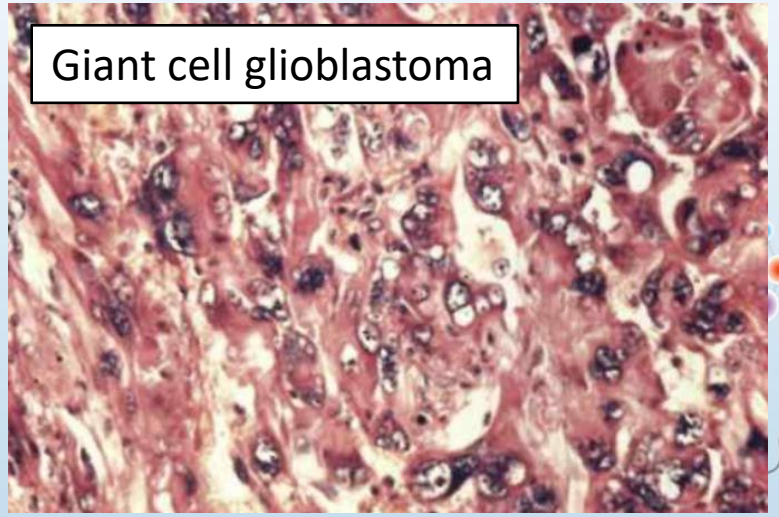






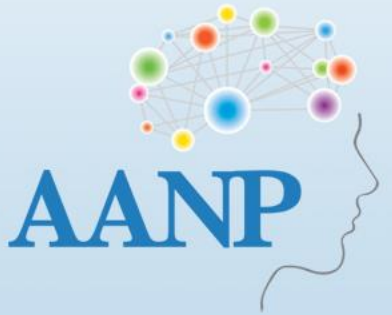




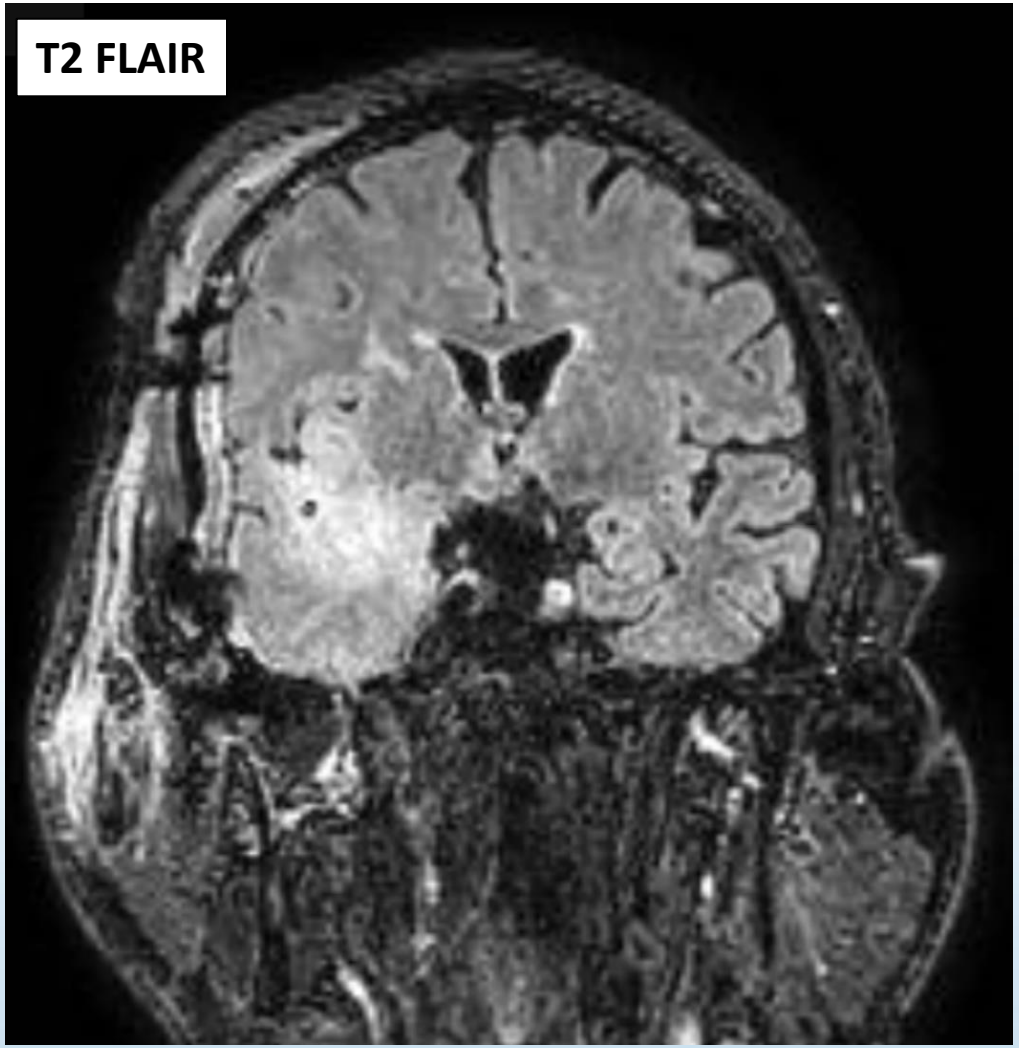


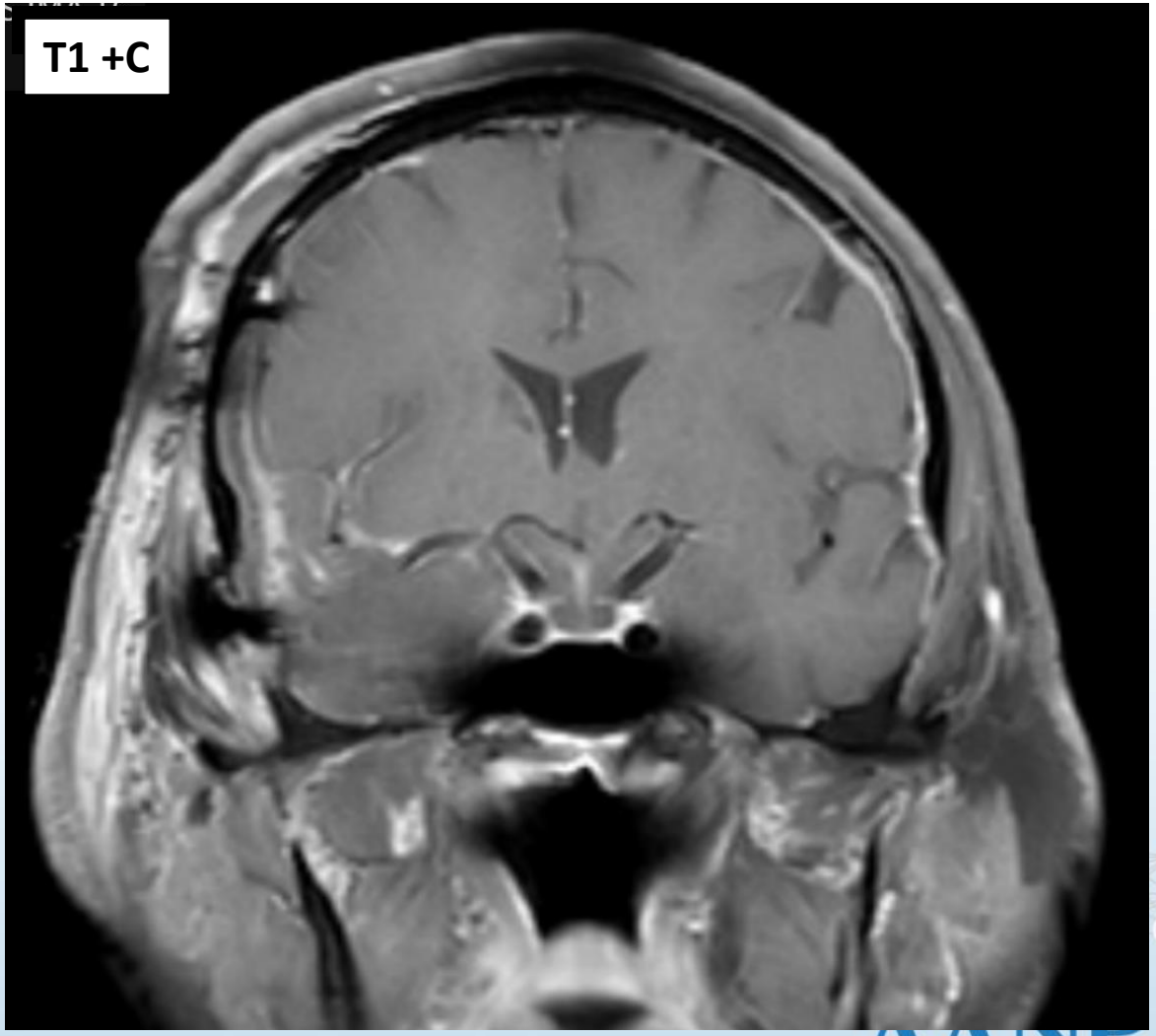
Feature/Pattern/Subtype	WHO CNS 1 (1979)	WHO CNS 2 (1993)	WHO CNS 3 (2000)	WHO CNS 4 (2007)	WHO CNS 4R (2016)	WHO CNS 5 (2021)
Giant cell	Variant	Variant	Variant	Variant	Variant	Subtype
Gliosarcoma	Variant	Variant	Variant	Variant	Variant	Subtype
Gemistocytic	Variant	Variant	Pattern	Pattern	Pattern	Pattern
Epithelioid			Pattern	Pattern	Variant	Subtype
Granular cell			Pattern	Pattern	Pattern	Pattern
Oligodendrocyte-like cells				Pattern	Pattern	Pattern
Small cell				Pattern	Pattern	Pattern
Primitive neuronal component					Pattern	Pattern
Gliomatosis cerebri	Type	Type	Type	Type		
Glioblastoma, IDH-mutant					Type	

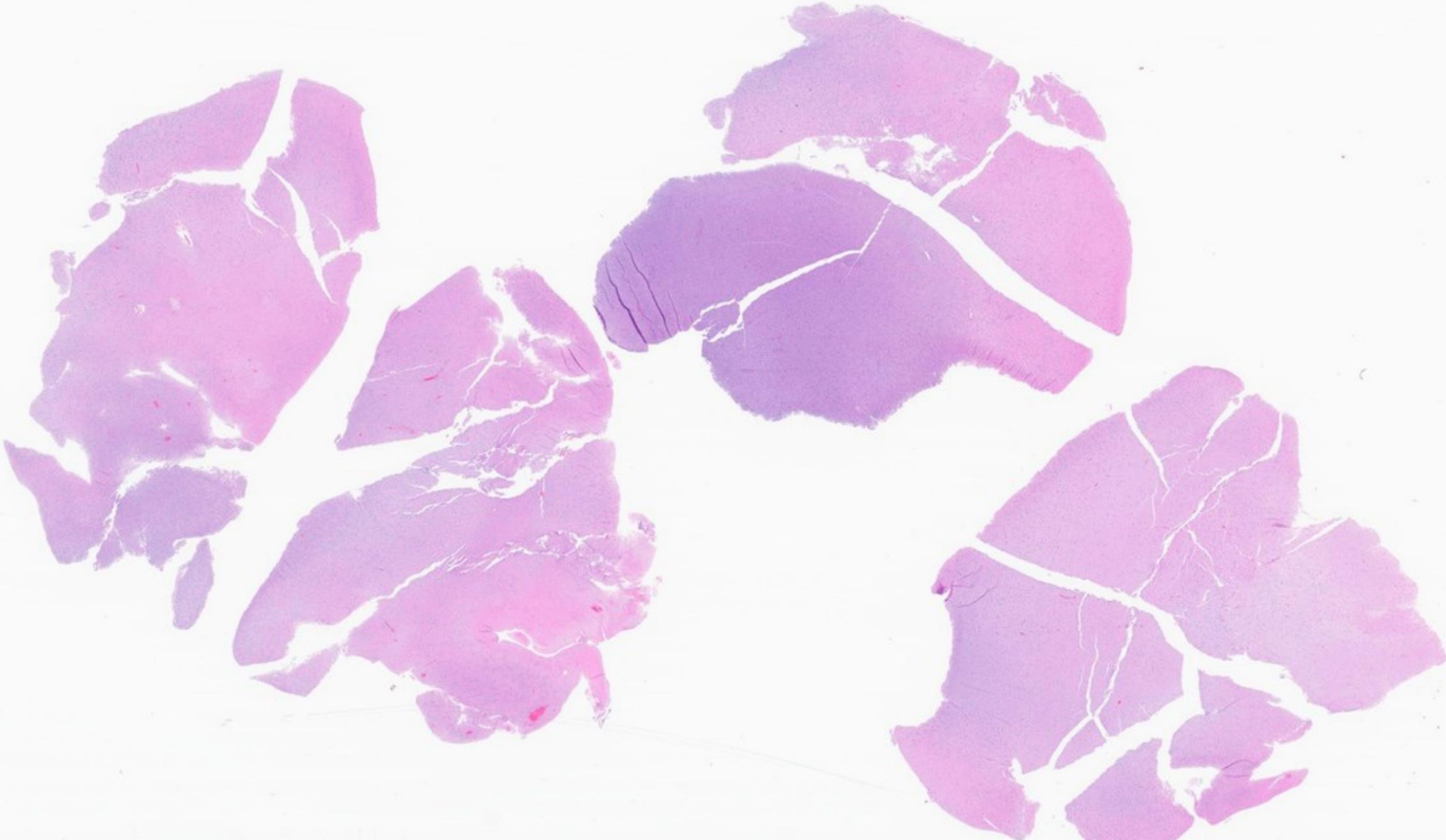
- What is the foundation of glioblastoma subtypes/patterns?
- What do these subtypes/patterns mean in the current era?

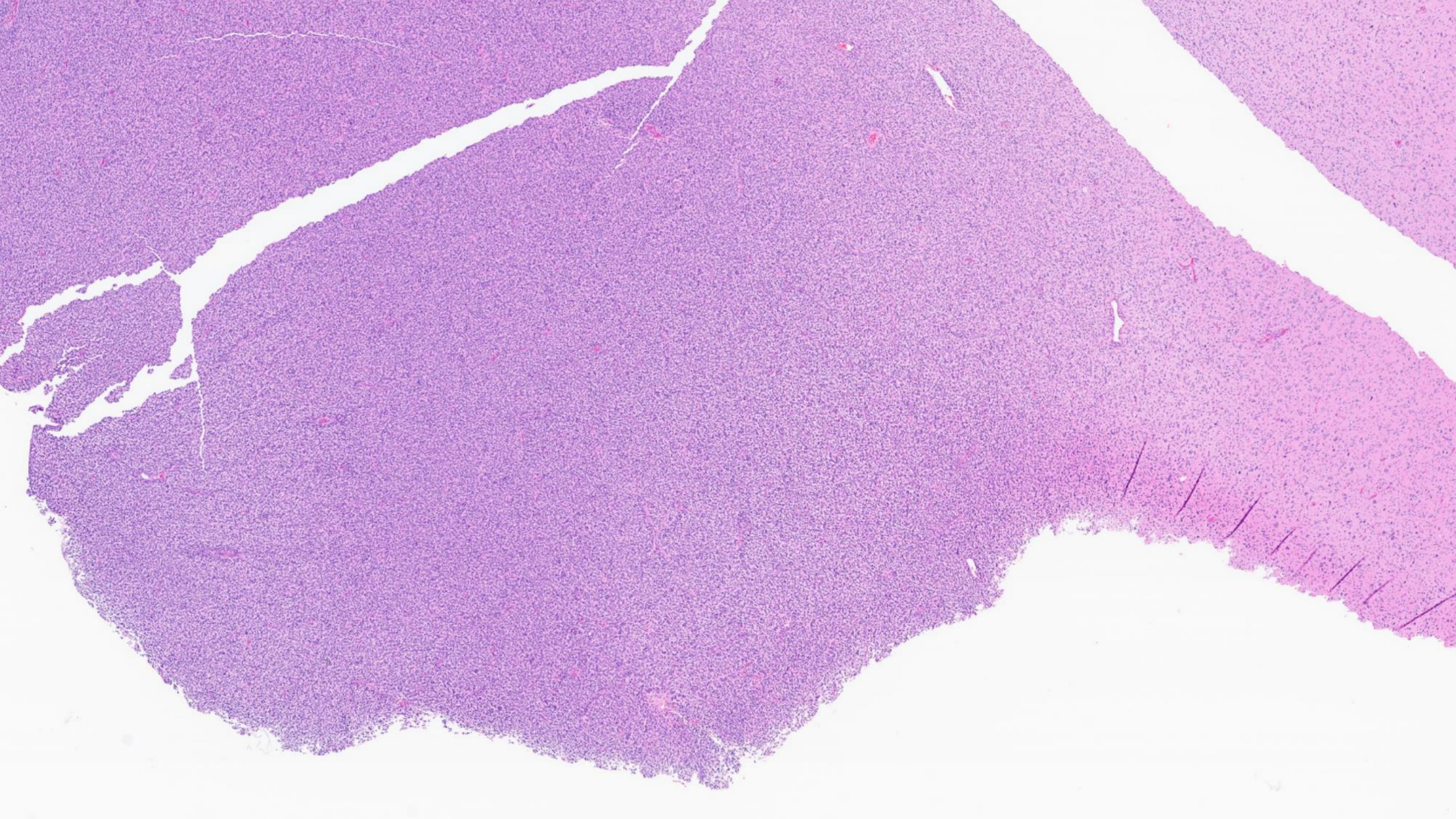


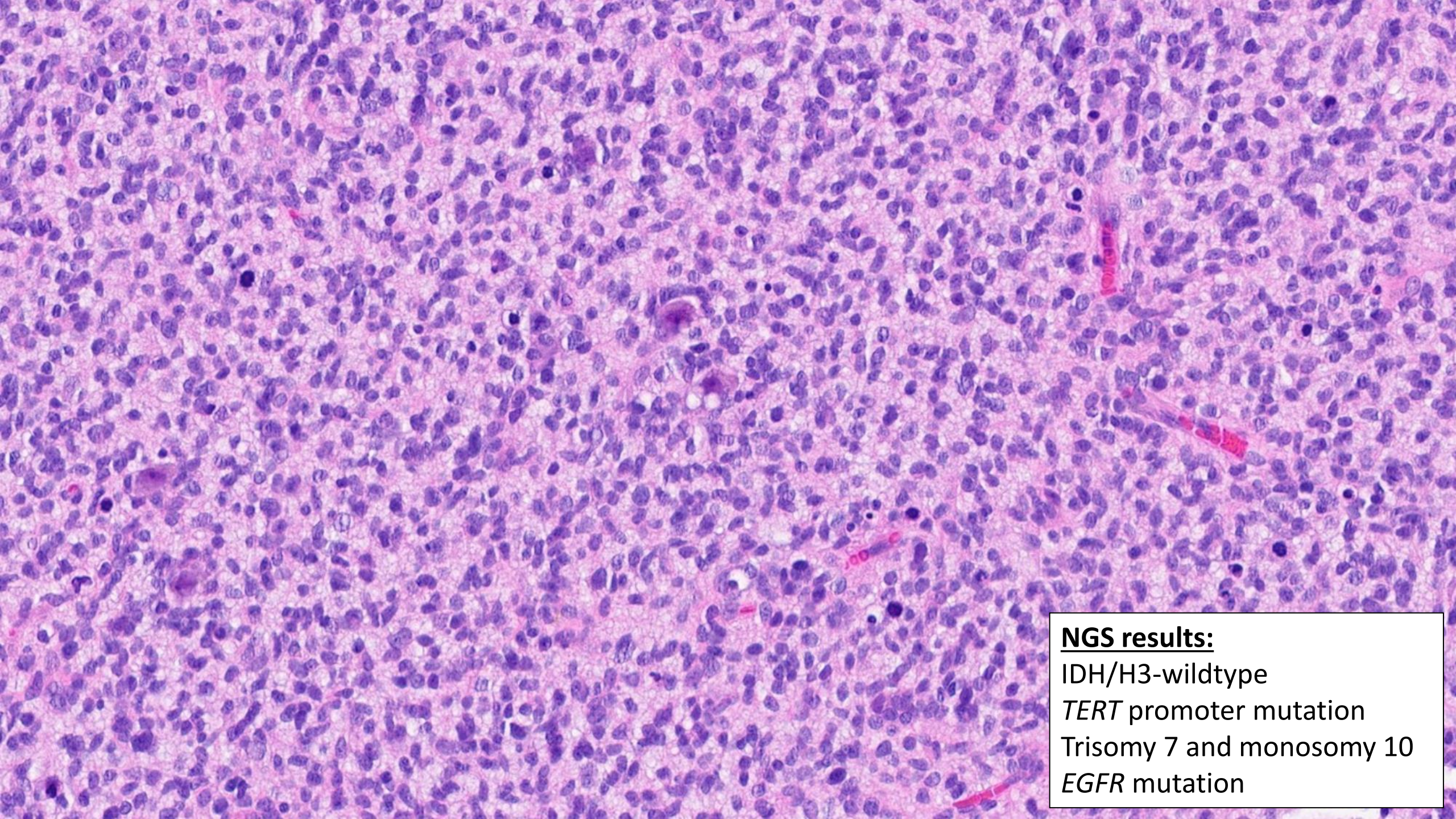
Case 1 – 79-year-old man



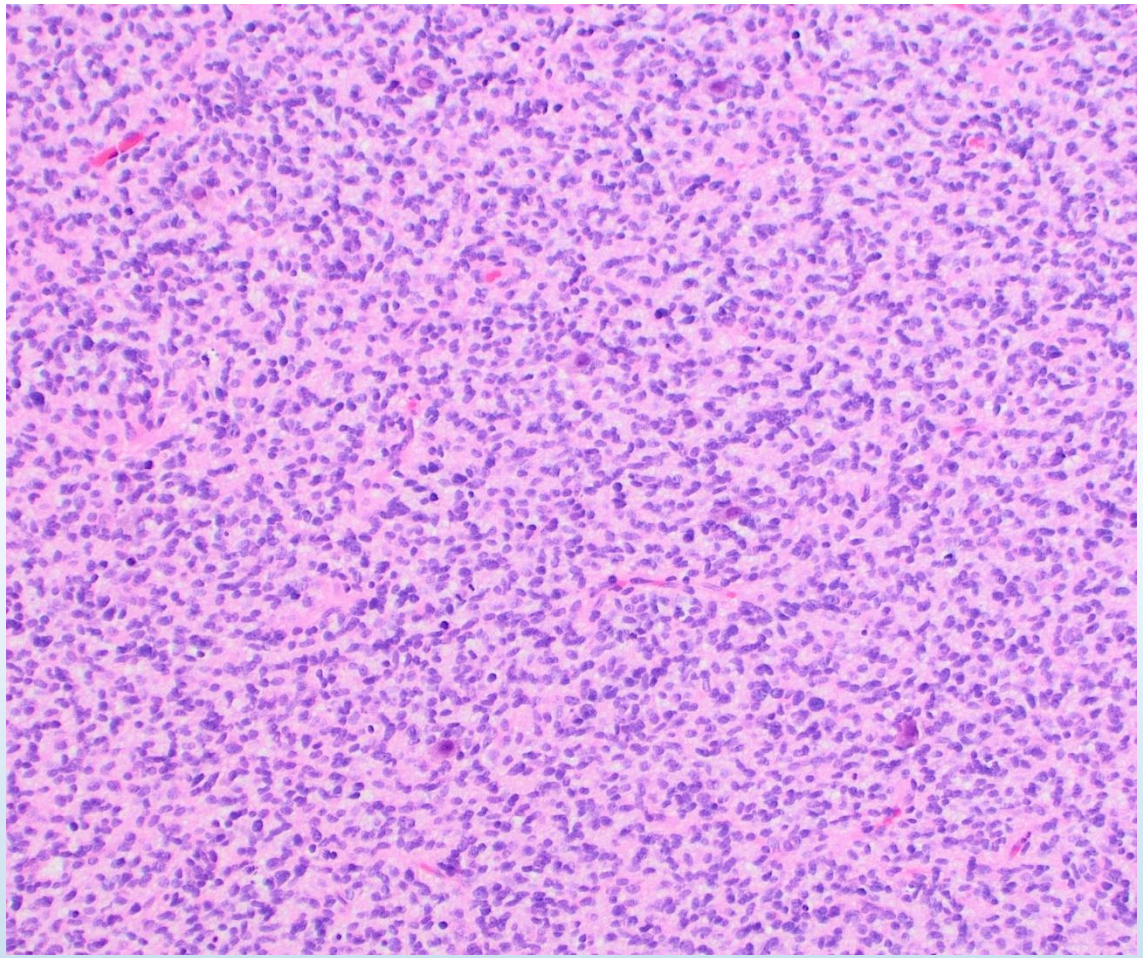







NGS results:
IDH/H3-wildtype
TERT promoter mutation
Trisomy 7 and monosomy 10
EGFR mutation

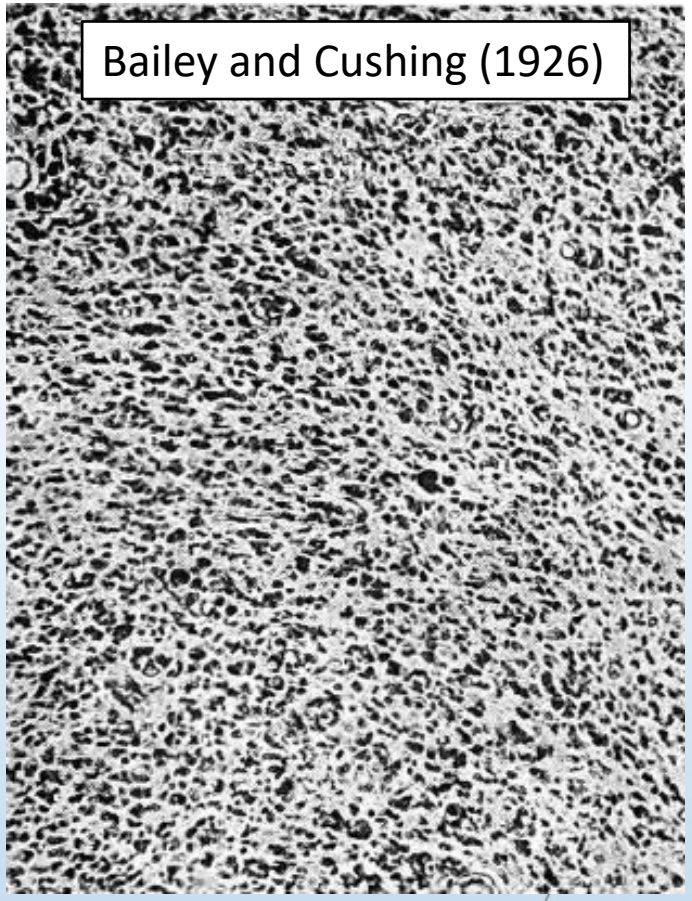
Case 1 – Small cell glioblastoma



- Highly monomorphic, small, round to elongated hyperchromatic nuclei
- Brisk mitotic activity
- ~30% non-contrast-enhancing
- May lack microvascular proliferation or necrosis

PMID 2539242

● Small undifferentiated cells
▲ Fibrillary astrocytes
△ Gemistocytic astrocytes



Bailey and Cushing (1926)

Primary glioblastoma

- Age >50 years
- No prior glioma history
- Rapid clinical course
- *Glioblastoma, IDH-wt**

EGFR amplification ⟷

Secondary glioblastoma

- Age <50 years
- May have prior low-grade glioma
- Relatively favorable outcome
- *Astrocytoma, IDH-mutant, CNS WHO gr. 4**

*Often but not always

Small Cell Architecture—A Histological Equivalent of EGFR Amplification in Glioblastoma Multiforme?

Peter C. Burger, MD, Dennis K. Pearl, PhD, Kenneth Aldape, MD, Allan J. Yates, MD, PhD, Bernd W. Scheithauer, MD, Sandra M. Passe, Robert B. Jenkins, MD, PhD, and C. David James, PhD

PMID 11706939

Small Cell Astrocytoma: An Aggressive Variant That Is Clinicopathologically and Genetically Distinct from Anaplastic Oligodendroglioma

Arie Perry, M.D.[1]
Kenneth D. Aldape, M.D.[2]
David H. George, M.D.[3]
Peter C. Burger, M.D.[4]

PMID 15470710

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Small cell glioblastoma – differential and workup

Oligodendroglioma, IDH-mutant and 1p/19q-codeleted (grade 3)

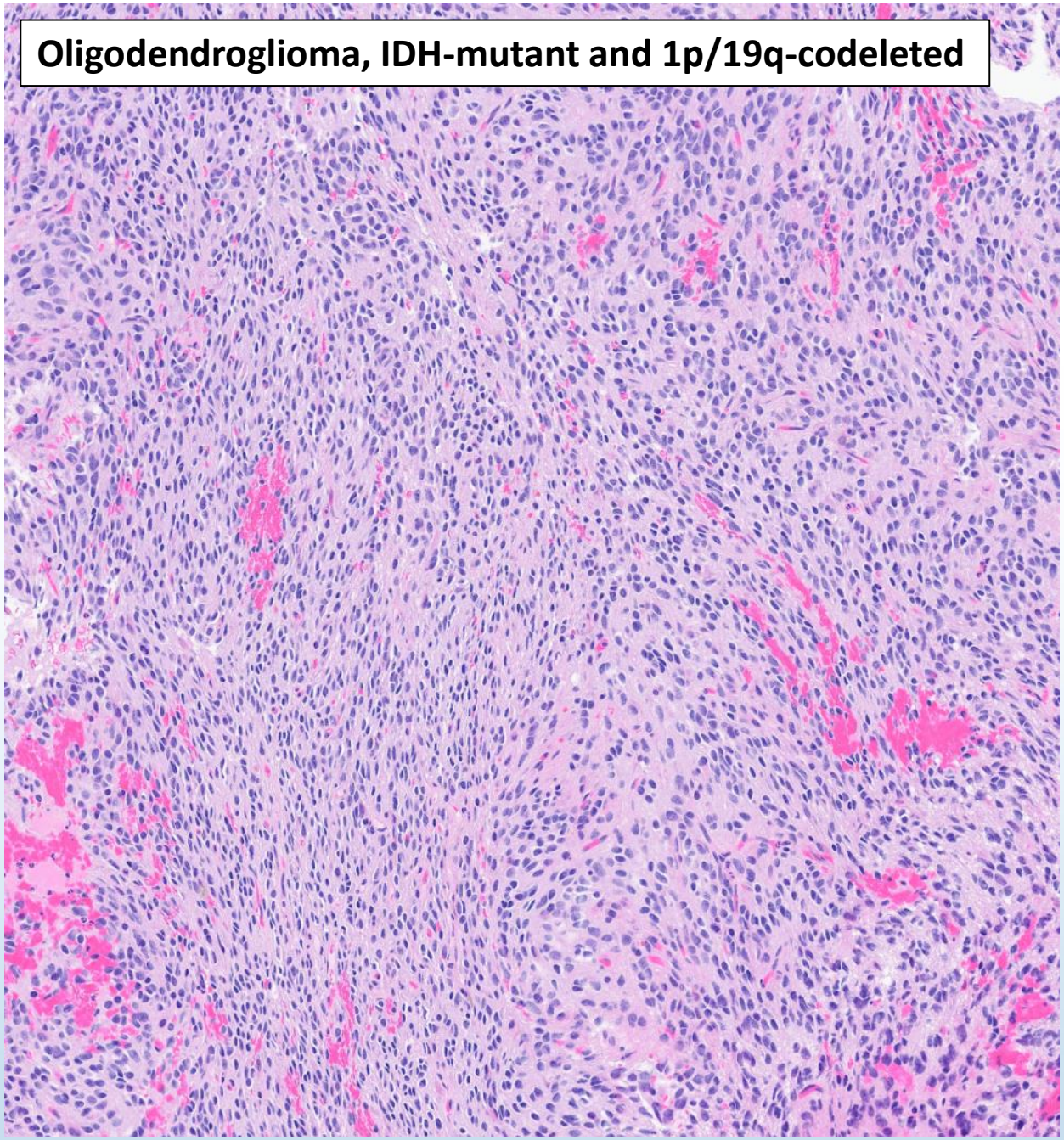
- Rounded > elongated nuclei, perinuclear halos, mucinous microcystic spaces
- ~90% (+) IDH1 R132H by IHC; remainder *IDH1/2* mutant by sequencing
- Younger age (usually)

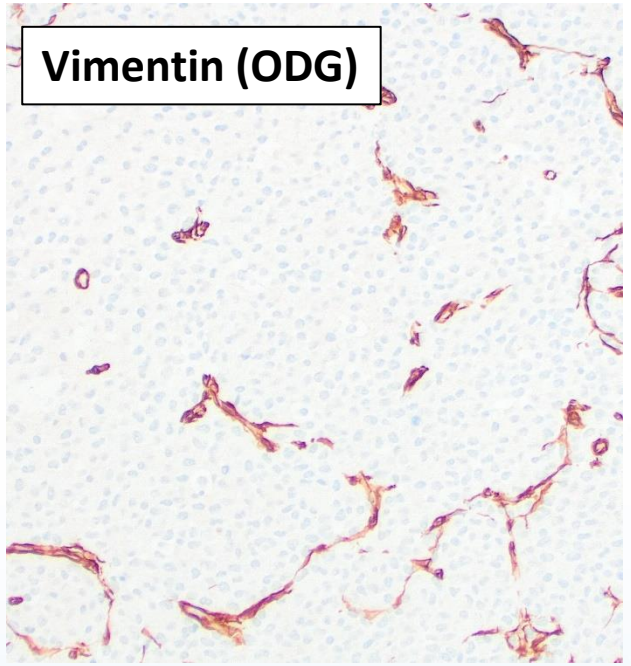
Metastatic/systemic tumors e.g. small cell carcinoma, lymphoma

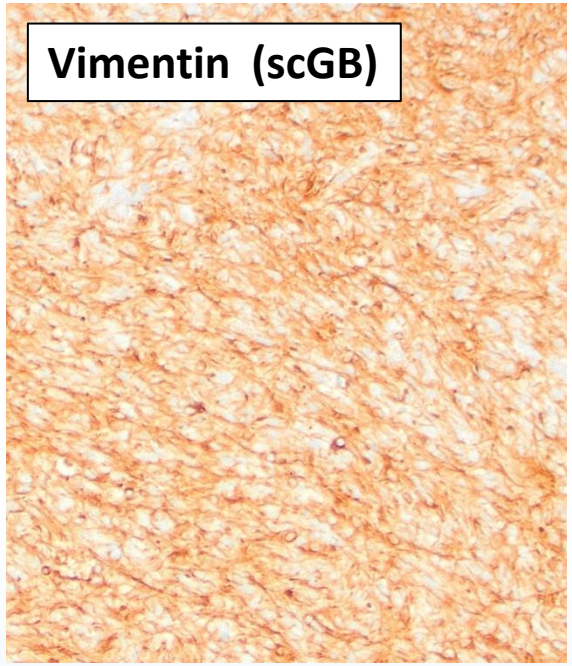
- Clinical history, radiology, lineage markers, morphology, fibrillary processes on smear

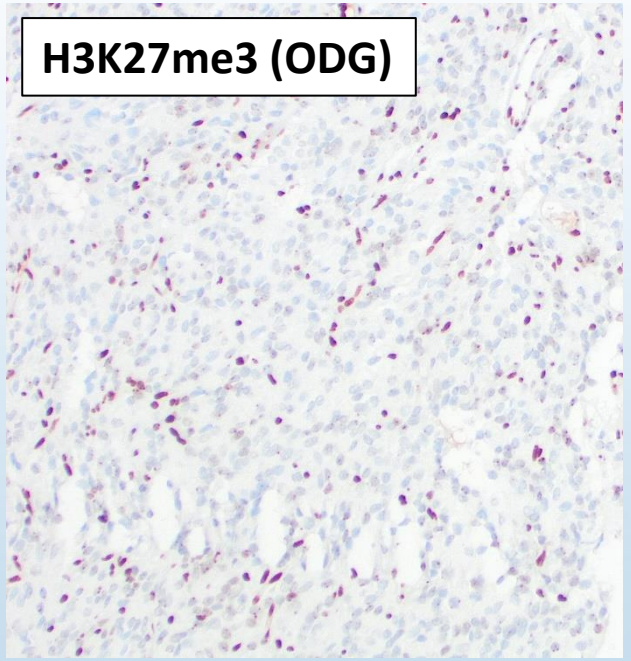
Malignant glioma with primitive neuronal component

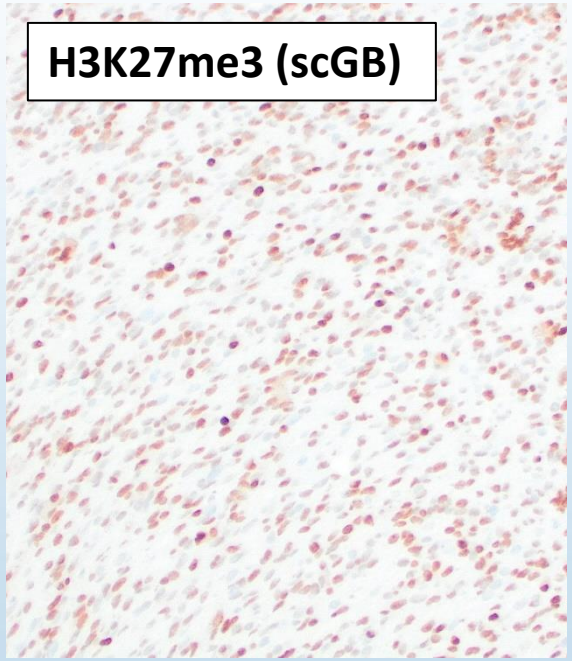
- Nodular pattern of hypercellular, embryonal-appearing cells
- Less glial fibrillary processes
- Lower GFAP and greater neuronal marker immunoreactivity


