Intraoperative Neuropathology

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Disclosures

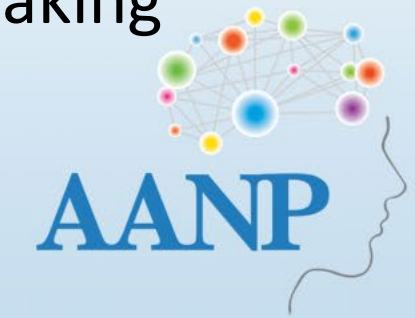
- Nothing to disclose

Learning Objectives

1. Describe the role of pathologists in intraoperative consultations of neurosurgical specimens

2. Discuss clinical and radiologic data to formulate a concise differential diagnosis prior to intraoperative consultation of neurosurgical specimens

3. Identify key cytological and histopathological features to provide a helpful intraoperative diagnosis that helps surgical decision making



Basic Principles of Intraoperative (IO) Neuropathology

- Get to know the neurosurgeons at your institution
- Gather basic clinical and radiologic information
- What is the question?
- What is needed to achieve and IO Dx? Cytologic preparation and/or Frozen section
- **Report only what you see, if you need more tissue, ask for it**
- Before hanging up ask the surgeon if there are any additional questions that need to be addressed

Role of Pathologists in IO Consultations

Guide the surgeon

- Is the surgeon in the lesion?
- Will your IO Dx change the course of the surgery? Bx vs resection

Provide necessary information

- **Does the lesion explain the clinical presentation?**
- Put the lesion in a category, if possible, most of the time no need for final diagnosis

Allocate tissue for ancillary studies

- Standard histopathology
- Molecular testing
- Clinical trials
- Brain banking

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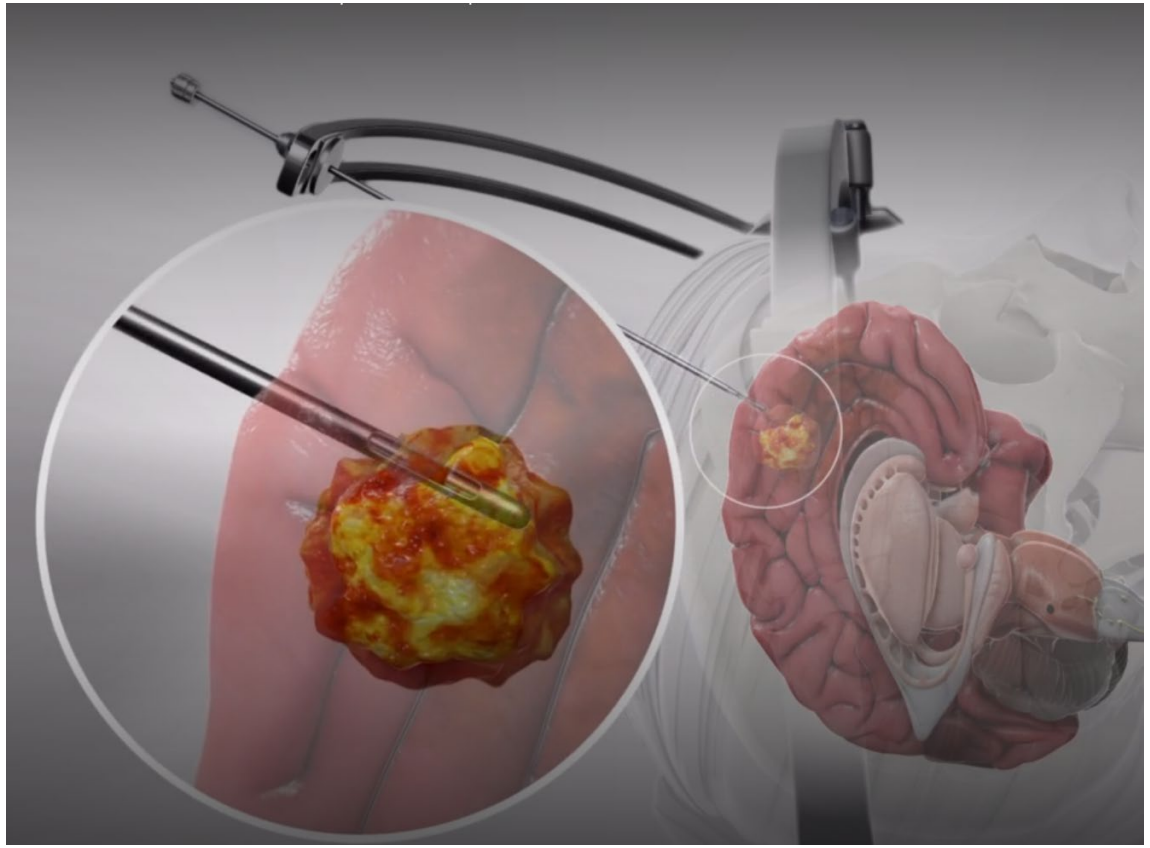
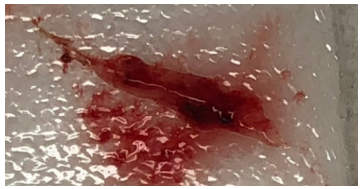
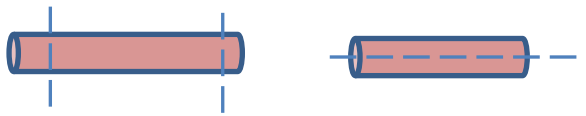
Neurosurgical Specimens for IOC

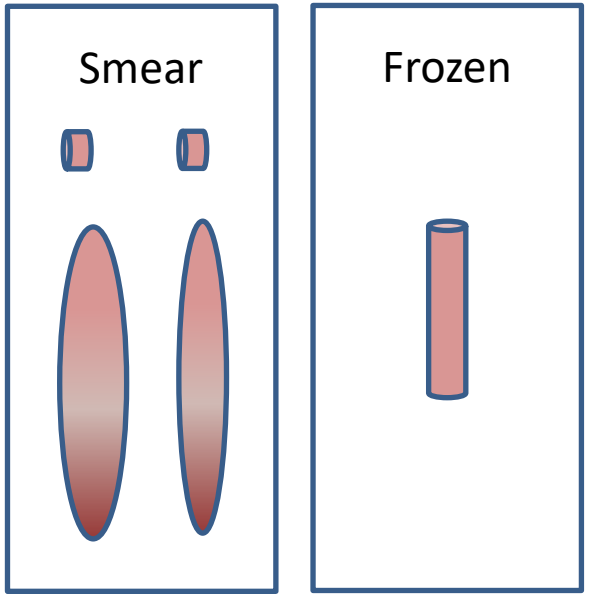
Needle stereotactic biopsies



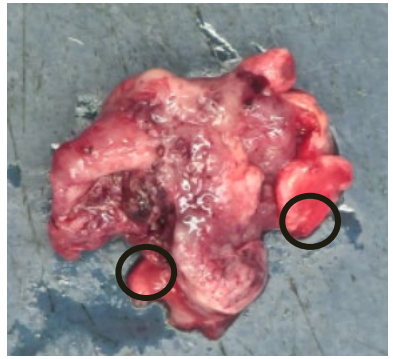
https://www.princetonneurologicalsurgery.com

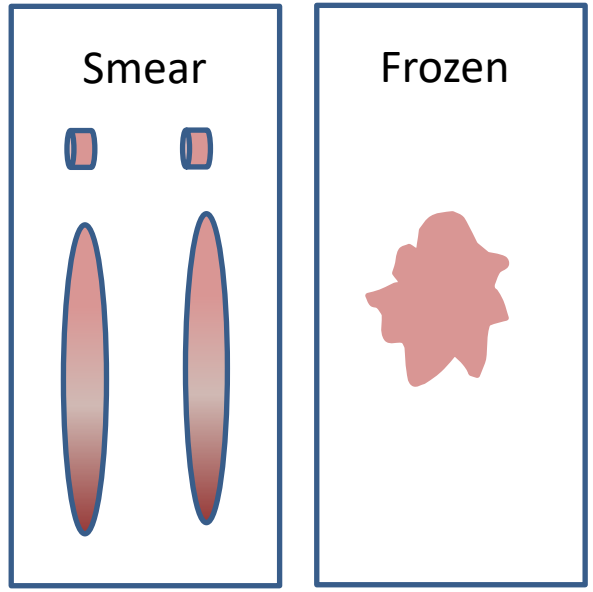




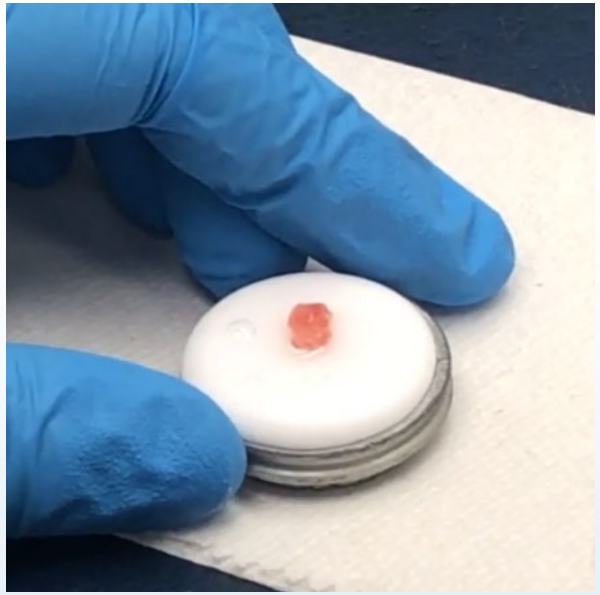


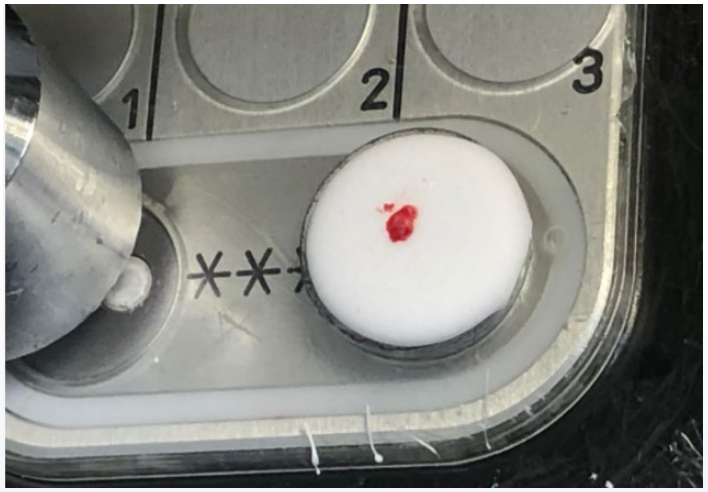
Open biopsies





Frozen Section Techniques





Video

Suggestions:
Hematoxylin:Eosin ratio 3:1

Scant material:
Smear Vs. Frozen section

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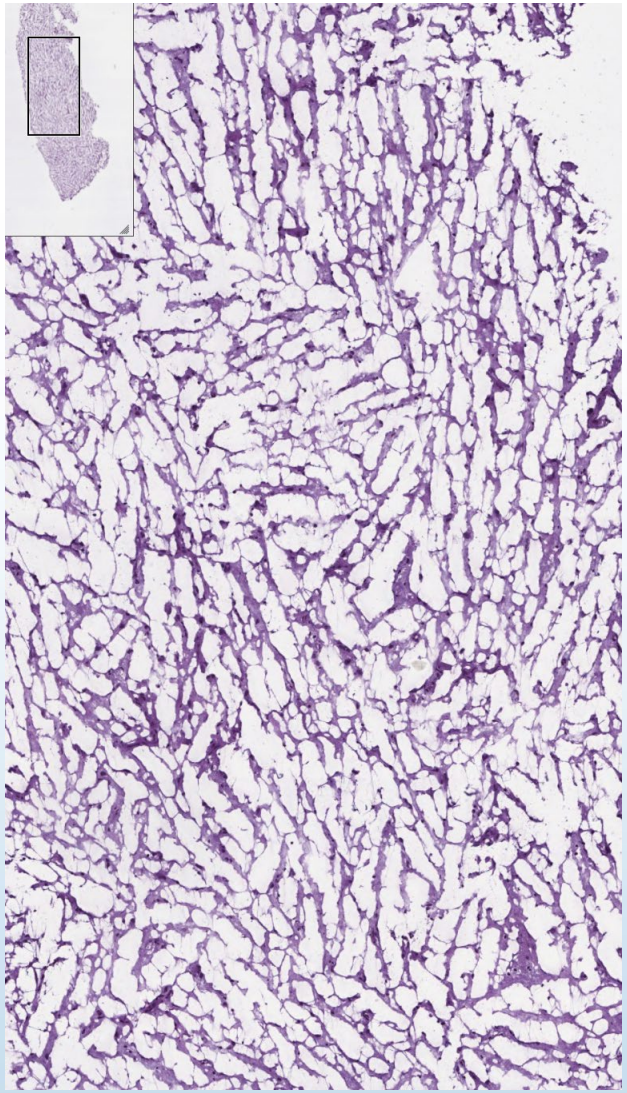
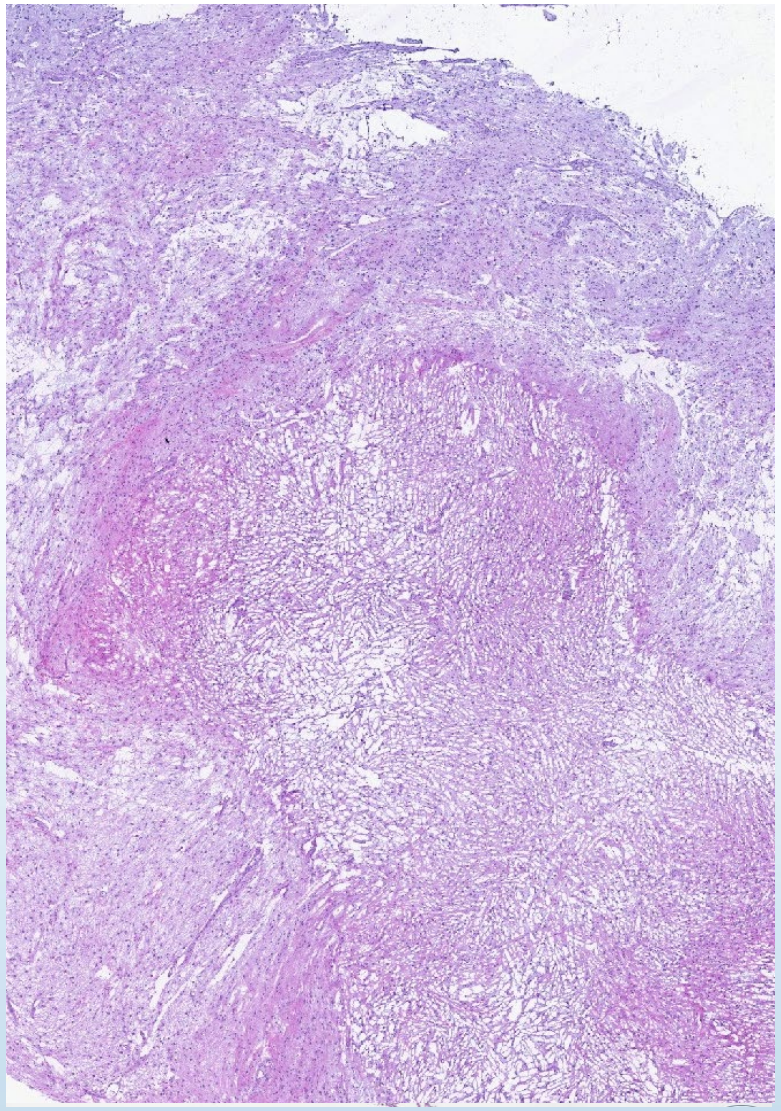
Artifacts

Ice crystals



Slow Freezing



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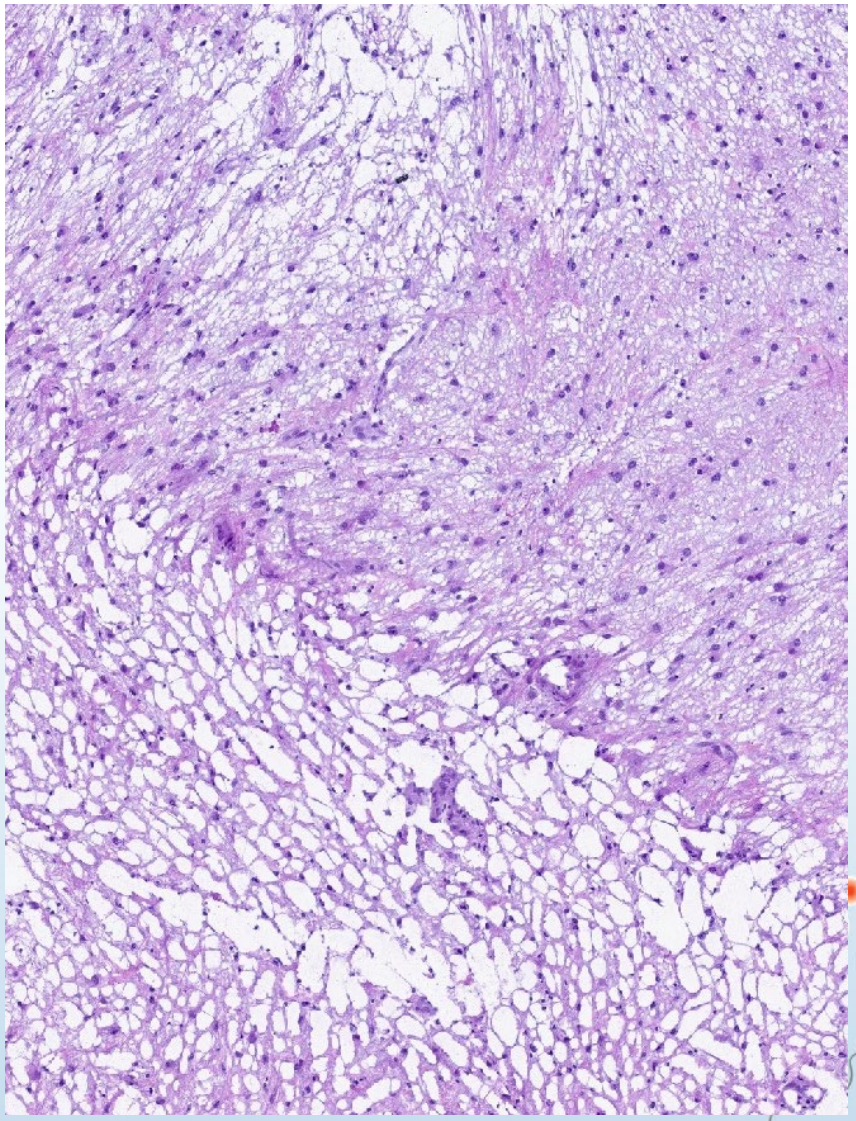
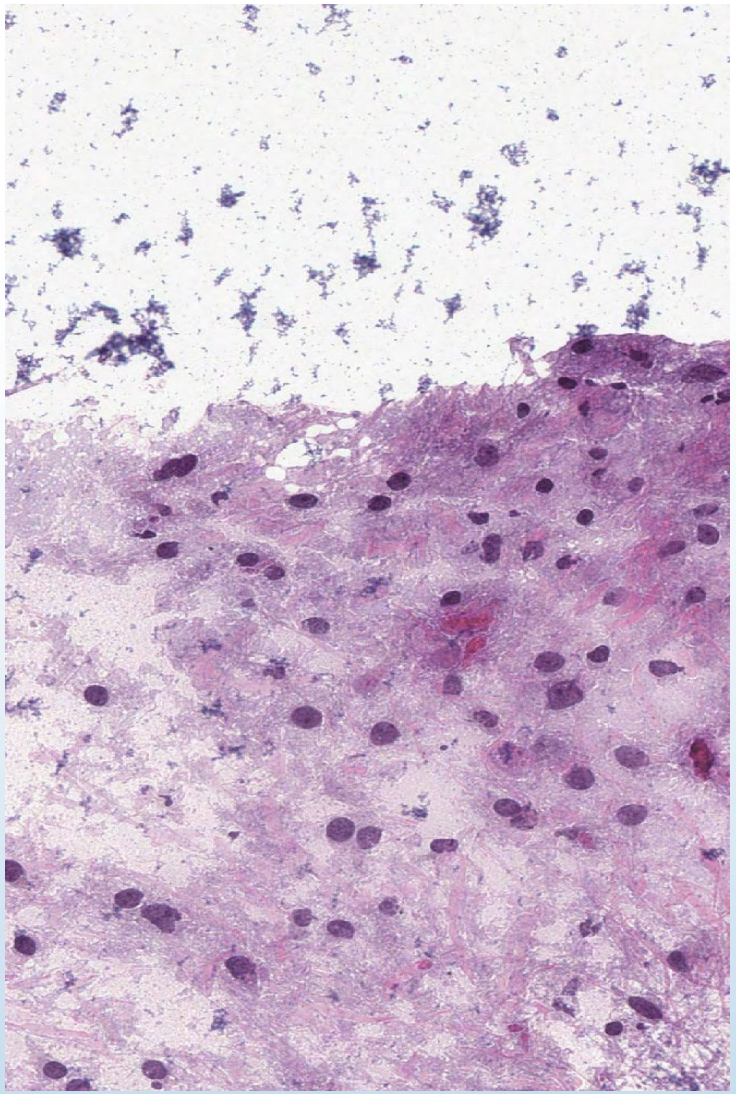