Oligodendroglioma, IDH-mutant and 1p/19q-codeleted

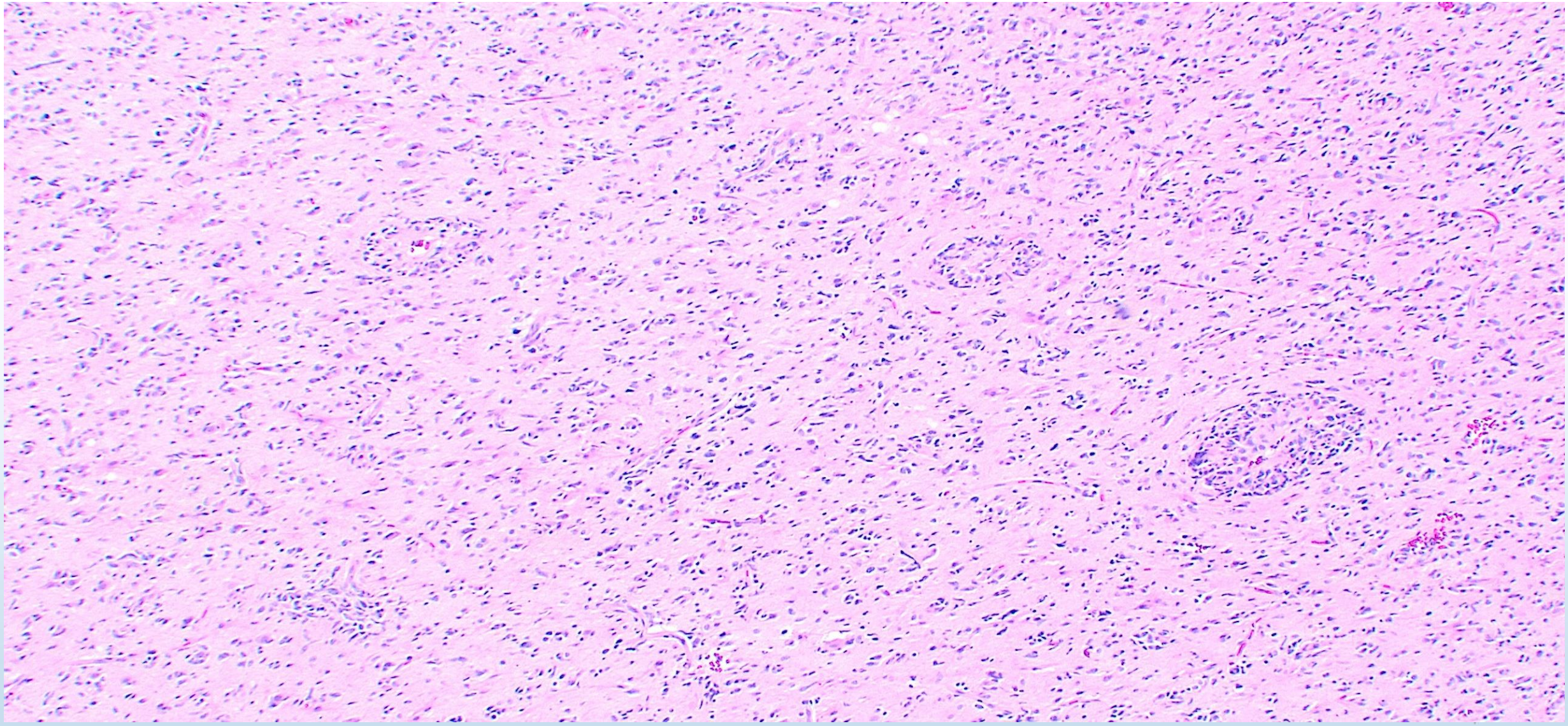

Vimentin (ODG)


Vimentin (scGB)

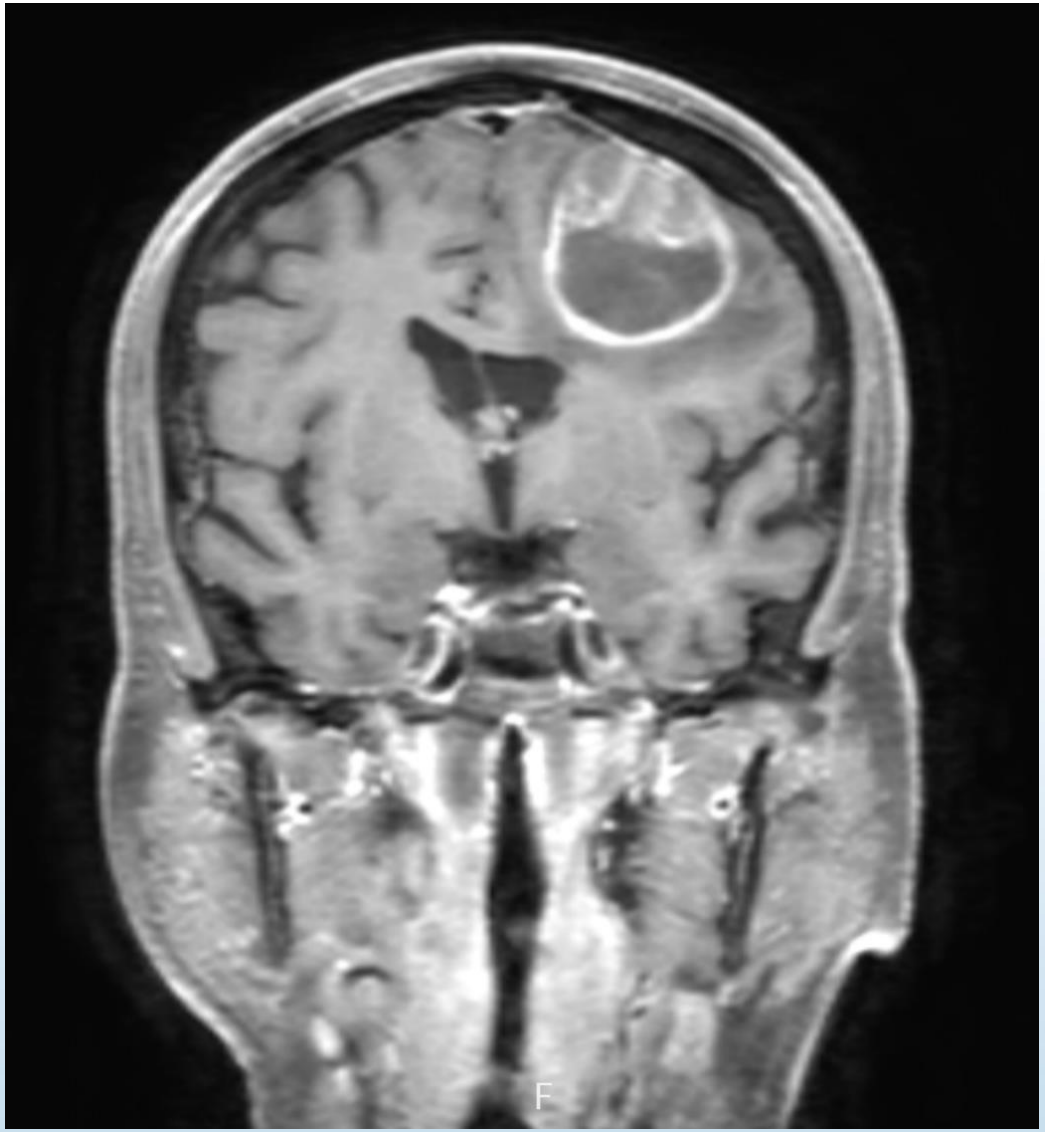

H3K27me3 (ODG)

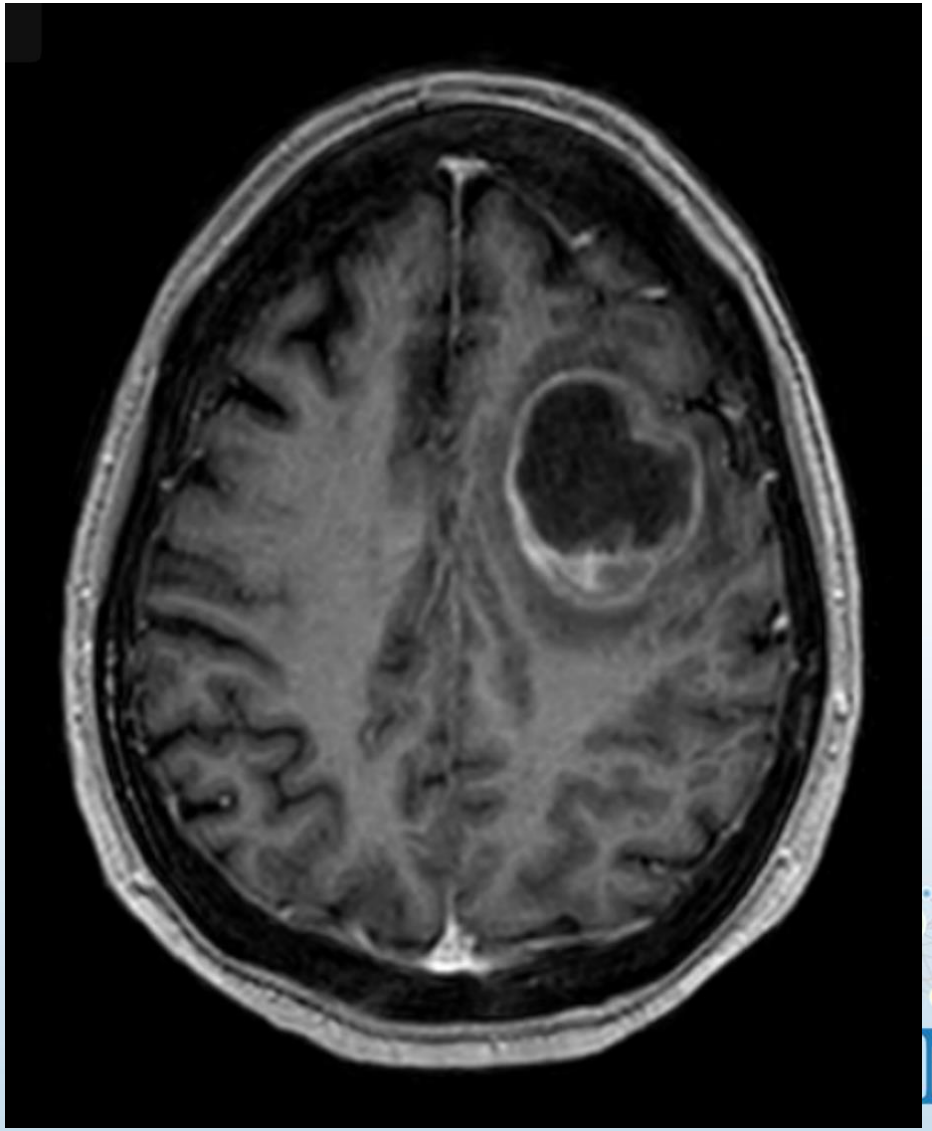

H3K27me3 (scGB)

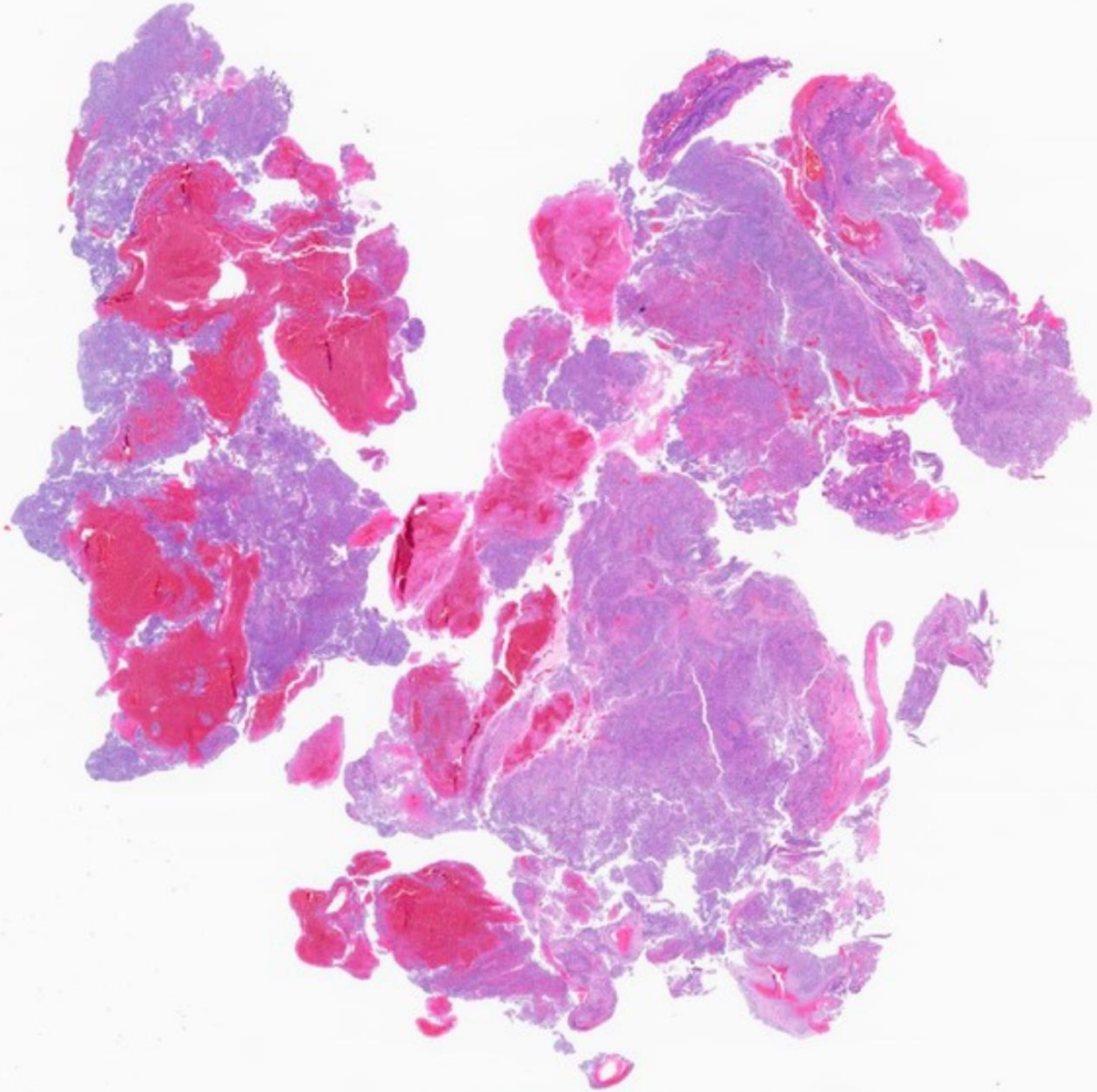
Pronounced perivascular satellitosis in scGB

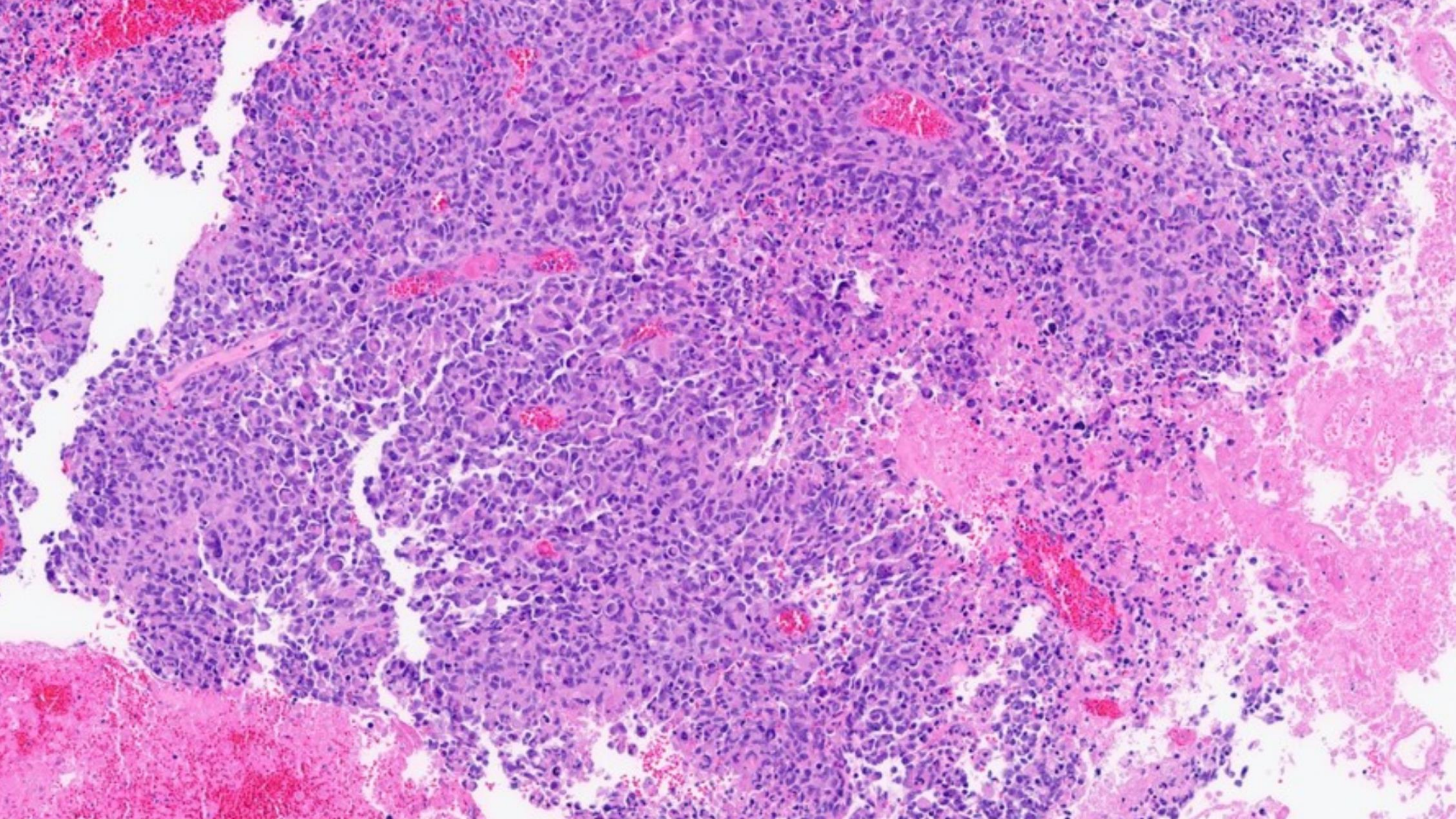


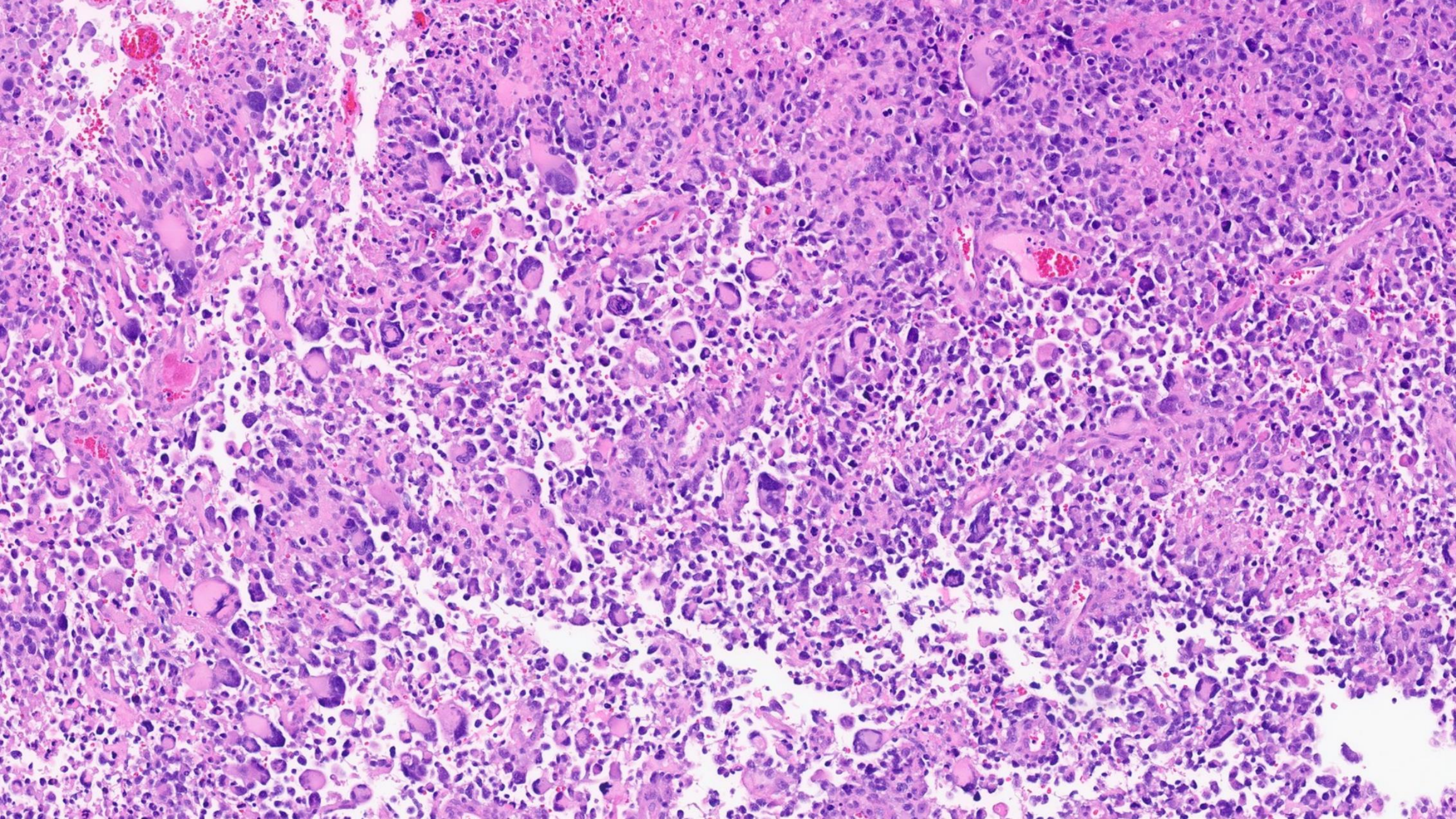
Case 2 – 71-year-old woman



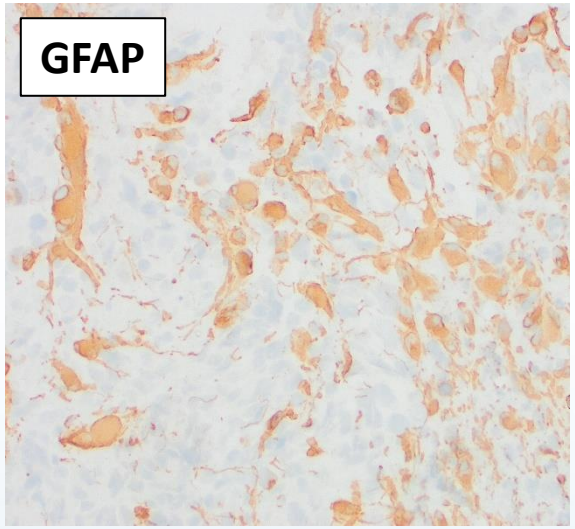


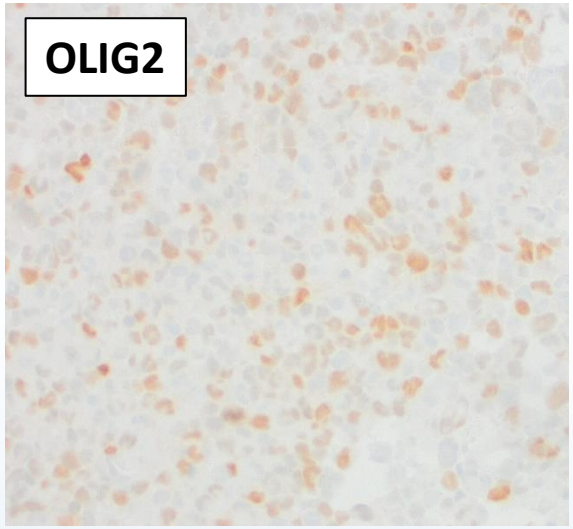


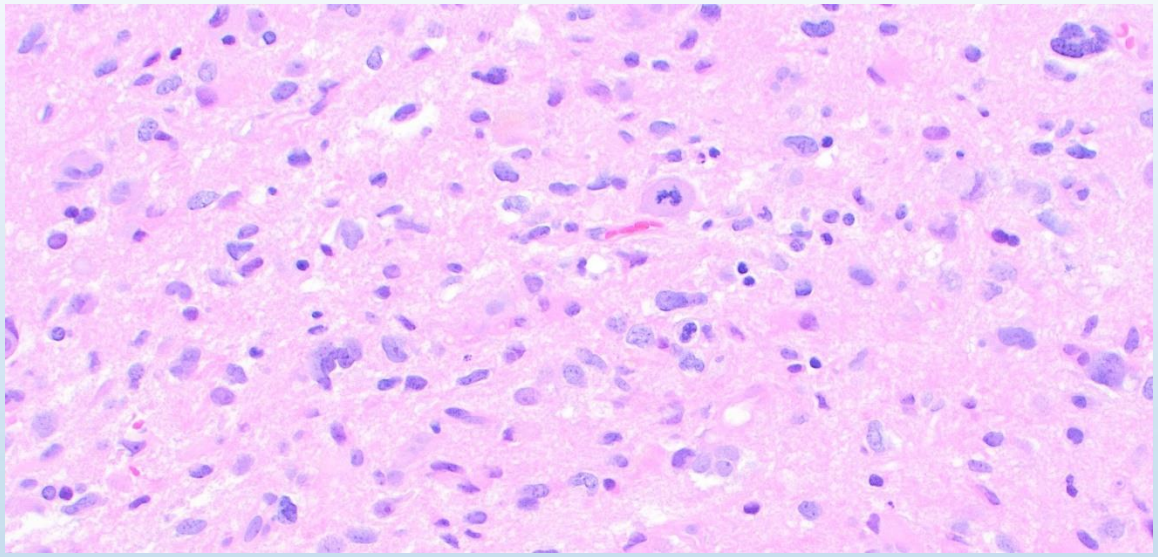




Case 2 – Immunohistochemistry and molecular results







Relevant next-generation sequencing results:

IDH-wildtype and H3-wildtype

TERT promoter region mutation

Trisomy 7 and monosomy 10

CDKN2A homozygous deletion

MET amplification

TP53 and *PIK3CA* mutations

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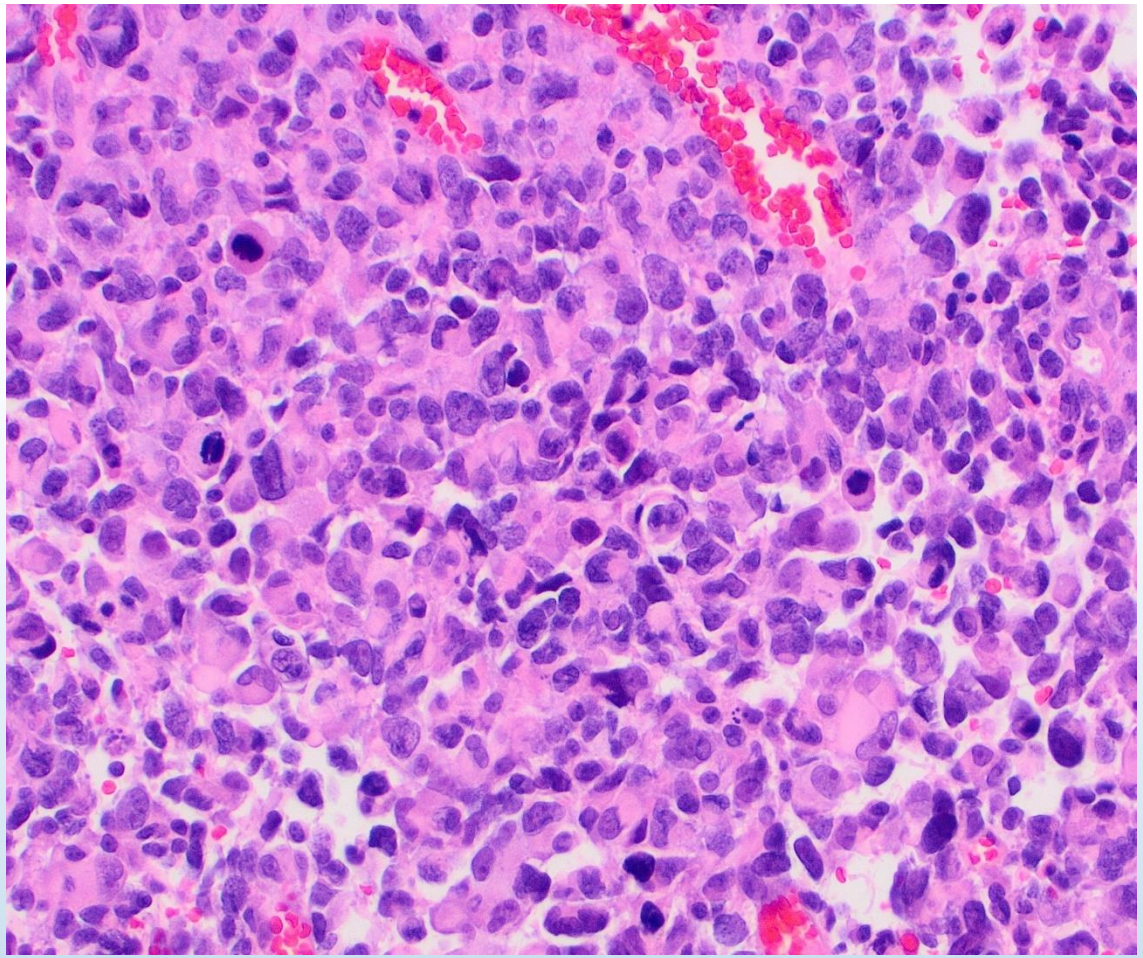
Case 2 – Epithelioid glioblastoma



- Dyscohesive, large, epithelioid to rhabdoid cells
- Mimicking metastatic carcinoma or melanoma
- “Adenoid” with formation of glandular structures
- May express cytokeratin, EMA
- Increased frequency of *BRAF* V600E mutation

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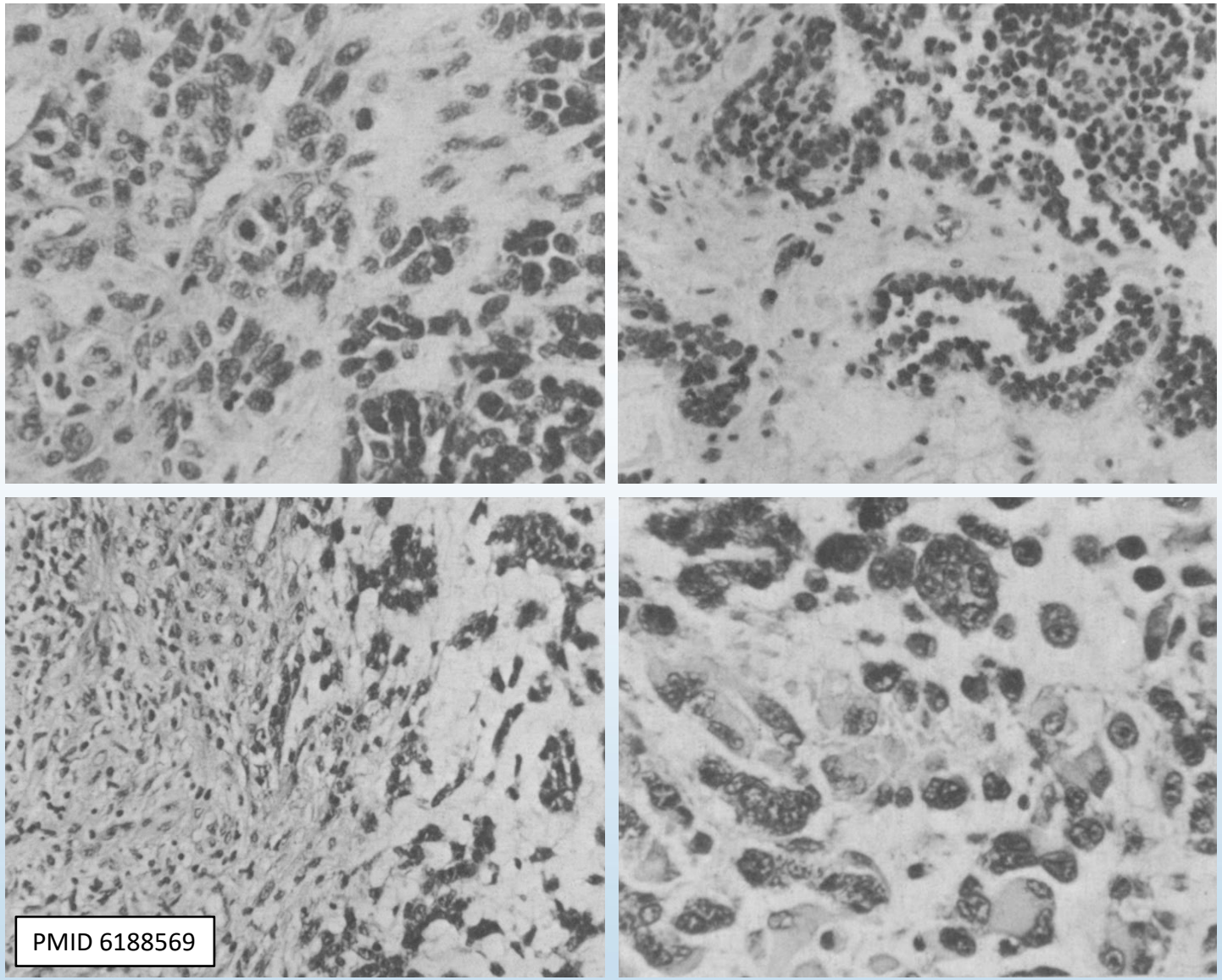
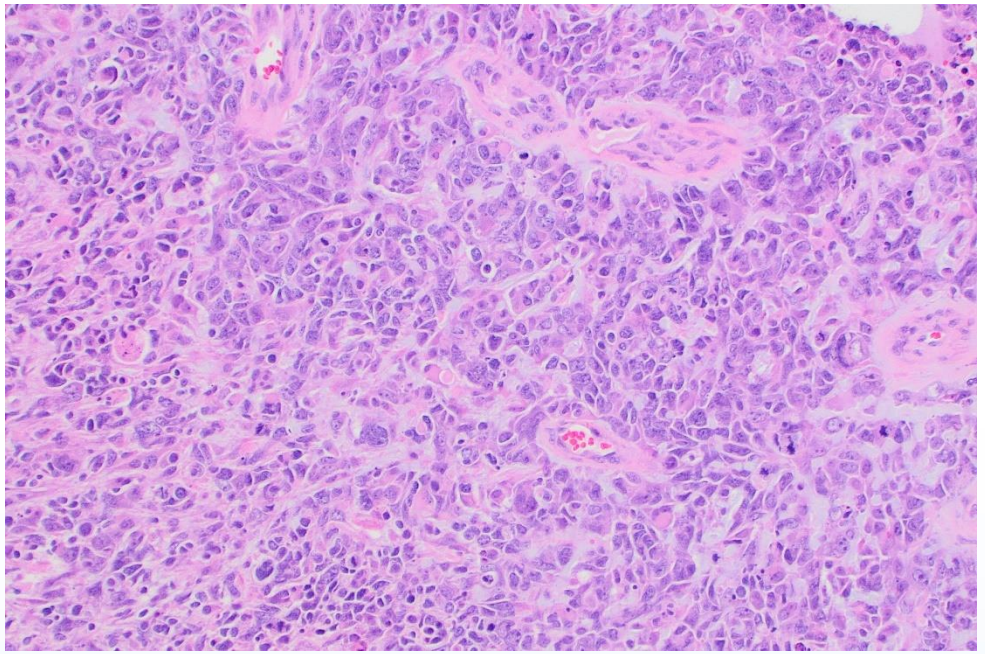
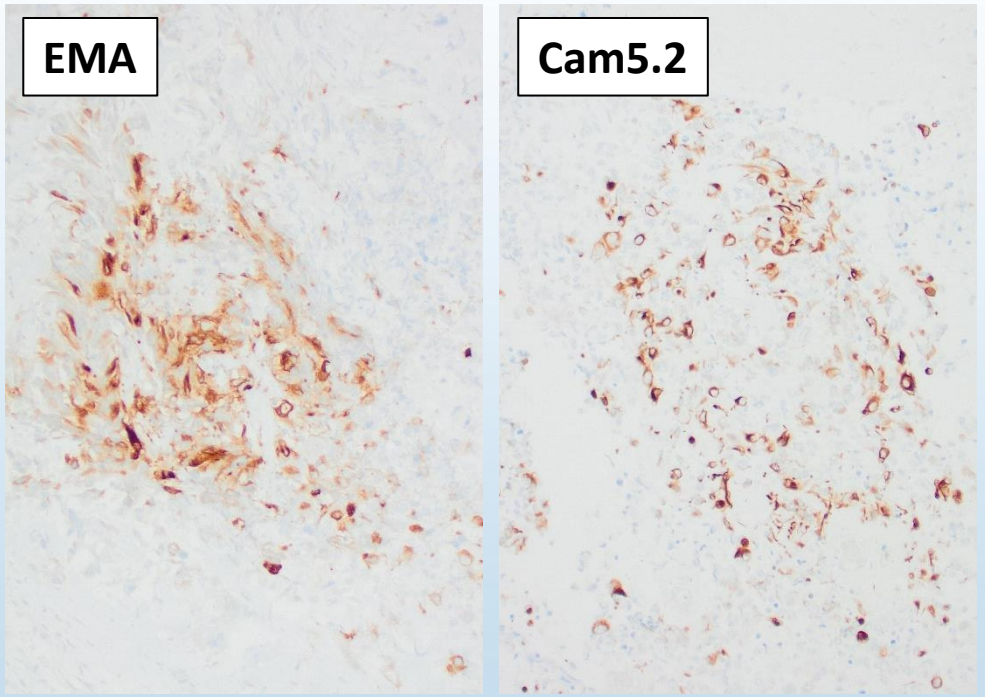
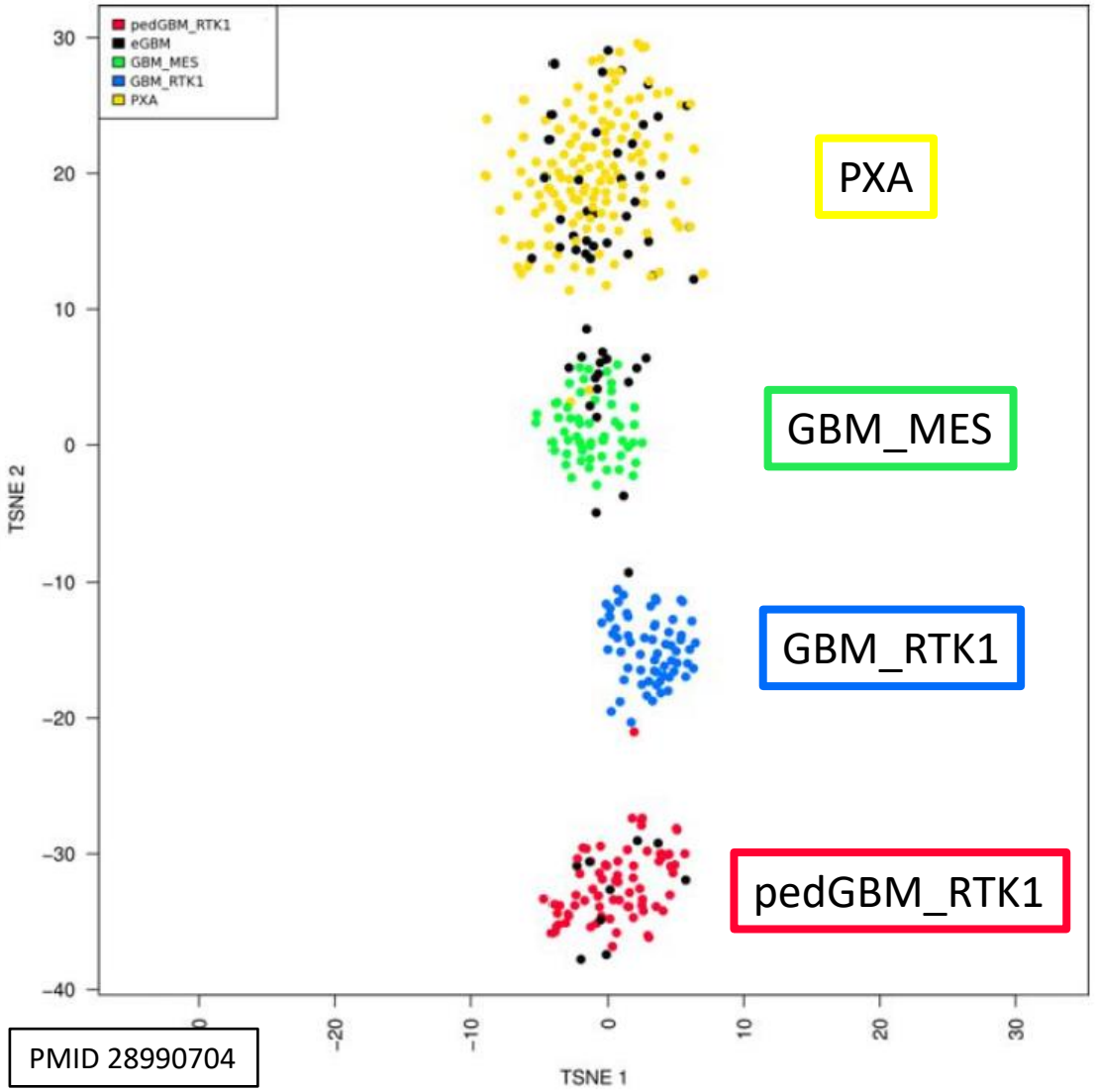
Kepes 1982 "The recognition of these cells as being astrocytic was made possible partly by finding **transitional zones to more typical, "classic" neoplastic astrocytes** and partly by the **positive staining of the tumor cells for glial fibrillary acidic protein** (GFAP) by the immunoperoxidase method"







Diverse methylation-based classes in histological epGB

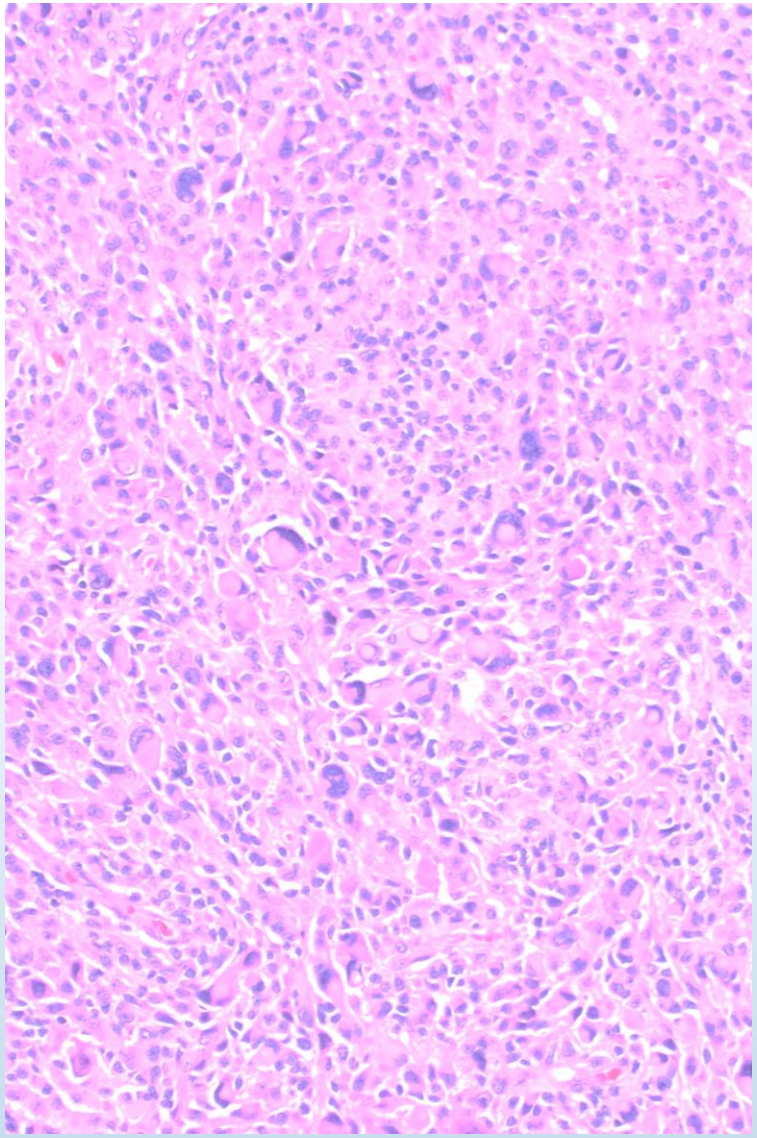


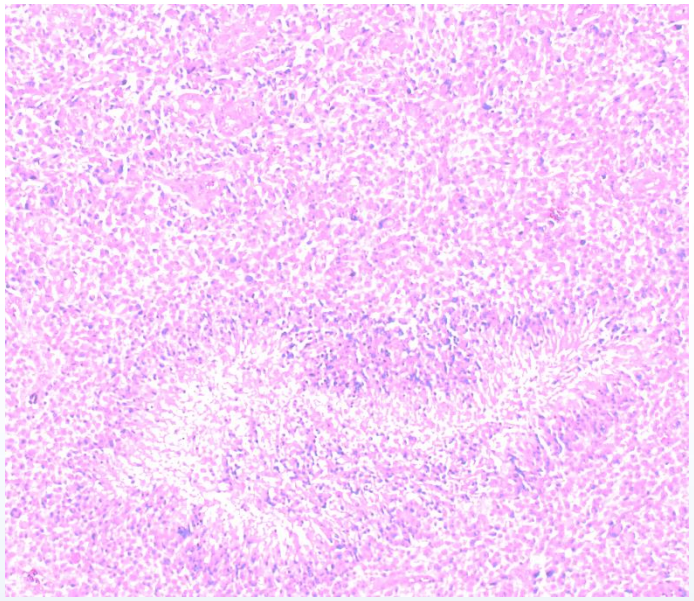
PMID 28990704

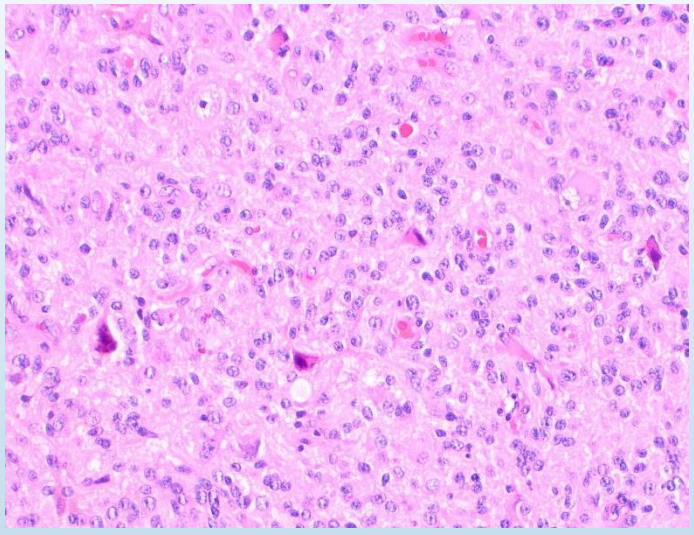
Table 1. Clinical and molecular variables in eGBM adjusted for various related CNS tumor clusters.

Variable	Clustered with PXA ($n = 38$)	Clustered with adult IDHwt GBM ($n = 17$)	Clustered with pediatric RTK1 GBM ($n = 9$)
Median age	17	50 ←	18
Children*	55%	0	56%
Gender M vs. F	58%/42%	94%/6%	56%/44%
PXA-like foci	34%	24% ←	22%
Median OS	34 months	11 months	18 months
Mean MIB1 LI	47%	53%	48%
Amplifications	0	25%	89%
CDKN2A homo del	61%	53%	33%
7 gain	53%	88%	30%
10q loss	28%	88%	70%
BRAF V600E mut	79%	35% ←	0
pTERT mut	30%	83%	0
MGMT methyl	21%	47%	33%
Chromothripsis	0	0	100%

(Epithelioid) glioblastoma-like histology within mcPXA

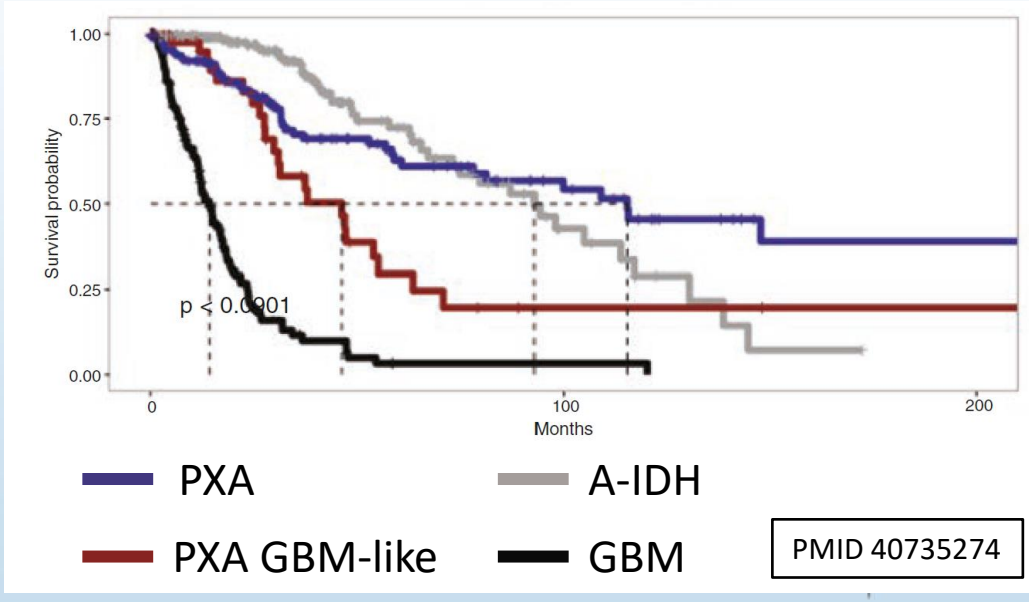






CD34 and Collagen-IV negative
Eosinophilic granular bodies present
BRAF V600E and *TERT* promoter mut.
CDKN2A homozygous deletion

Methylation class: PXA (score 1.0)



PMID 40735274

Epithelioid glioblastoma – differential and workup

Pleomorphic xanthoastrocytoma

- *Opinion*: no single histologic/genetic/clinical factor can differentiate
- Epigenetic classification can classify; caution when discordant to histopathology

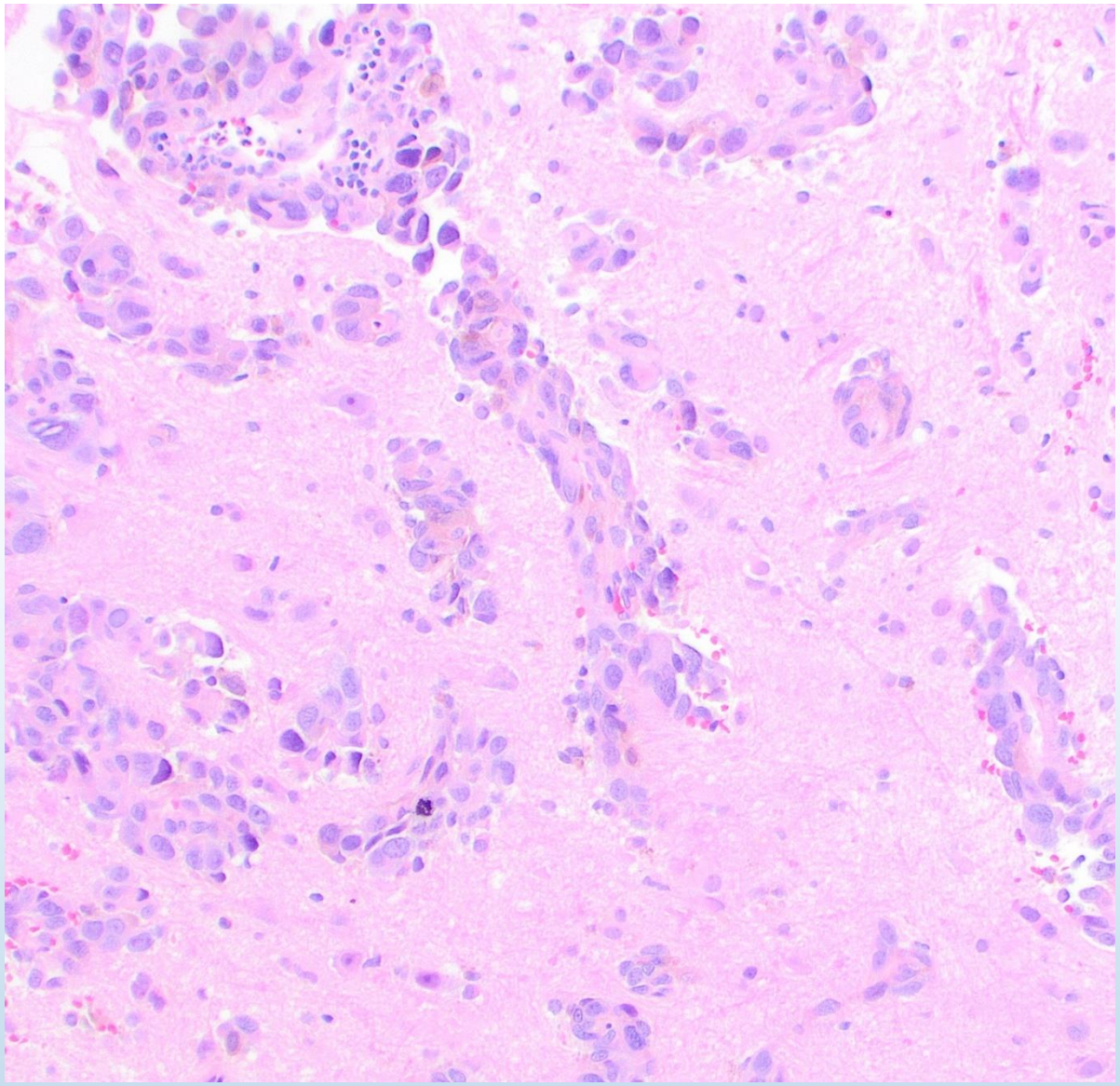
Metastatic carcinoma

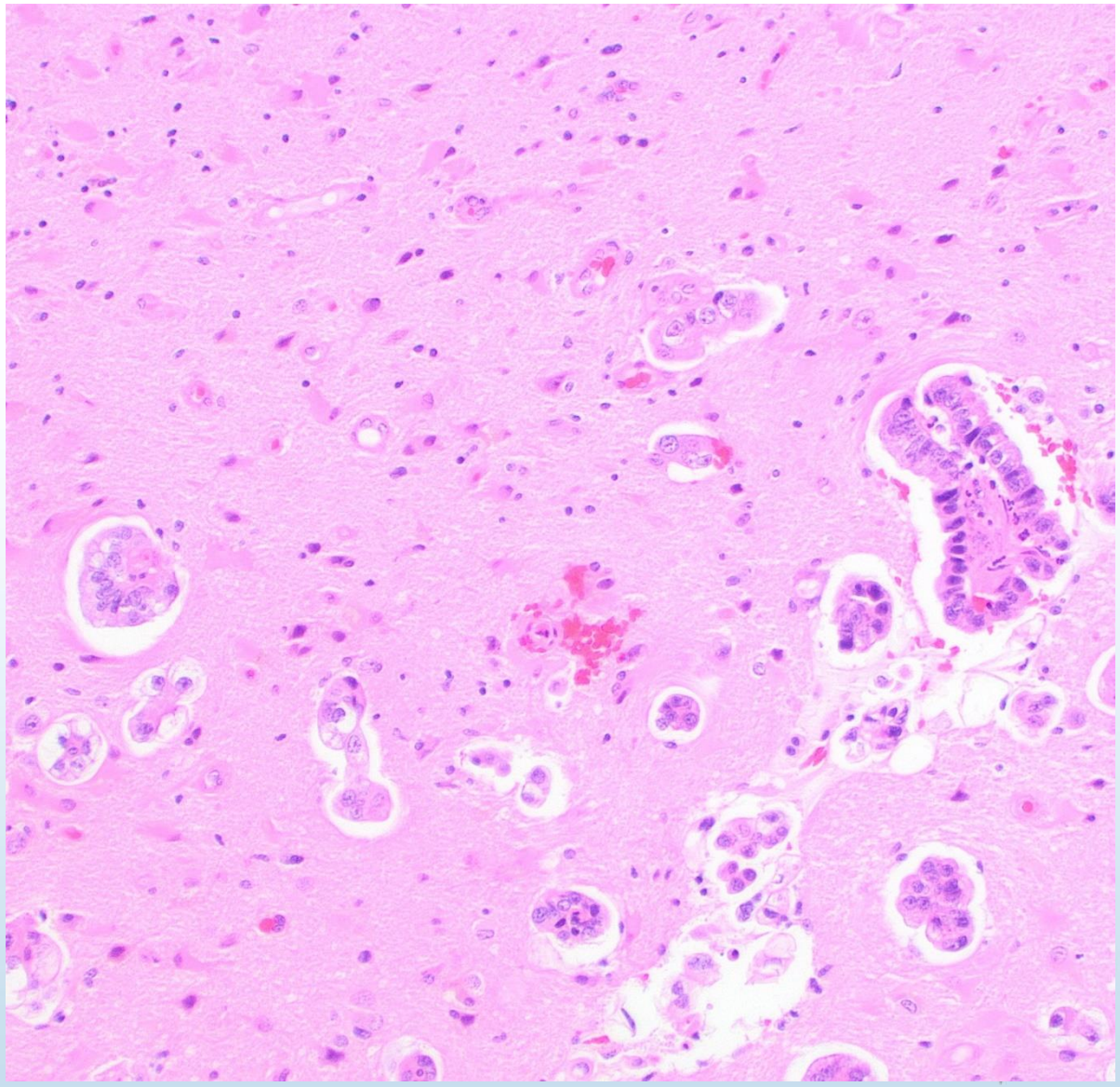
- Compact/non-infiltrative, multifocal, history/imaging
- Pitfall of EMA, cytokeratin positivity in epGB

Metastatic melanoma

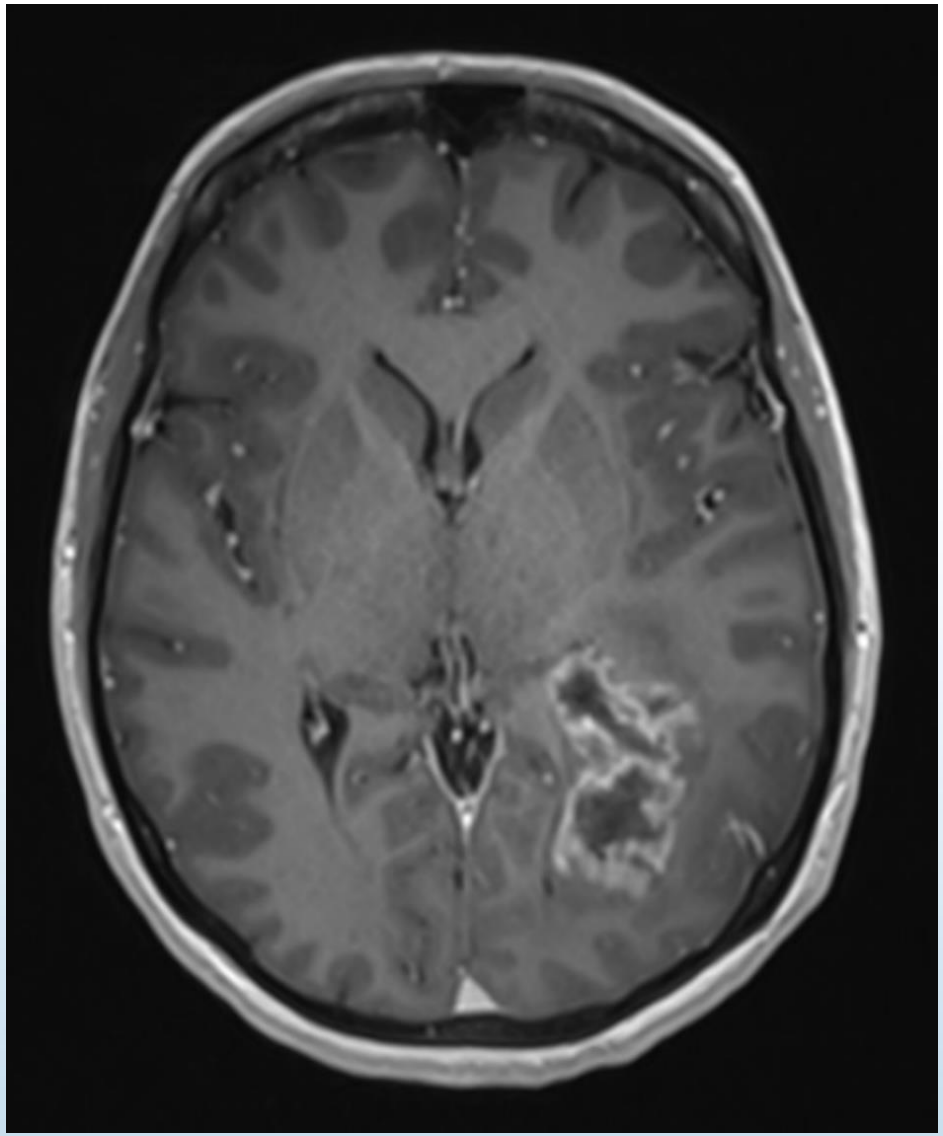
- Lacks a neoplastic high-grade astrocytic component
- Positivity for melanocytic markers (HMB45, MELANA, PRAME)
- May have overlapping feature of BRAF V600E mutation with epGB

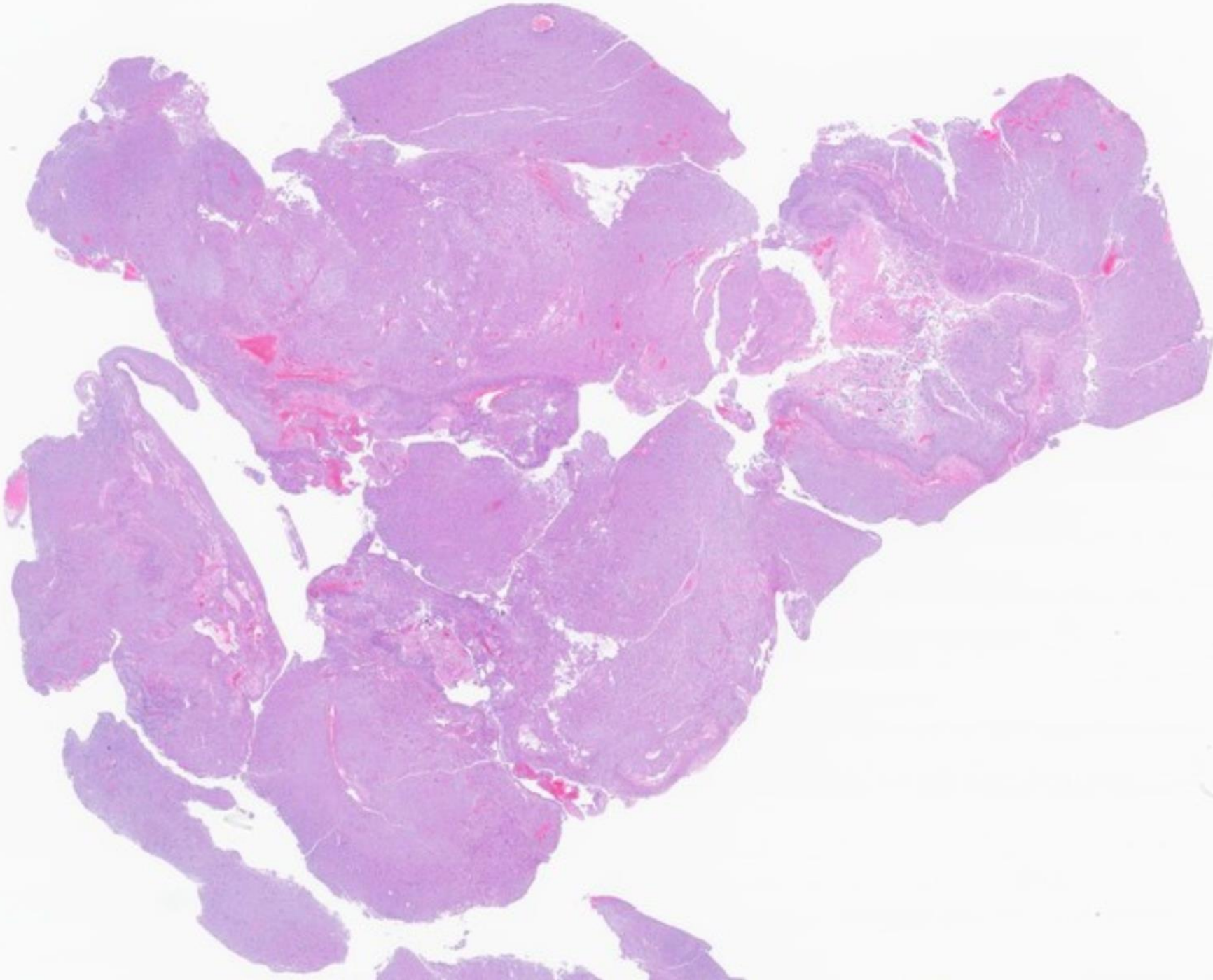
Tumor-parenchyma interface in metastatic tumors

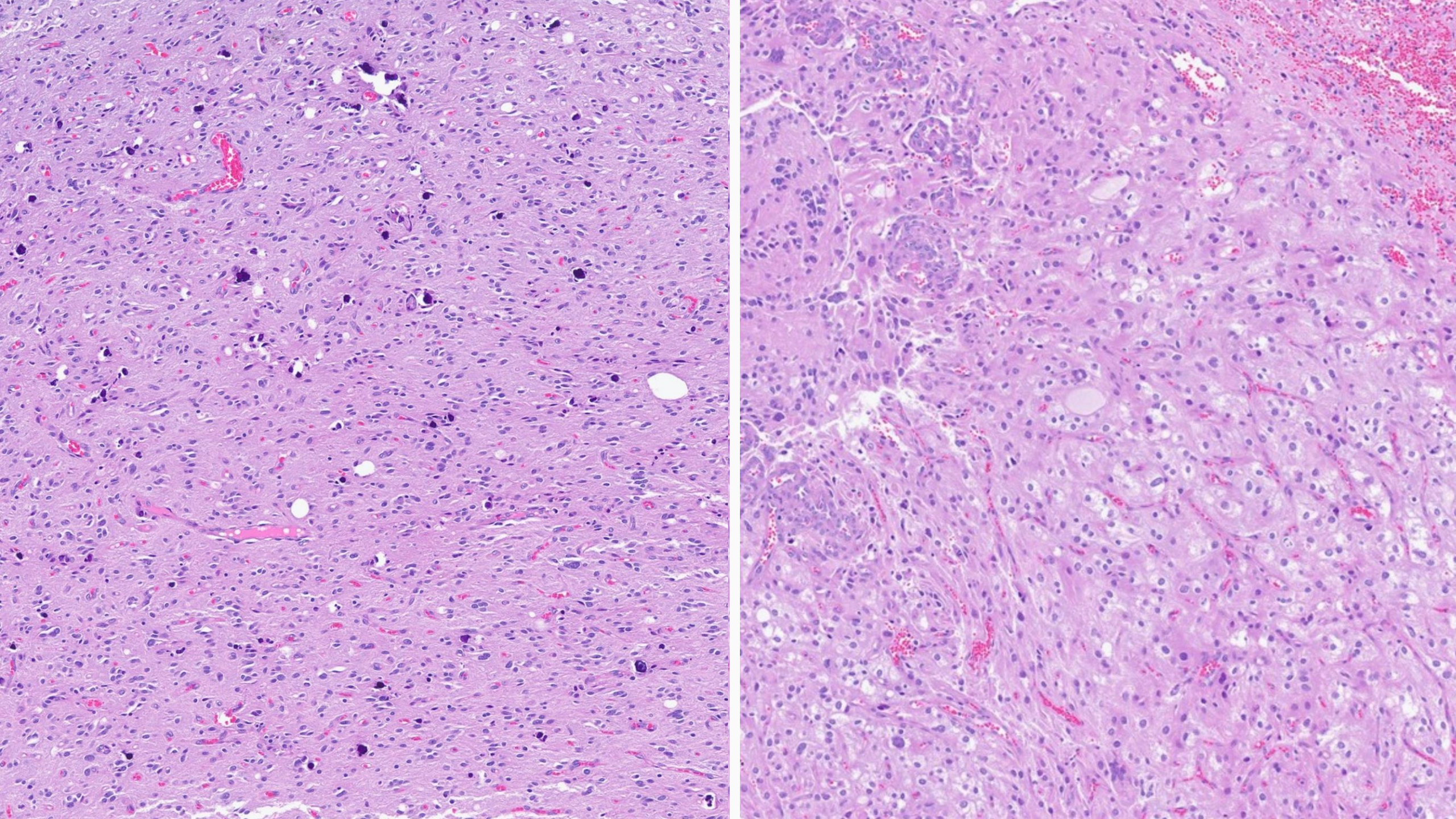


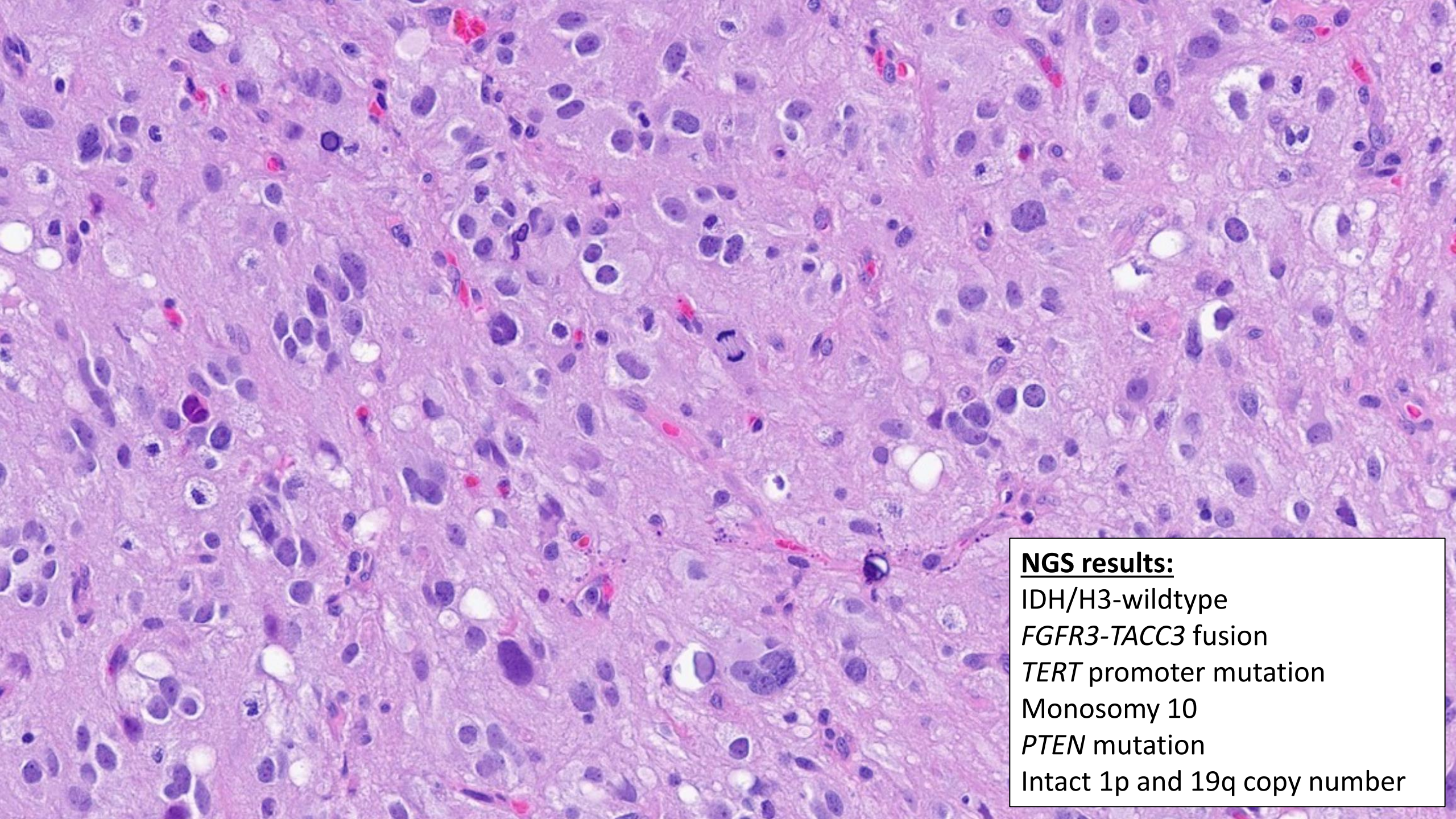


Case 3 – 40-year-old woman

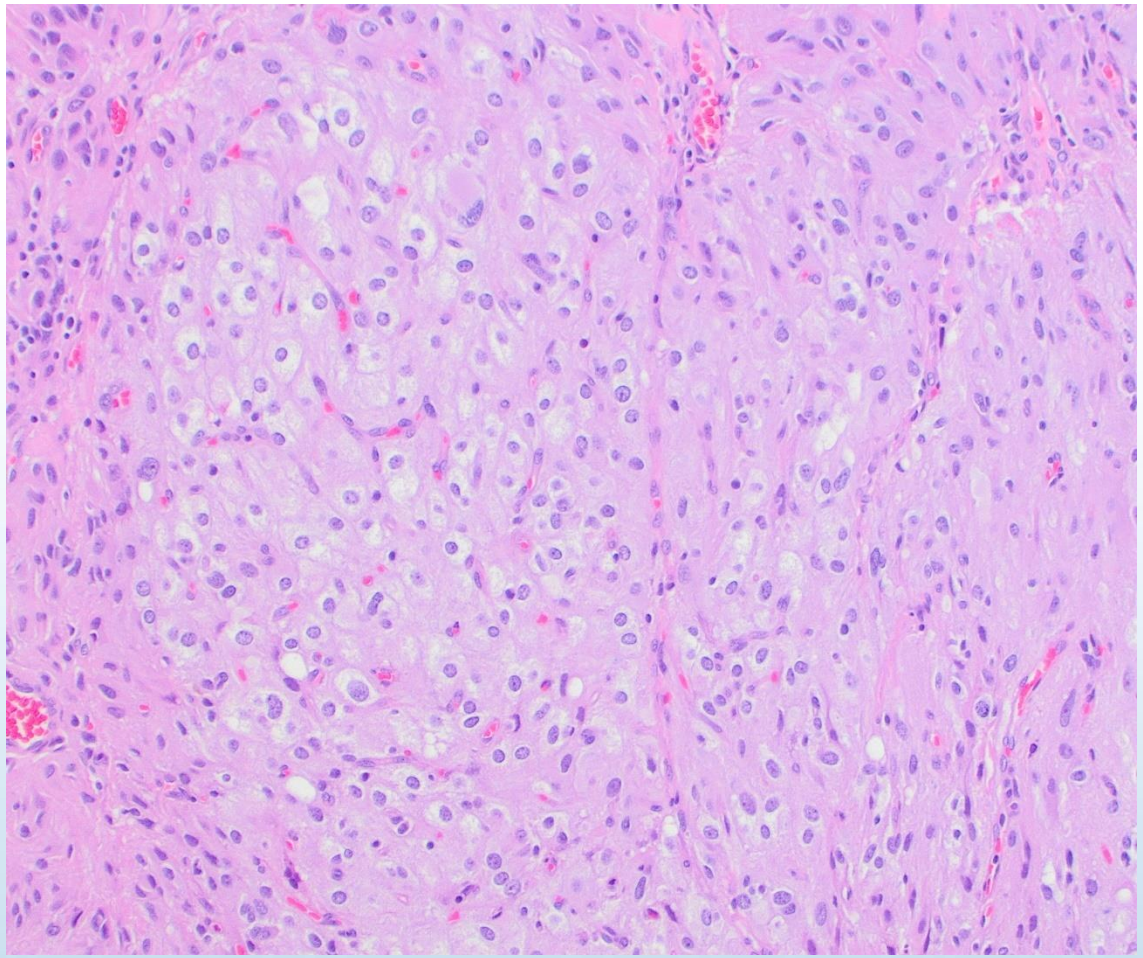







NGS results:
IDH/H3-wildtype
FGFR3-TACC3 fusion
TERT promoter mutation
Monosomy 10
PTEN mutation
Intact 1p and 19q copy number

Case 3 – Glioblastoma with oligodendrocyte-like cells

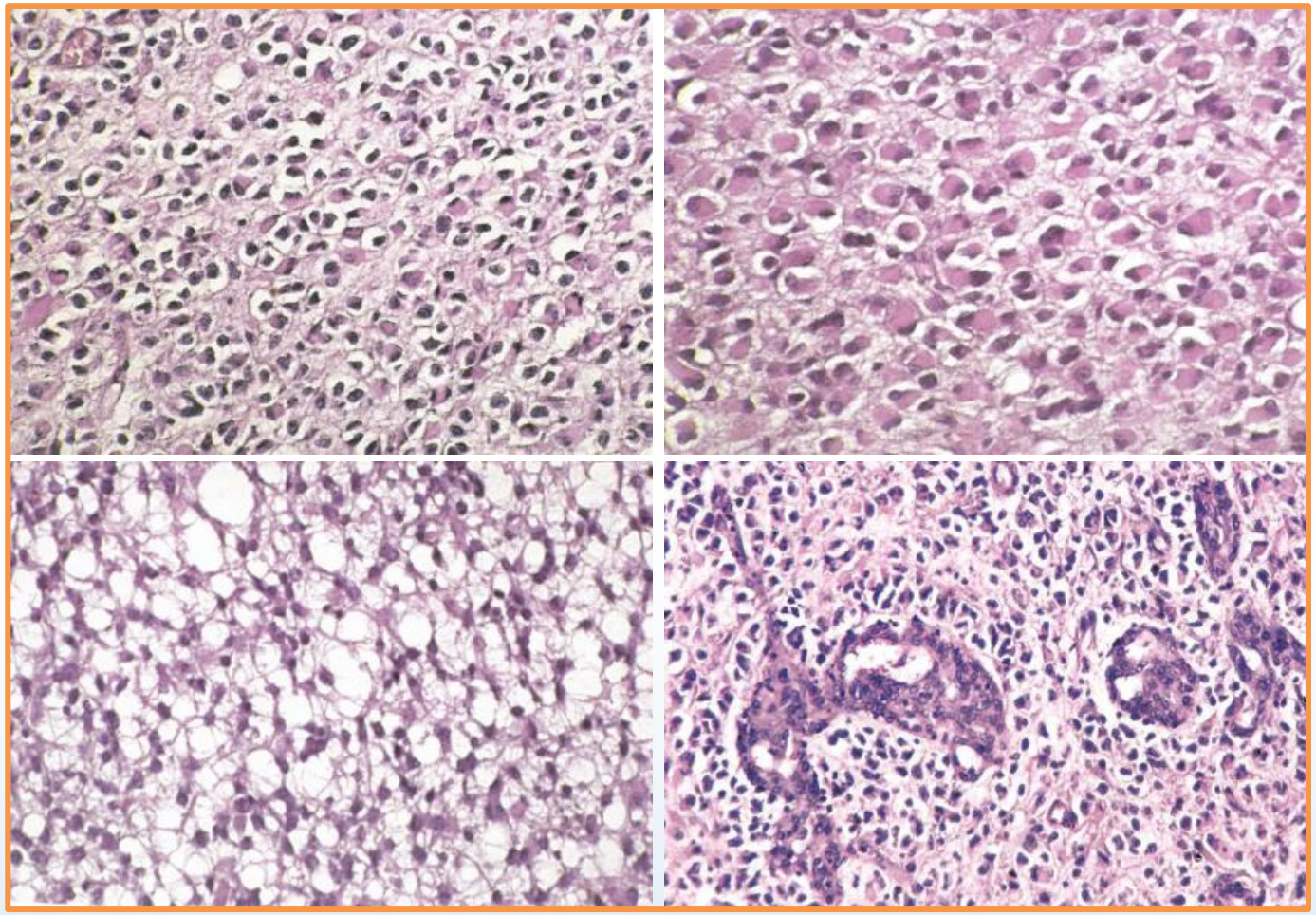


- Focal or diffuse component of cells with rounded nuclei and clear cytoplasm
- Microcalcifications
- Delicate branching background capillaries