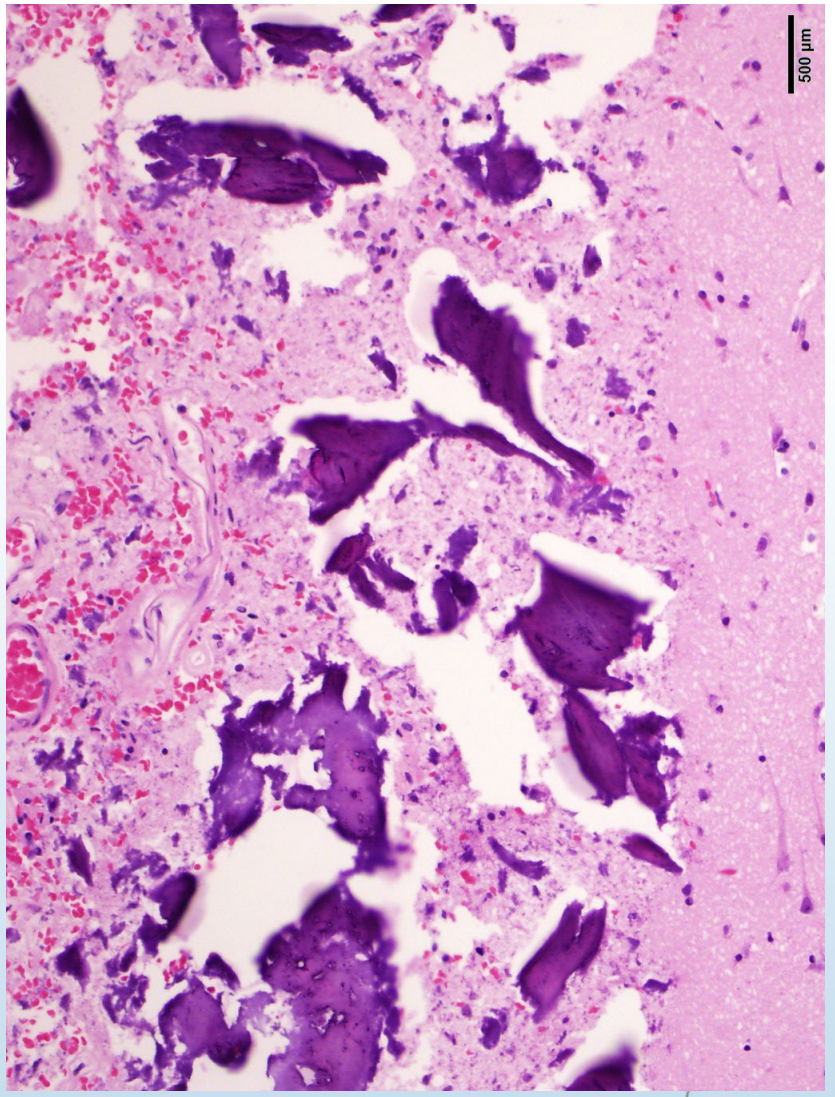
Artifacts

Stain precipitate



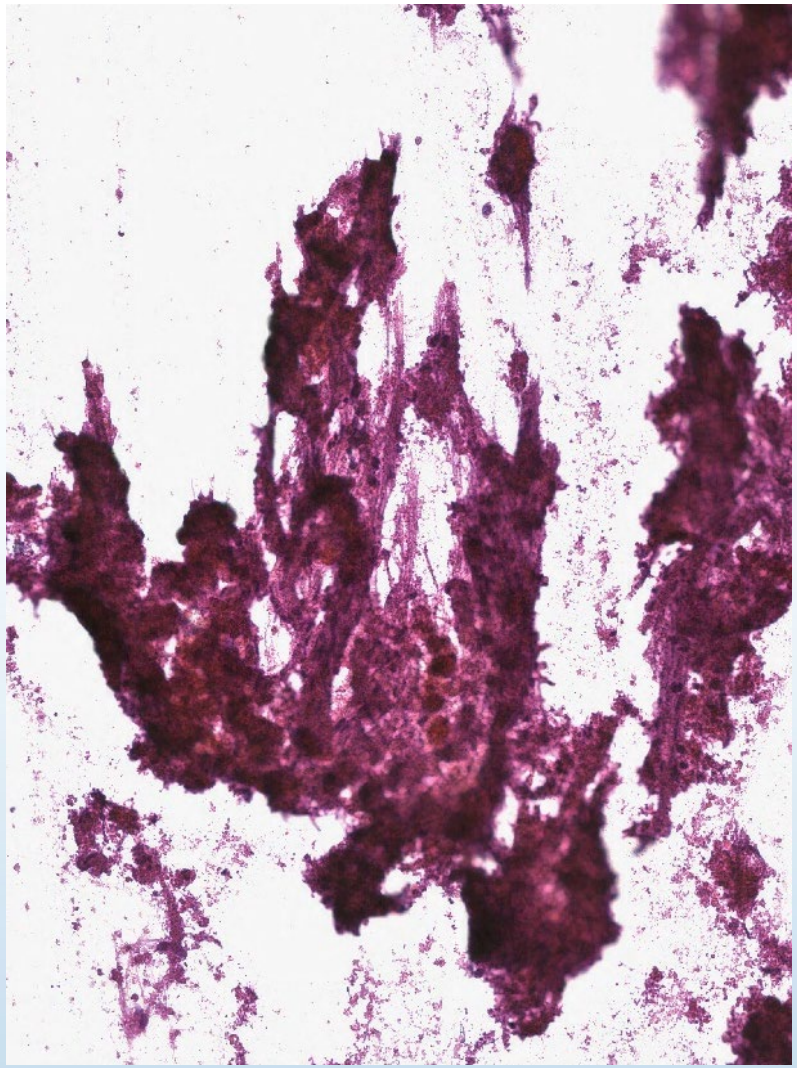
Gel Foam

Bone dust

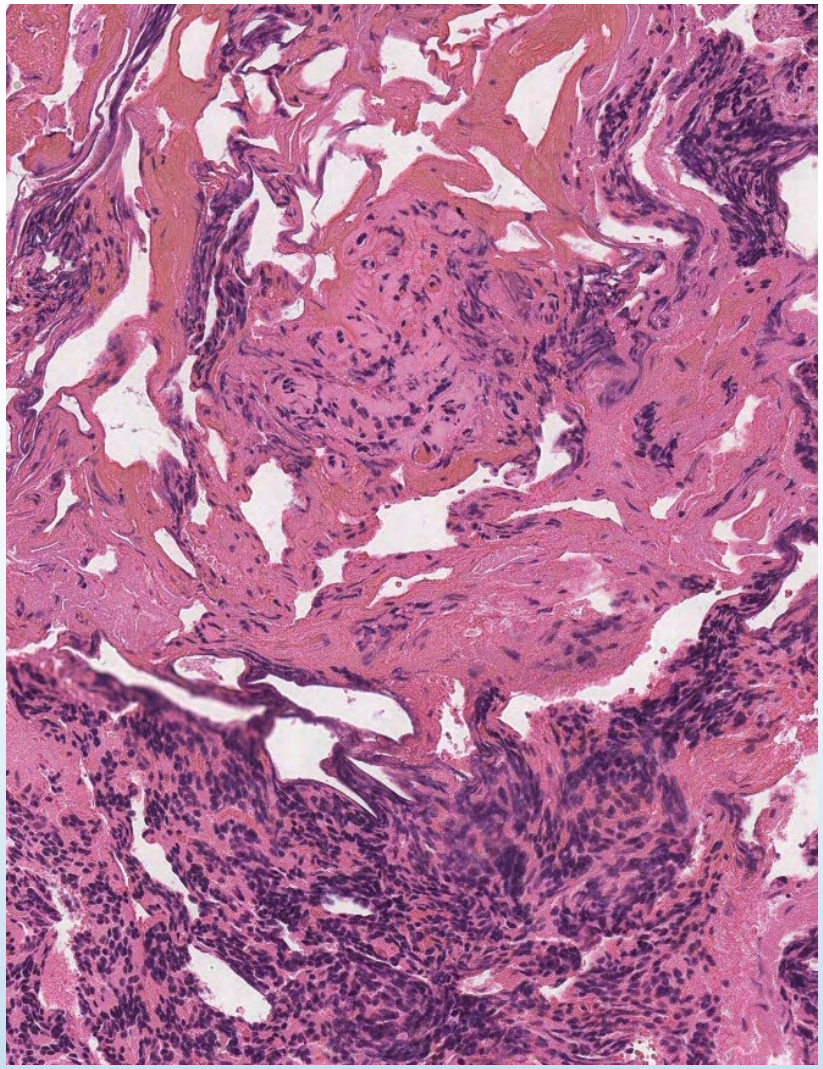


Artifacts

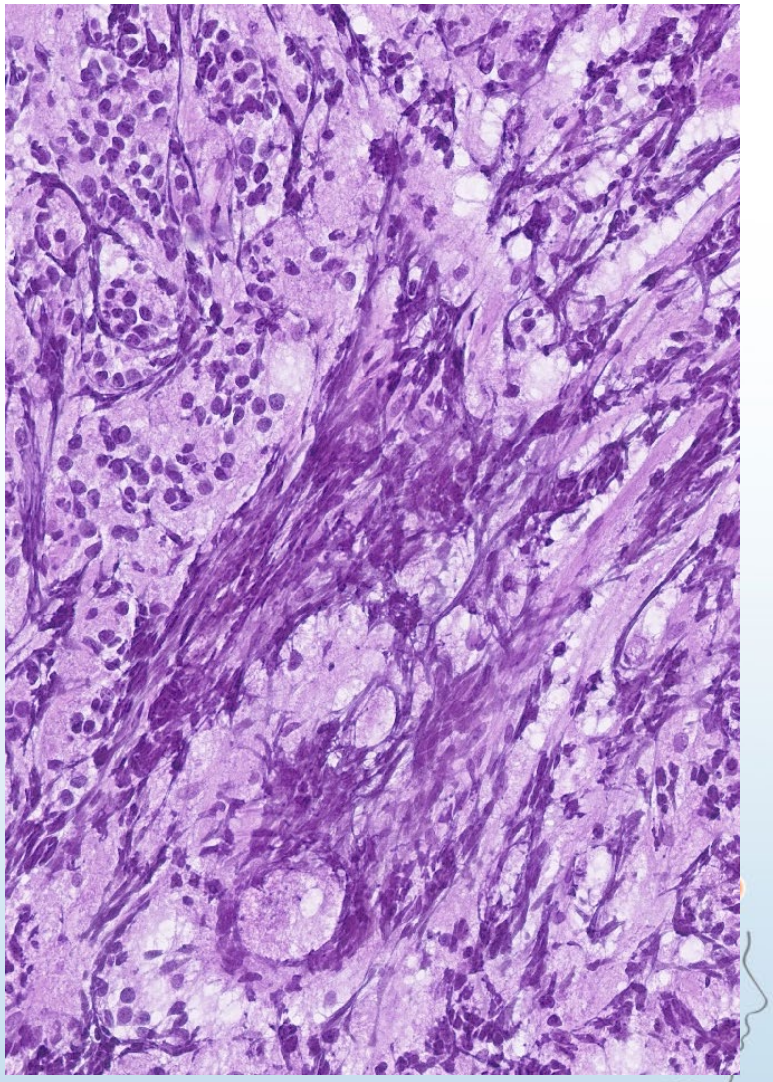
Thermal artifact Smear



Thermal artifact Frozen

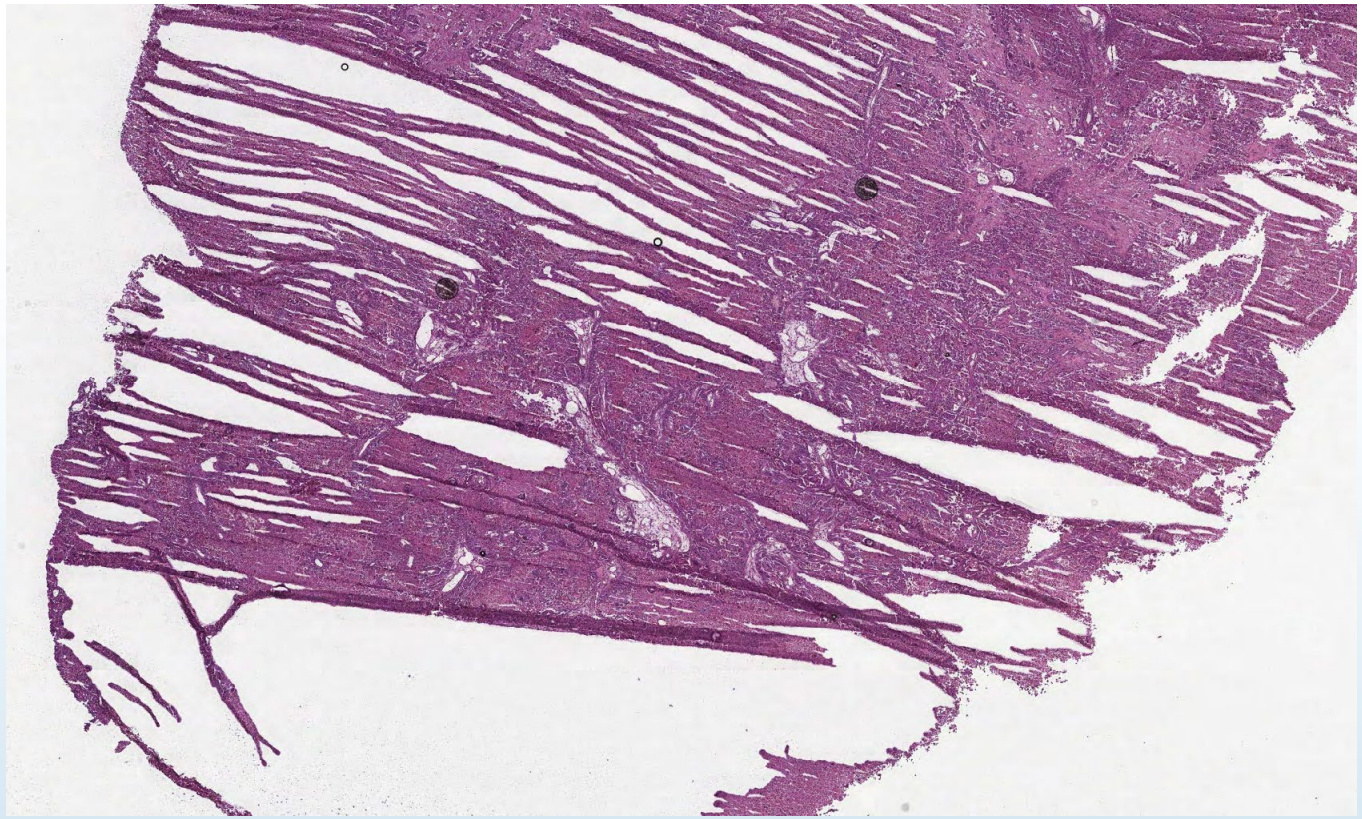


Crush artifact

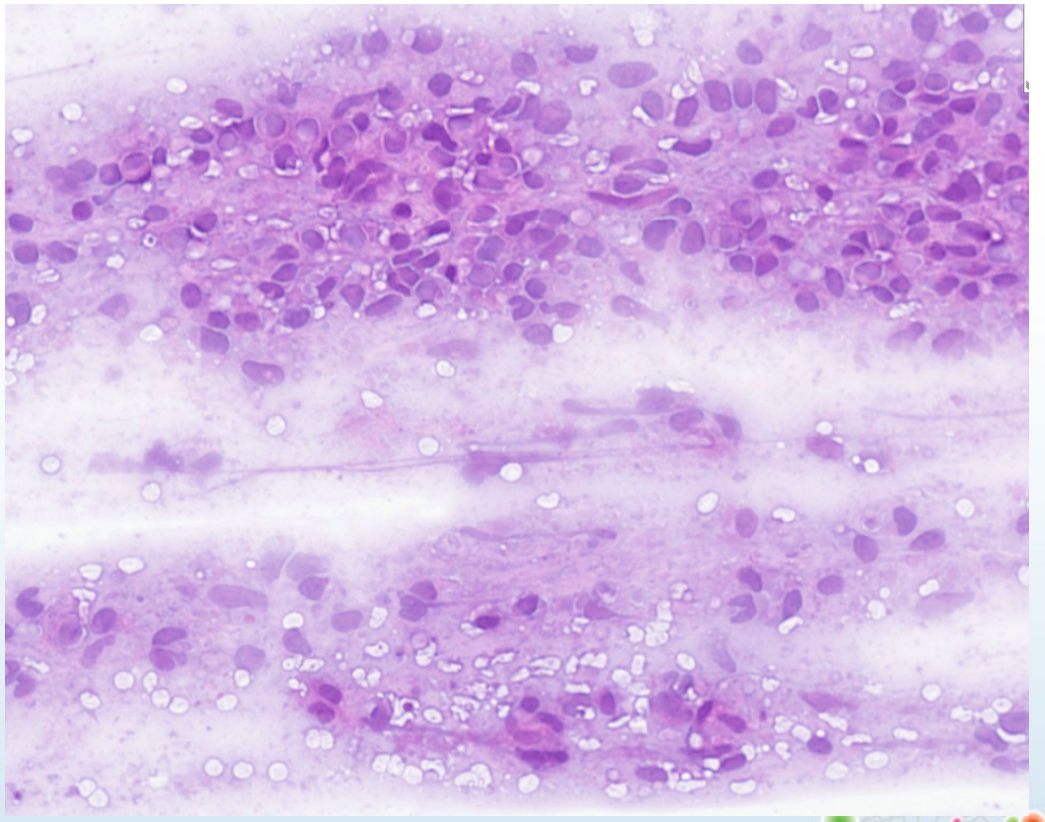


Artifacts

Knife artifact

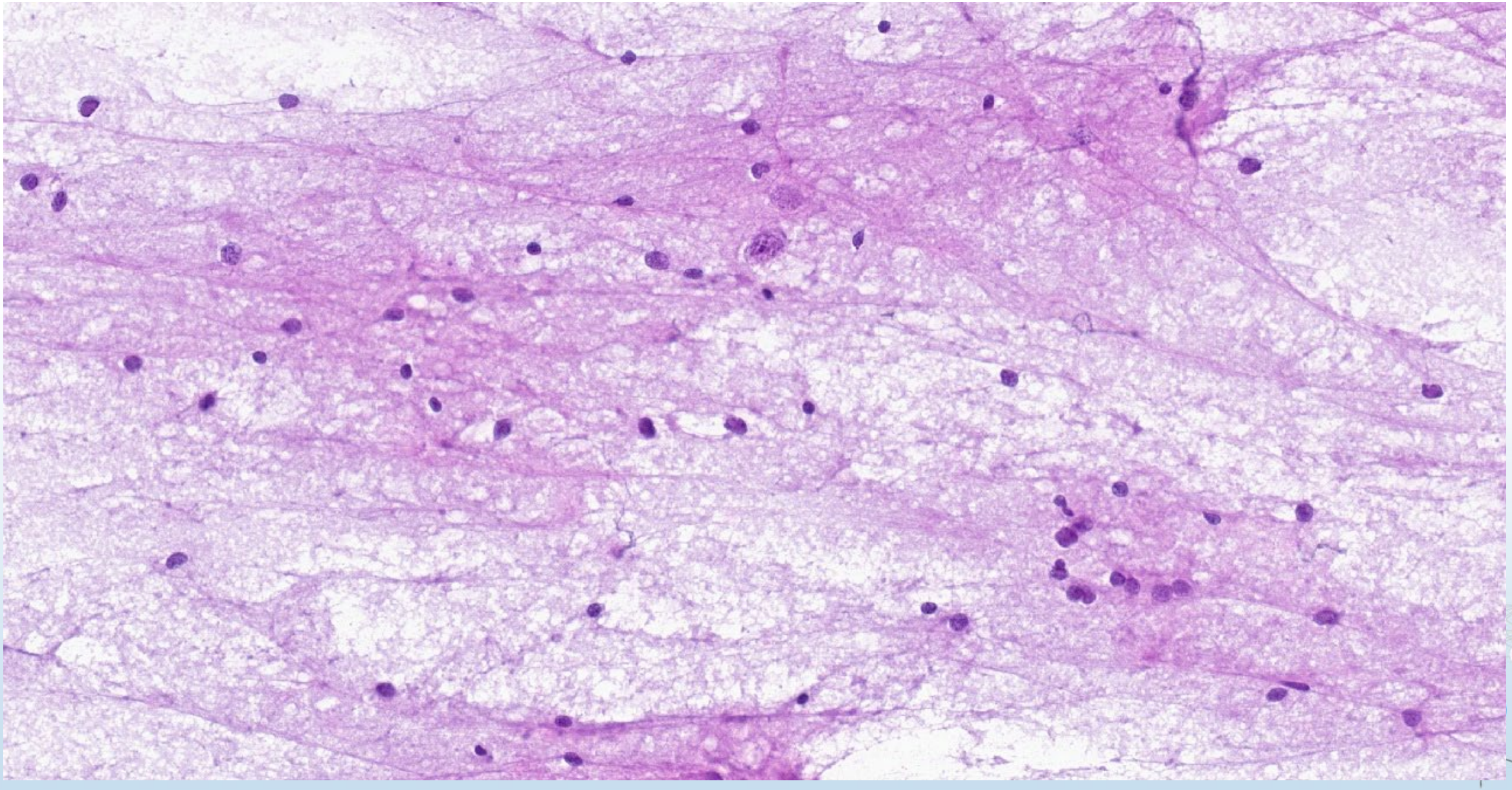


Smear, air dry artifact



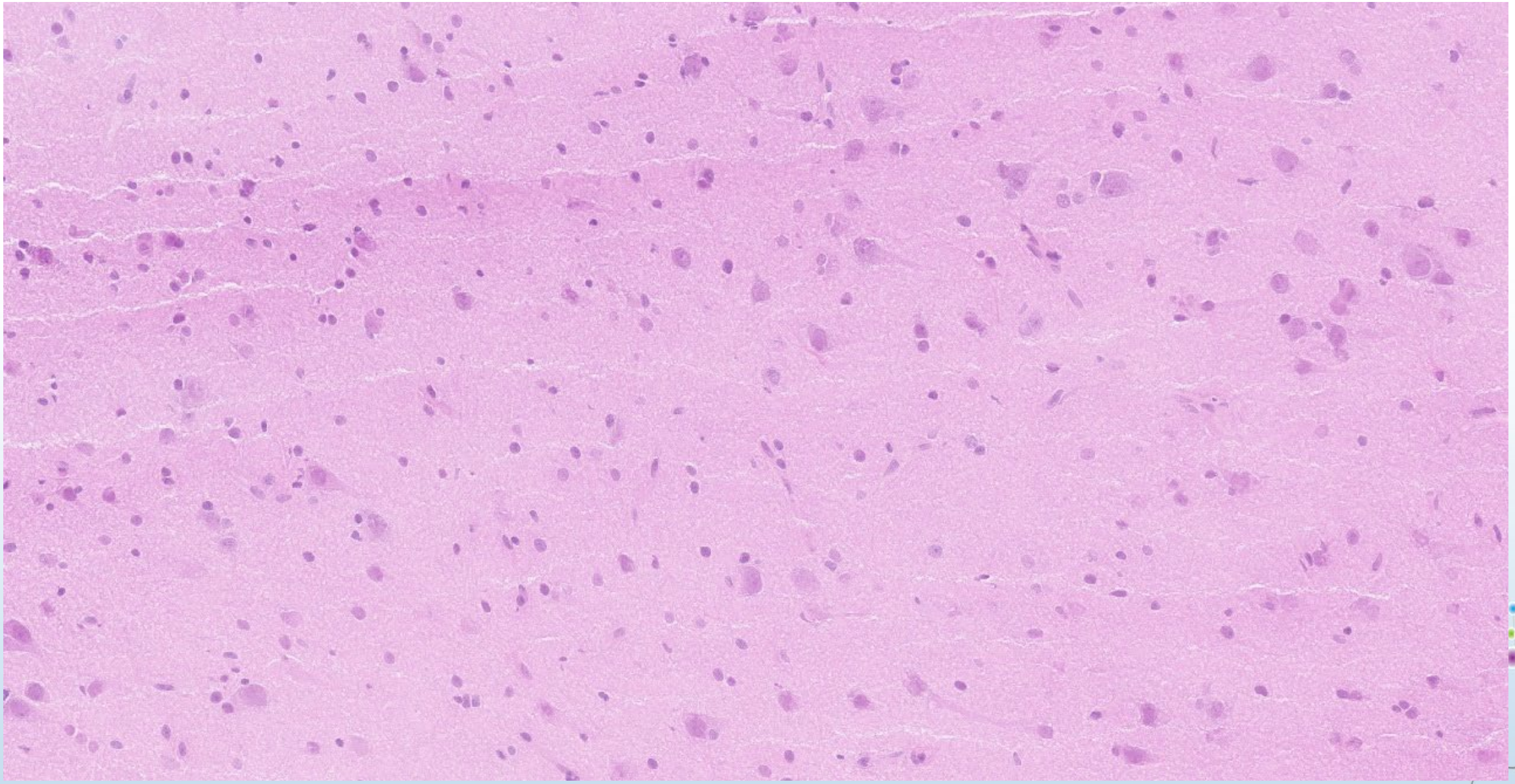
Normal Brain

Normal Brain

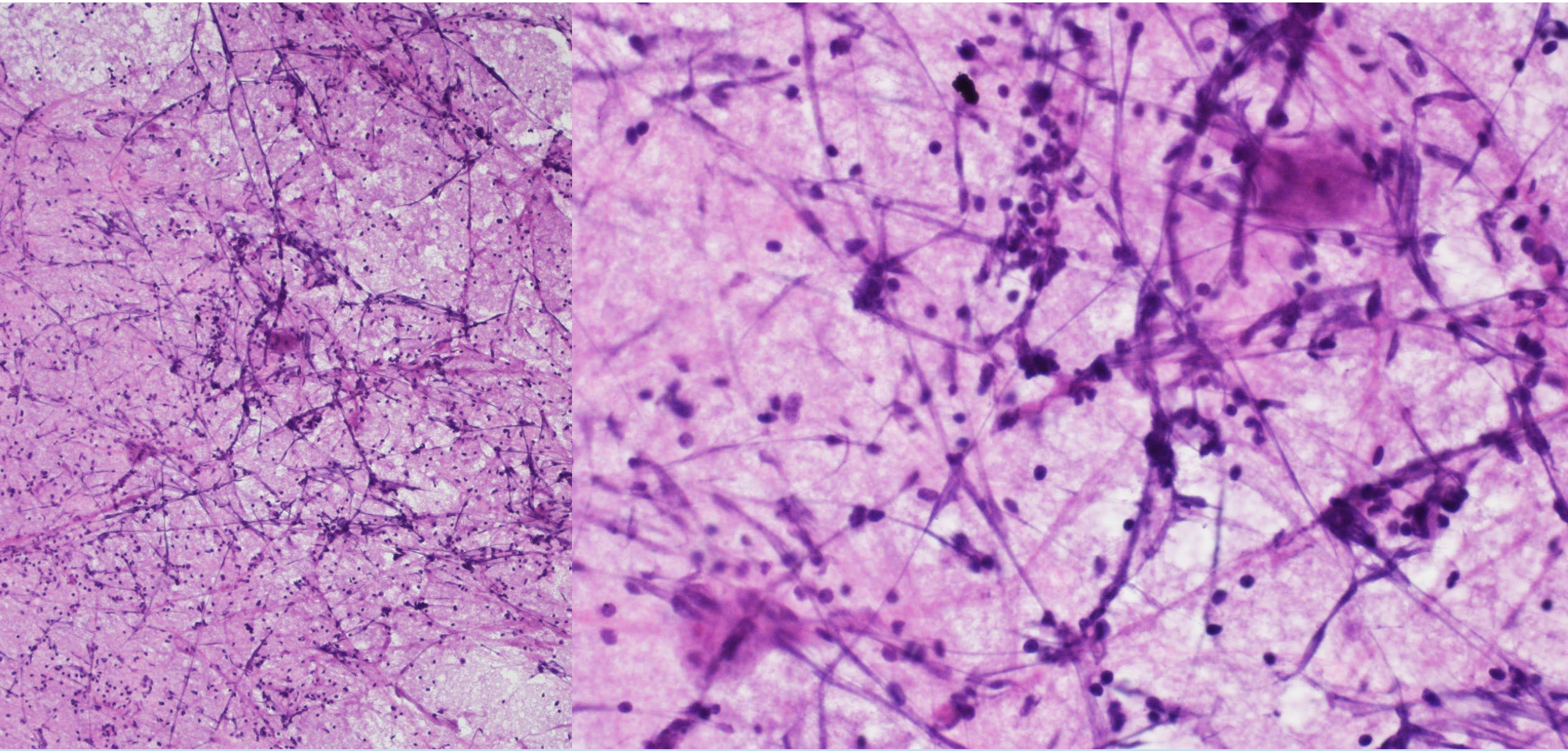


CP

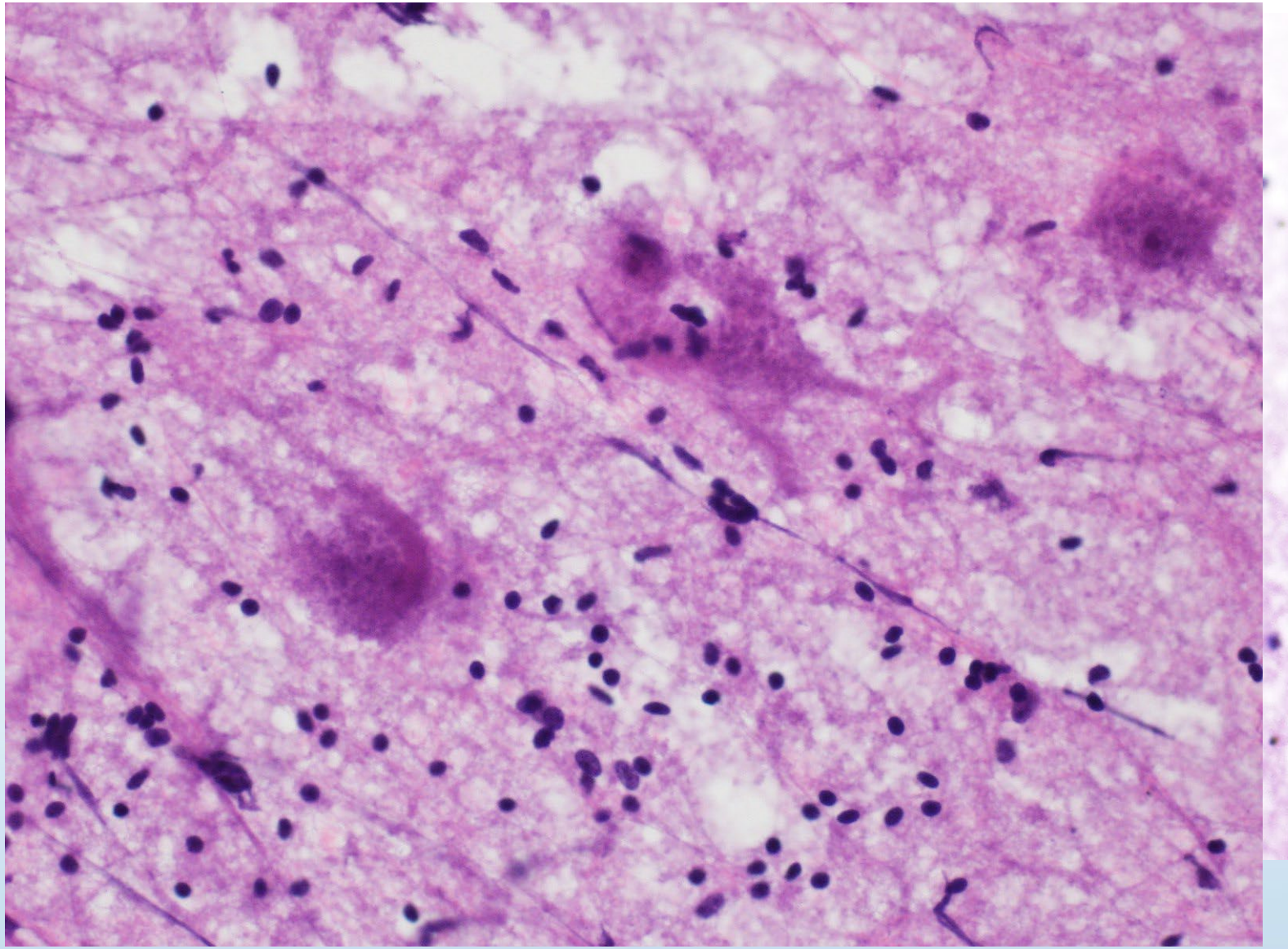