WHO CNS 3 (2000)

1. **Astrocytic tumours**
   - Diffusely infiltrating astrocytomas
   - Diffuse astrocytoma
   - Anaplastic astrocytoma
   - Glioblastoma
   - Giant cell glioblastoma
   - Gliosarcoma
   - Pilocytic astrocytoma
   - Pleomorphic xanthoastrocytoma

2. **Oligodendroglial tumours and mixed gliomas**
   - Oligodendroglioma
   - Anaplastic oligodendroglioma
   - **Oligoastrocytoma (OA)**
   - **Anaplastic oligoastrocytoma (AOA) – Fig. 2.14**
   - Other mixed gliomas



OA *… diagnosis … requires the recognition of two different glial components both of which must be unequivocally neoplastic … may be divided into biphasic ("compact") and intermingled ("diffuse") variants [juxtaposed or intimately admixed]*
WHO grade II (2)

AOA *… oligoastroctyomas with histological features of anaplasia …*
… microvascular proliferation and necrosis may be present …
WHO grade III (3)

AANP

WHO CNS 3 (2000)

1. **Astrocytic tumours**
   - Diffusely infiltrating astrocytomas
   - Diffuse astrocytoma
   - Anaplastic astrocytoma
   - Glioblastoma
   - Giant cell glioblastoma
   - Gliosarcoma
   - Pilocytic astrocytoma
   - Pleomorphic xanthoastrocytoma

2. **Oligodendroglial tumours and mixed gliomas**
   - Oligodendroglioma
   - Anaplastic oligodendroglioma
   - **Oligoastrocytoma (OA)**
   - **Anaplastic oligoastrocytoma (AOA) – Fig. 2.14**
   - Other mixed gliomas

WHO CNS 4 (2007)

Two large studies of malignant gliomas suggest that necrosis is associated with significantly worse prognosis in the setting of anaplastic gliomas with both oligodendroglial and astrocytic components …

Such tumors should be classified as "glioblastoma with oligodendroglial component", *although they may have a better prognosis than standard glioblastoma*

WHO CNS 4R (2016)

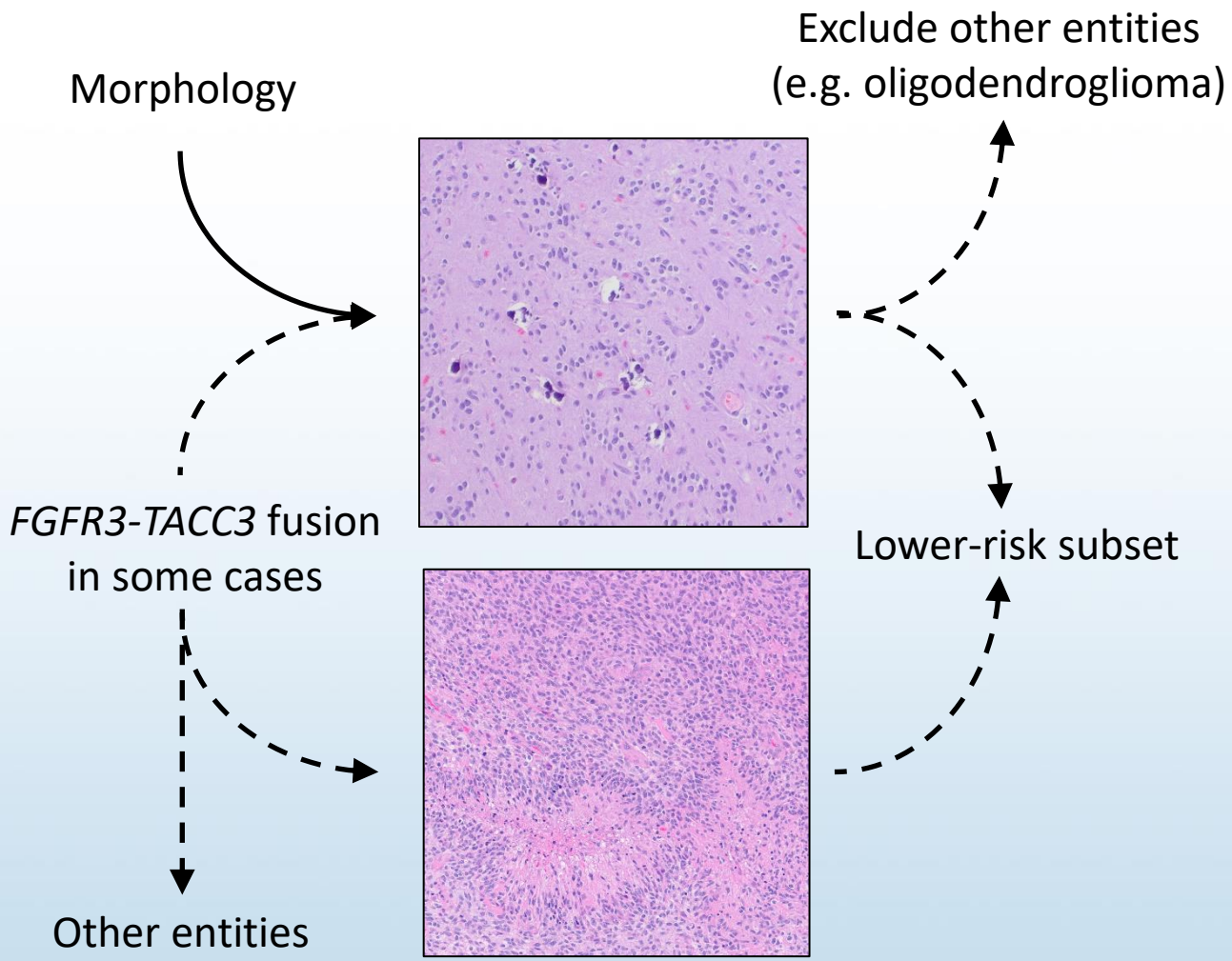
More recent studies suggest that this is a heterogeneous tumor group and that some cases are IDH1- or IDH2-mutant glioblastomas. ***The current WHO classification does not consider glioblastoma with an oligodendroglioma component to be a distinct entity****; with genetic analysis, it should be possible to classify such tumors as IDH-wildtype glioblastoma ... IDH-mutant glioblastoma … or IDH-mutant and 1p/19q-codeleted anaplastic oligodendroglioma*

OA *… diagnosis … requires the recognition of two different glial components both of which must be unequivocally neoplastic … may be divided into biphasic ("compact") and intermingled ("diffuse") variants [juxtaposed or intimately admixed]*
WHO grade II (2)

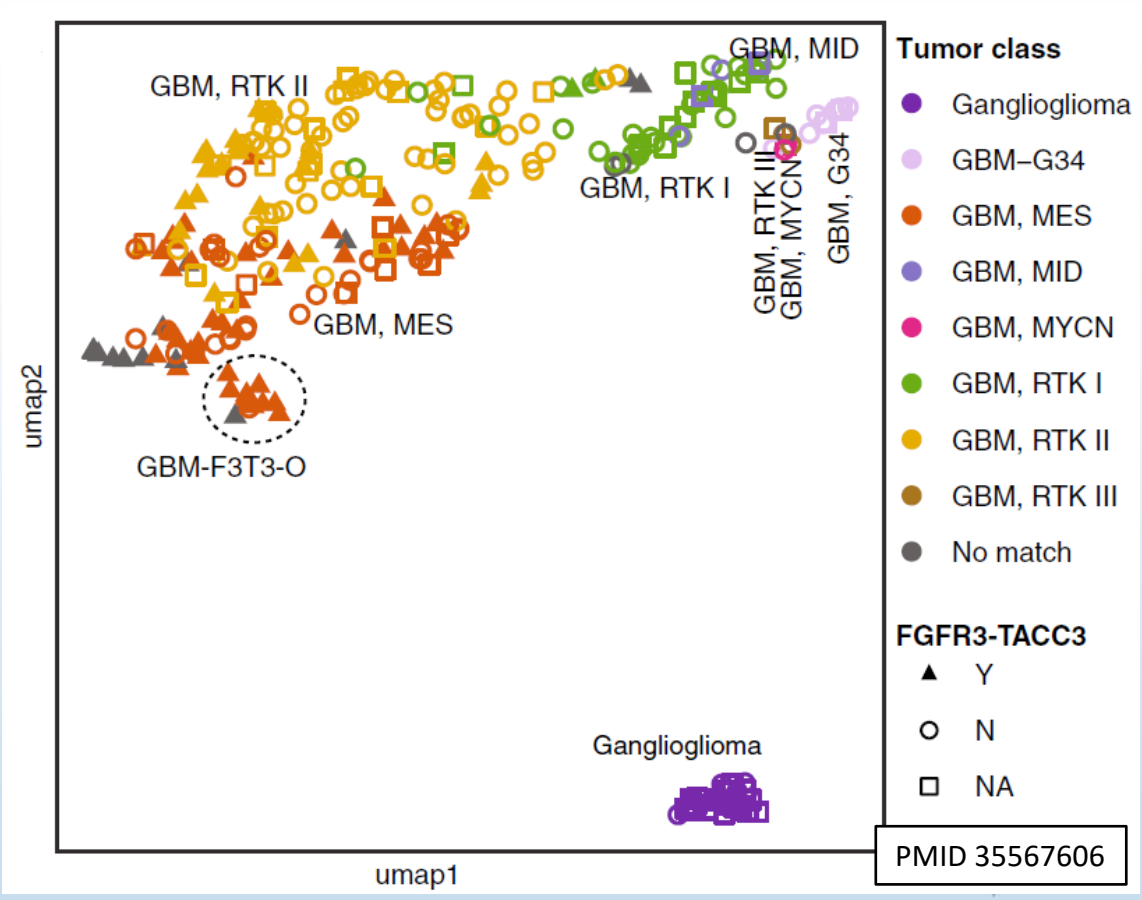
AOA *… oligoastroctyomas with histological features of anaplasia … … microvascular proliferation and necrosis may be present …*
WHO grade III (3)

AANP

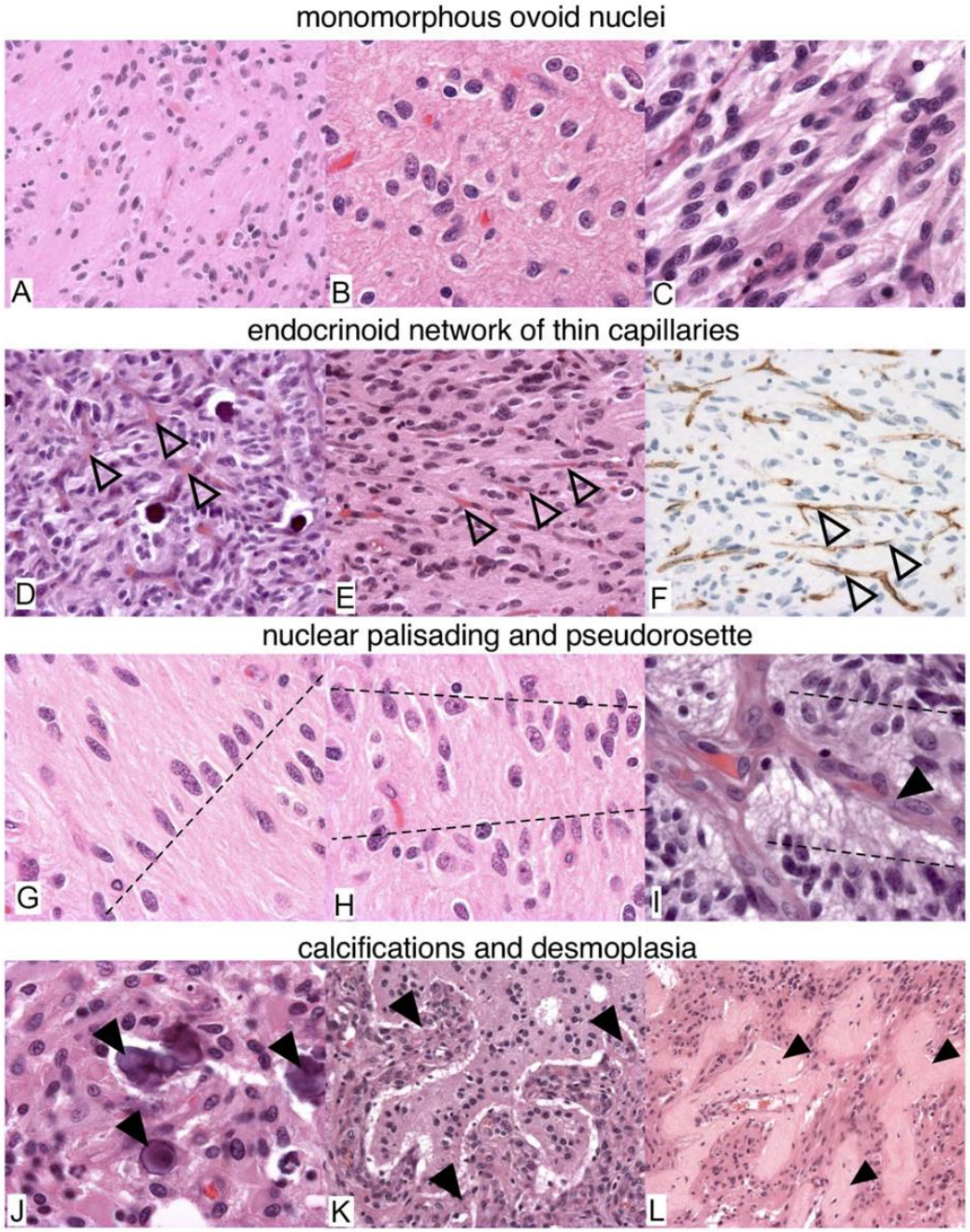
Molecular features of GB with oligodendrocyte-like cells

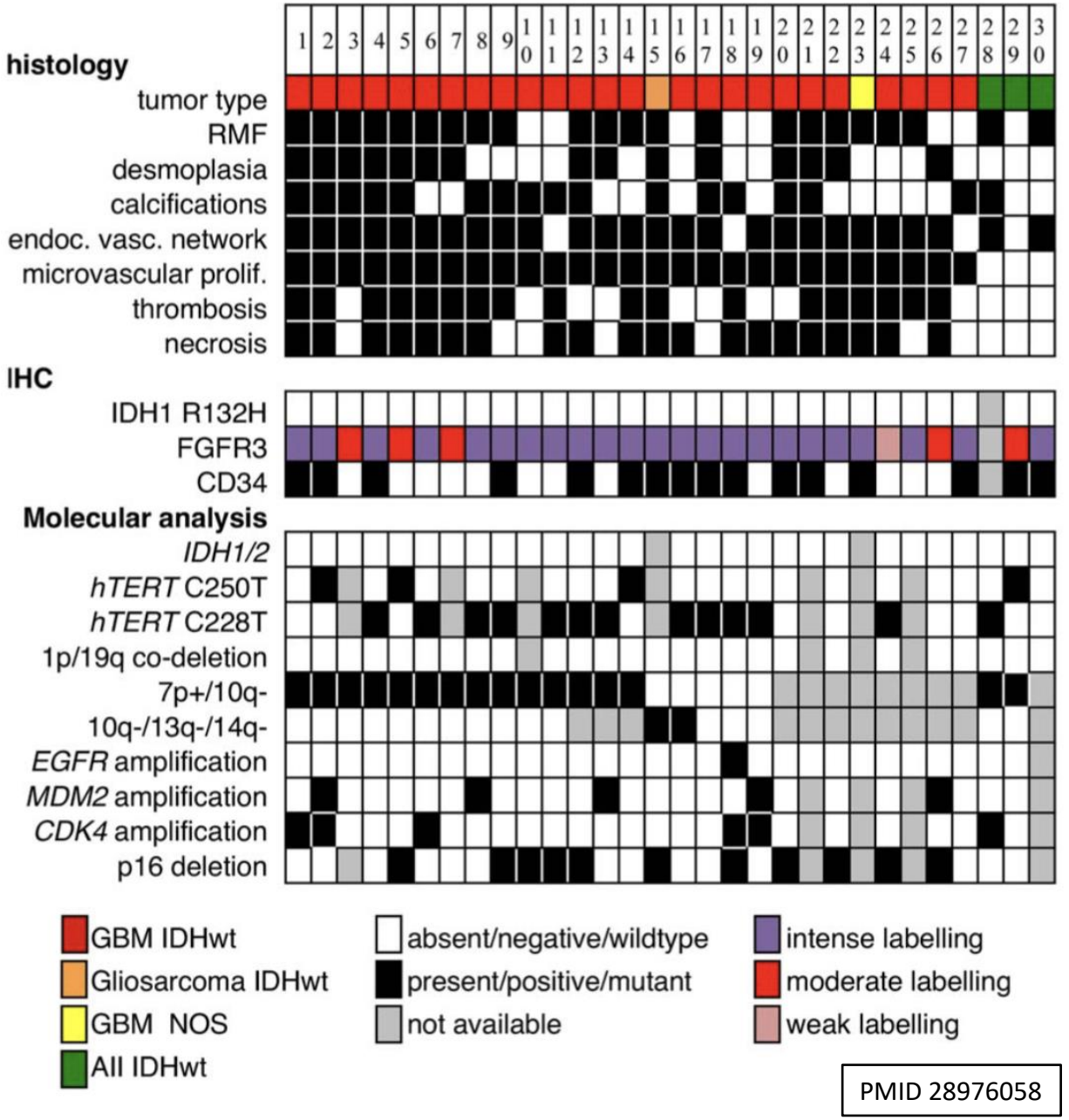


Methylation-based classes in glioblastomas with *FGFR3-TACC3* fusion



PMID 35567606





PMID 28976058

Glioblastoma c oligo-like cells – differential and workup

Glioblastoma, IDH-wildtype (small cell pattern)

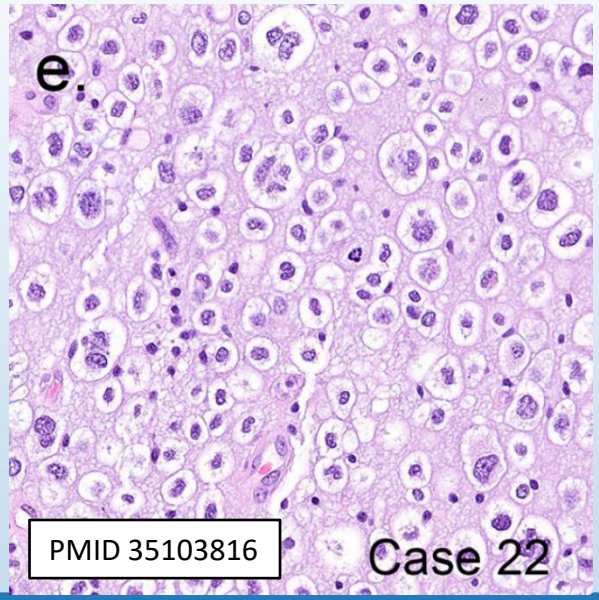
- Less pronounced oligodendrocyte-like cytology, distinctive vasculature or calcifications

Oligodendroglioma, IDH-mutant and 1p/19q-codeleted

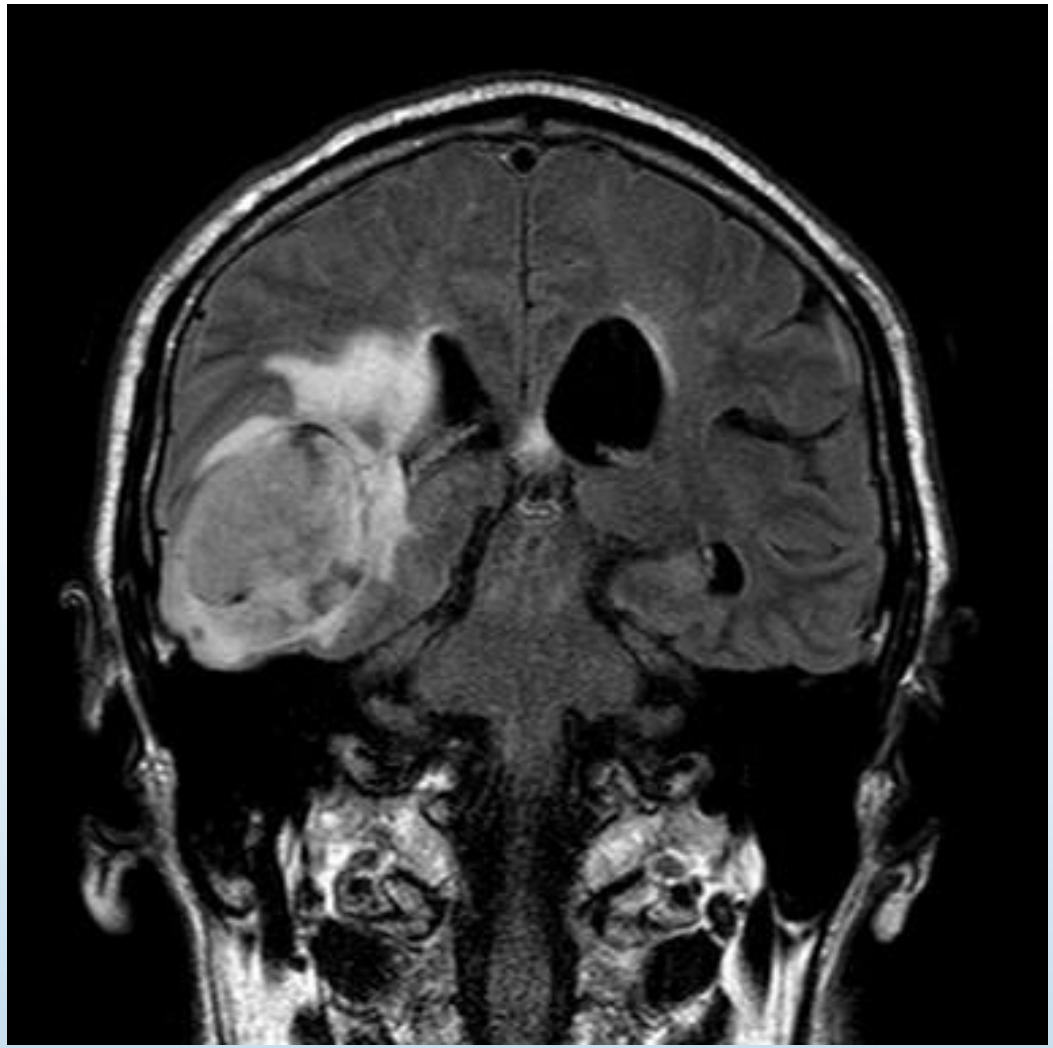
- Monotypic neoplastic population
- ~90% positive for IDH1 R132H by immunohistochemistry

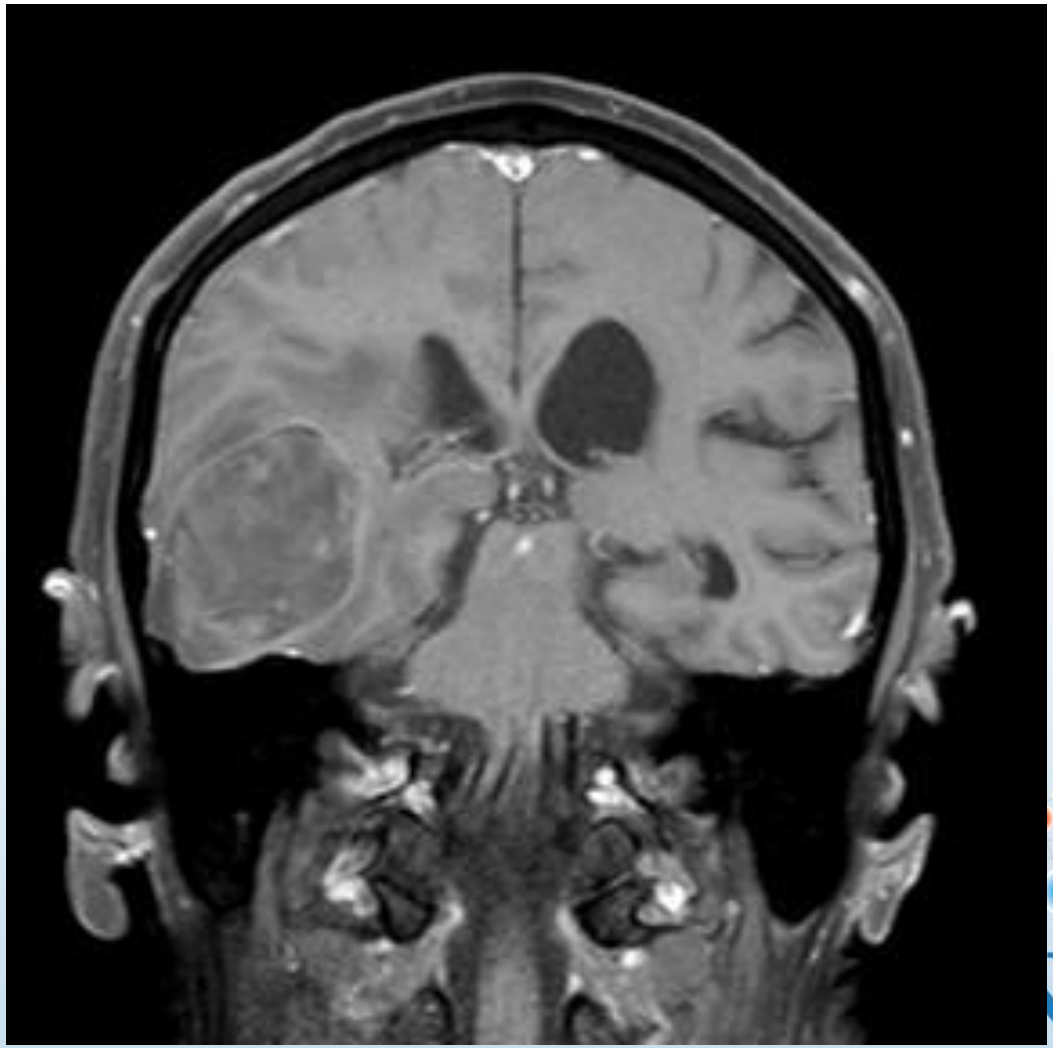
High-grade glioma with pleomorphic and pseudopapillary features

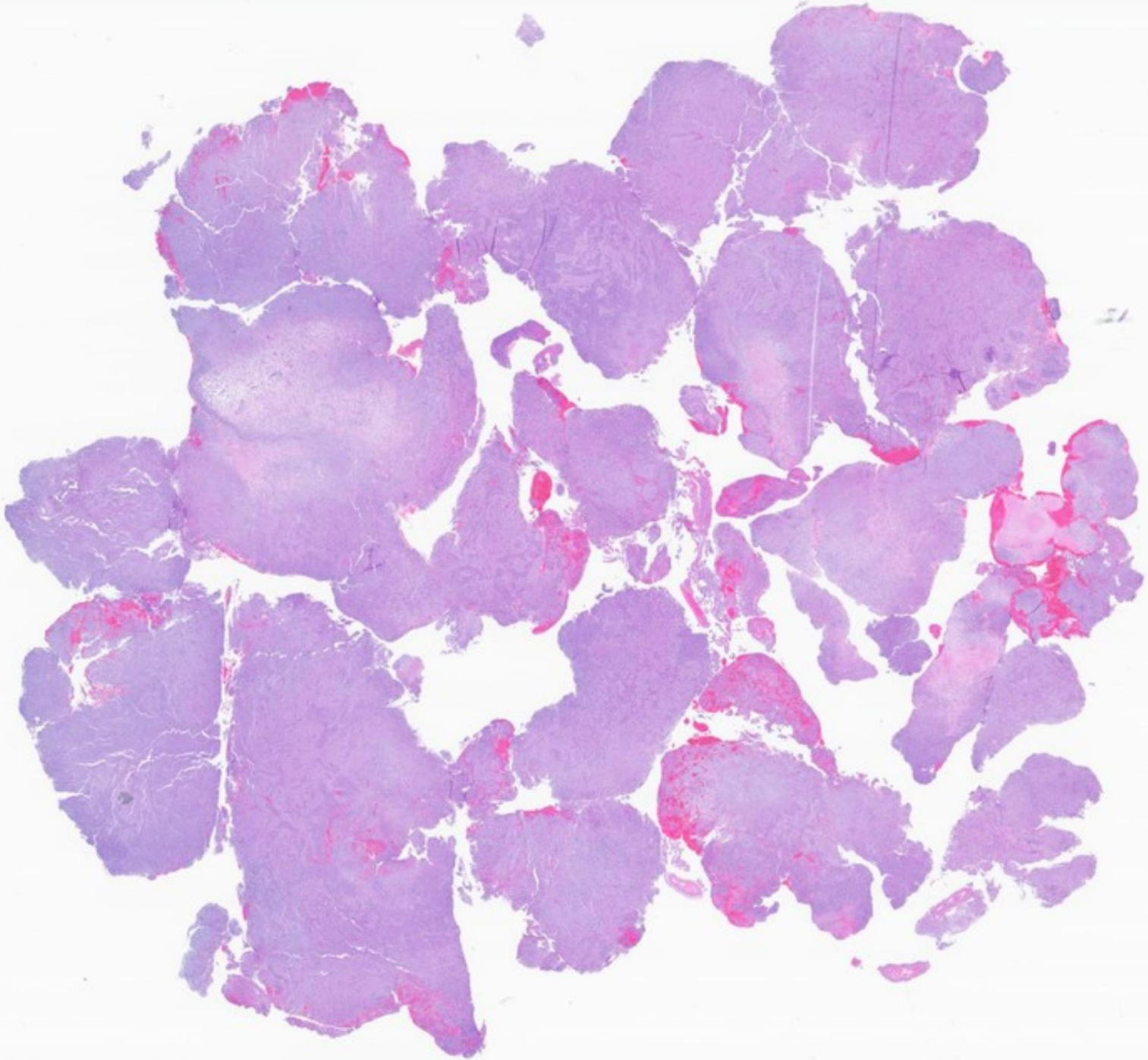
- Circumscription, pleomorphism, architecture
- Distinct methylation class
- Consider HPAP when NGS shows monosomy 13 -/+ *TP53, RB1 or NF1* mutation