Normal Brain

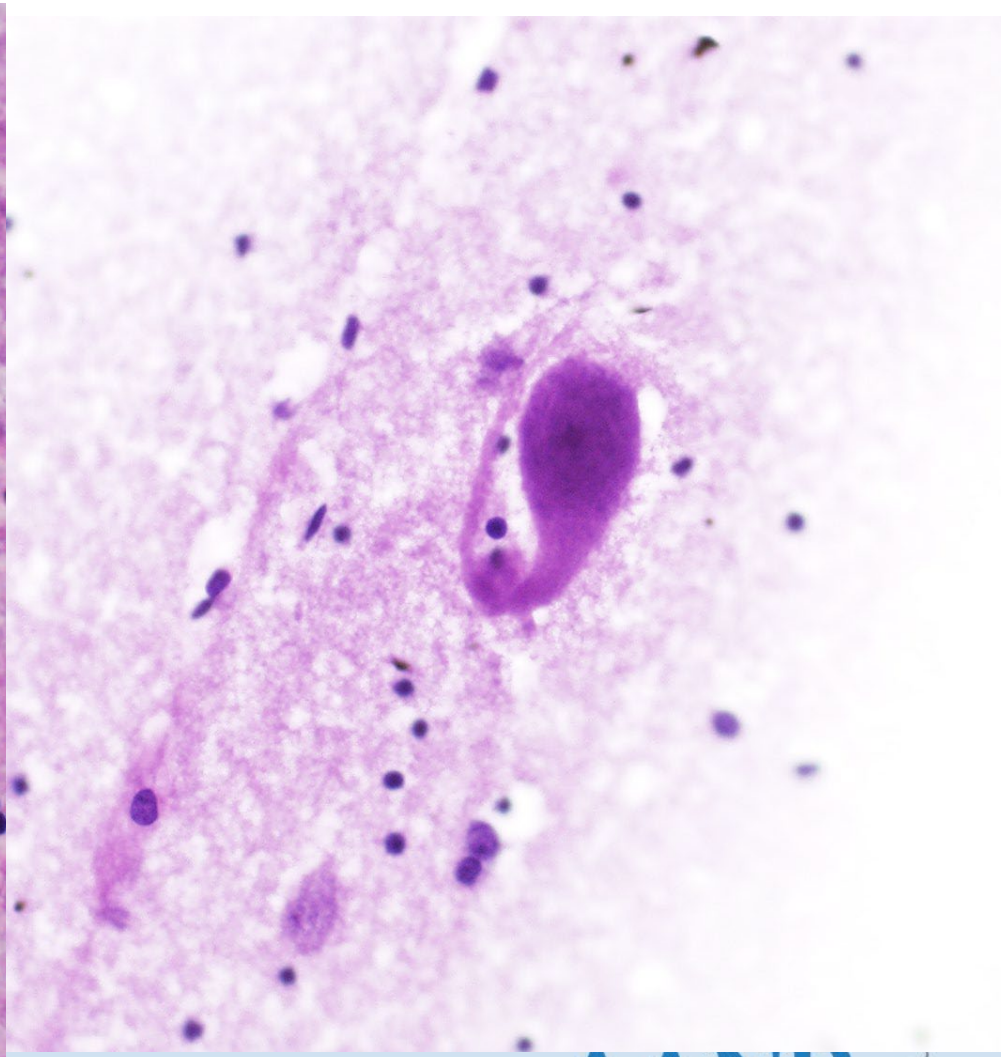


Normal Cerebellum



Normal Cerebellum





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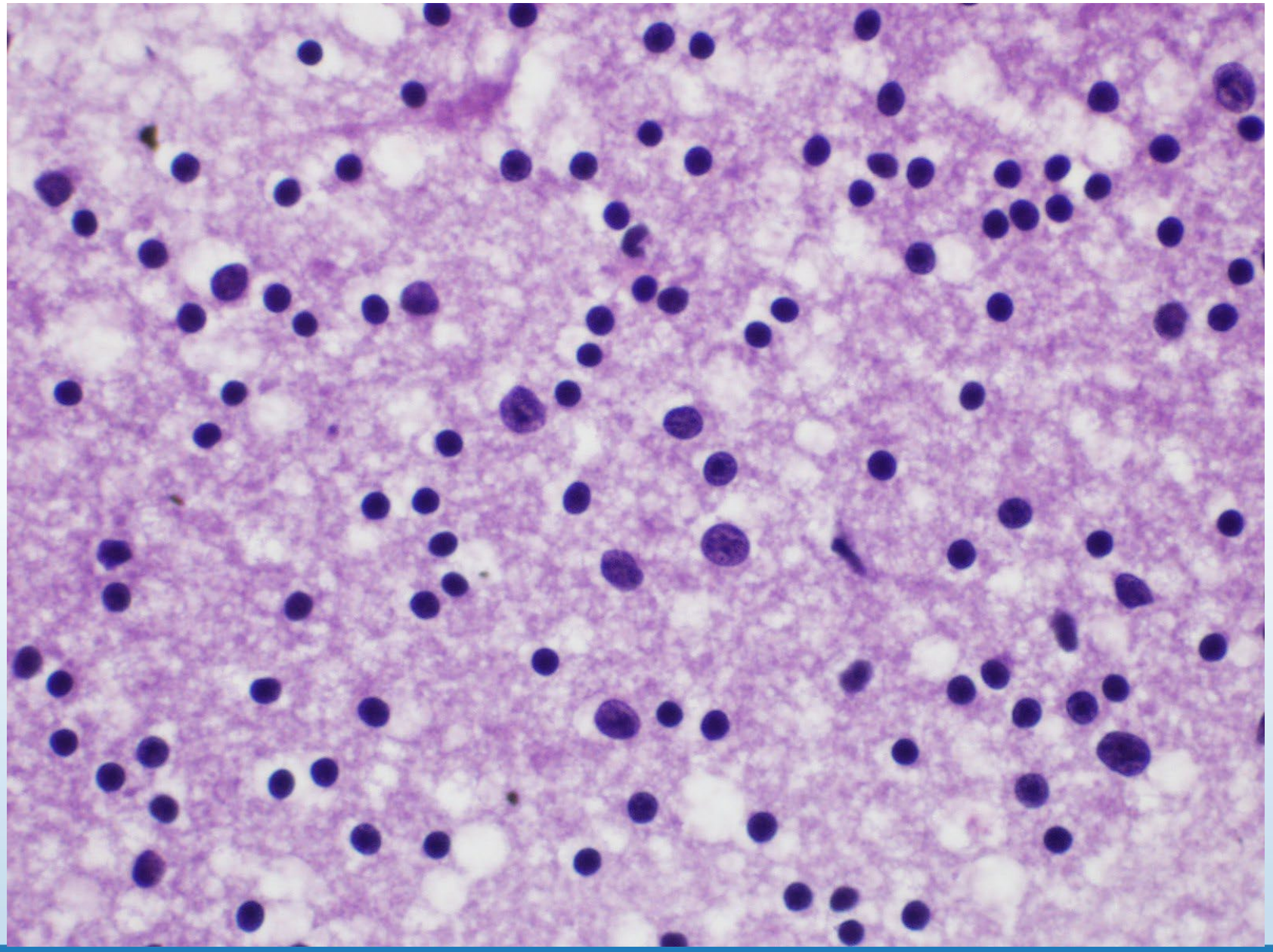
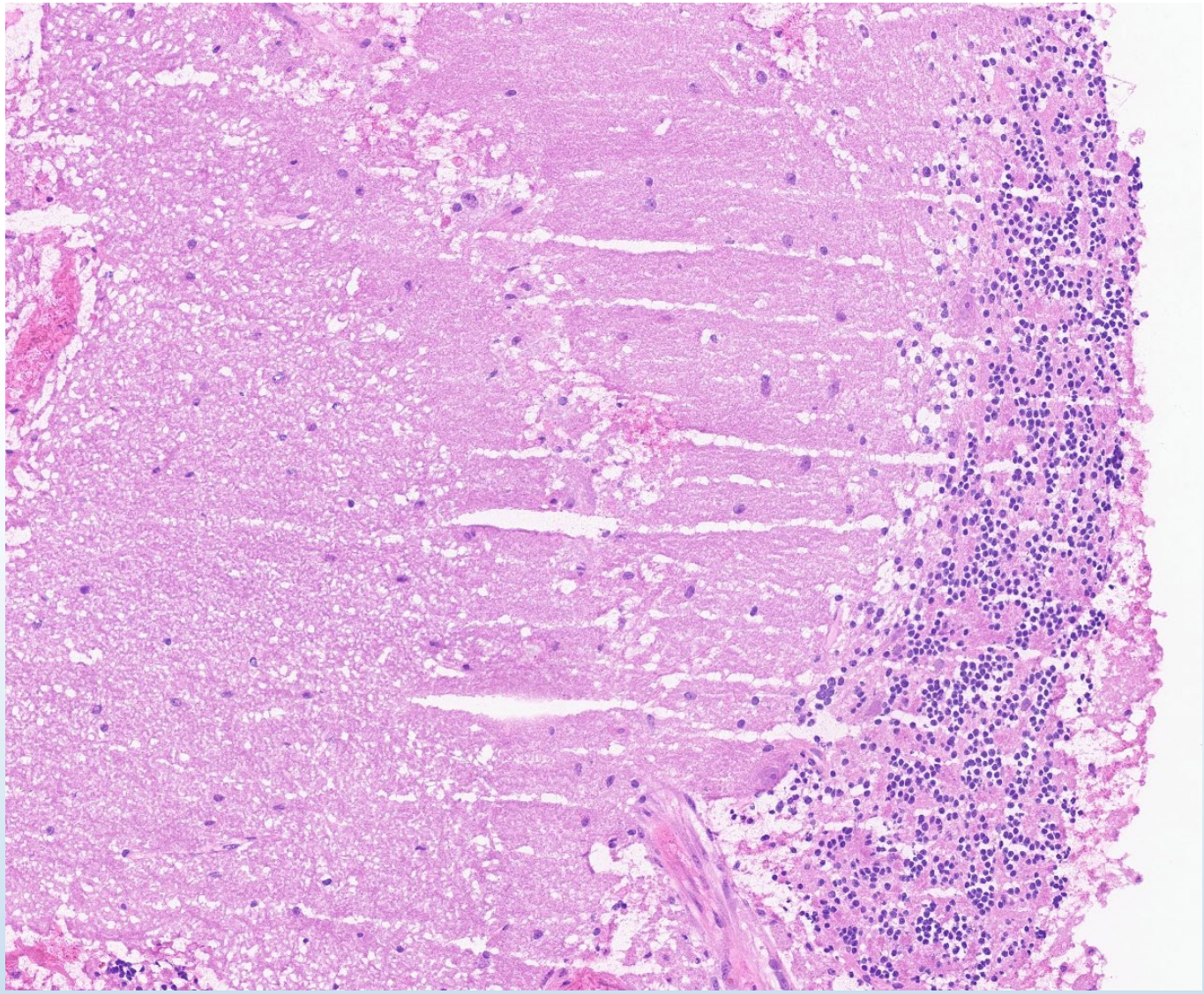
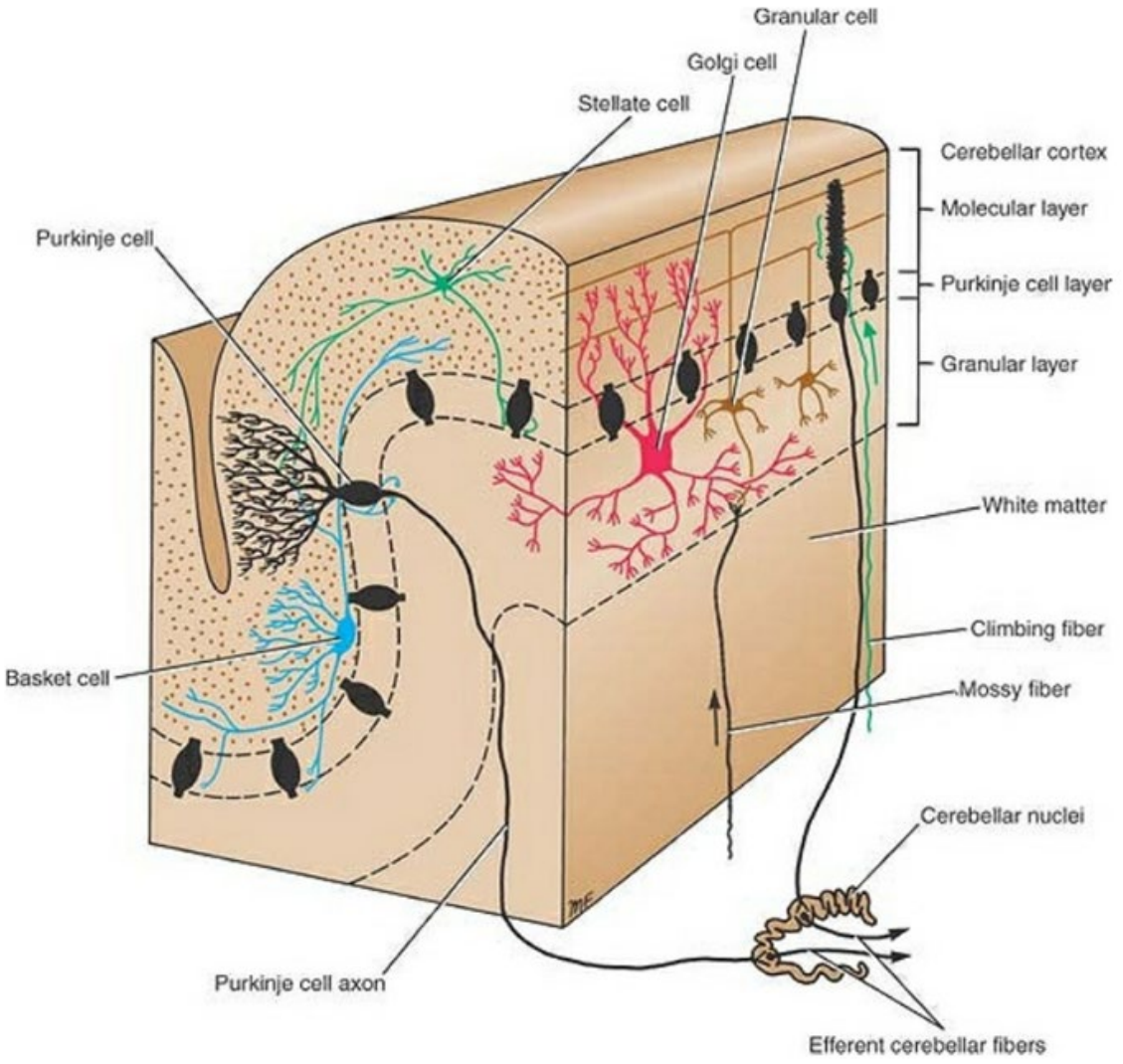
Normal Cerebellum