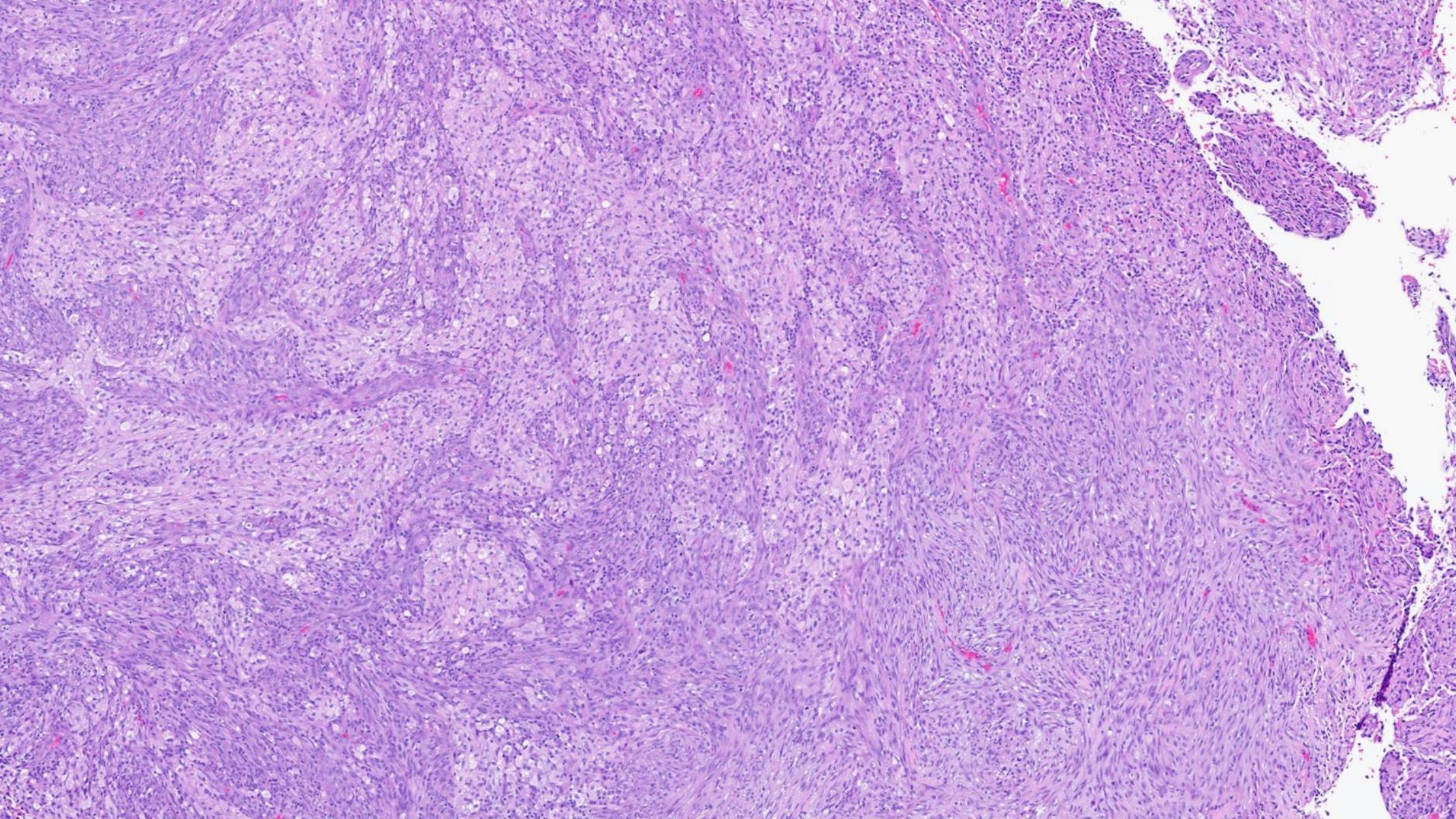


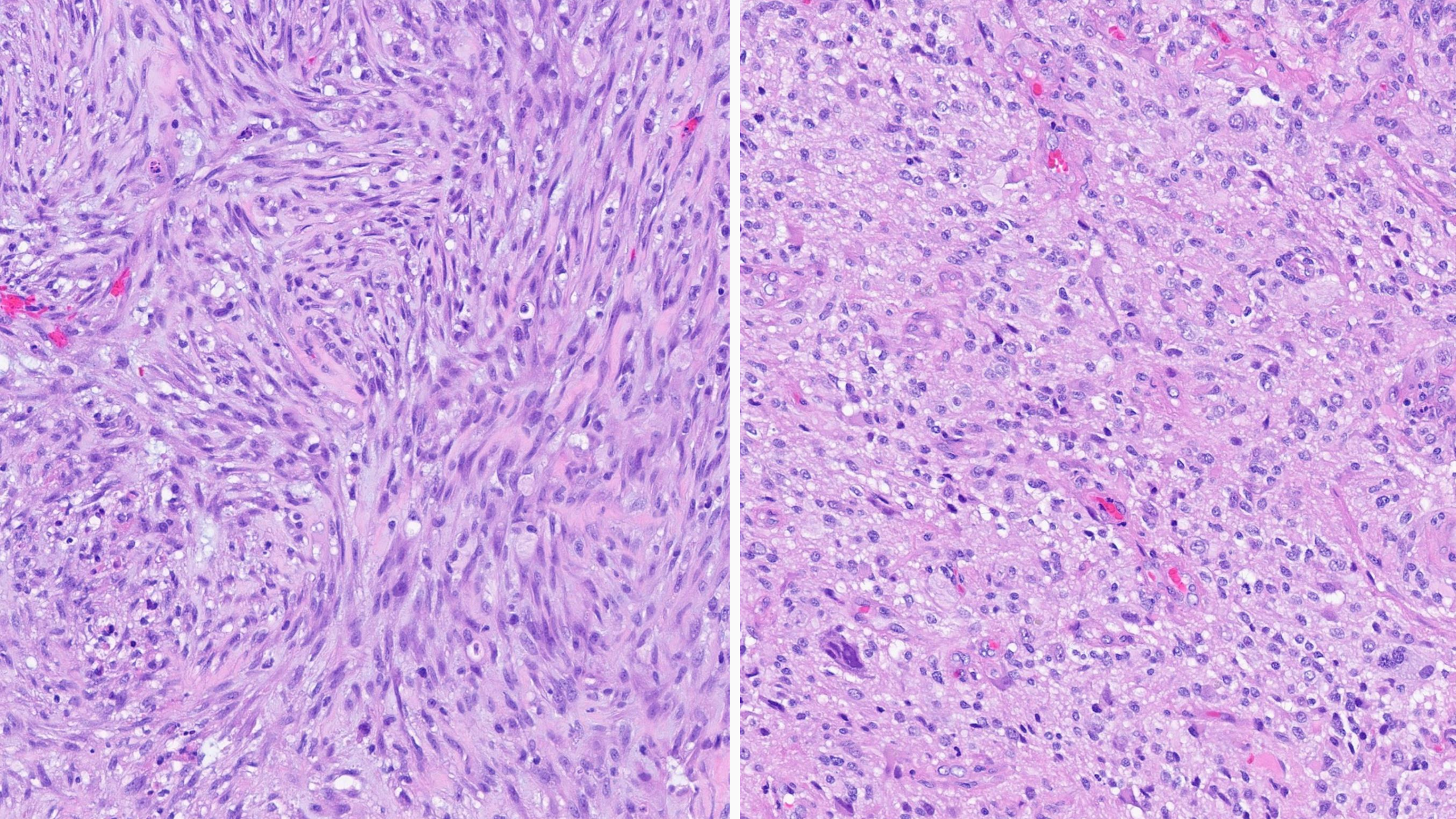
Case 4 – 70-year-old man



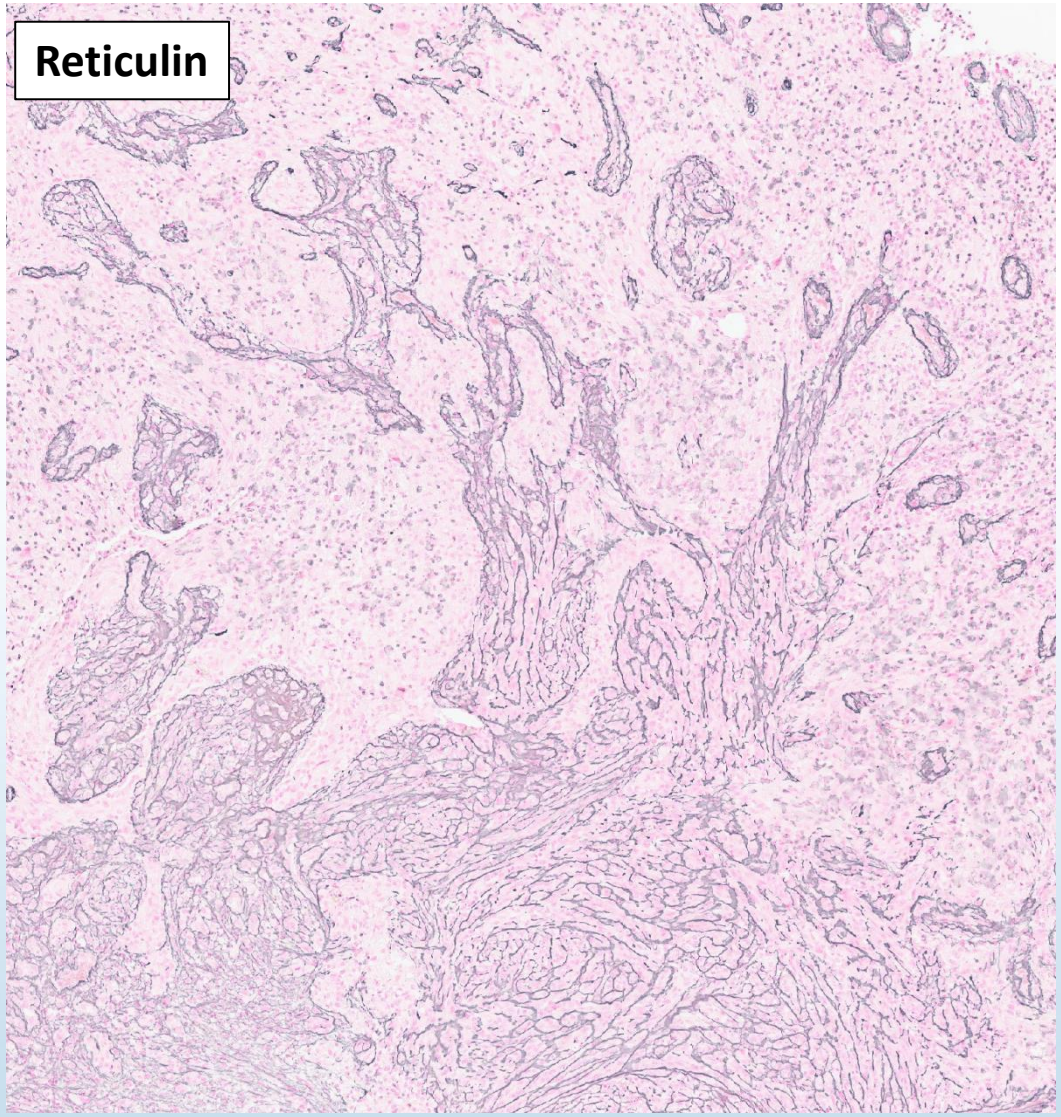


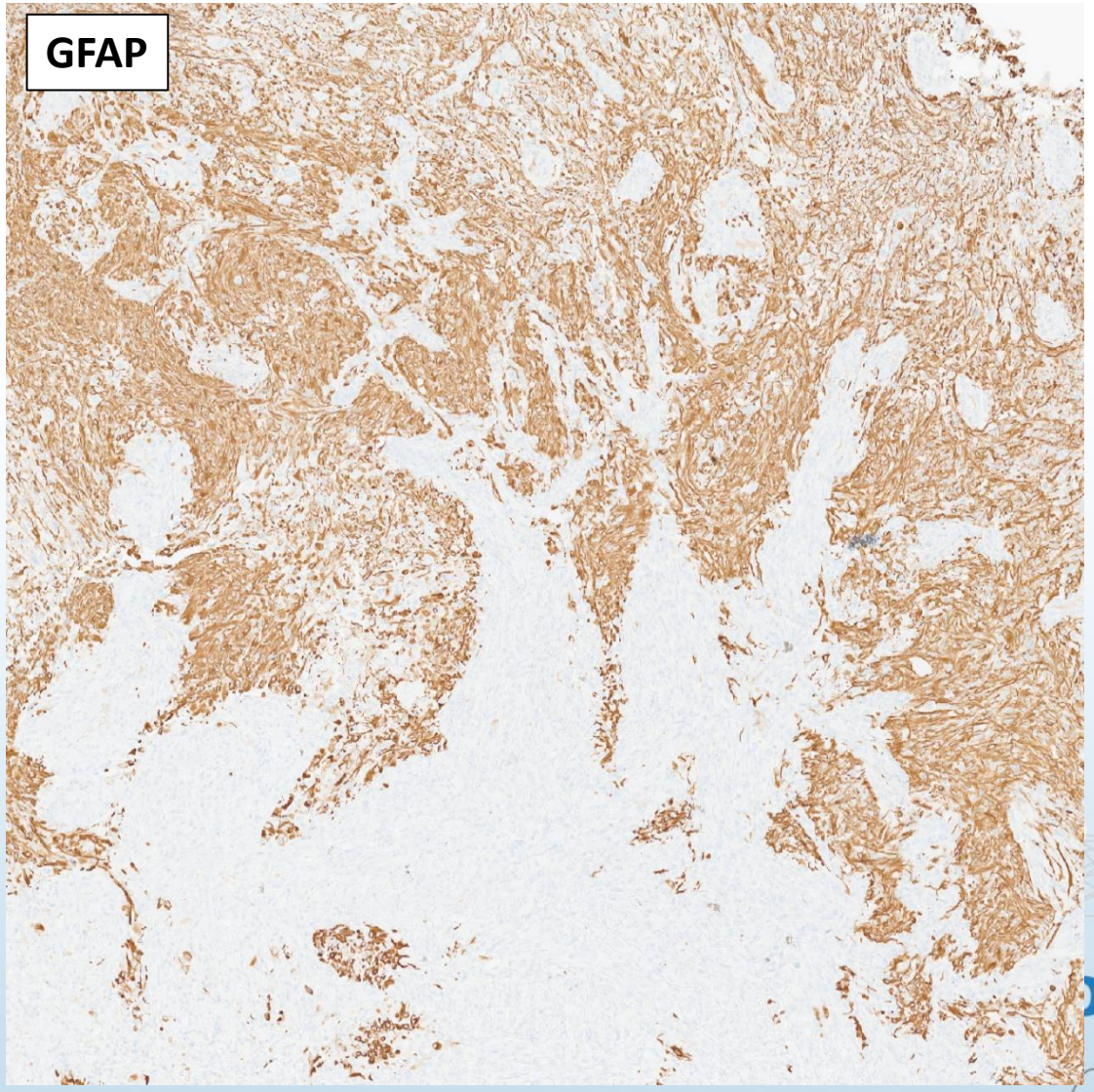




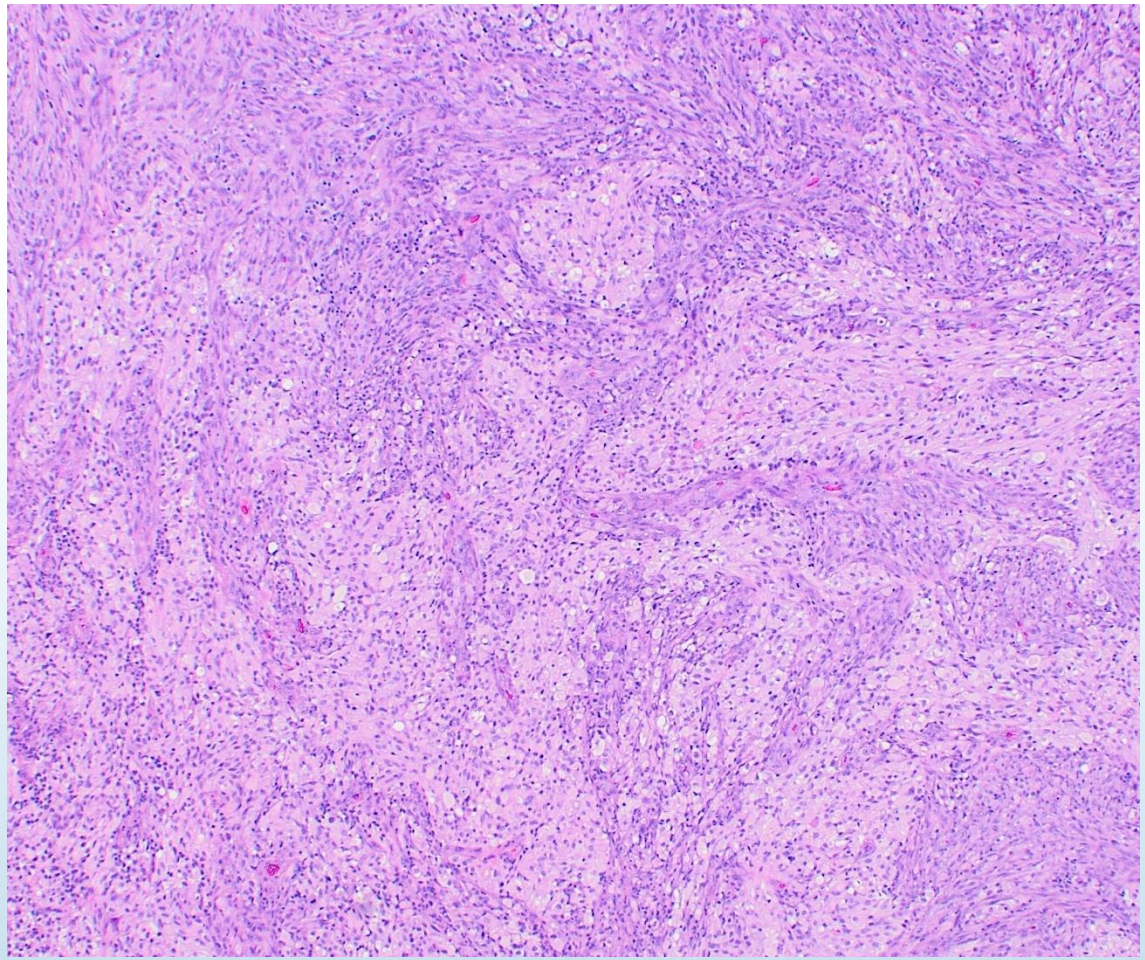


Case 4 – Histochemical stains





Case 4 – Gliosarcoma

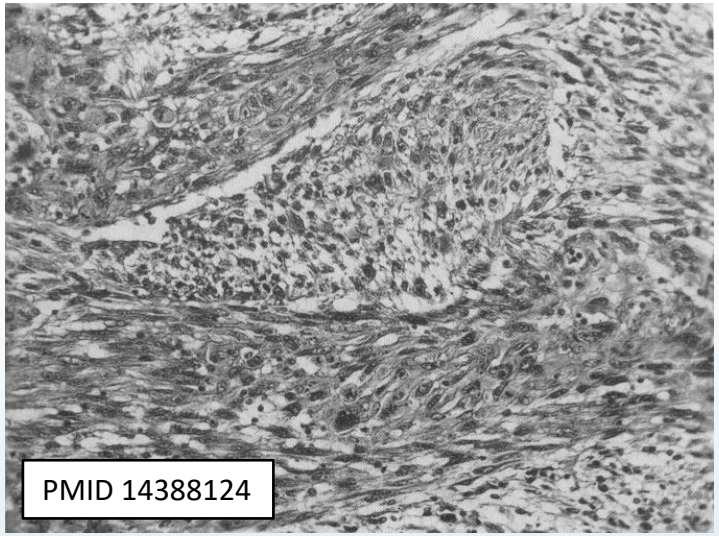


- Biphasic/alternating areas displaying glial and mesenchymal differentiation
- Cartilage, bone, osteoid, chondroid, lipomatous, myogenic elements may be present
- Sarcomatous overgrowth or limited sampling (biopsy) can complicate diagnosis

AANP

Feigin (1954)

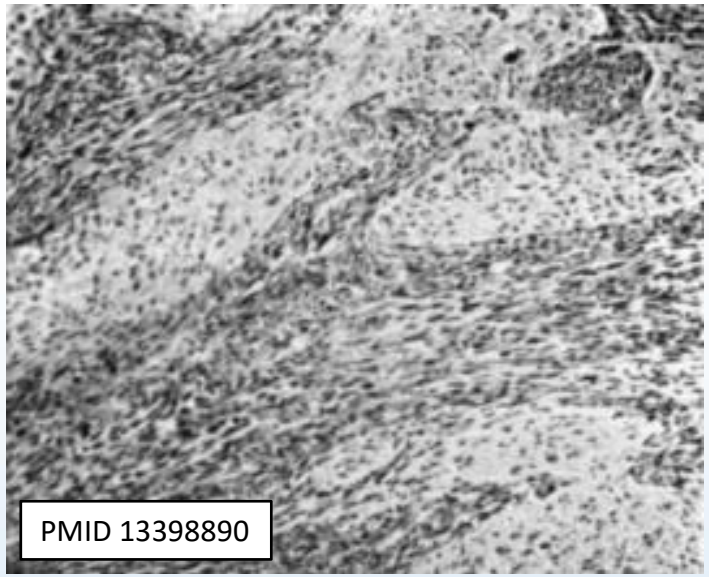
"It is concluded that the sarcomatous tissue did develop as a result of **neoplastic change in hyperplastic blood vessel walls** … as part of the reaction to the presence of the malignant glioma"



PMID 14388124

Rubinstein (1956)

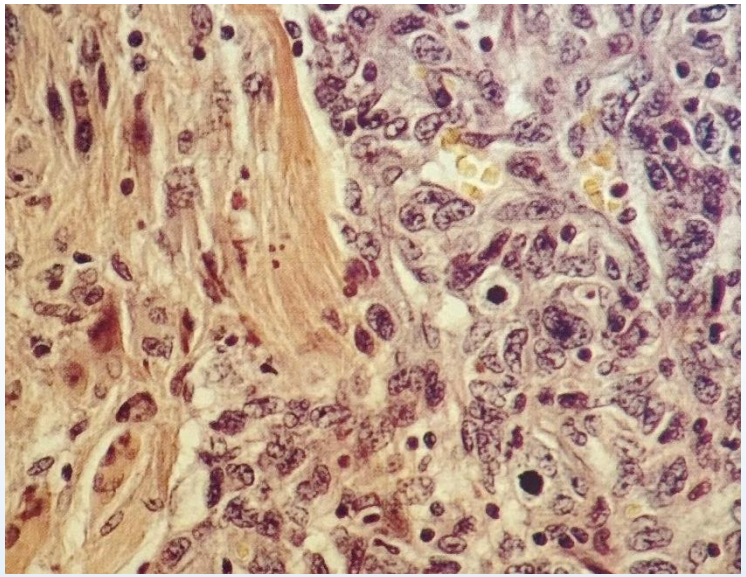
"Three of these cases … are considered to be **meningeal sarcomas which have promoted a malignant change** in the contiguous neuroglia"



PMID 13398890

WHO CNS 1 (1979)

"The sarcomatous component, which originates from a malignant transformation of the hyperplastic vascular elements, may predominate in some cases"



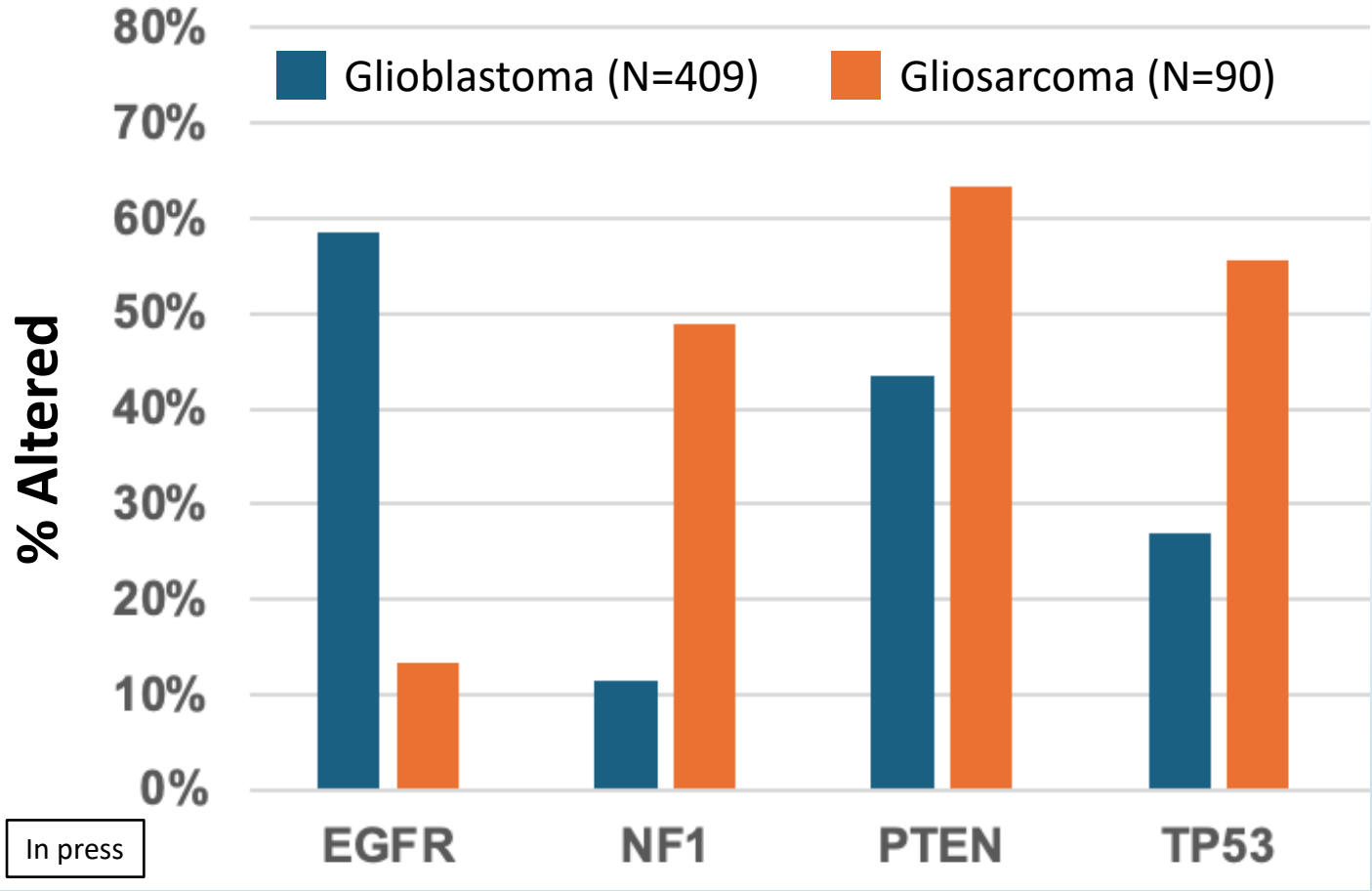
Multiple investigators (ca. 1995-2000)

- Biernat W et al. *Identical Mutations of the p53 Tumor Suppressor Gene in the Gliomatous and the Sarcomatous Components of Gliosarcomas Suggest a Common Origin from Glial Cells* (1995)
- Boerman RH et al. *The Glial and Mesenchymal Elements of Gliosarcomas Share Similar Genetic Alterations* (1996)
- Reis RM et al. *Genetic Profile of Gliosarcomas* (2000)
- Actor B et al. *Comprehensive analysis of genomic alterations in gliosarcoma and its two tissue components* (2002)

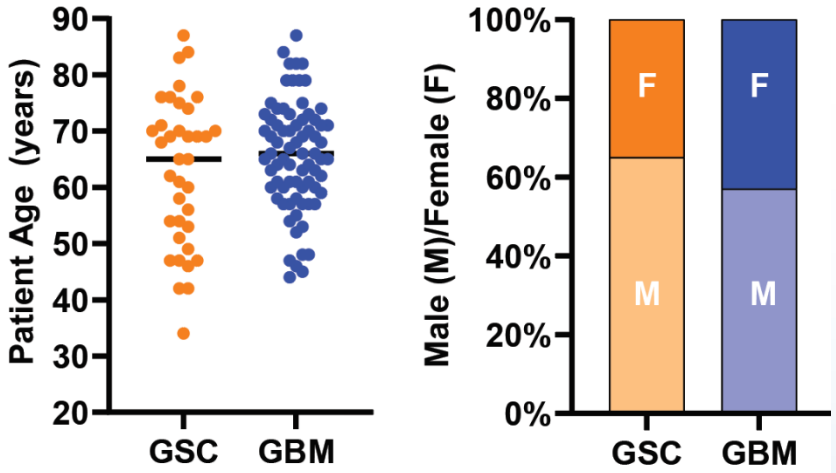
AANP

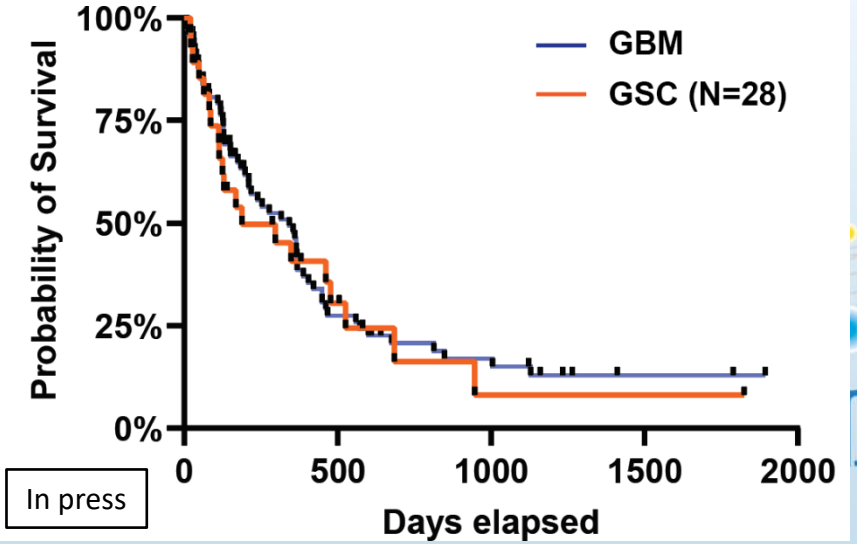
Gliosarcoma molecular features and clinical behavior

Molecular features in multiple studies and TCGA



In press

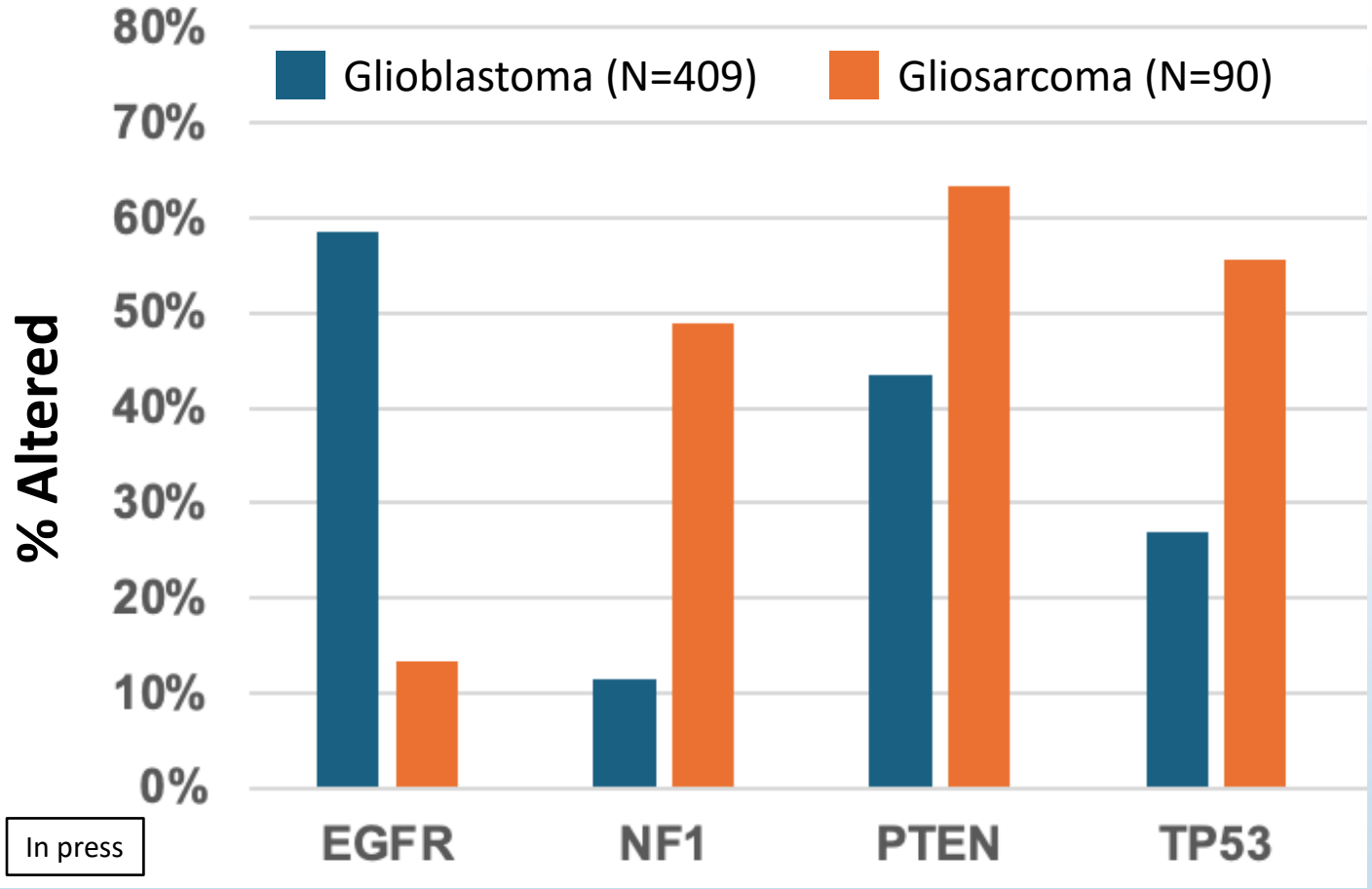




In press

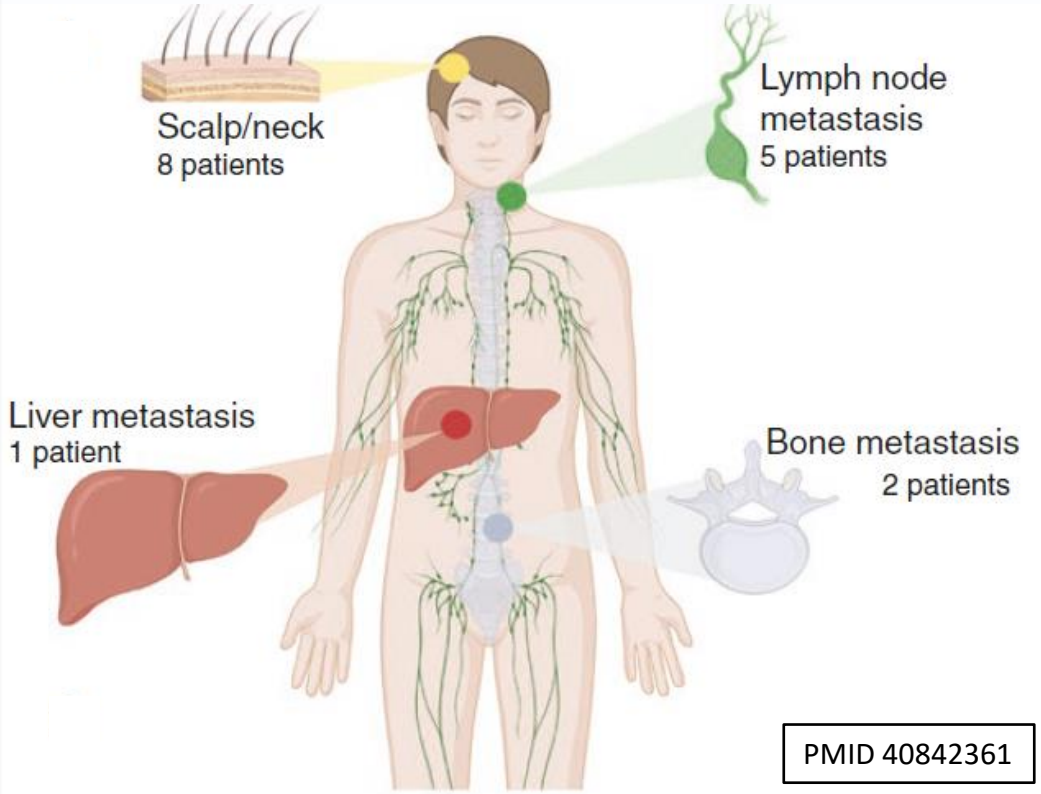
Gliosarcoma molecular features and clinical behavior

Molecular features in multiple studies and TCGA



In press

Jacobsen *et al* (2025) – Extra-cranial metastasis in adult gliomas – six of 14 glioblastomas were consistent with gliosarcoma (versus 1-2% gliosarcoma incidence in glioblastoma)



PMID 40842361

Gliosarcoma – differential and workup

Metastatic sarcoma/sarcomatous neoplasm

- Consider sample size (biopsy/resection), overgrowth of sarcomatous component
- Lineage markers e.g. sarcomatoid carcinoma, desmoplastic melanoma
- Growth pattern, presence/absence of malignant glial/astrocytic component
- Identify other sites of systemic metastasis

Other primary intracranial sarcomatous tumor

- Primary intracranial sarcoma, *DICER1*-mutant
- Oligosarcoma, ependymosarcoma, IDH-mutant astrocytoma/sarcoma
- Grade 3 meningioma

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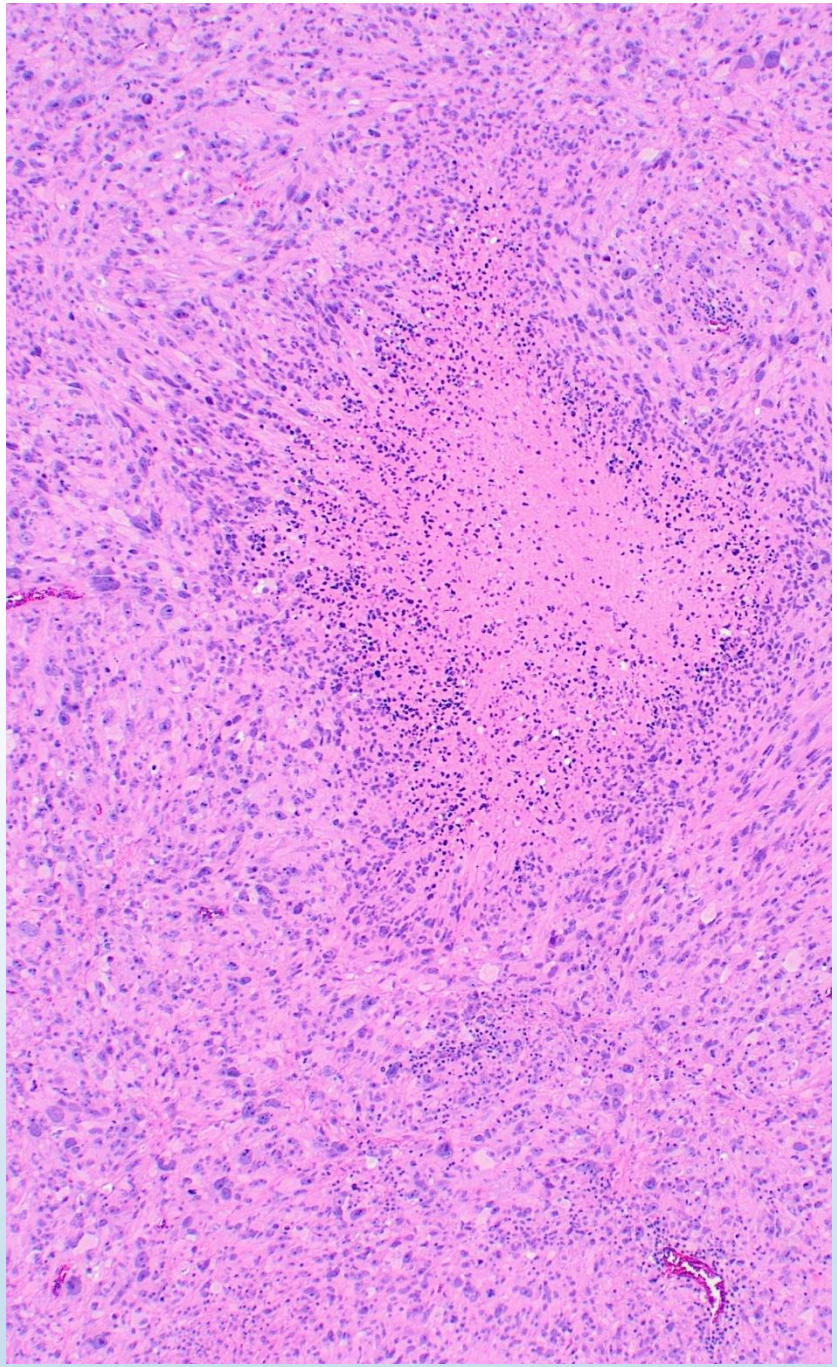
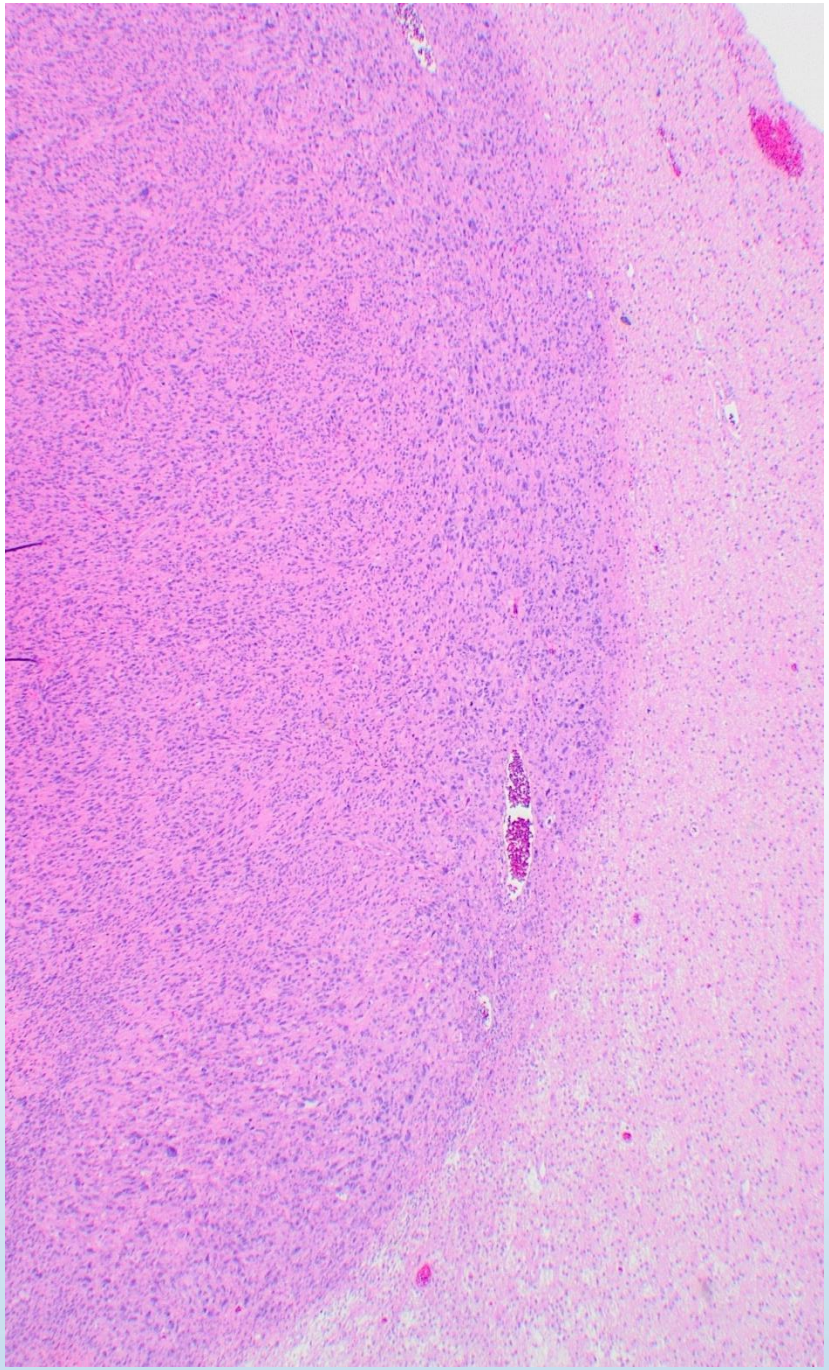
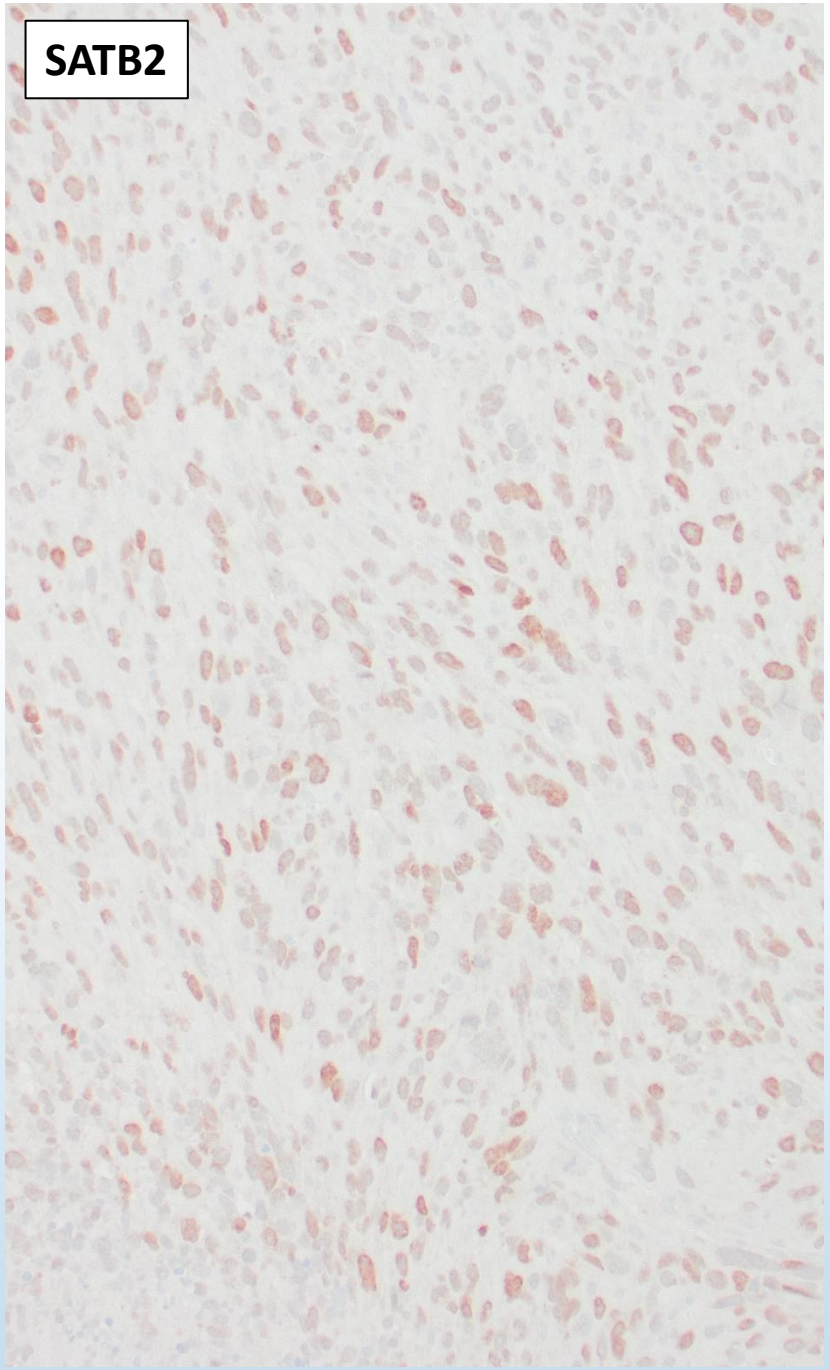
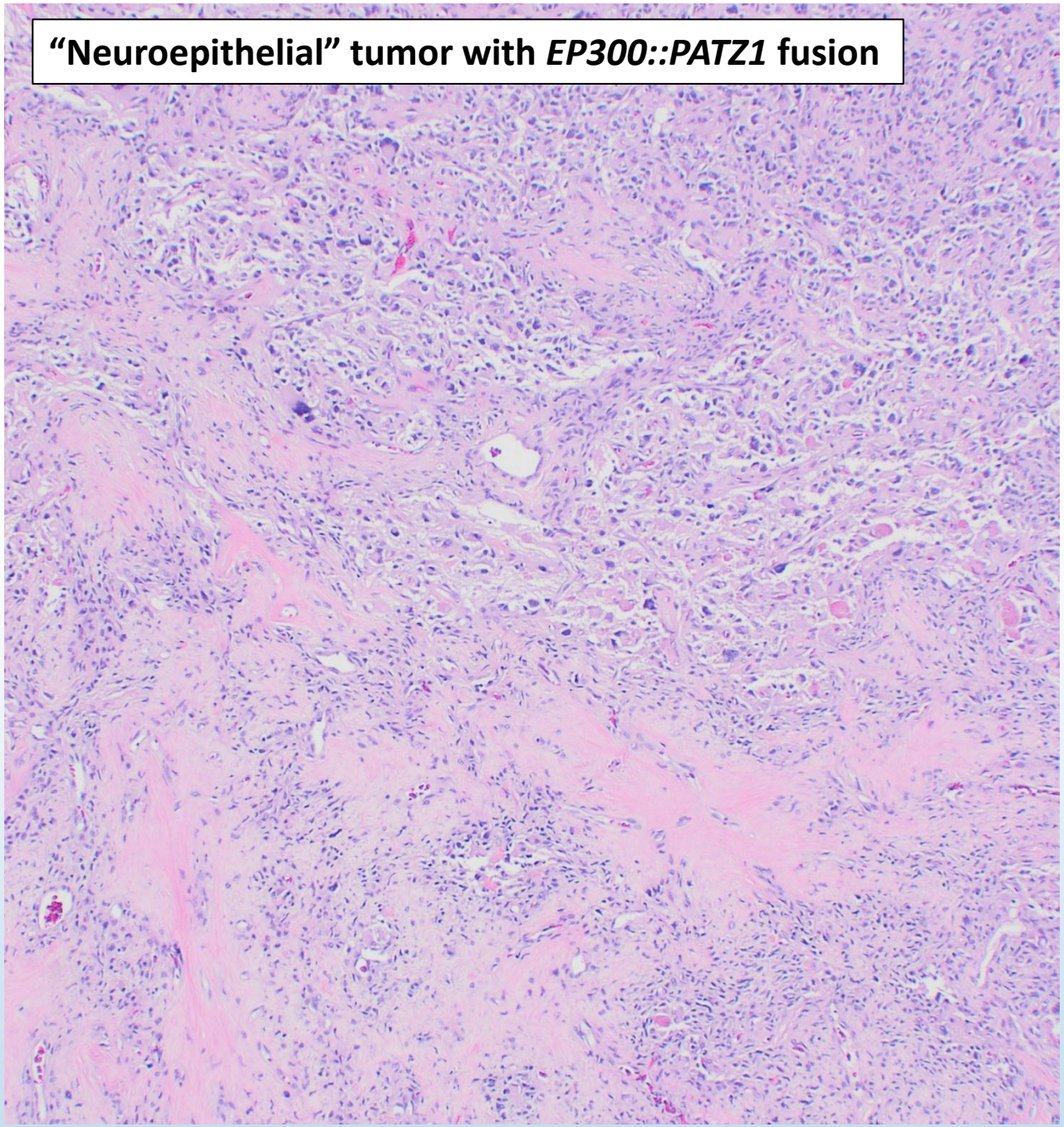
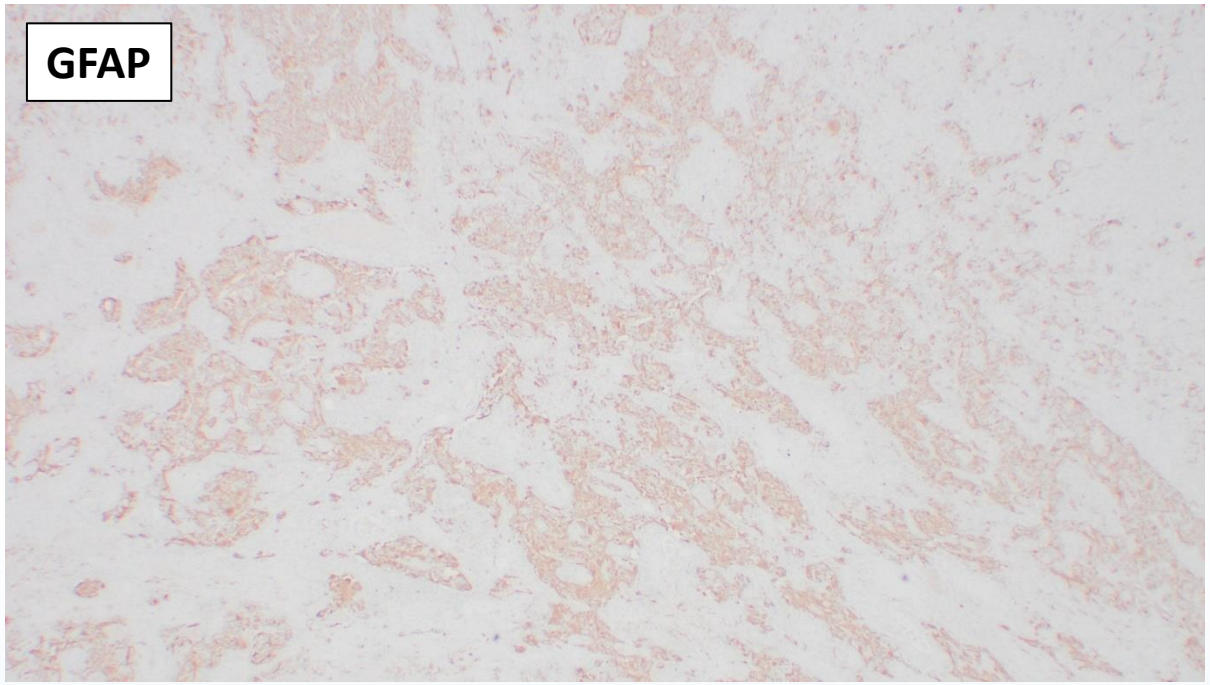
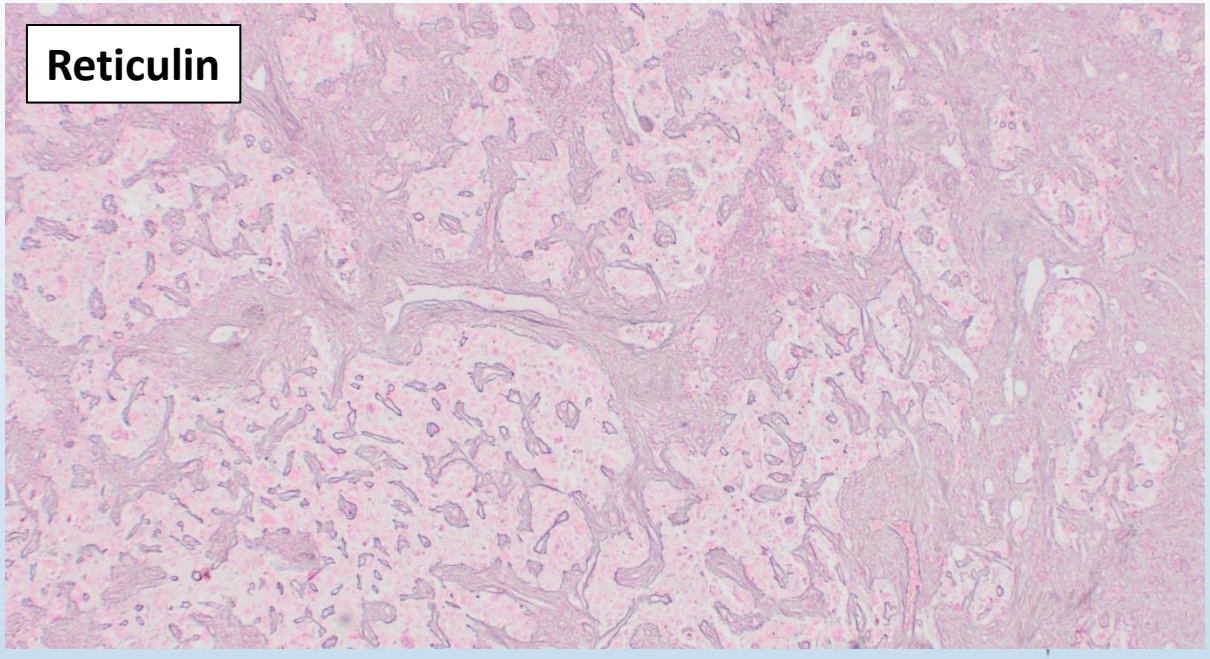




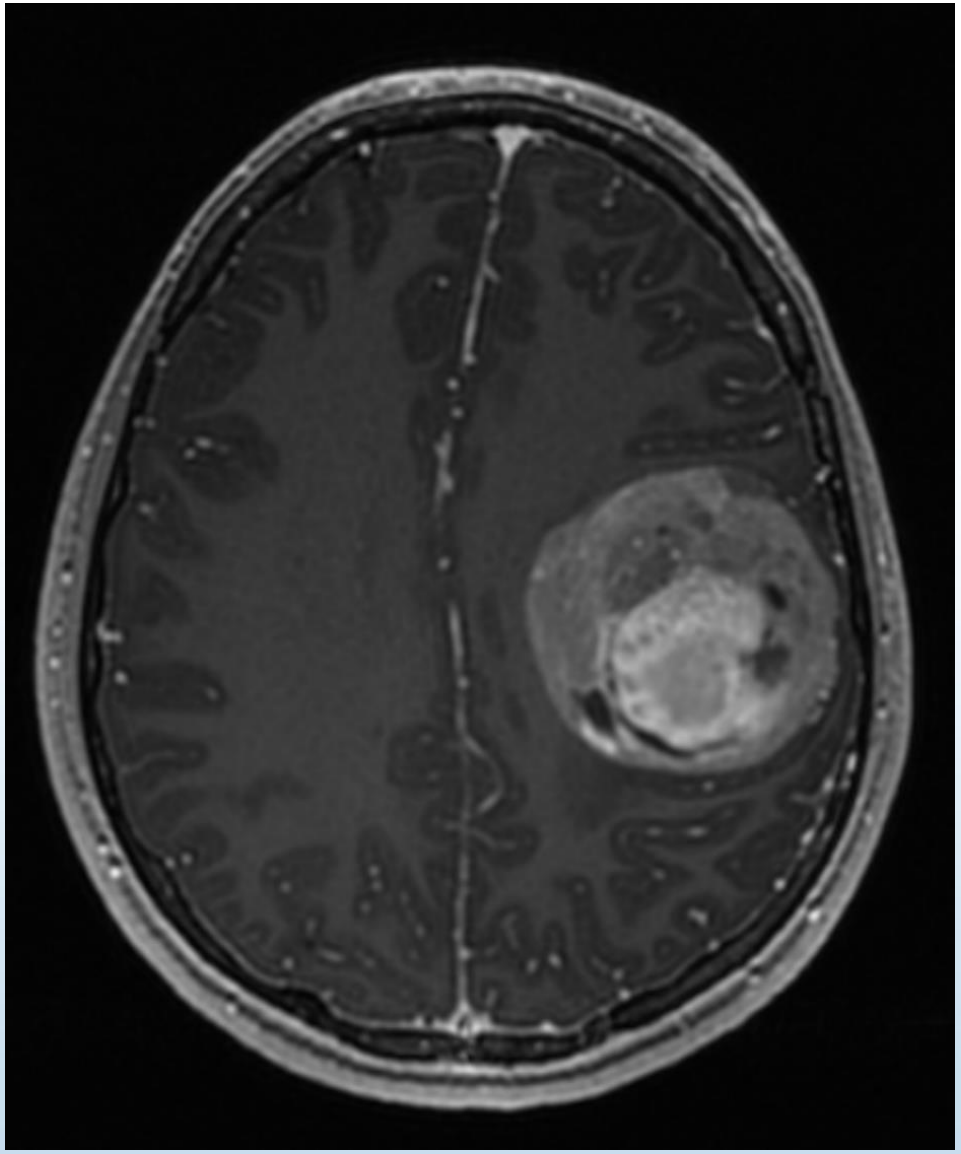

SATB2

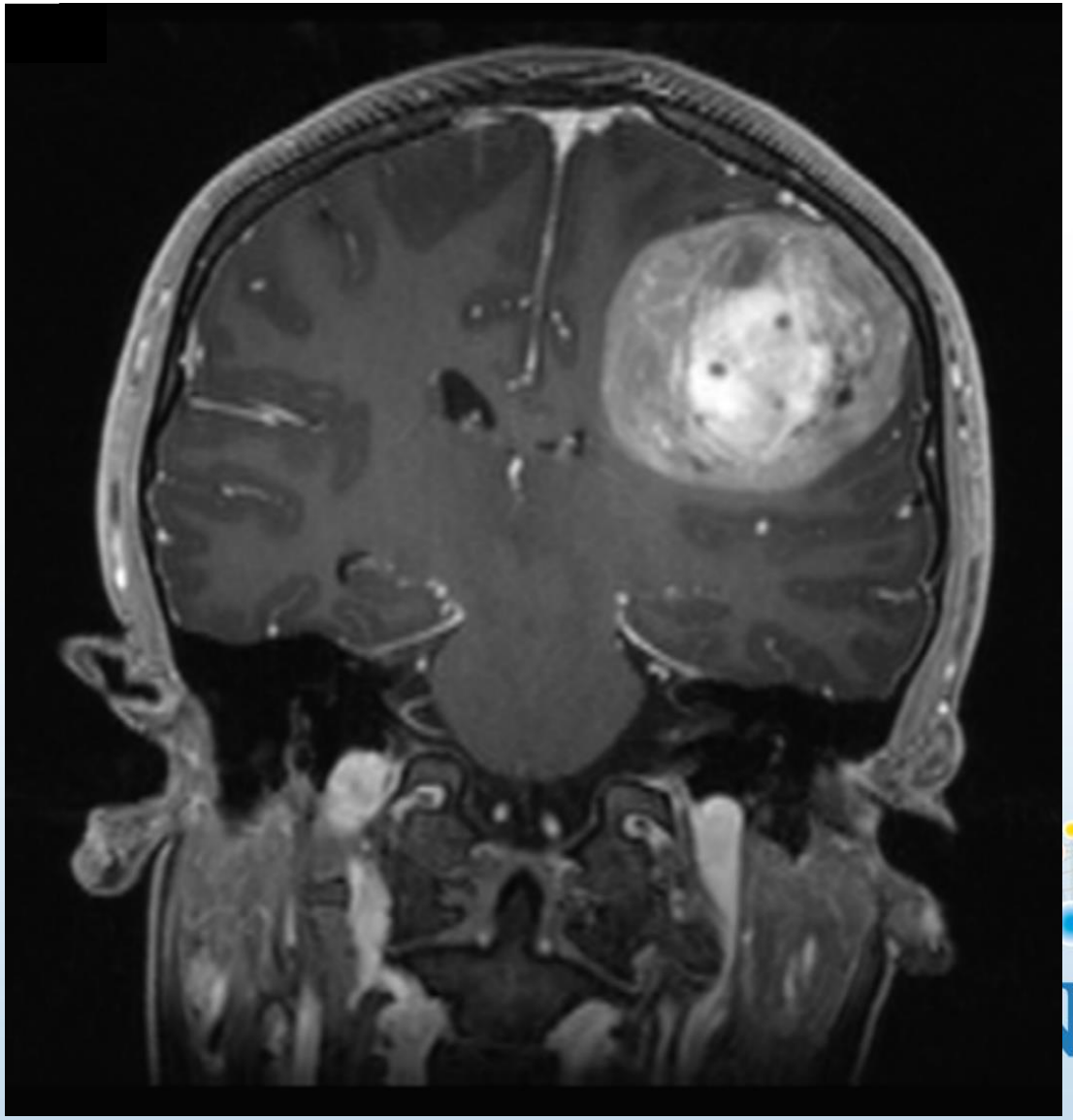

“Neuroepithelial” tumor with *EP300::PATZ1* fusion

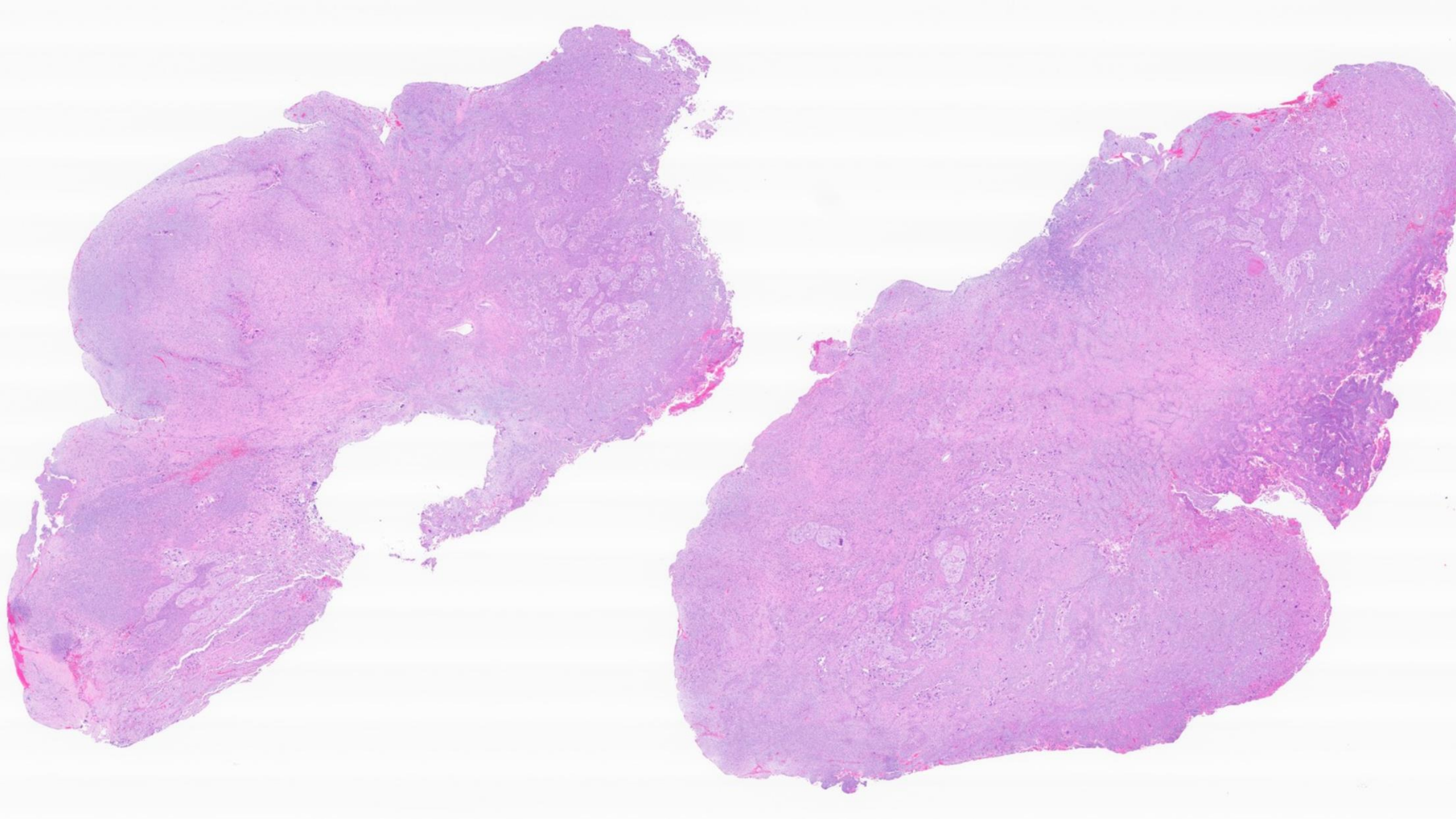

GFAP

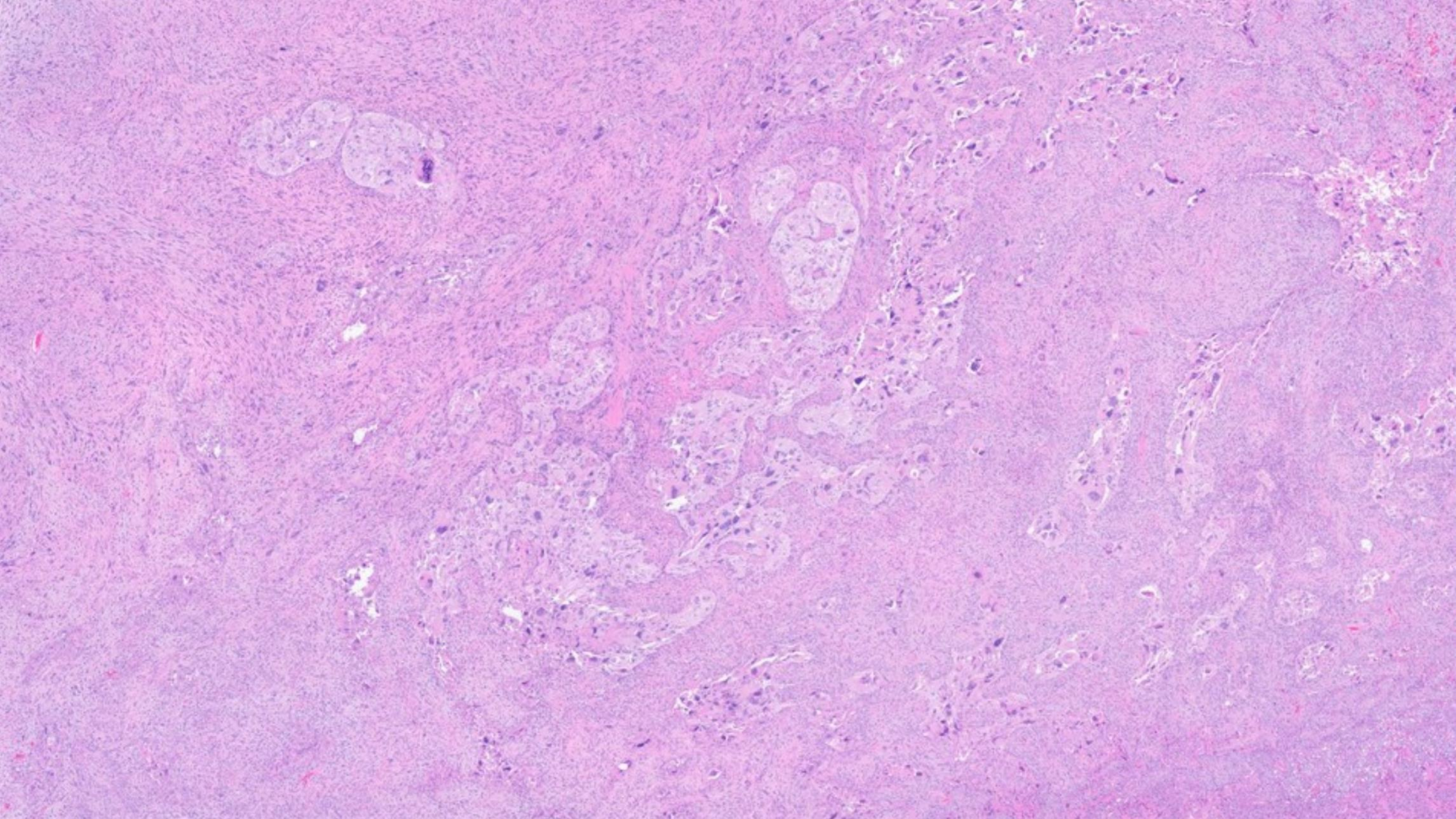

Reticulin

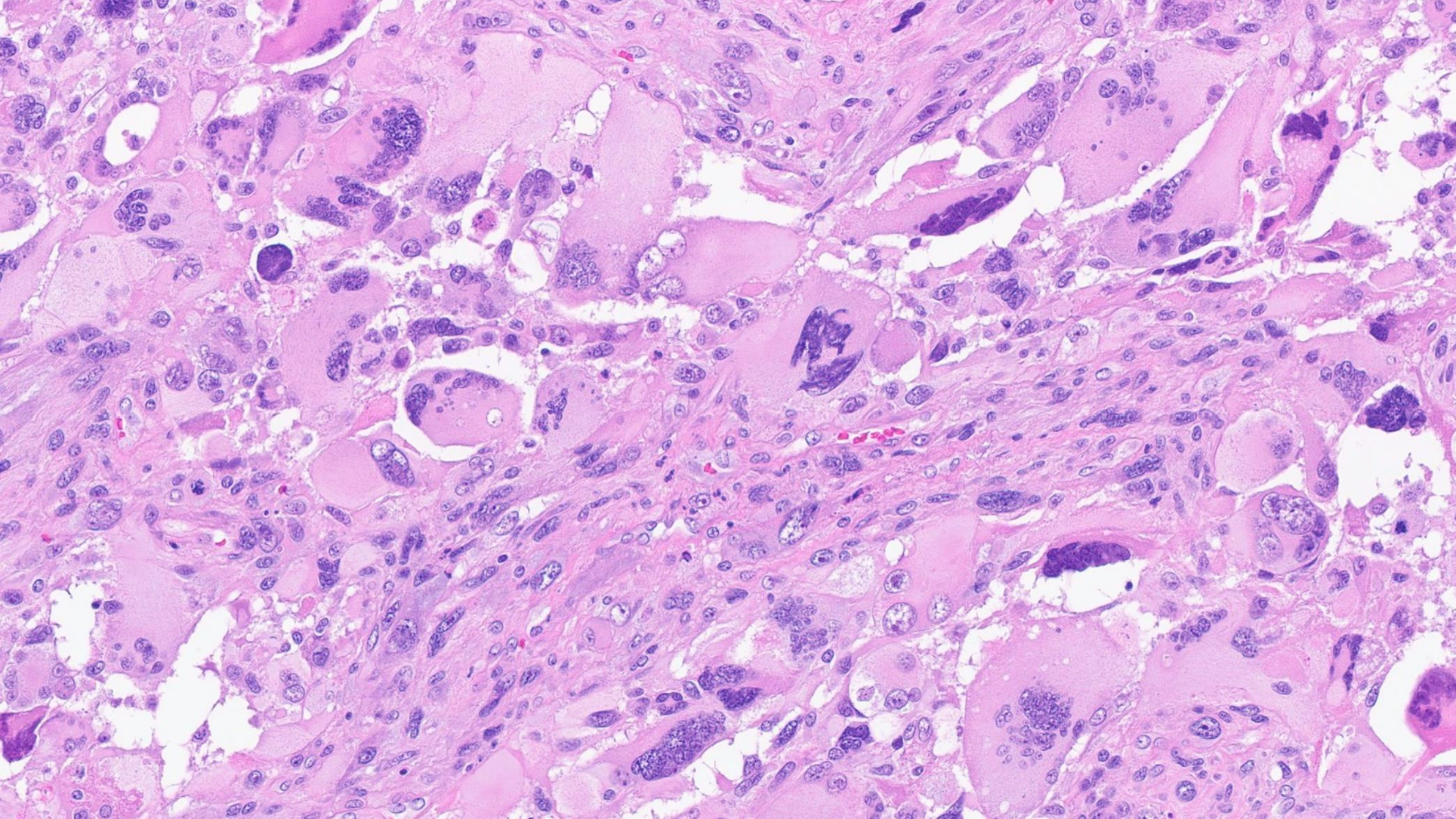
Case 5 – 15-year-old



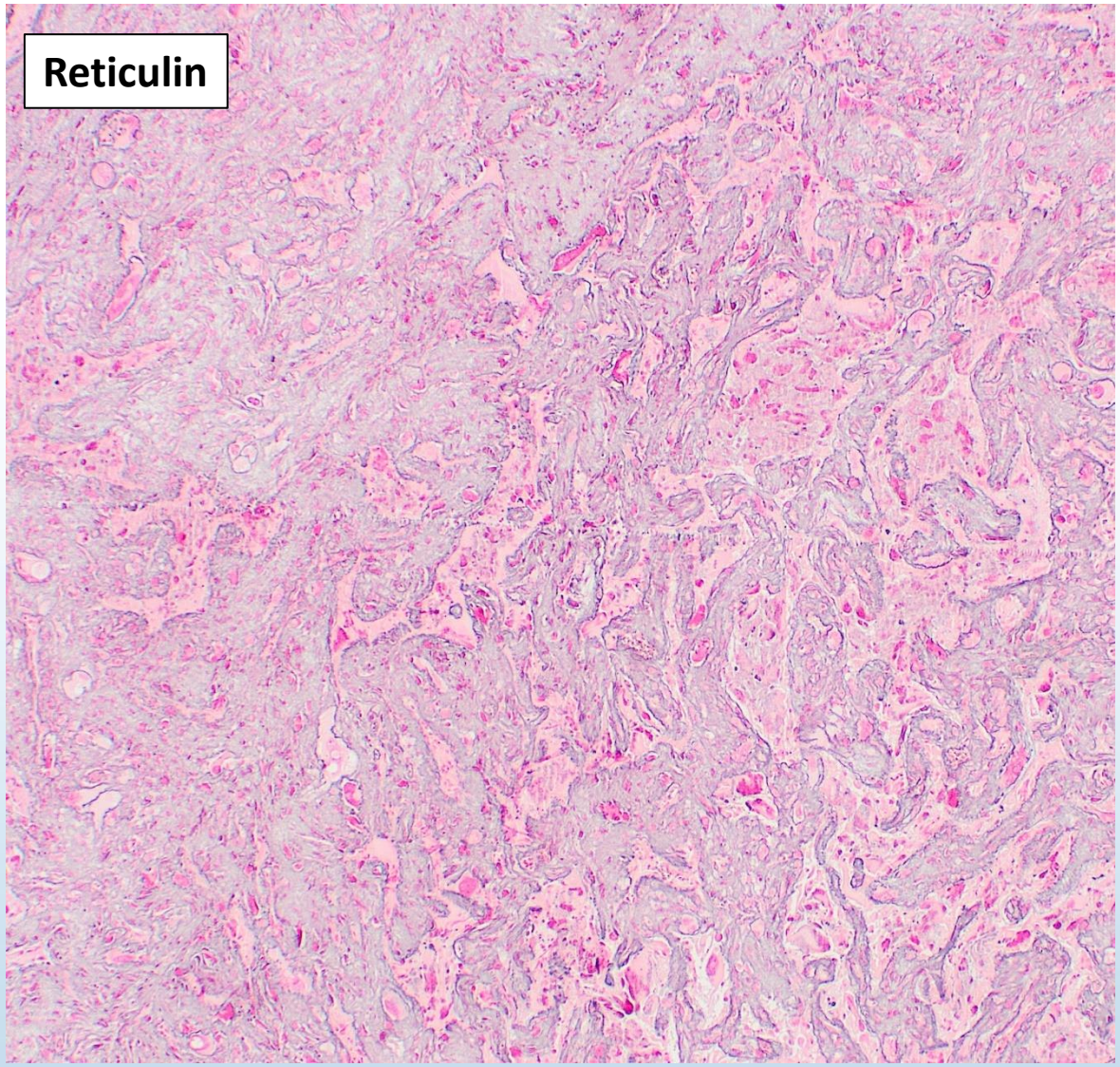


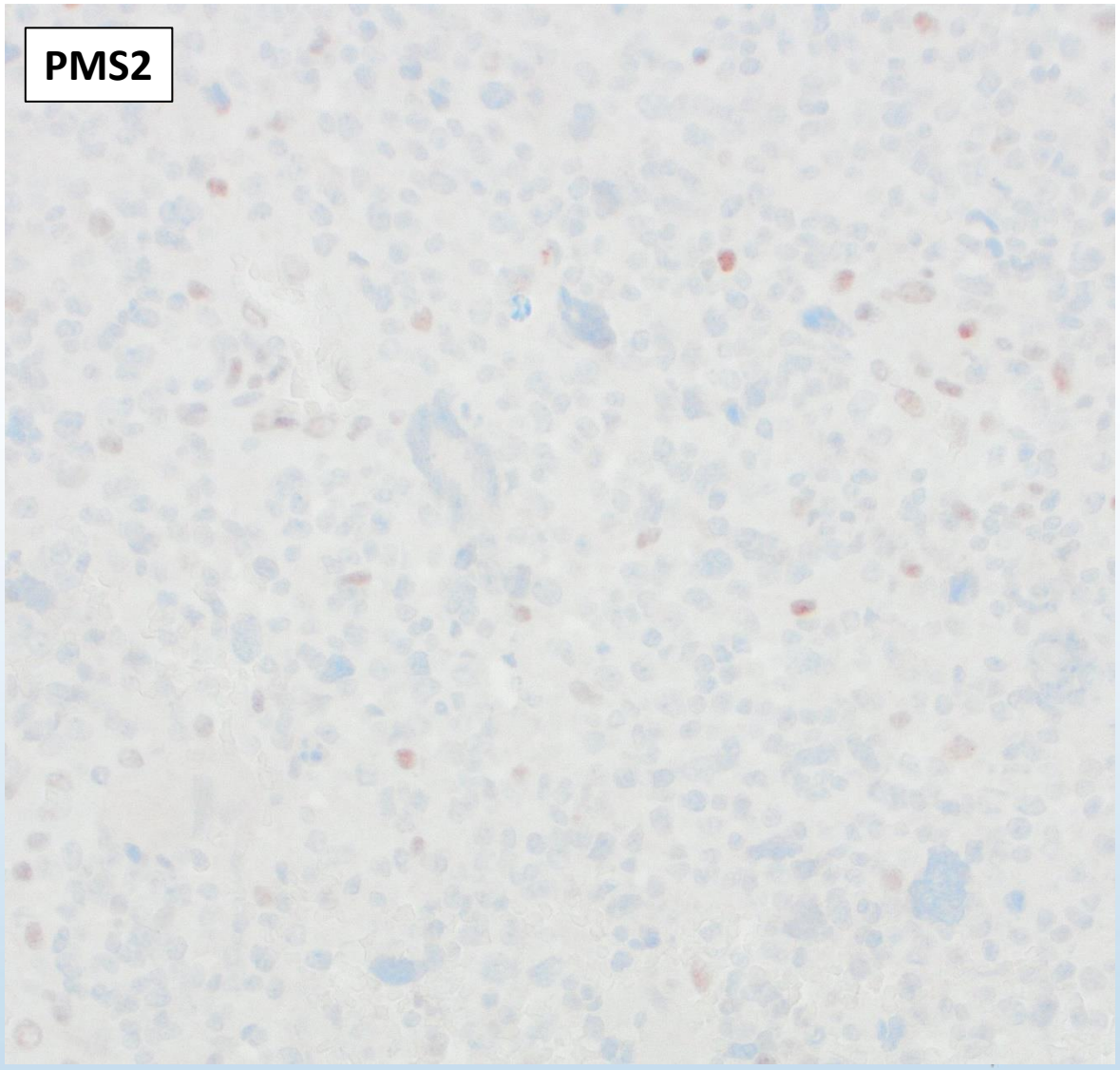




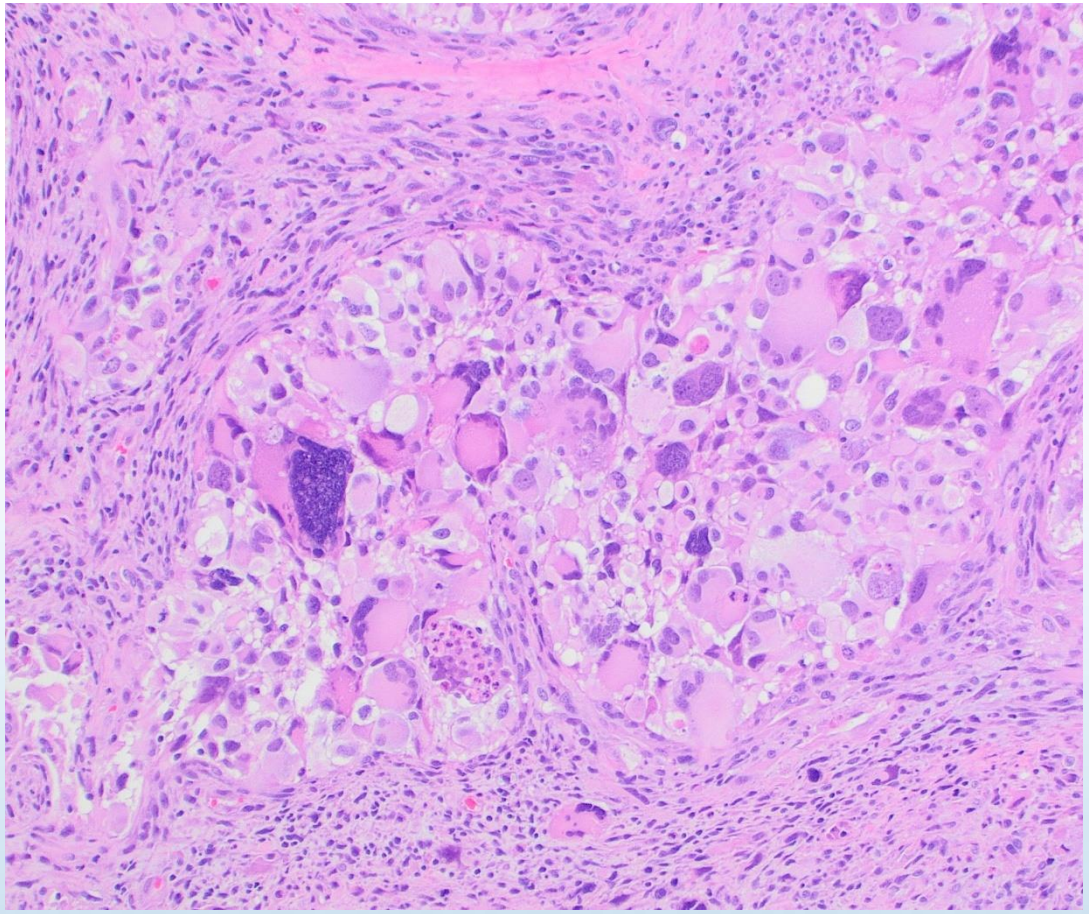


Case 5 – Histochemical stains





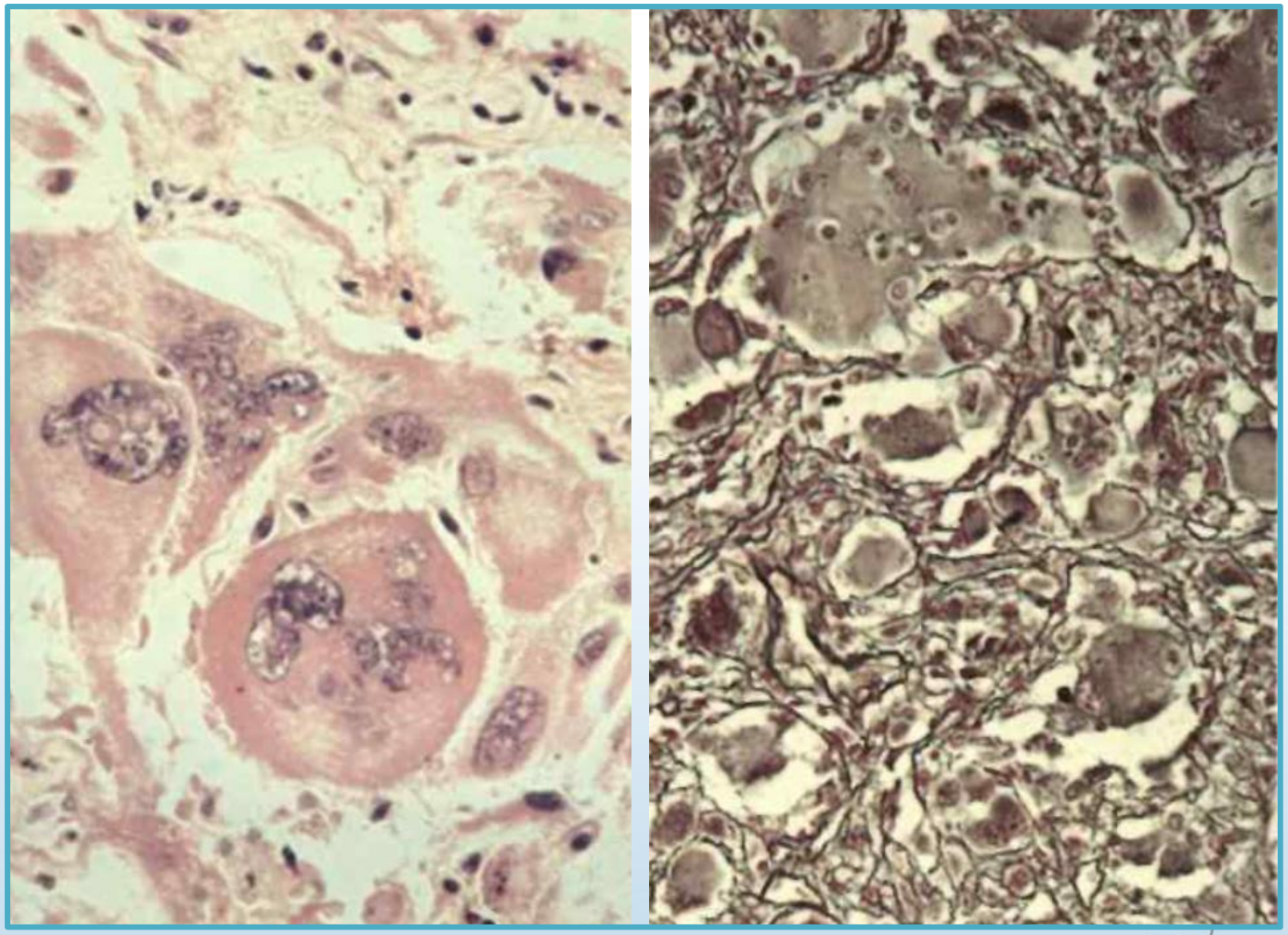
Case 5 – Giant cell glioblastoma



- Bizarre, multinucleated giant cells are a dominant histopathological component
- Often subcortically located and may be circumscribed
- Possibly better clinical outcome
- Increased reticulin