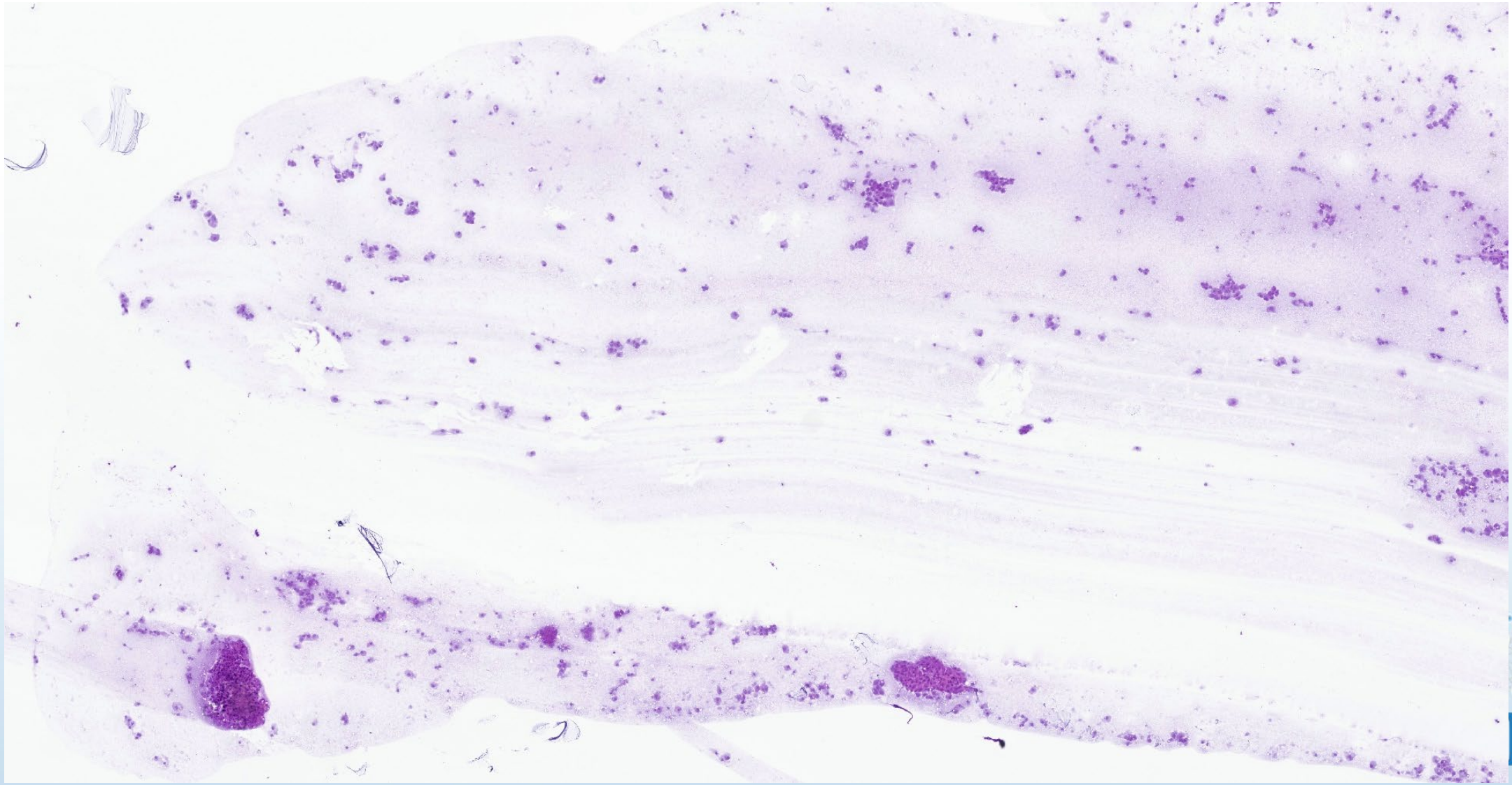


Normal Cerebellum



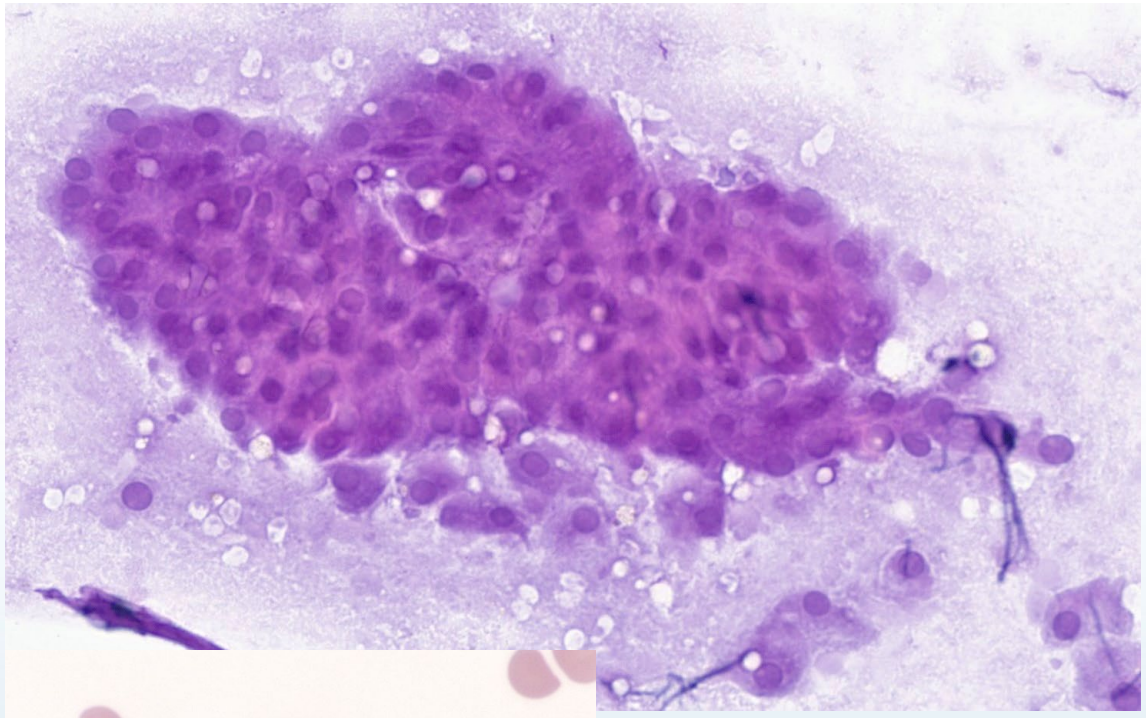


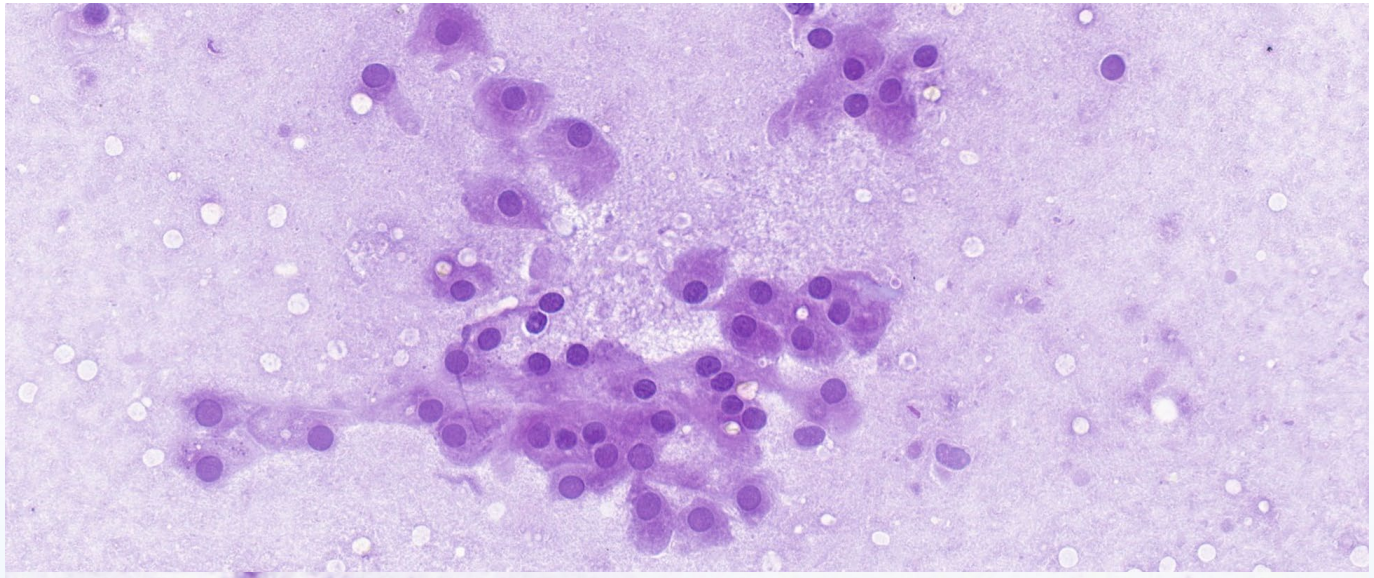
Normal Choroid Plexus

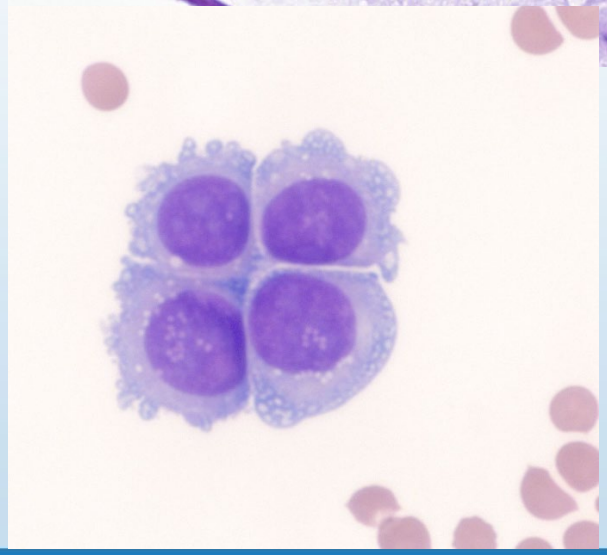


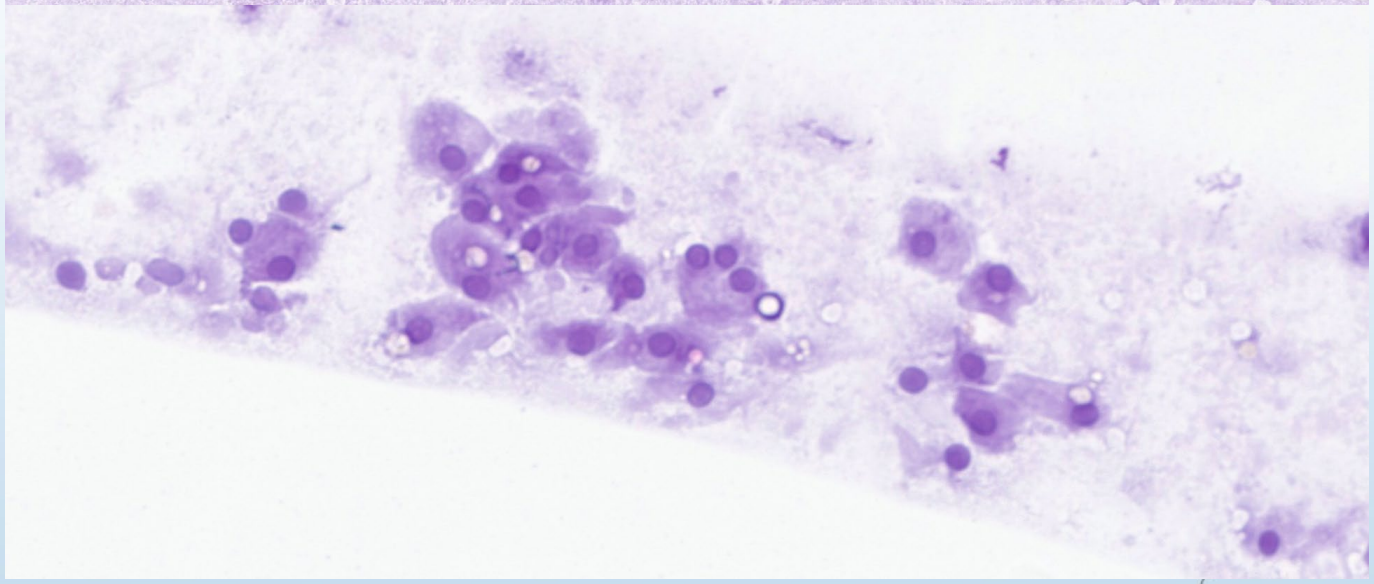
NB

Normal Choroid Plexus



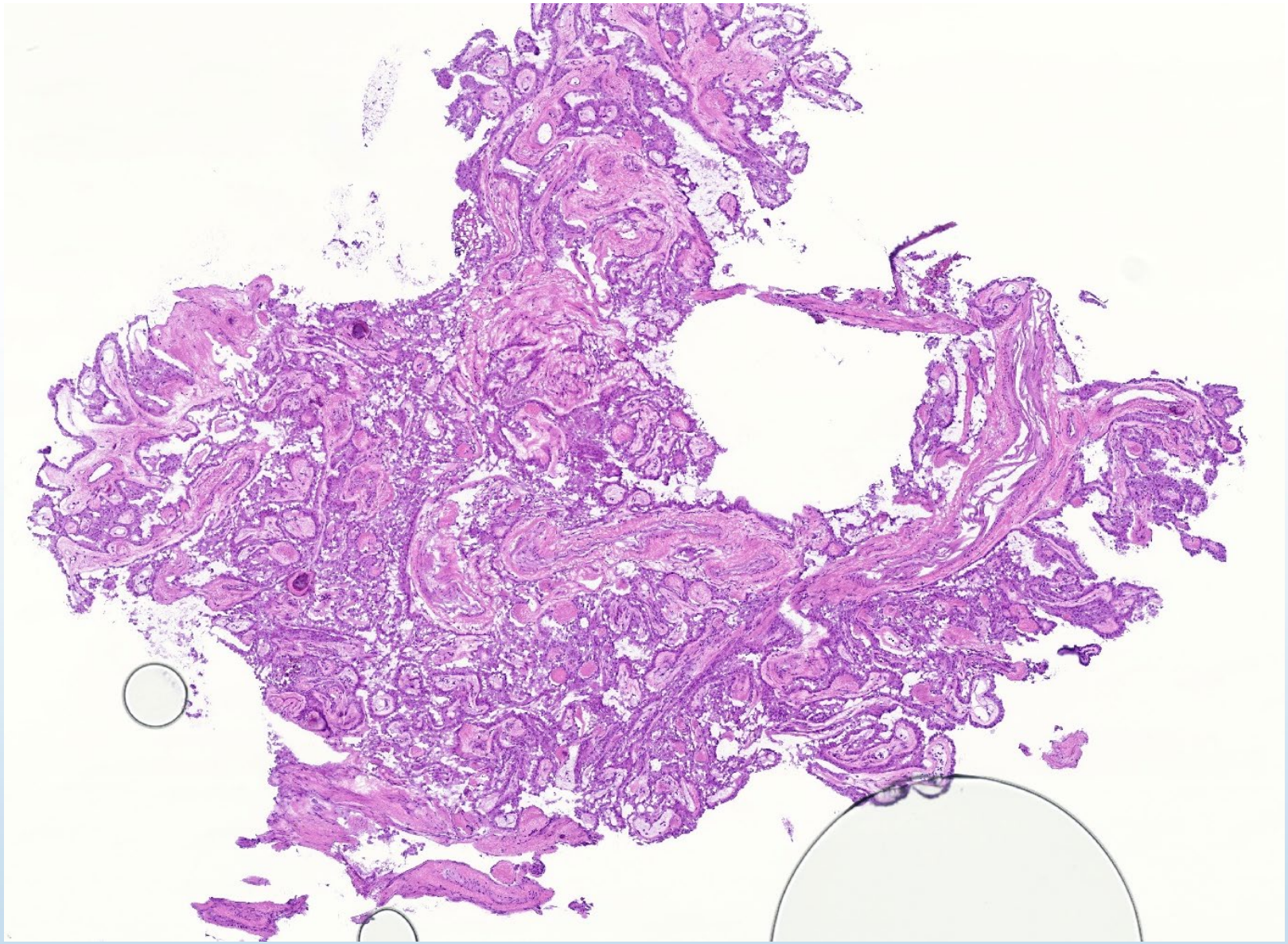


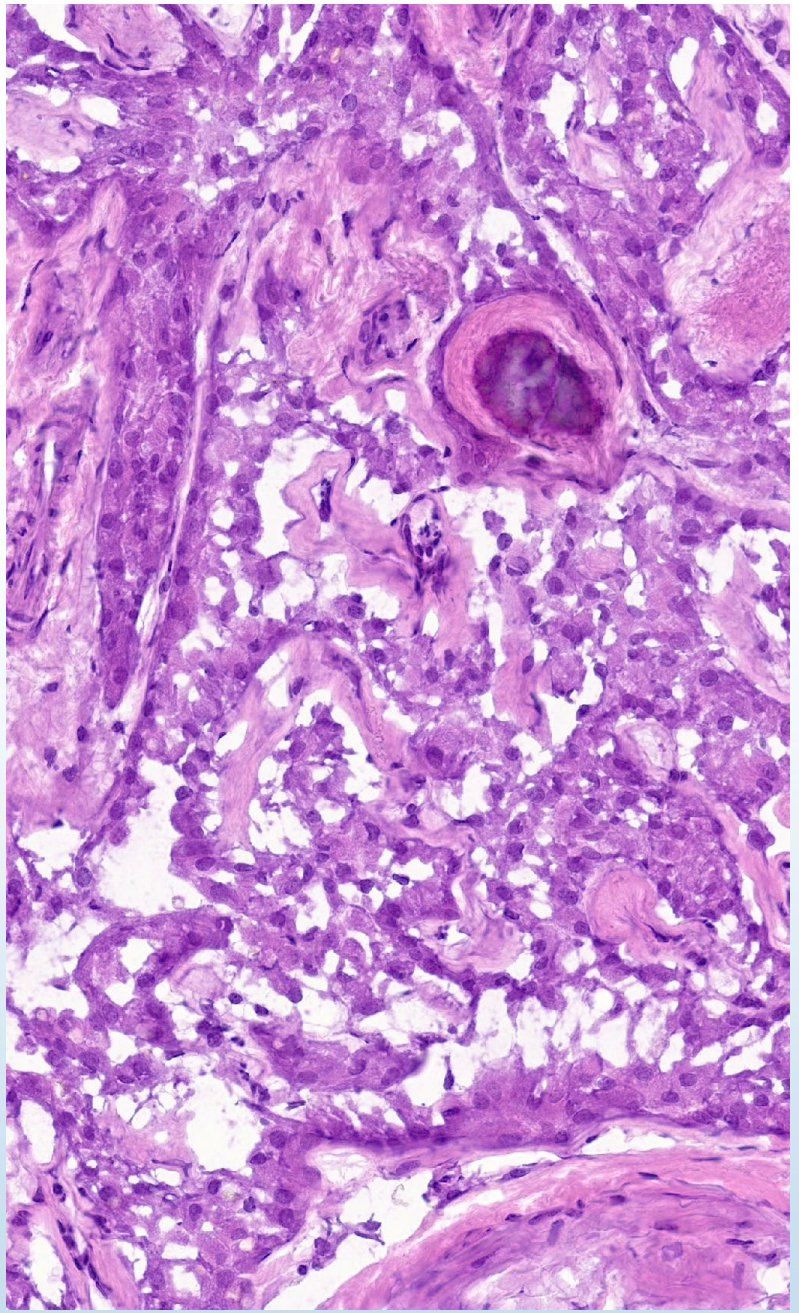




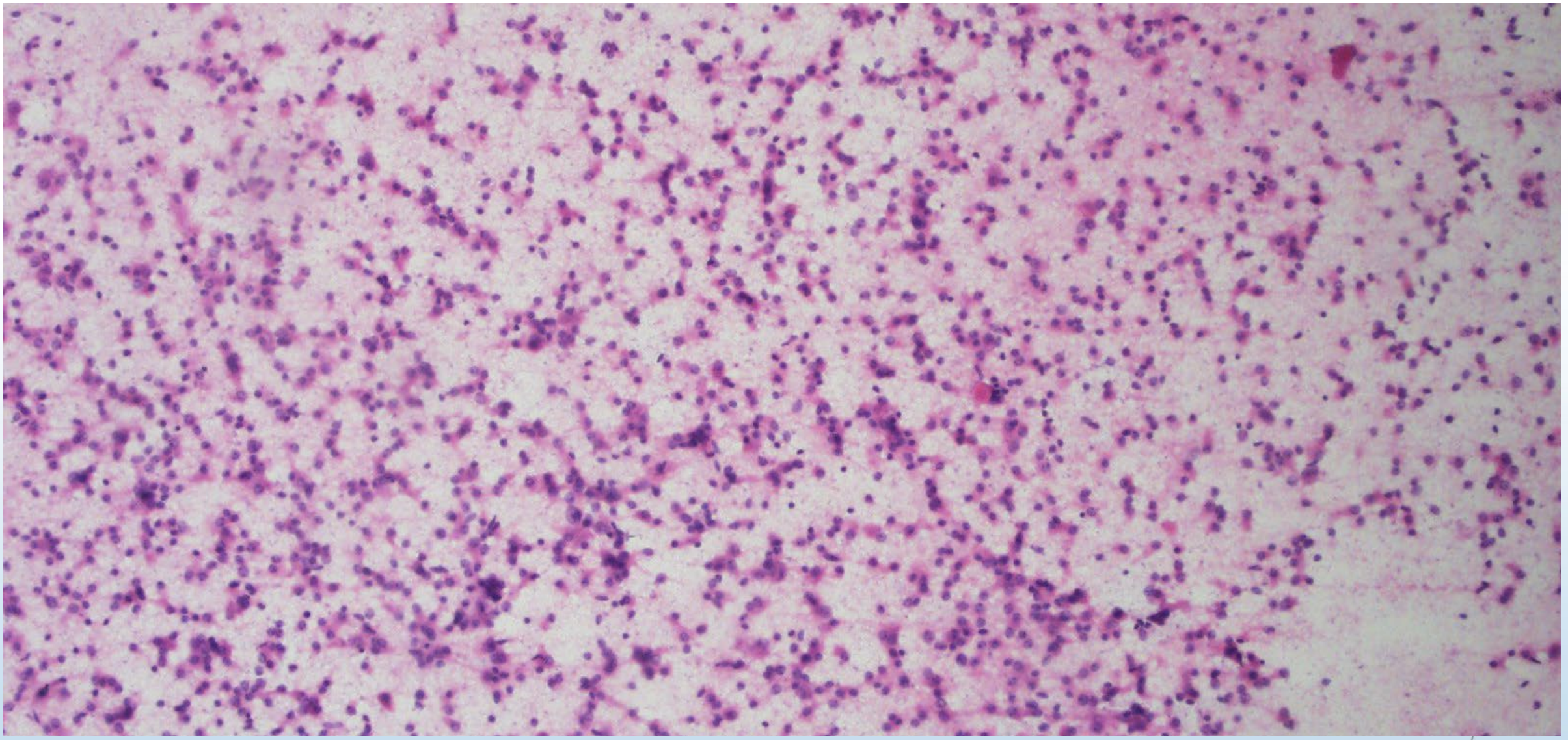
Normal Cytology
Springer 2022
Fig. 14.22