Giant cell glioblastoma vs. “monstrocellular sarcoma”

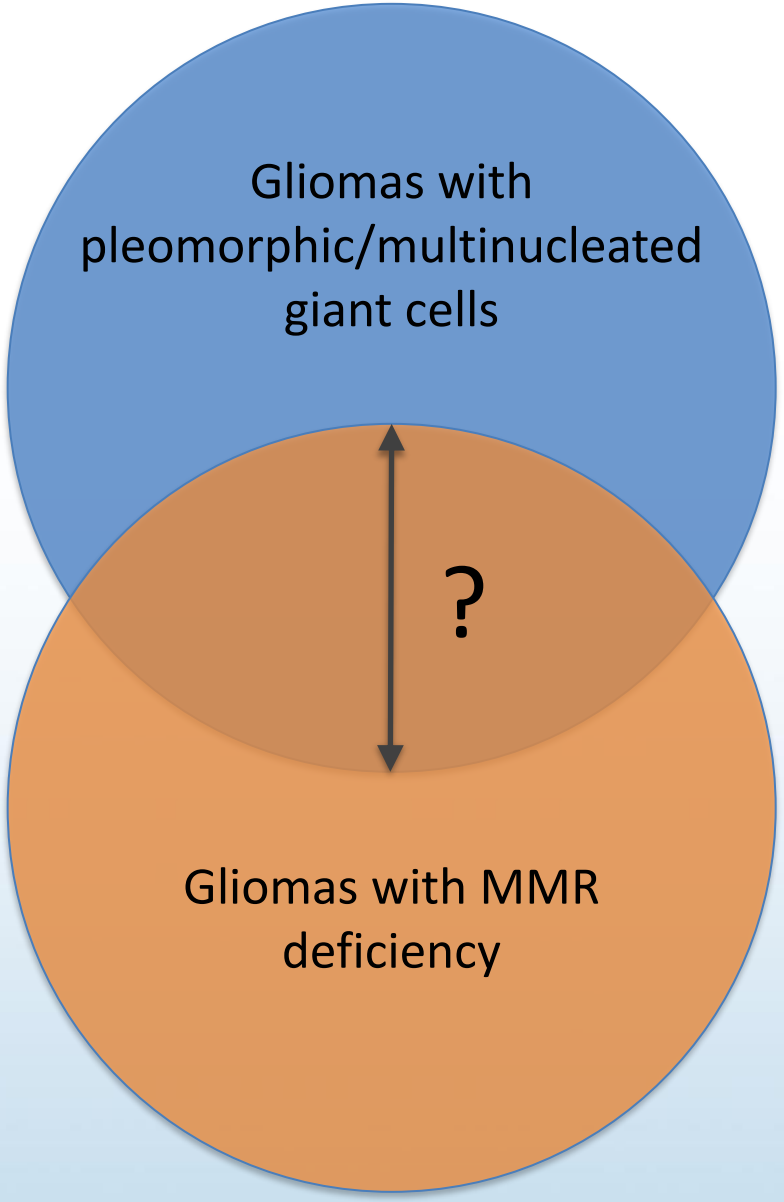
- “Sarcoma” was historically applied based on gross features, lack of differentiation, and/or reticulin content
- Monstrocellular sarcoma was classified as a tumor of blood vessel origin in **WHO CNS 1** (1979)
- Rubinstein reclassified the entity to (giant cell) glioblastoma
- Later supported by ultrastructure immunophenotype leading to reclassification in WHO CNS 2 (1993)



Glioma mismatch repair (MMR) deficient state

- Replication/repair deficient cancer predisposition syndromes
  - Constitutional Mismatch Repair Deficiency (CMMRD)
  - Lynch syndrome
  - Polymerase Proofreading Associated Polyposis (PPAP)
  - Reviewed recently in Kim *et al* PMID 31970492
- Treatment-related hypermutant state
- “De novo” MMR-deficient high-grade glioma (-/+ Lynch)
- Primary MMR-deficient IDH-mutant astrocytoma

AANP



A subset of gcGB show genome-wide loss of heterozygosity

Data suggest an enrichment in methylation subclass(es)

- “HGG_E” or “pedHGG RTK1A”

Screening for MMR protein loss by immunohistochemistry can be informative, especially in glioblastoma diagnosed under age 40

PMID 33392505, 34952640, 37262394

Giant cell glioblastoma – differential and workup

Pleomorphic xanthoastrocytoma

- CD34 reactivity, eosinophilic granular bodies
- ? Degree and extensiveness of severe pleomorphism and giant cells

Other adult- or pediatric-type diffuse high-grade glioma

- Giant cell morphology is reported in IDH or H3-mutant gliomas and ependymoma

High-grade glioma with pleomorphic and pseudopapillary features (HPAP)

- Might lack reticulin deposition

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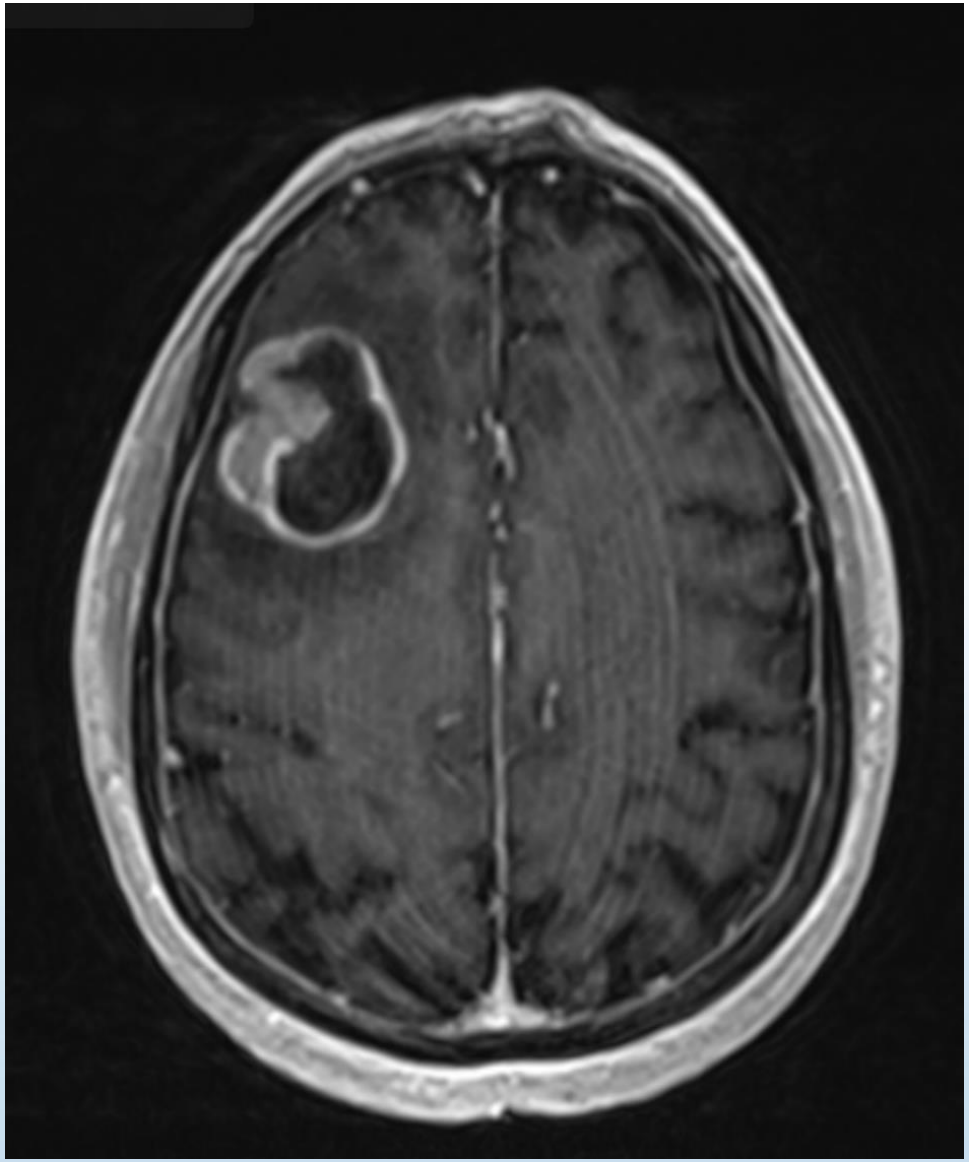
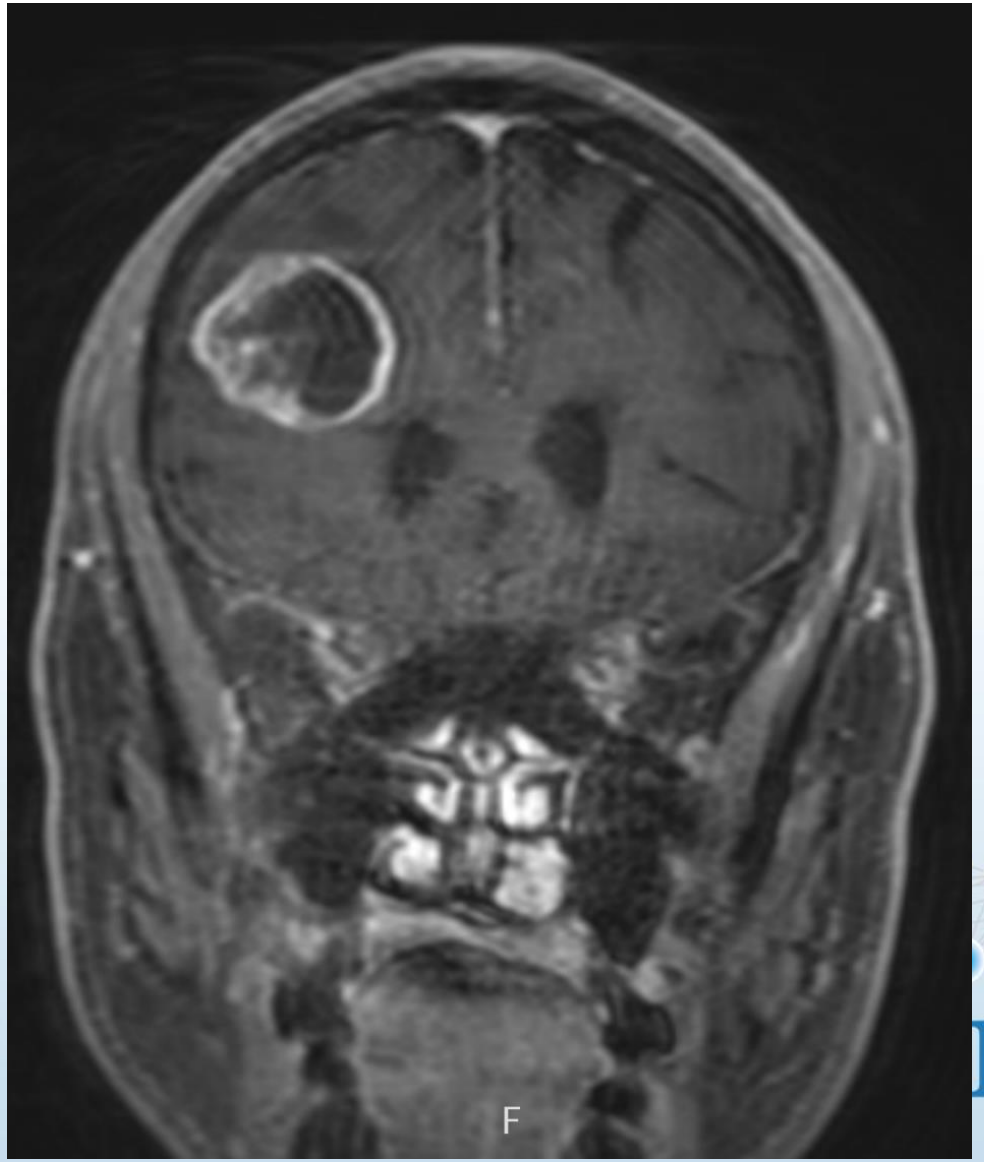
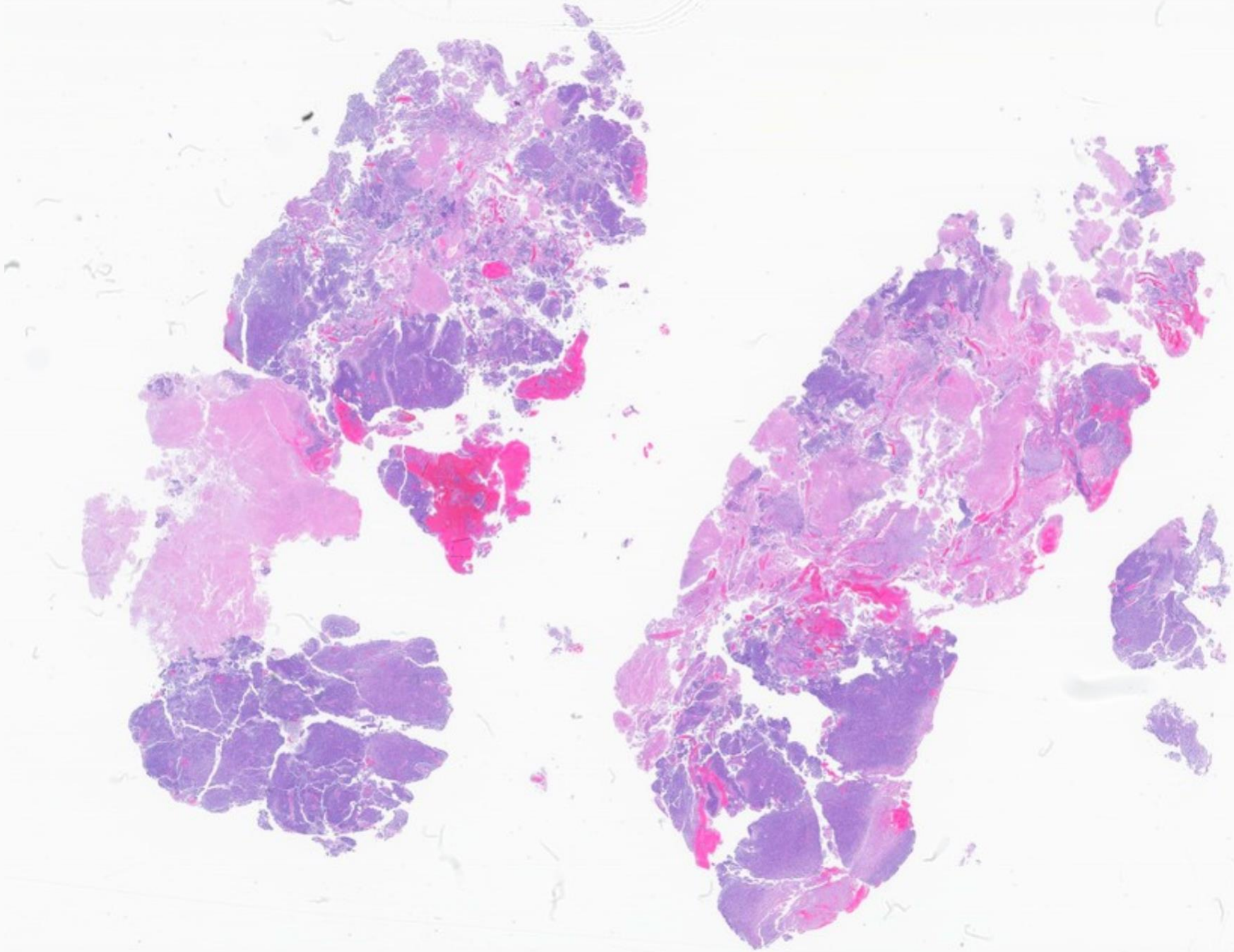
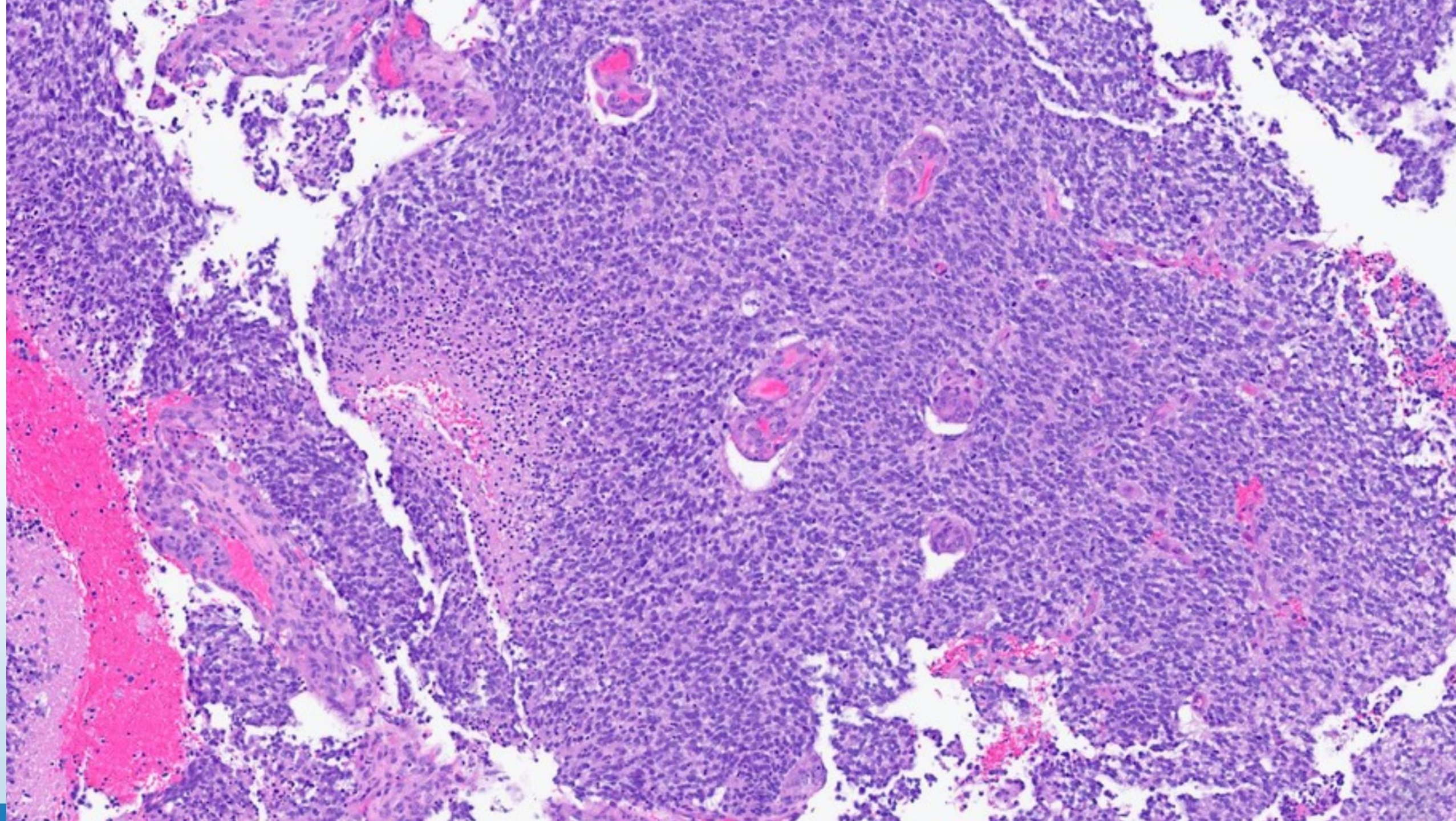
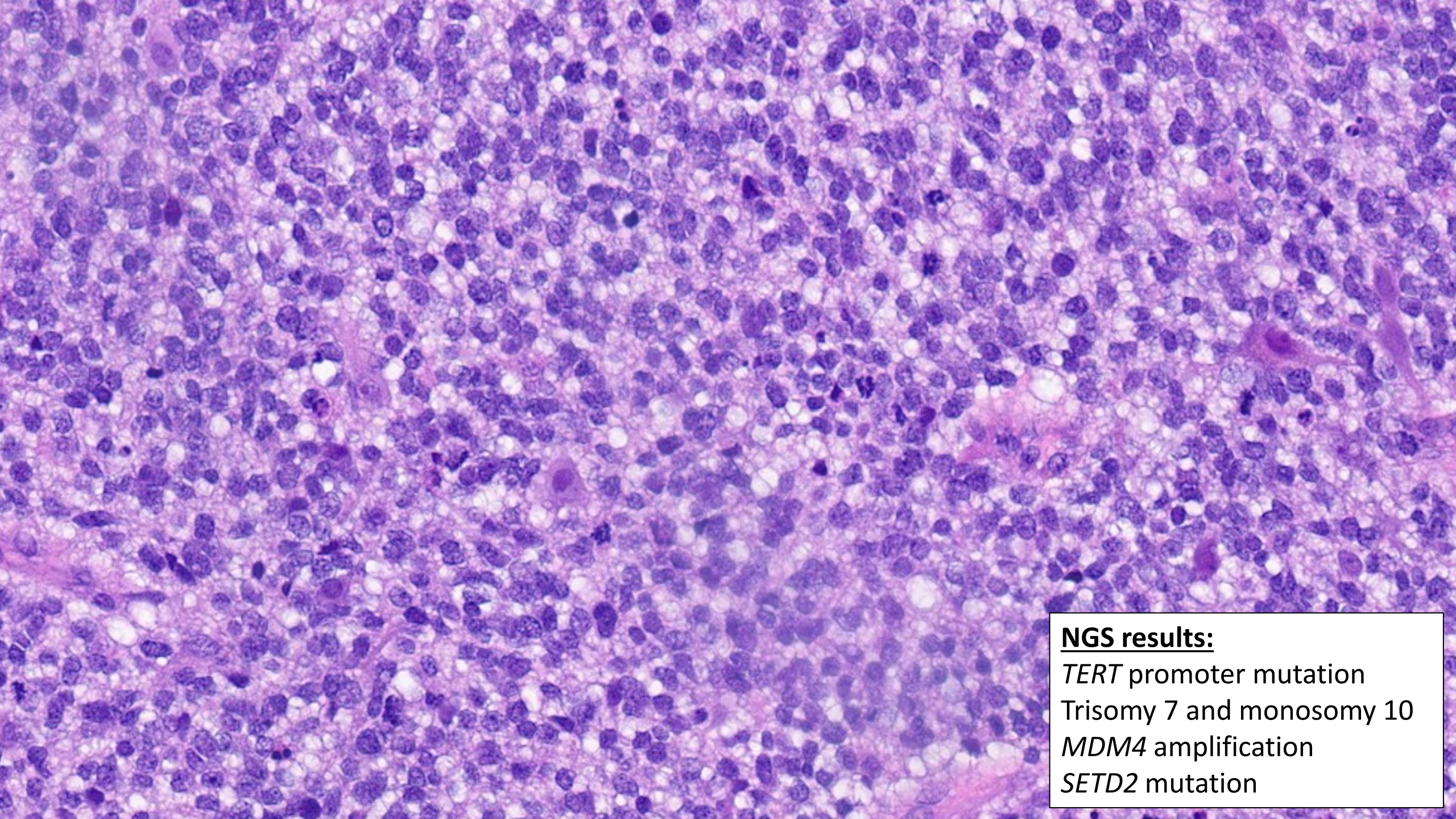
Case 6 – 72-year-old man



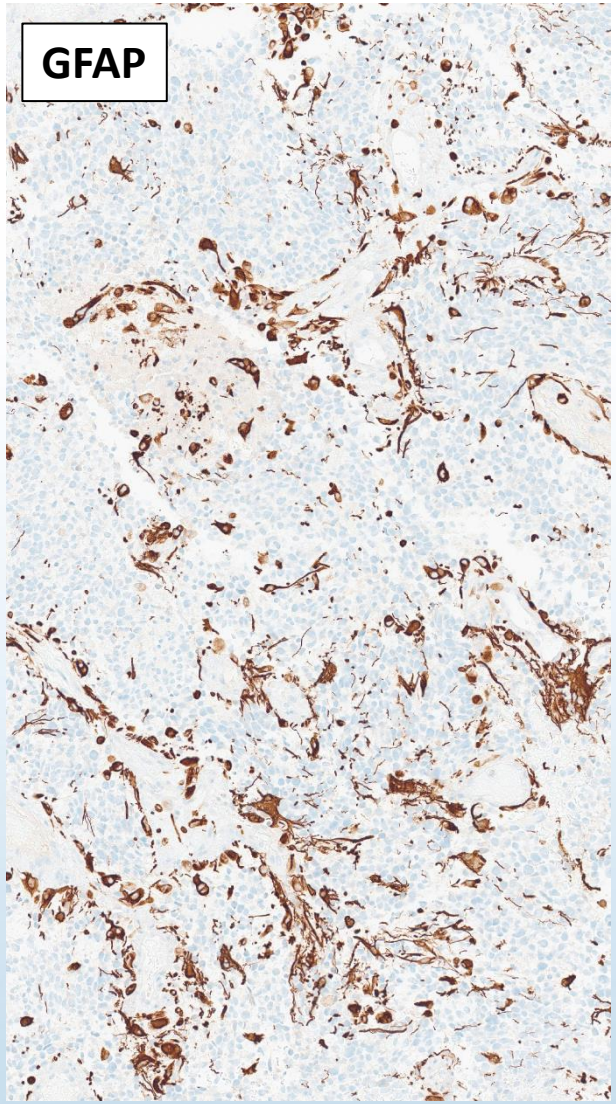


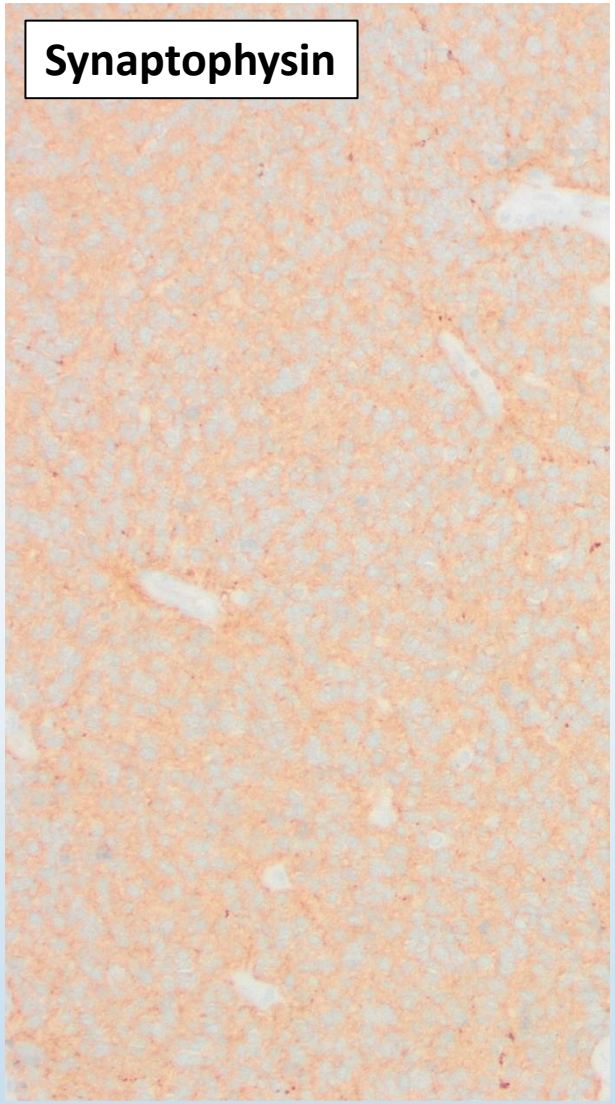


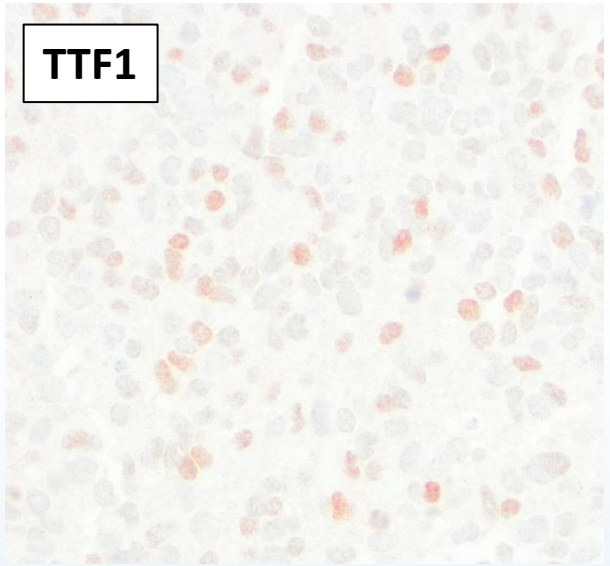


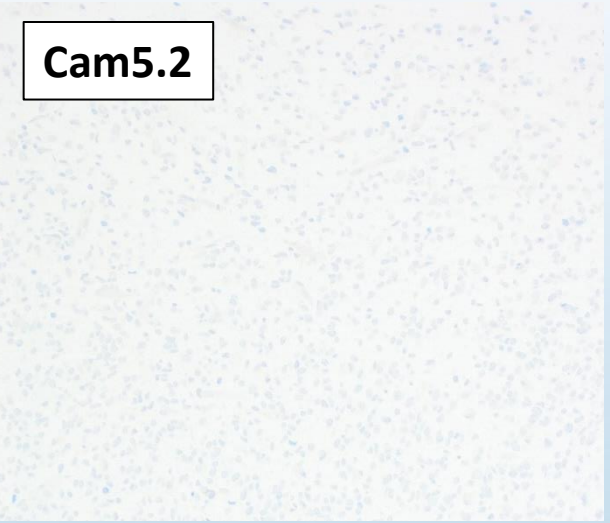

NGS results:
TERT promoter mutation
Trisomy 7 and monosomy 10
MDM4 amplification
SETD2 mutation