Normal Choroid Plexus





Normal Pituitary Gland



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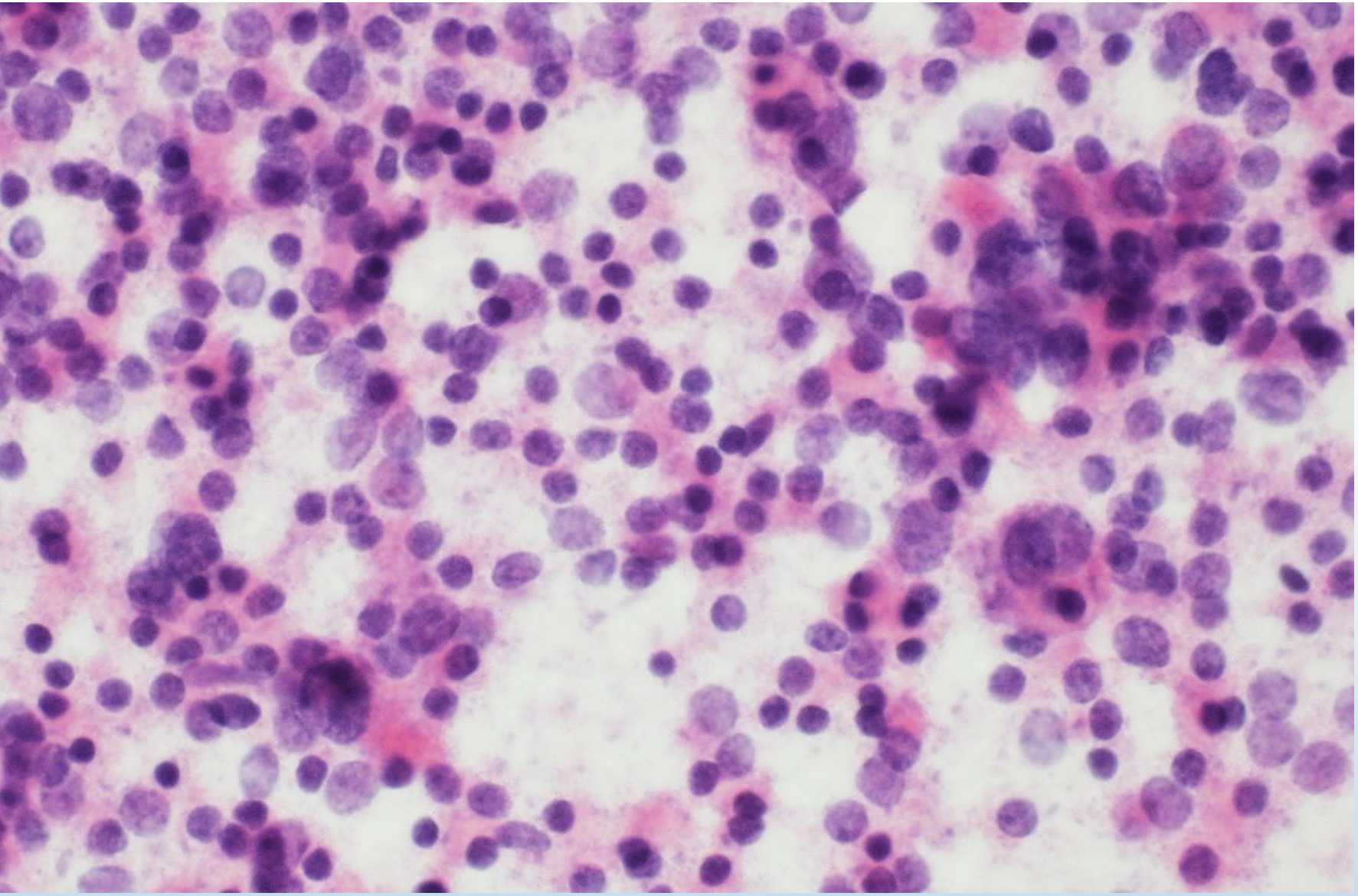
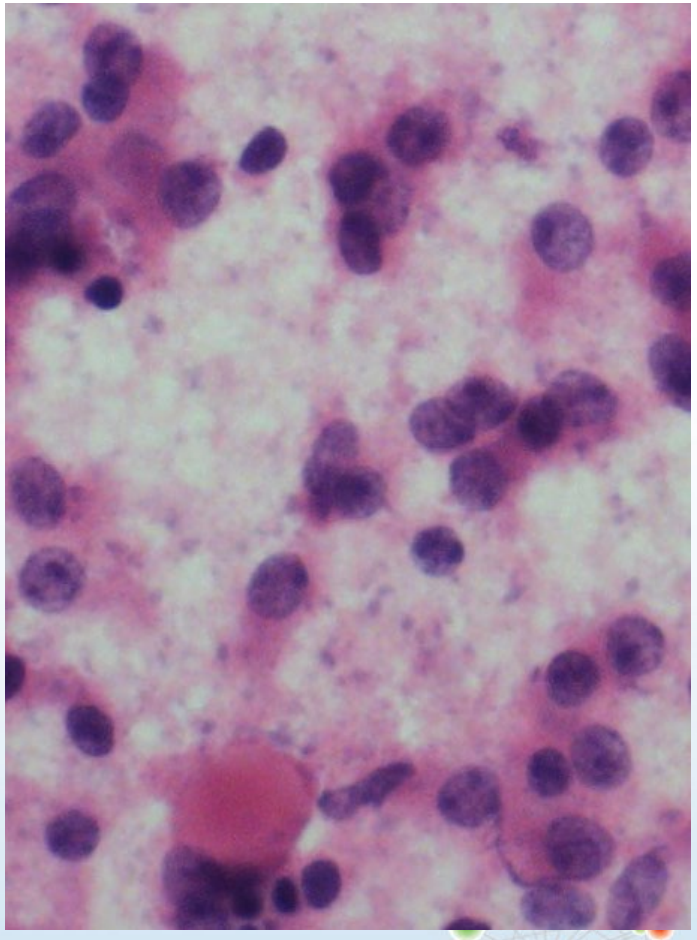
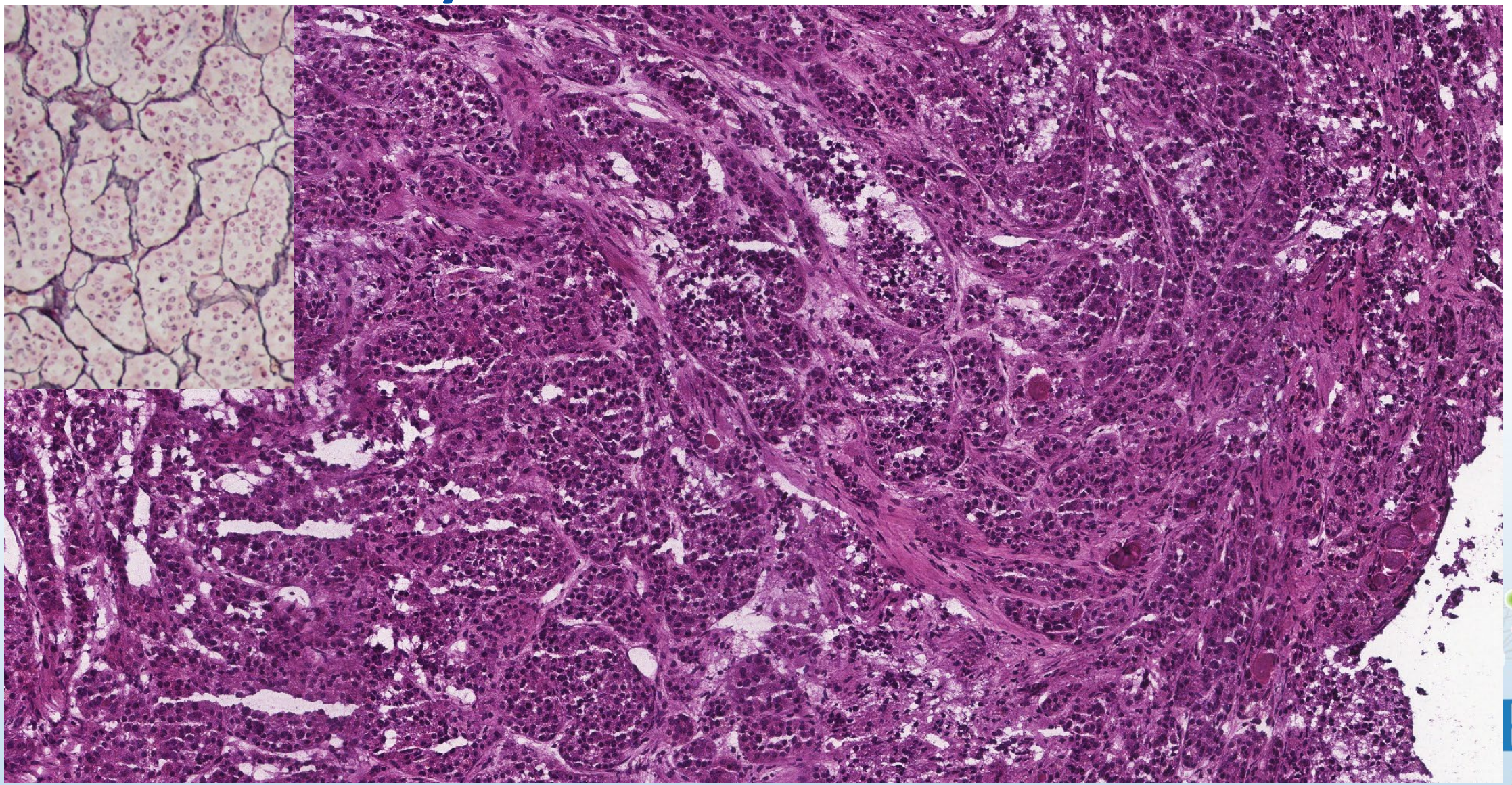
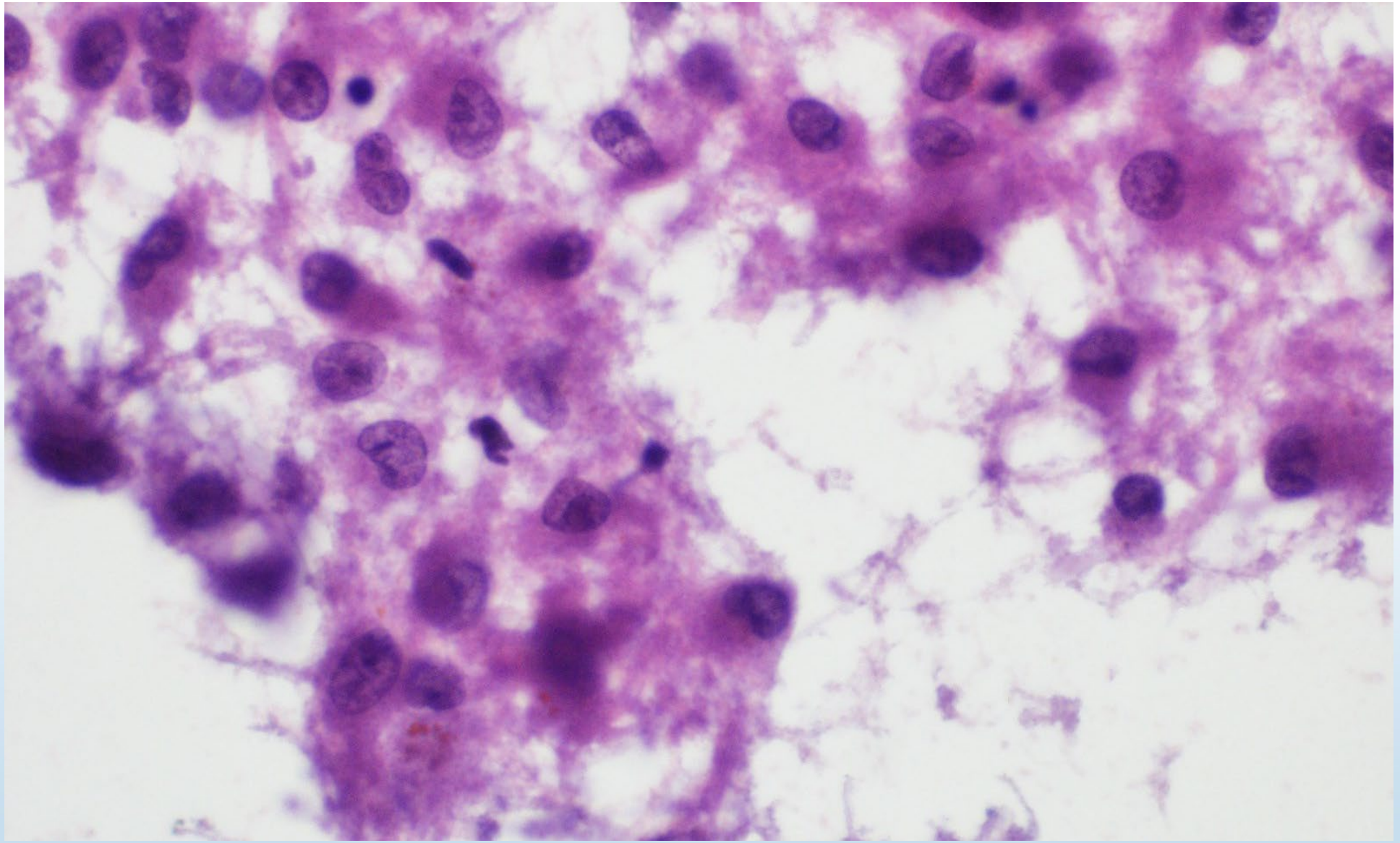