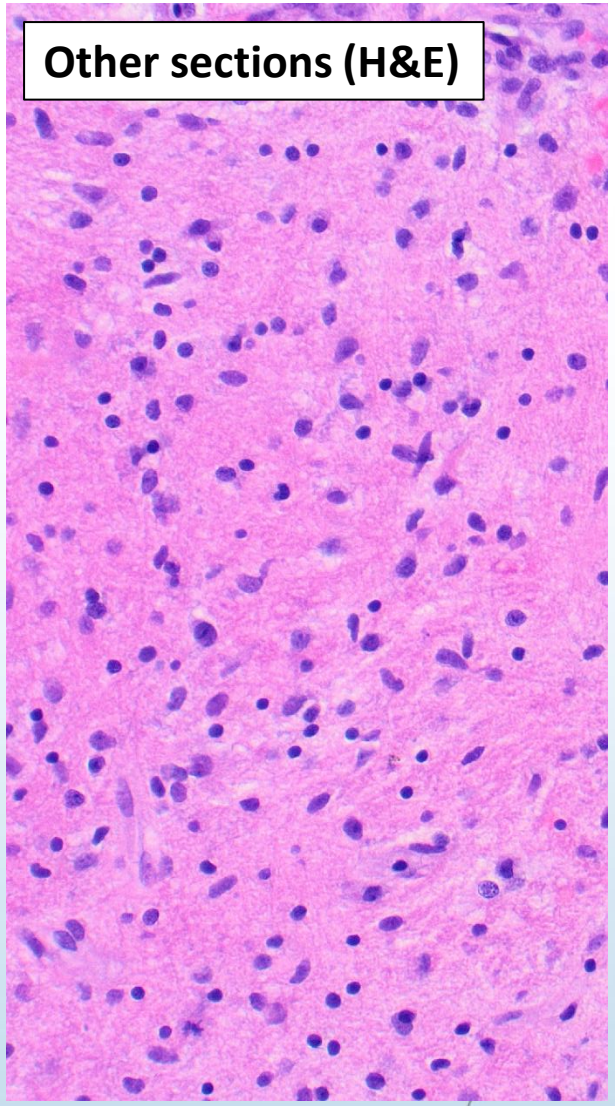
Case 6 – Immunohistochemical stains



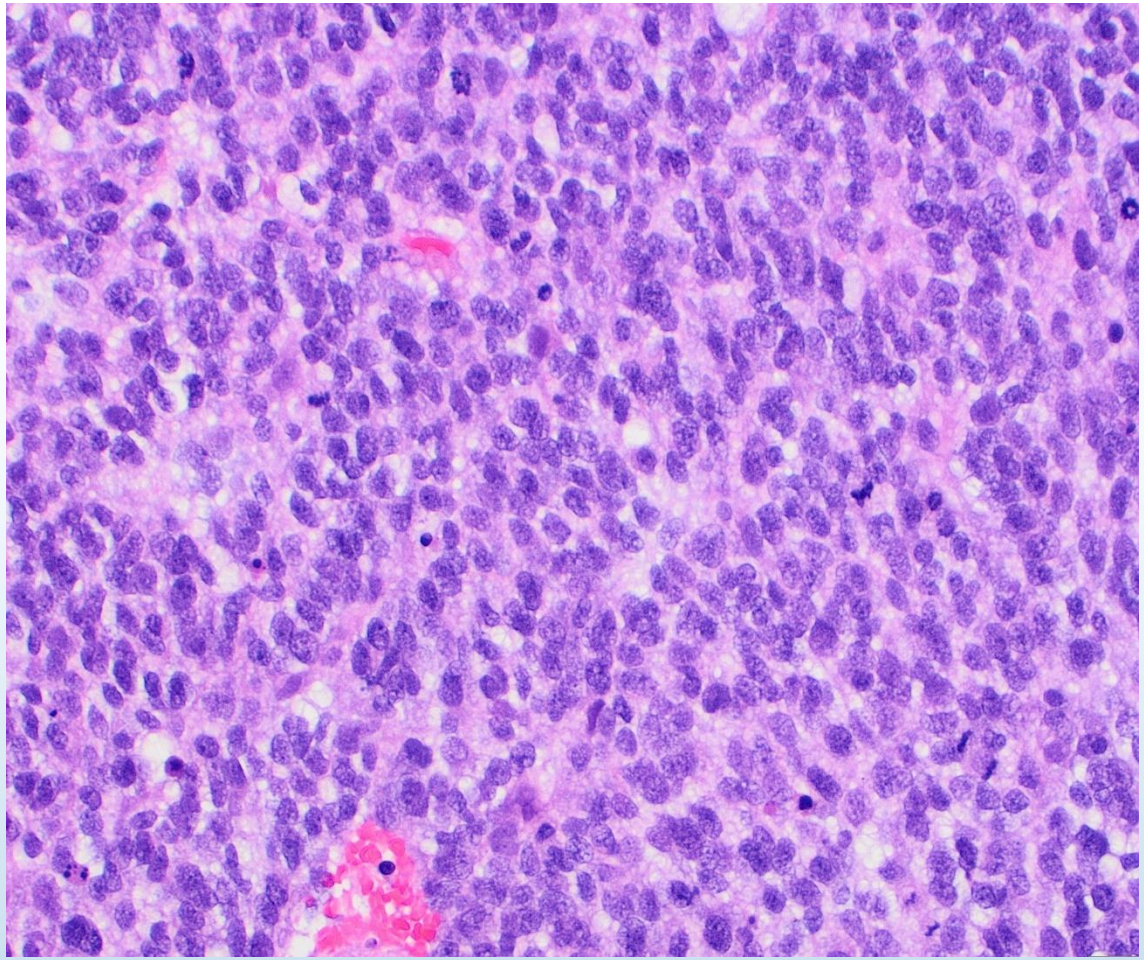






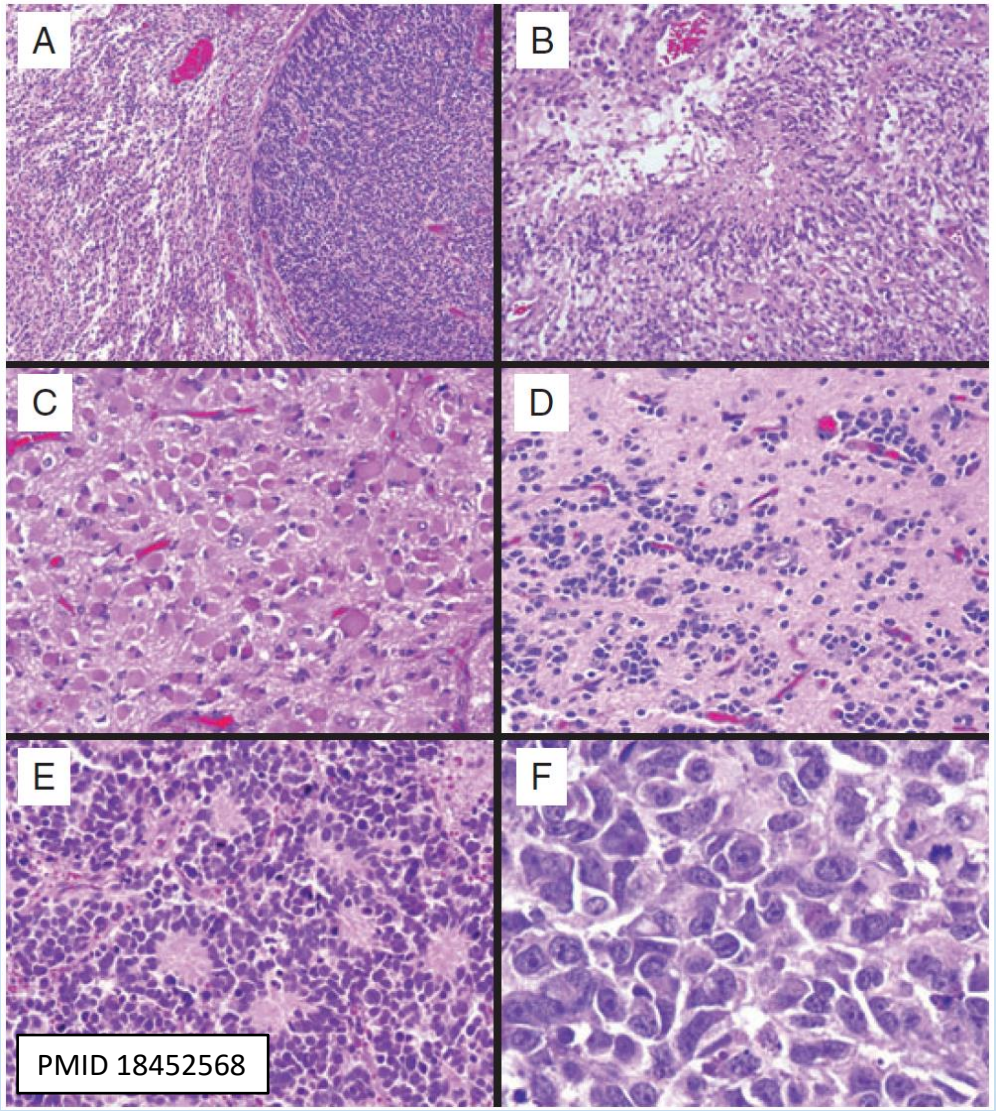


Case 6 – Glioblastoma with primitive neuronal component

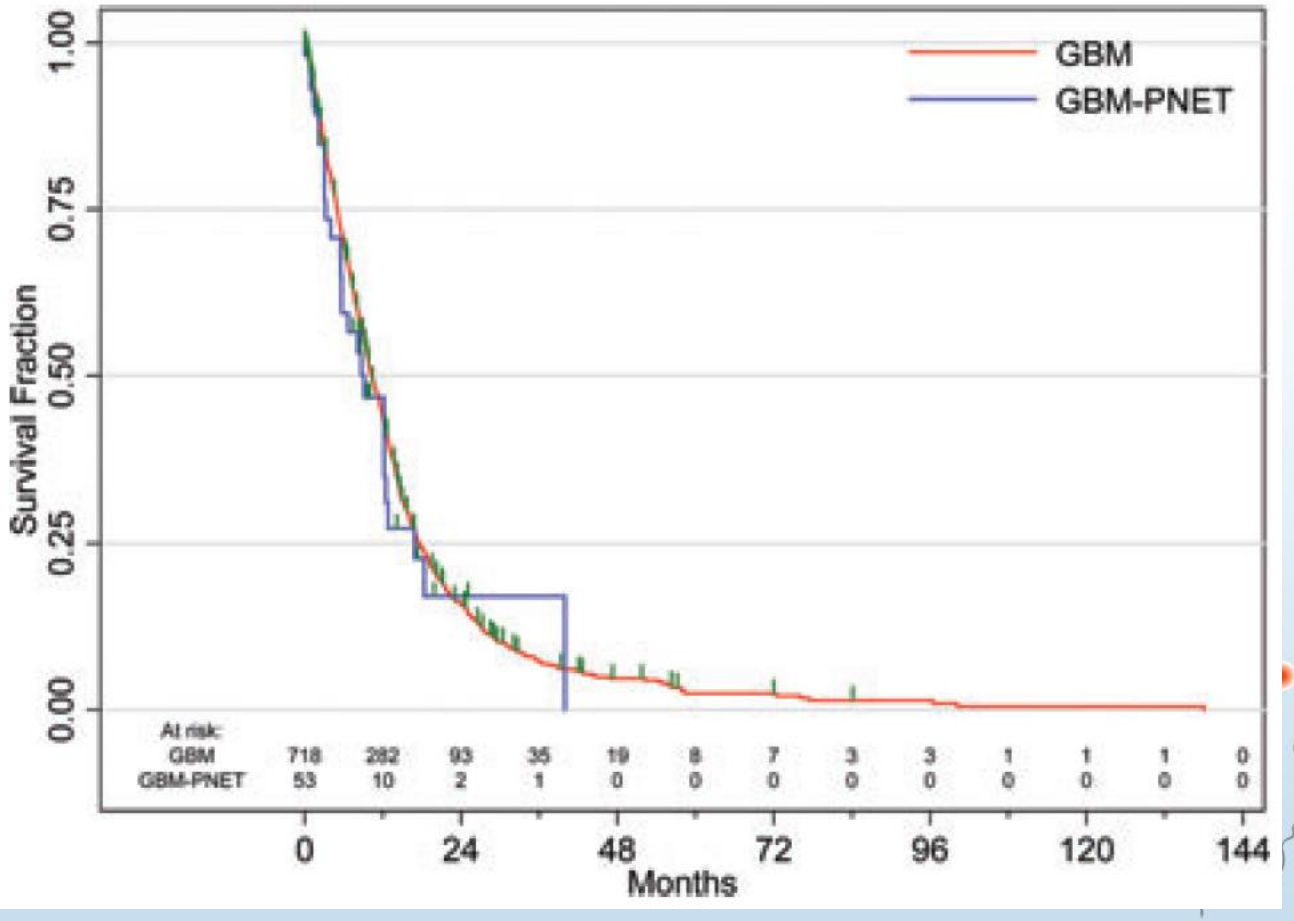


- One or more solid-looking hypercellular primitive nodules
- Immature cells with high N:C ratio, cell wrapping
- Lower GFAP and increased synaptophysin (or other neuronal marker) reactivity

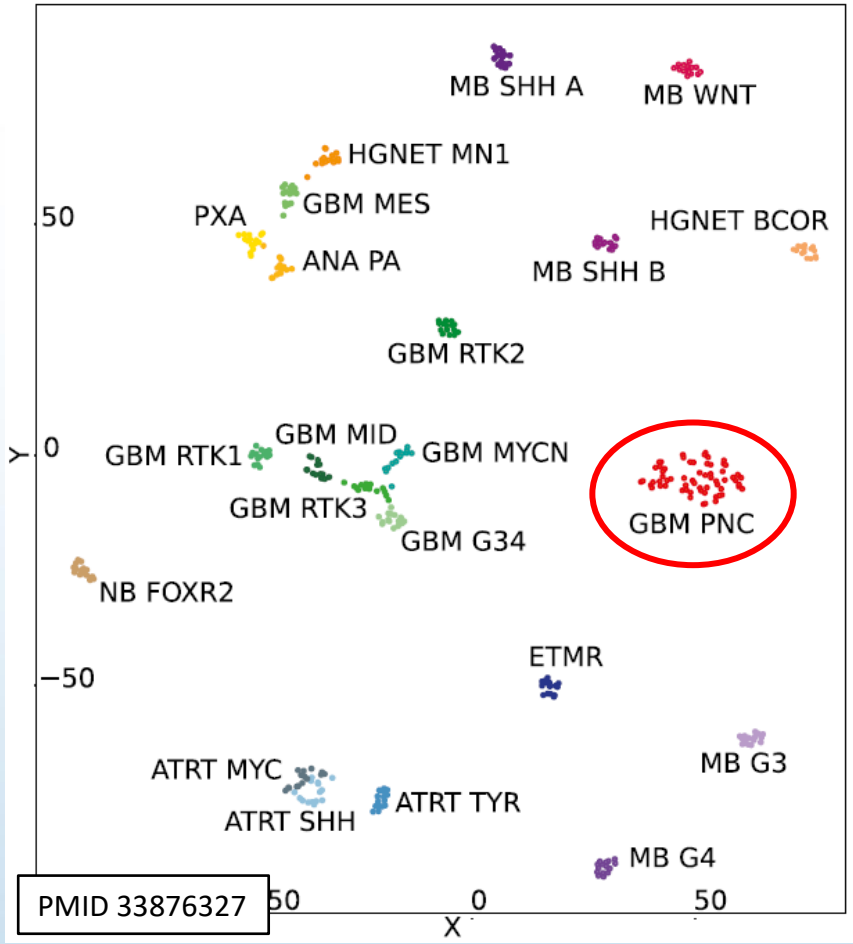
Malignant gliomas with PNET-like components (2008)



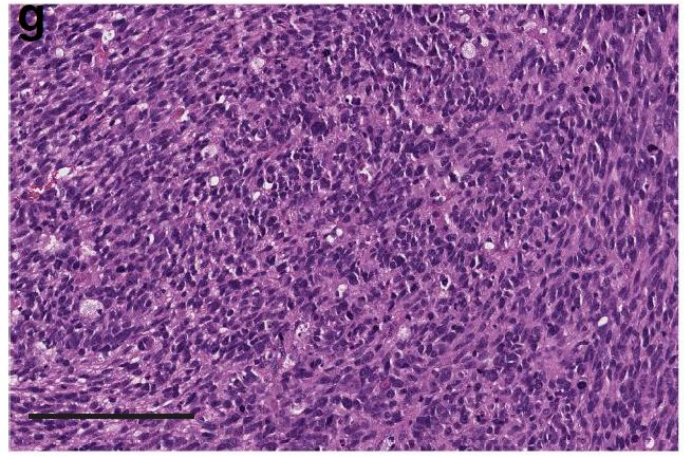
- *MYCN* (33%) or *MYCC* (10%) amplified
- Leptomeningeal spread in 21% with follow-up

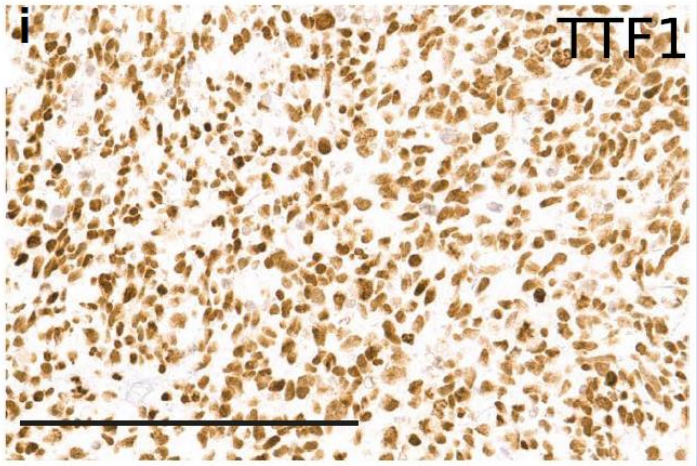


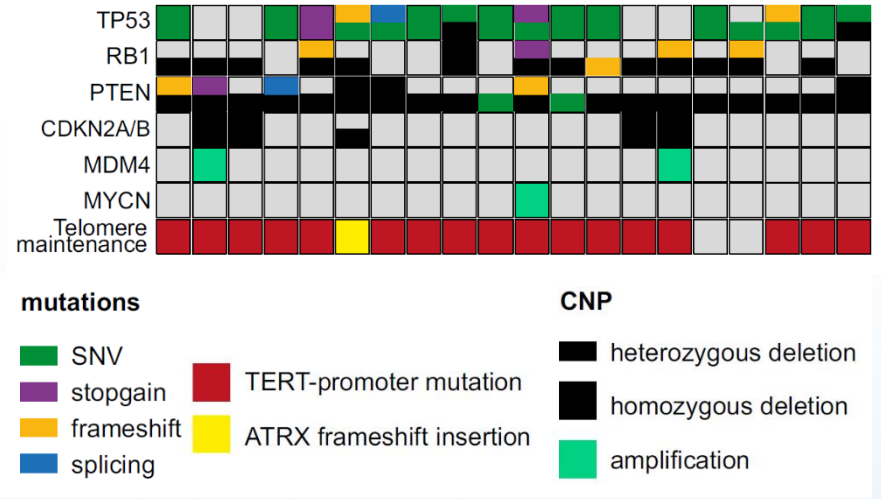
Molecular features of glioblastoma with PNC



PMID 33876327







- Distinct DNA methylation class
- Frequent mutation/deletion of *TP53*, *PTEN*, and *RB1*
- TTF1 positive (clone EP229) – also noted by Galloway & Seim 2007 (clone SPT24)
- 8G7G3/1 less frequently positive

Primitive neuronal component – differential and workup

Metastatic neuroendocrine tumor

- History, cytokeratin expression, lineage marker transcription factors (note TTF1)

Primitive neuronal component of another adult-type diffuse glioma

- Nature of the histopathology/genetics of the non-PN component

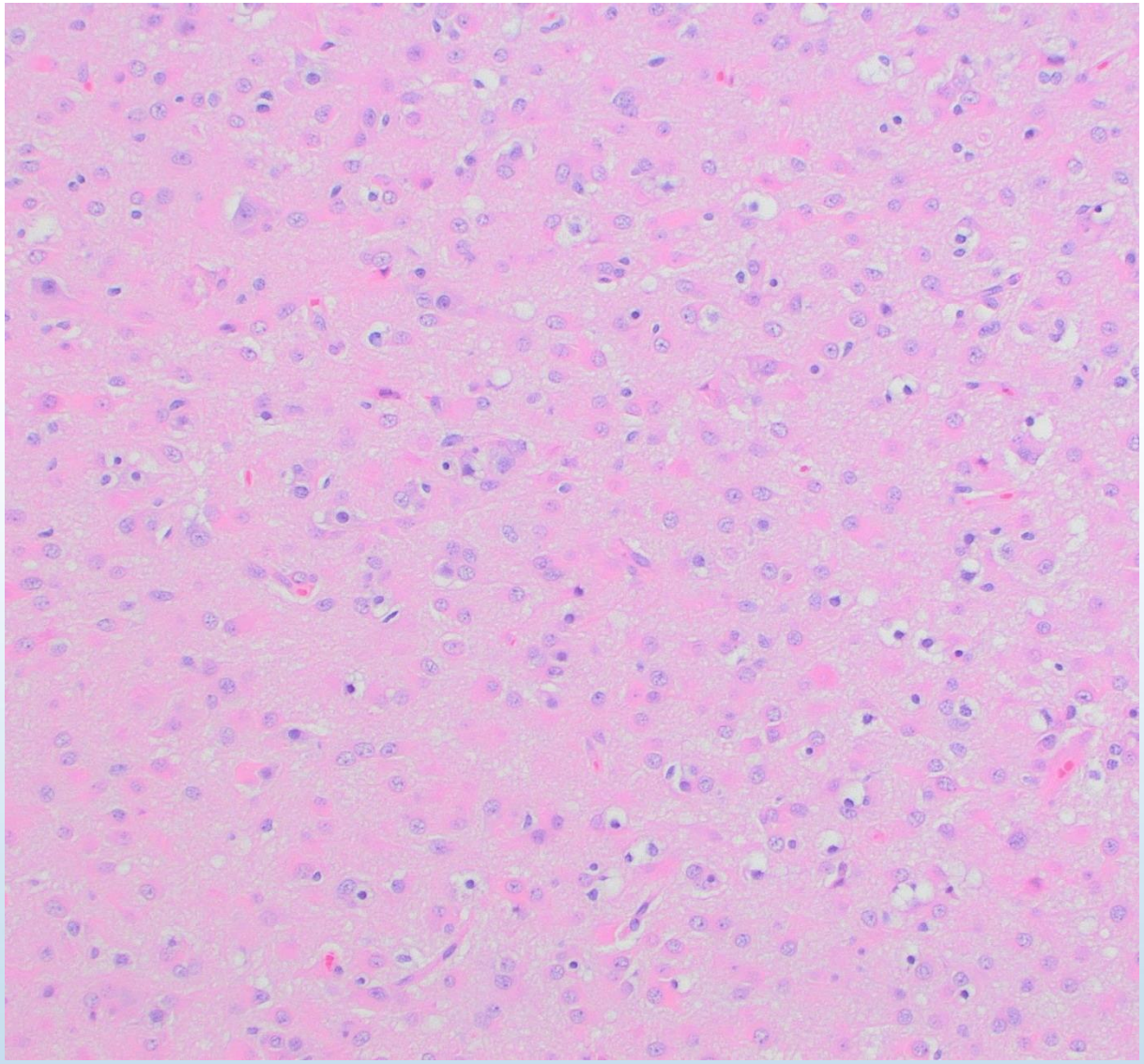
Other CNS embryonal tumor e.g. *FOXR2*-activated, *PLAGL* family amplified, etc.

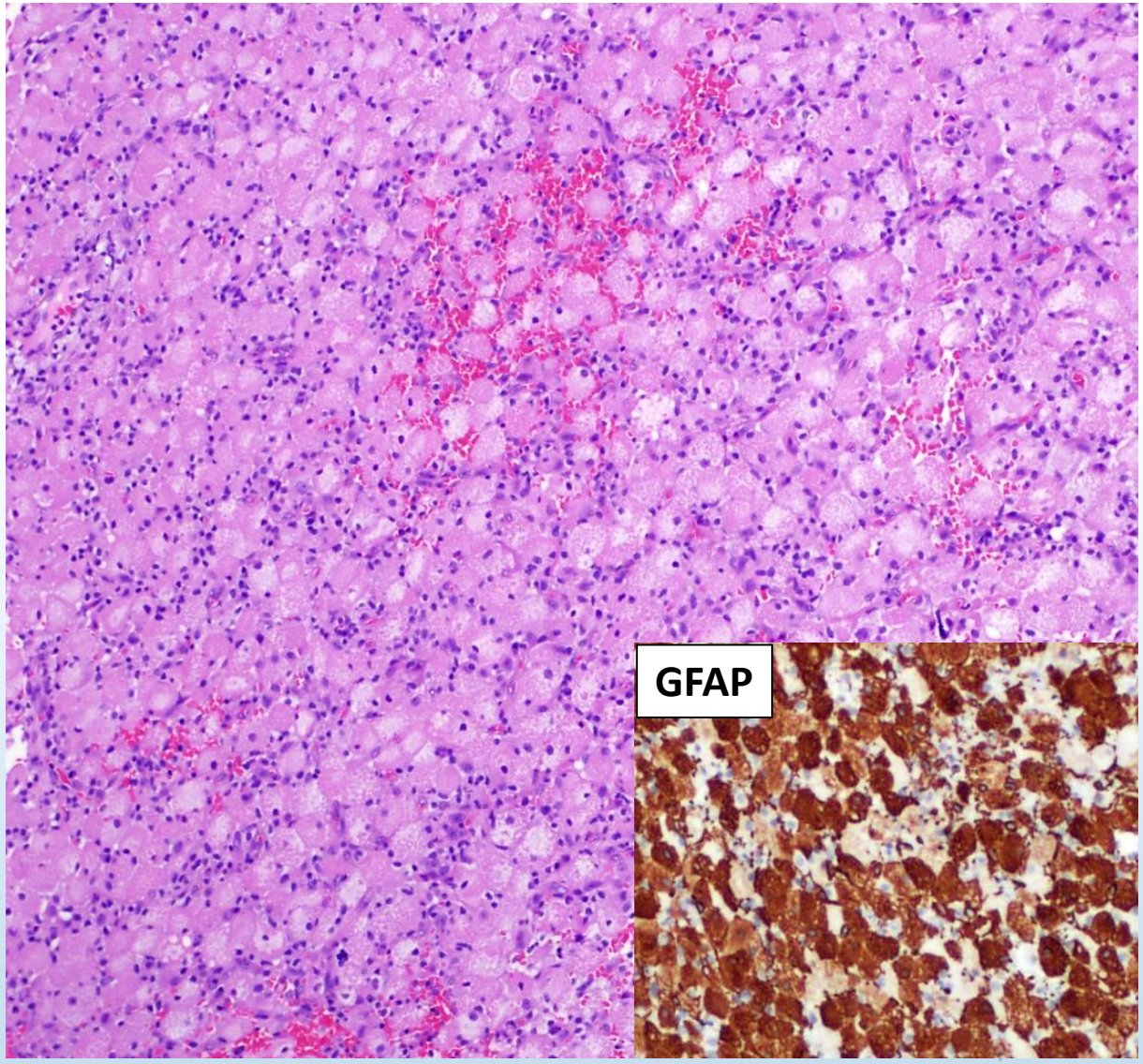
- Consider pure embryonal population vs. mixed/nodular with glial component

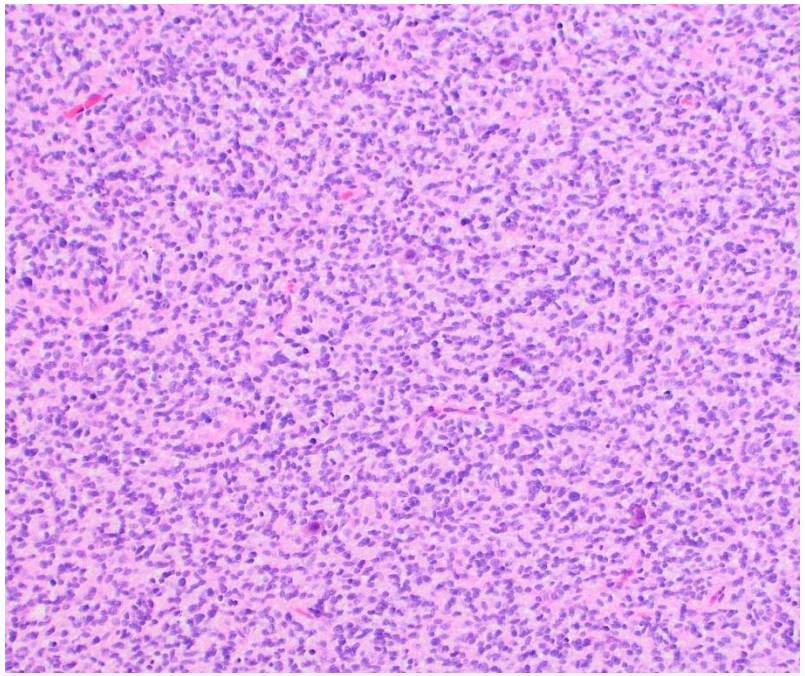
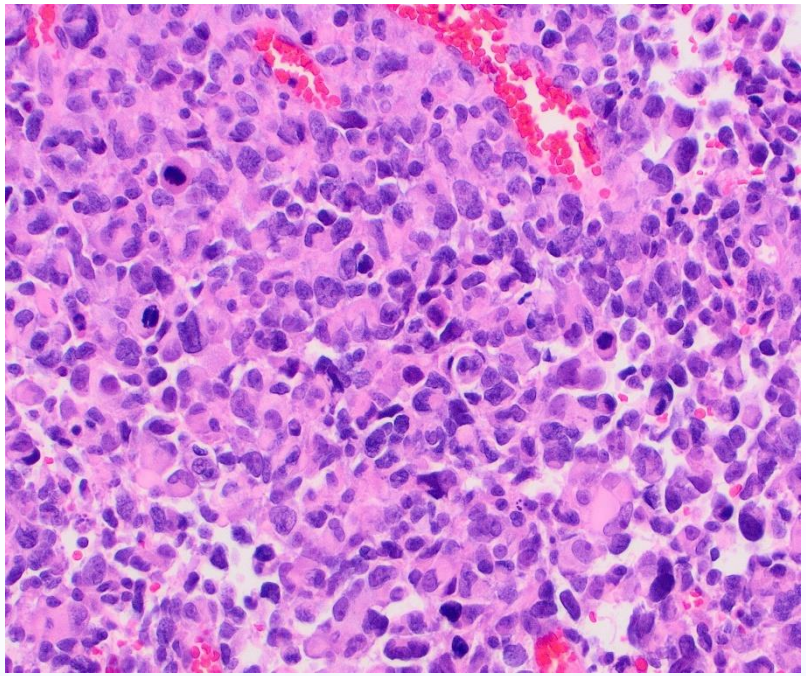
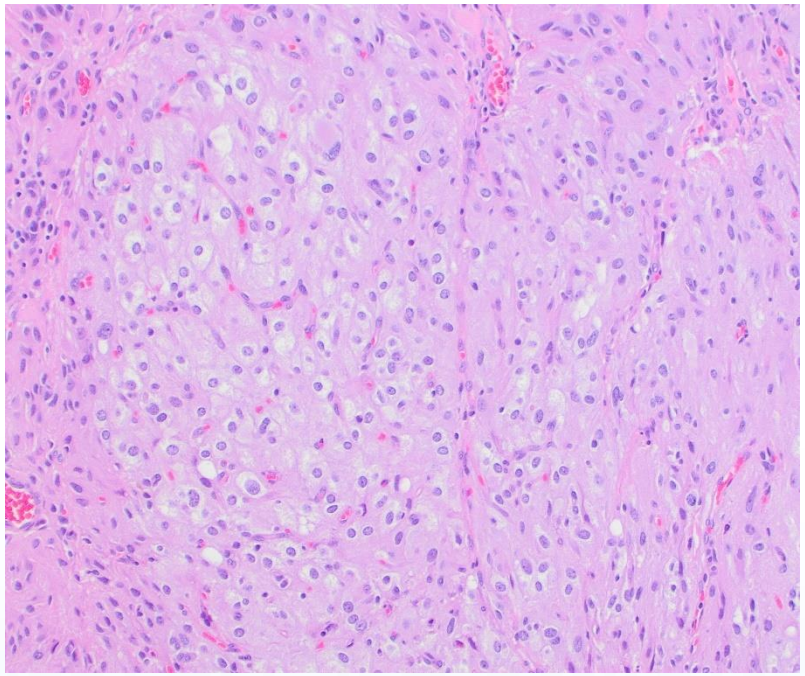
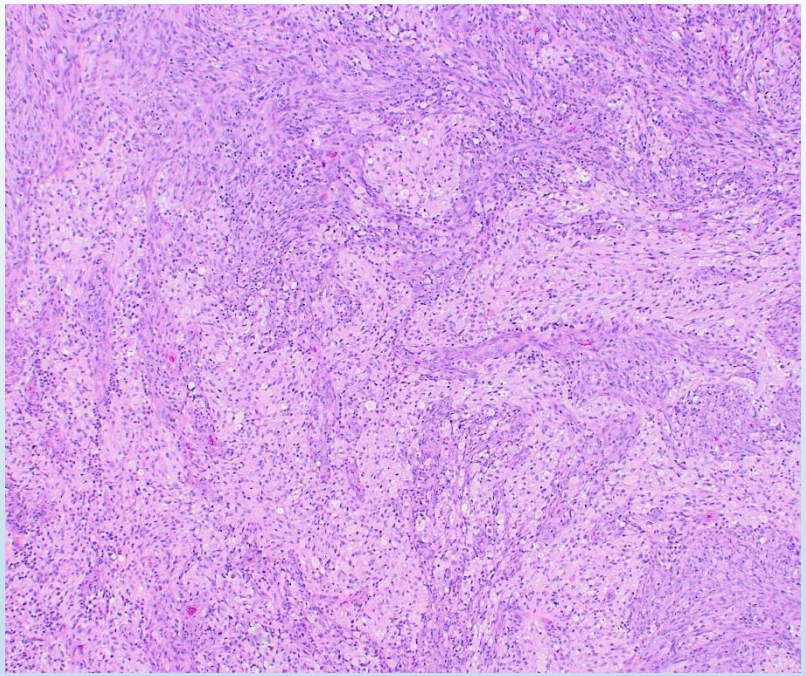
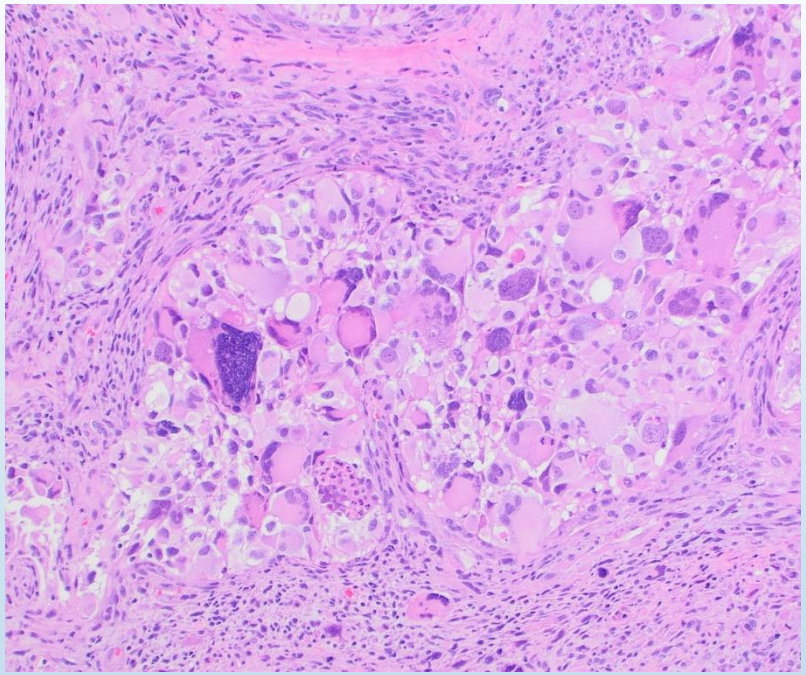
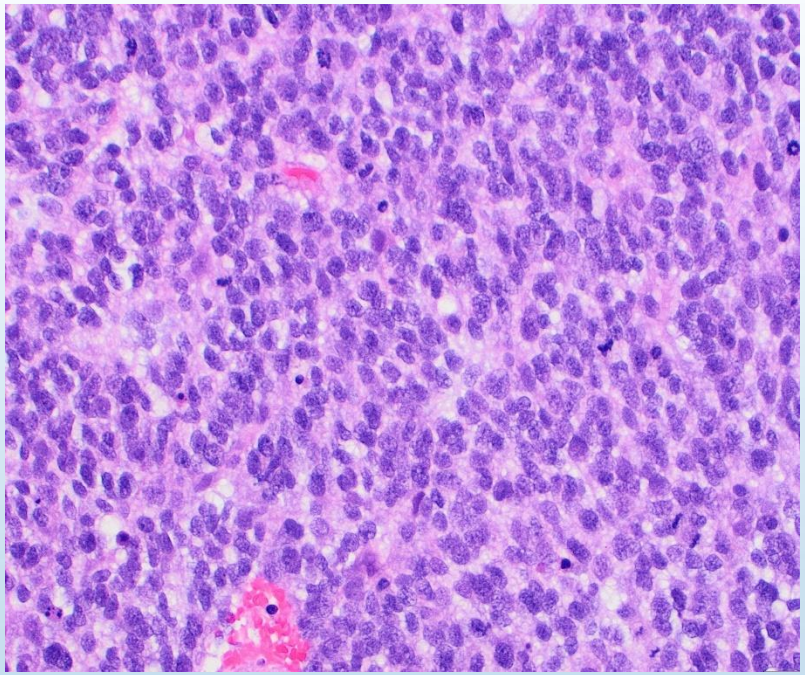
Diffuse hemispheric glioma, H3 G34-mutant – PMID 41649072

- Usually (but not always) younger patients (median age 21, range 12-50)
- ATRX loss by immunohistochemistry in 87%

Briefly noted - gemistocytic cells and granular cells





Summary

- Our framing of glioblastoma subtypes and patterns has changed with advances in molecular characterization of CNS tumors
- Clinical, histopathological, radiologic, and molecular context is essential

Small cell
- May be non-contrast-enhancing
- May lack vascular proliferation and necrosis
- High rate of *EGFR* amplification

Epithelioid
- Higher rate of BRAF pV600E mutation vs. traditional GB or other subtypes
- Challenging differential to grade 3 PXA, individual factors overlap
- May express cytokeratin, EMA, produce glandular structures

Oligodendrocyte-like cells
- Consider and exclude other oligodendrocyte-like tumors
- A subset are *FGFR3-TACC3* fusion-positive and this may have prognostic significance

Sarcomatous/gliosarcoma
- Consider sarcomatous metastasis or other sarcomatous primary CNS tumor
- Lower frequency of *EGFR* and higher frequency of *NF1* alterations
- Some evidence for increased extra-cranial metastasis

Giant cell
- A subset are associated with DNA mismatch repair deficient state
- Conflicting information on outcome, may be related to heterogeneity within the subtype

Primitive neuronal component
- Distinct epigenetic class
- Higher rate of CSF spread
- May be TTF1-positive, depending on antibody clone

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AANP

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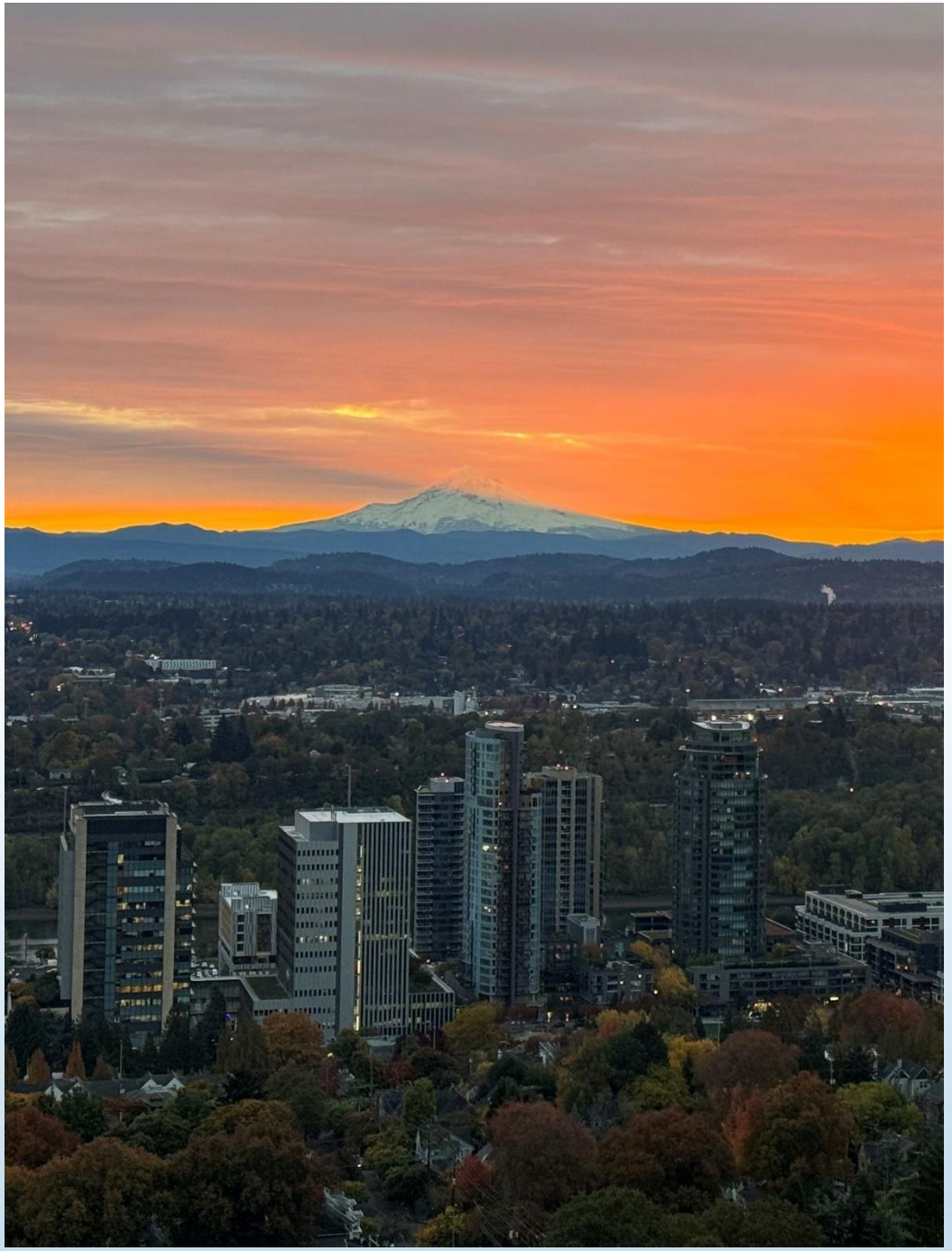

Q&A