Normal Pituitary Gland

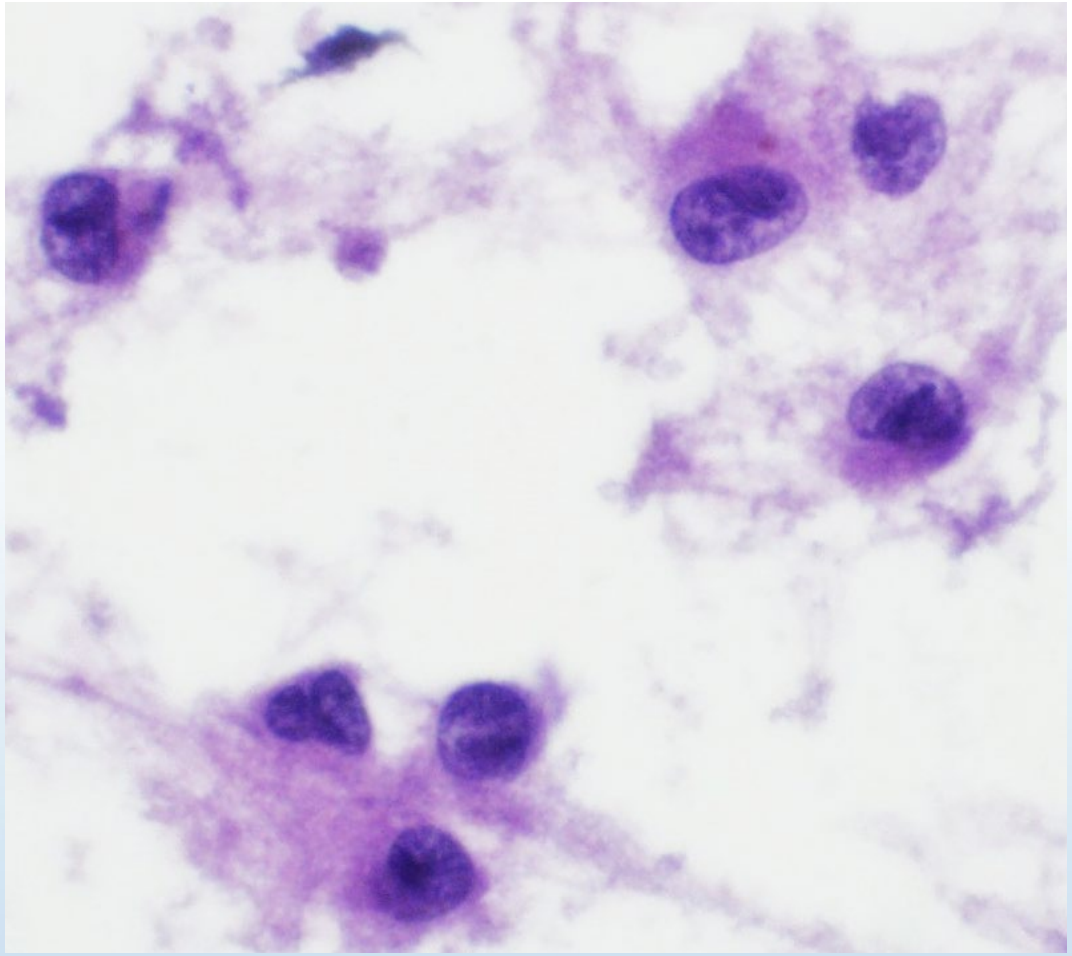


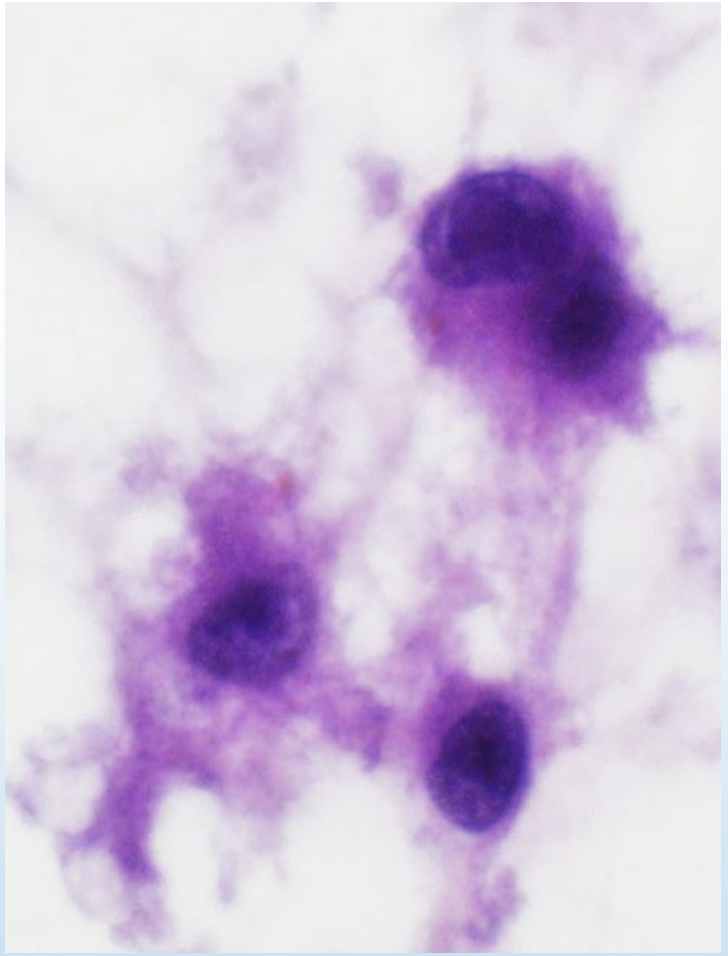
Normal Pineal Gland

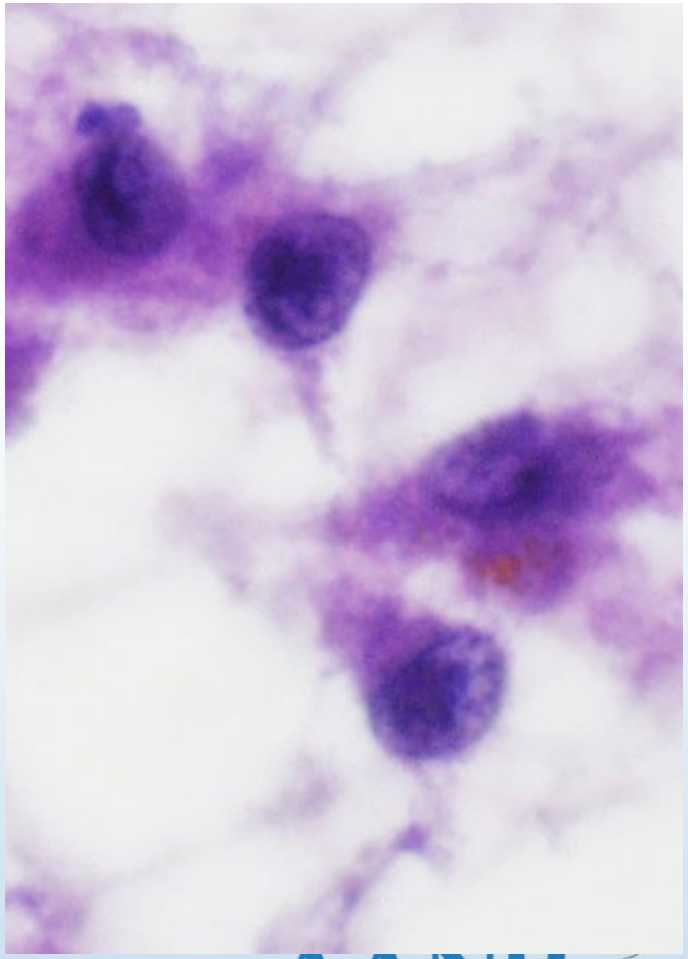


Pigments:
Melanin
Melatonin

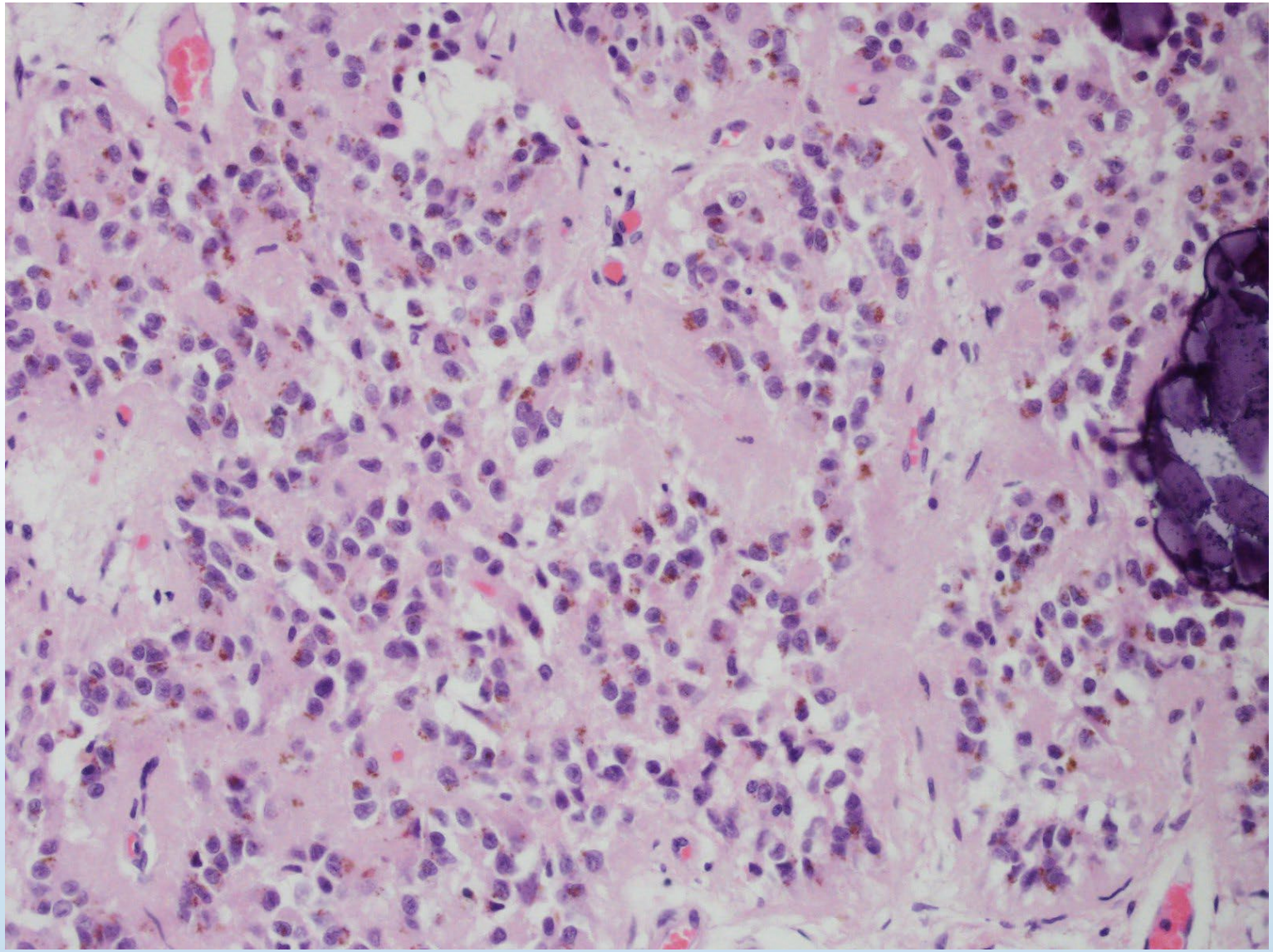
Normal Pineal Gland

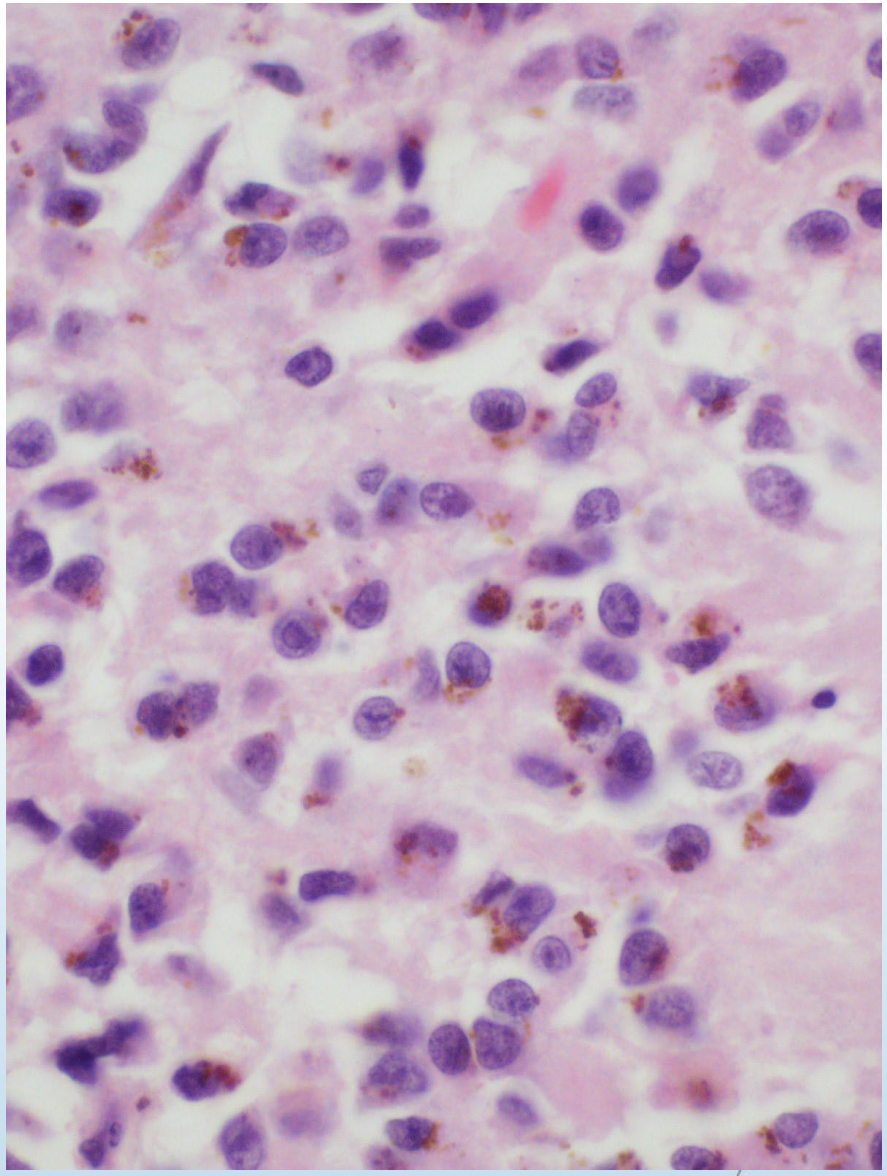




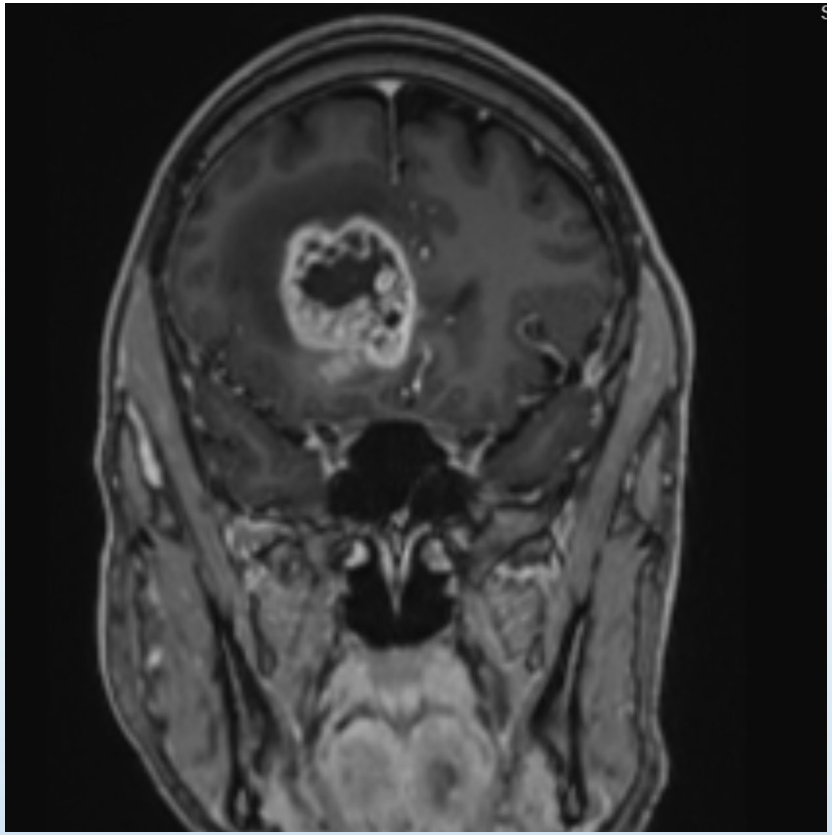


Normal Pineal Gland





DDX by Radiologic Features: Rim Enhancing lesions



- Glioblastoma/HGG
- Lymphoma *
- Metastasis
- Demyelination *
- Infectious (Toxo, bacterial, fungal, abscess) #

* NOT a surgical lesion
# May need to send tissue for culture from the OR

65-year-old patient with imbalance forgetfulness and behavioral changes

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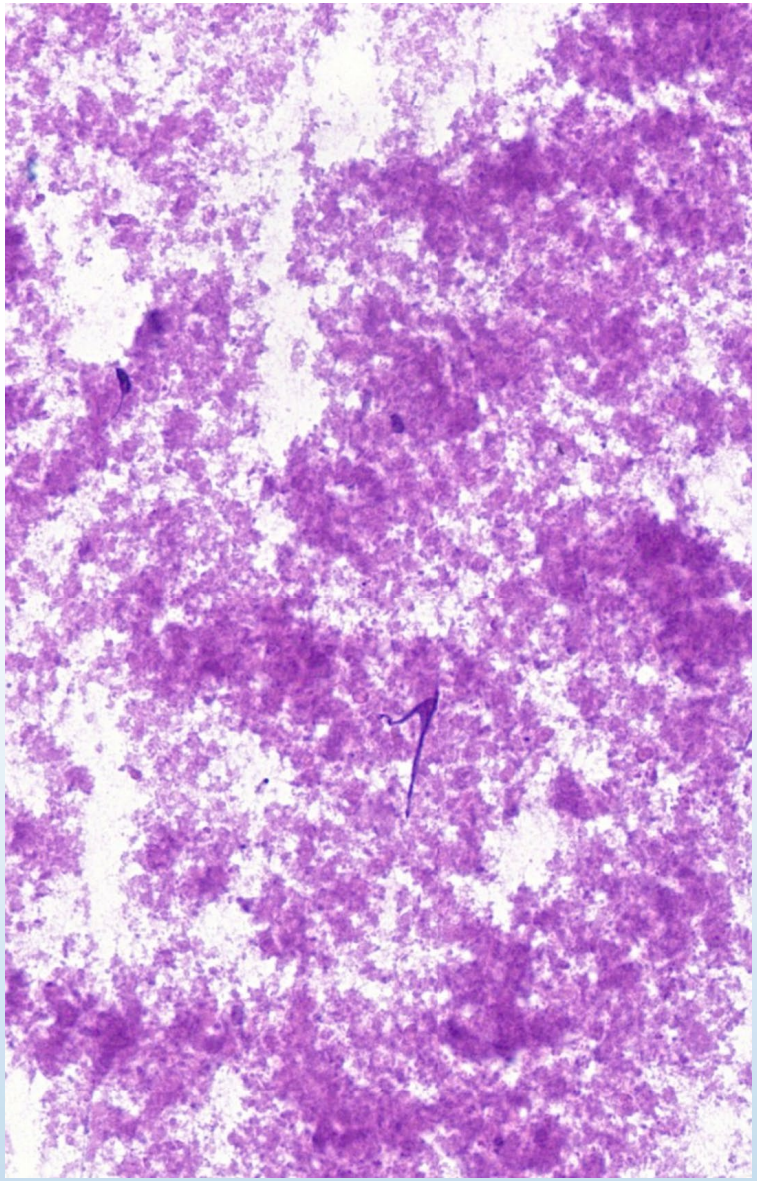
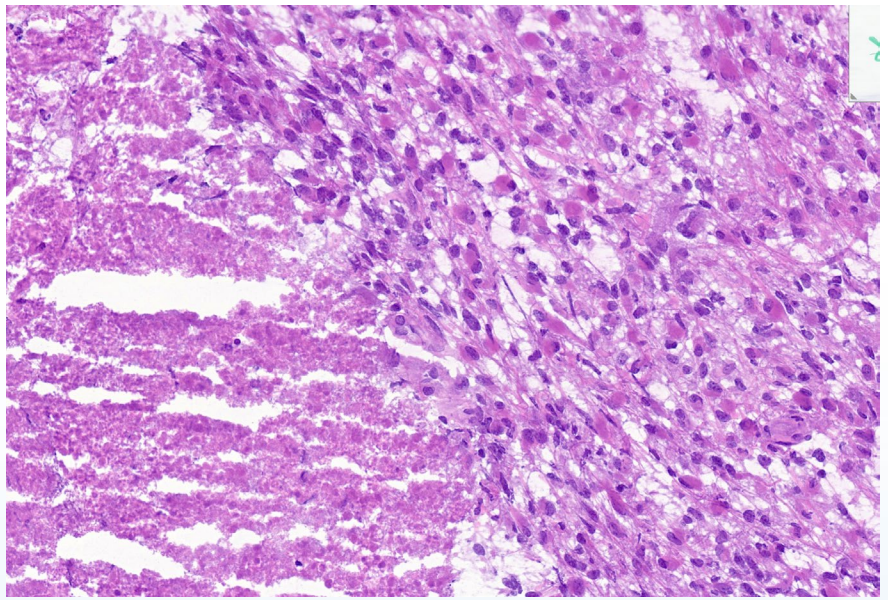
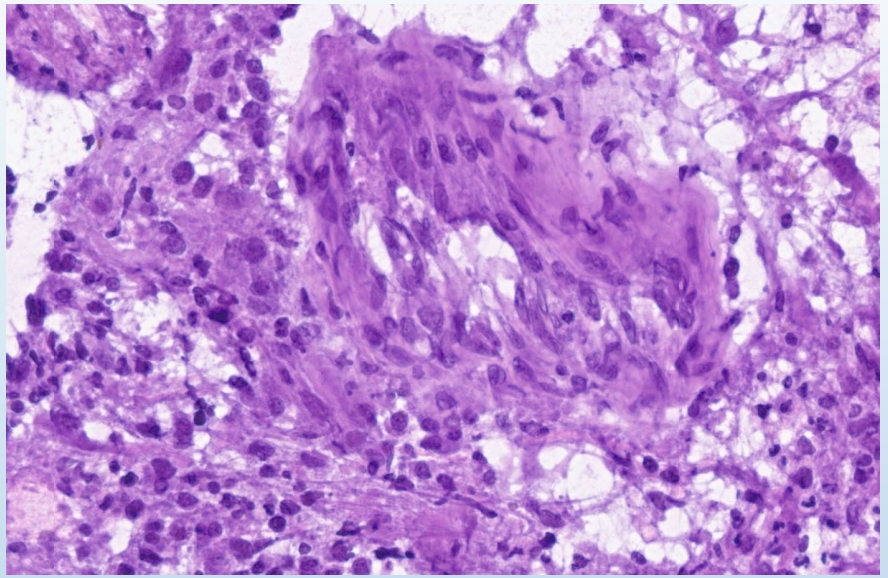
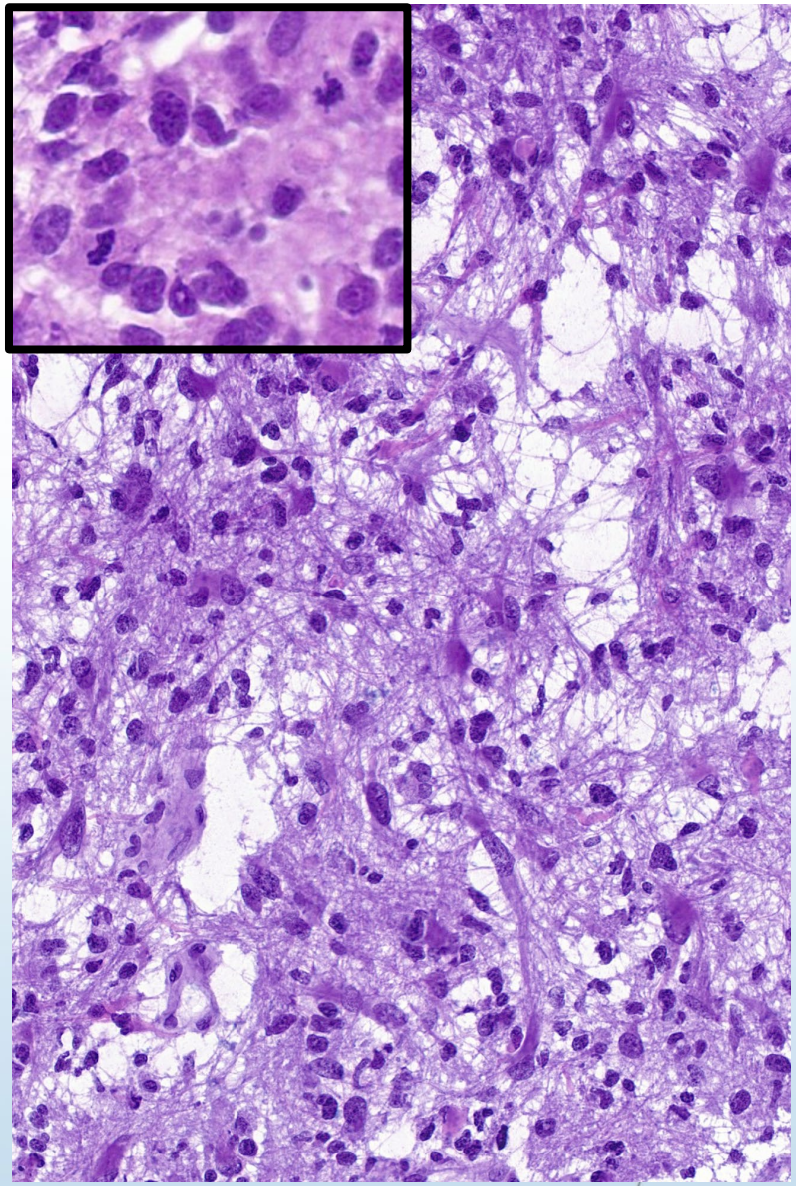
High Grade Glioma

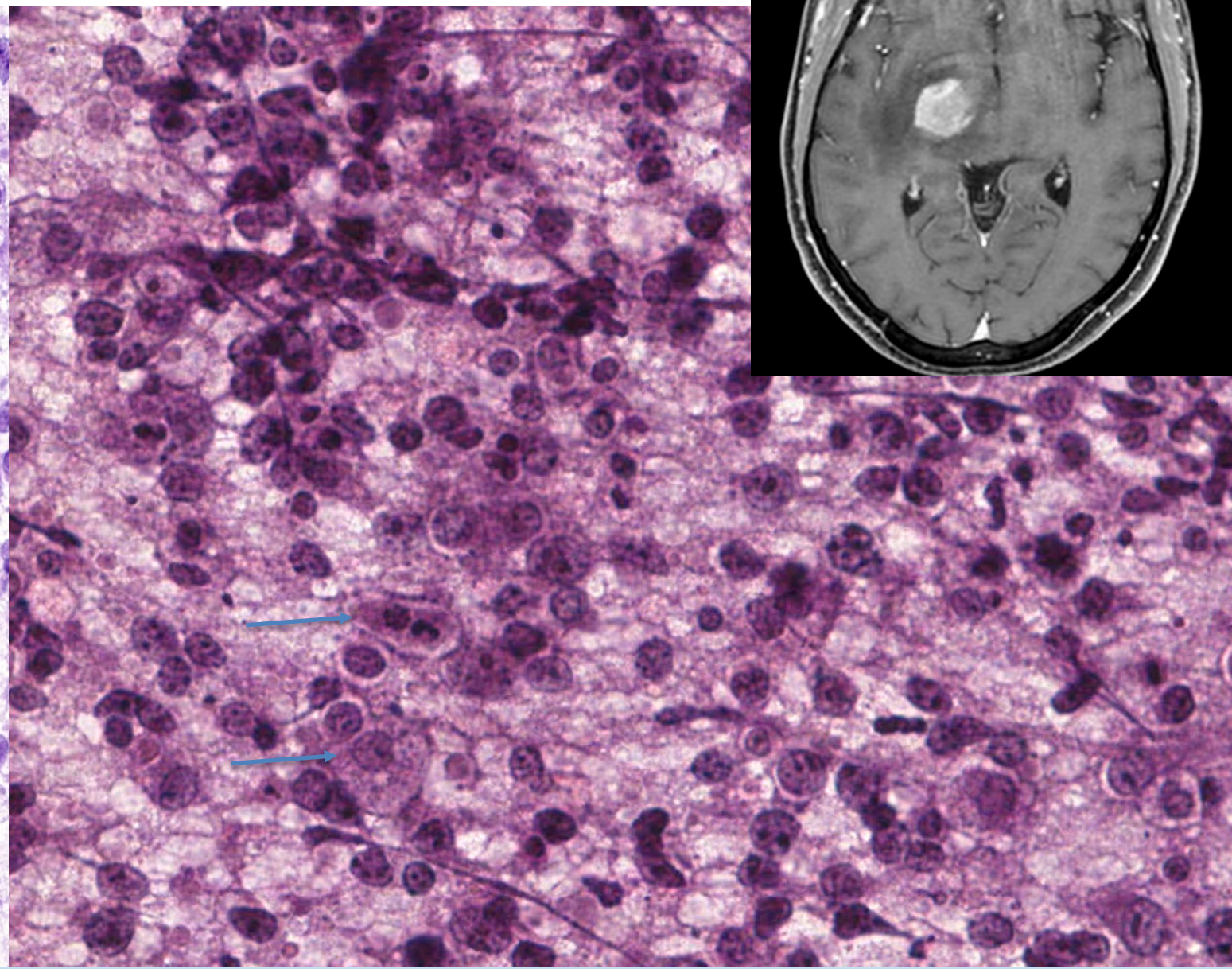




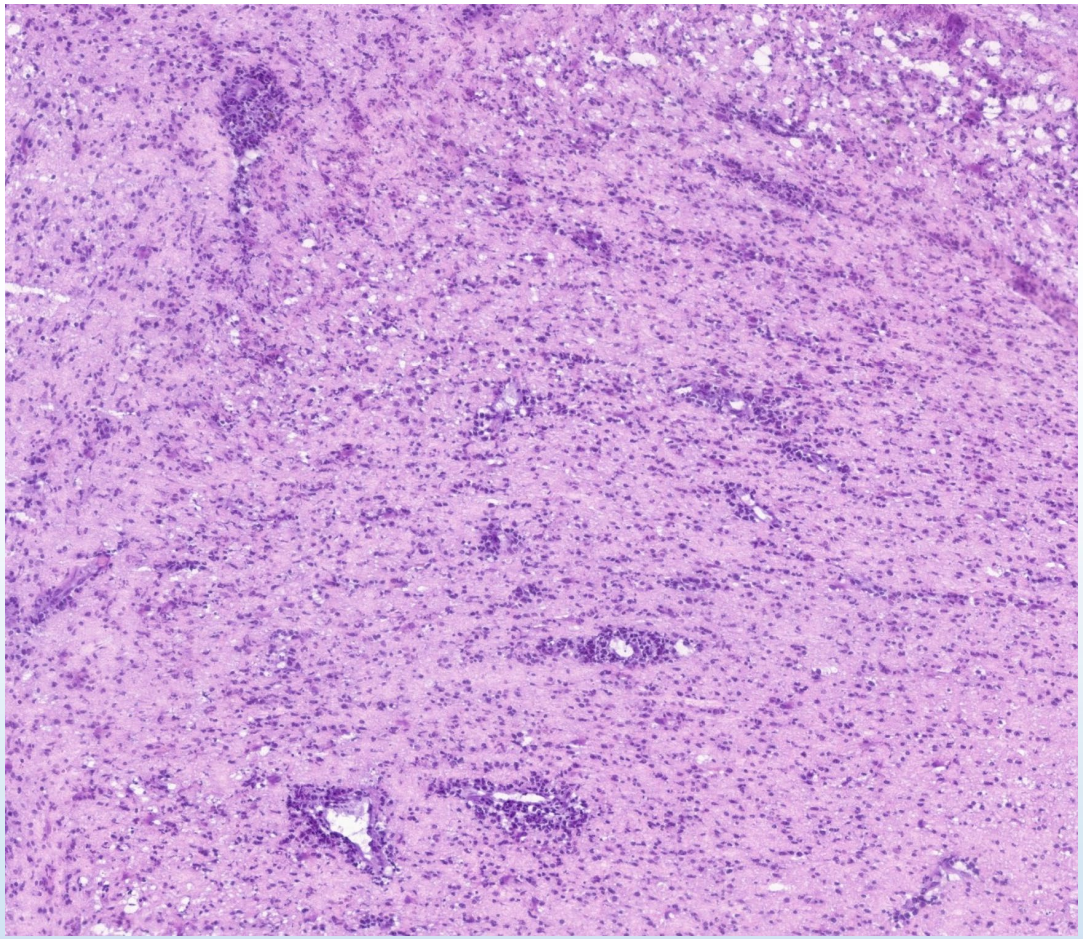


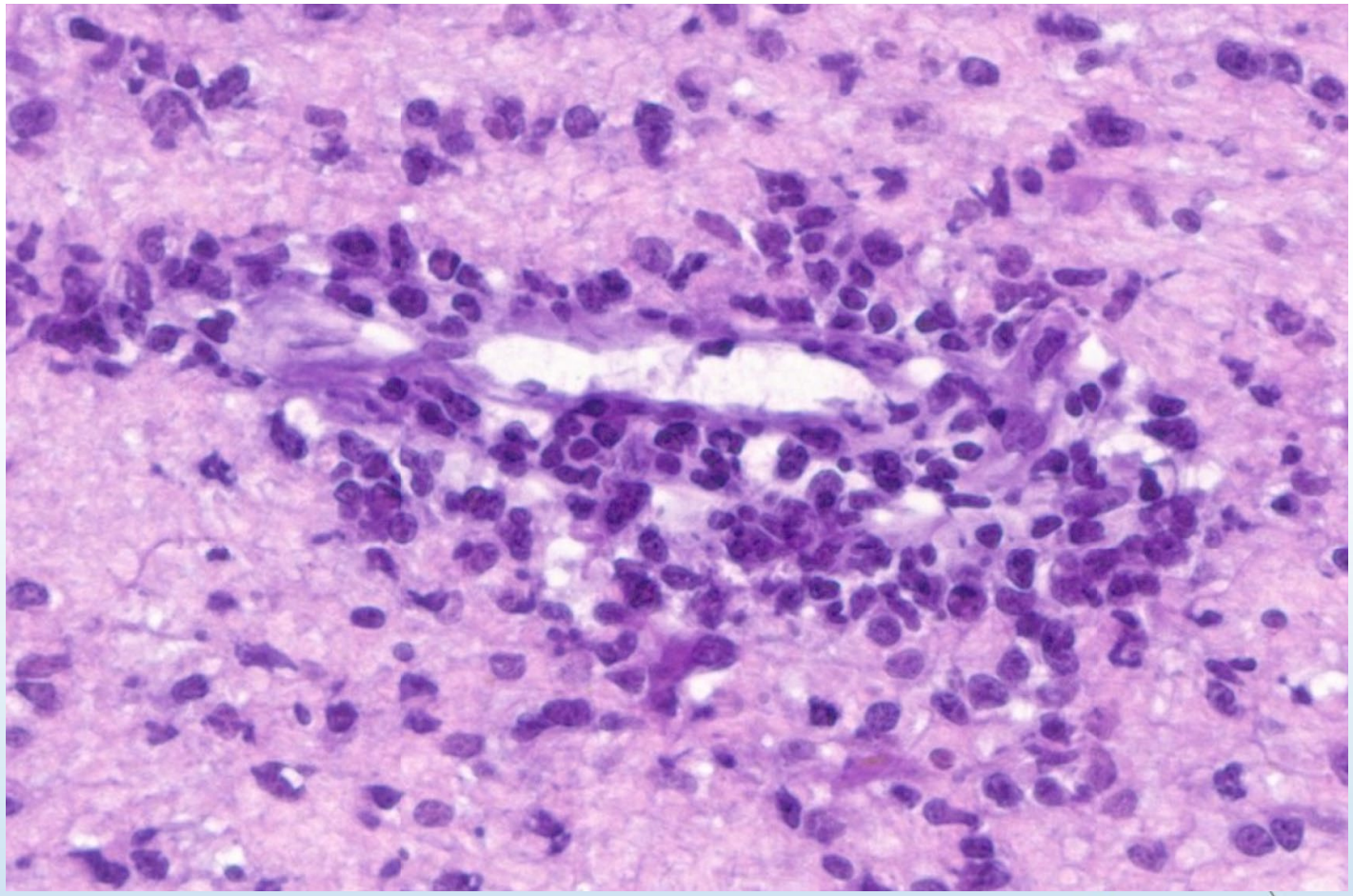


Lymphoma

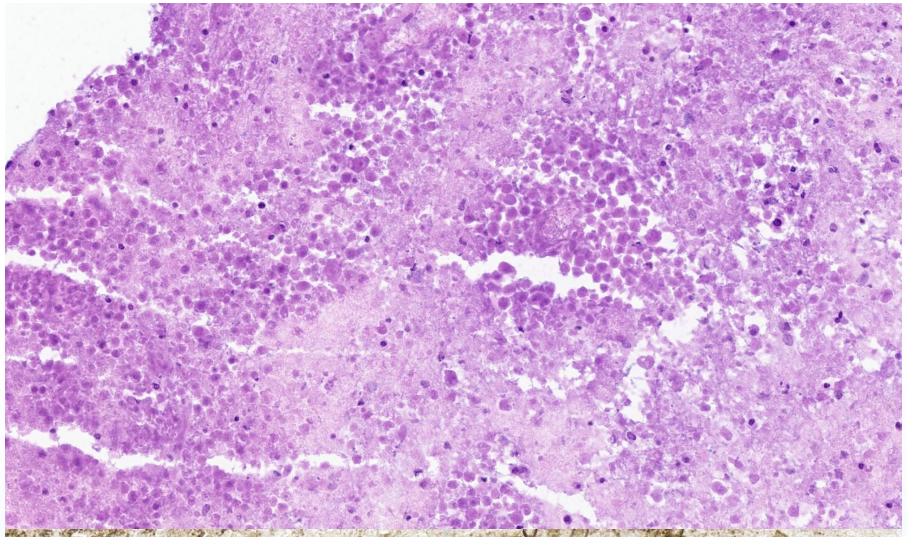


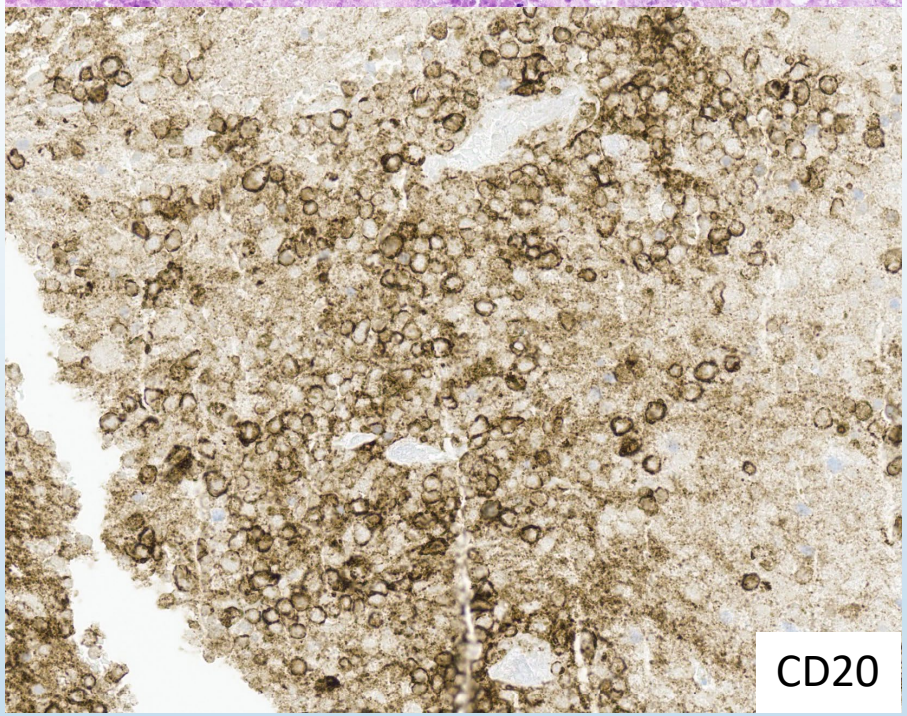
Lymphoma

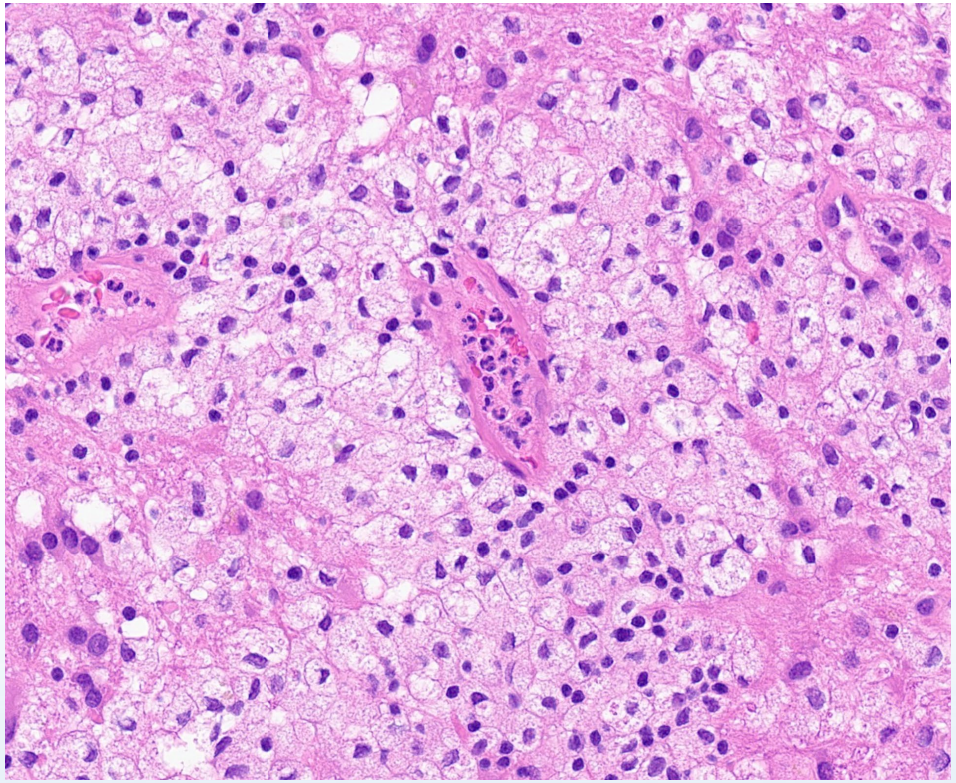


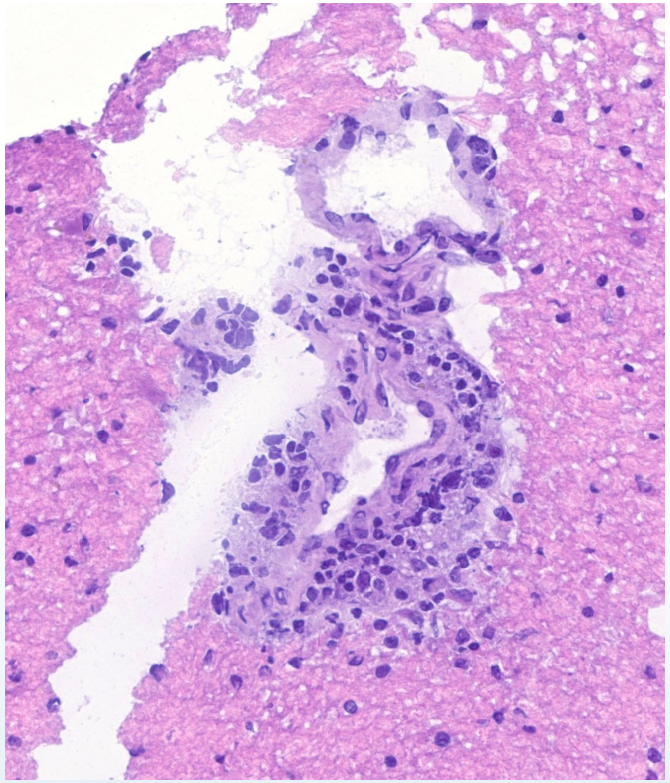


Treated Lymphoma









Positive for MYD88 L265P mutation

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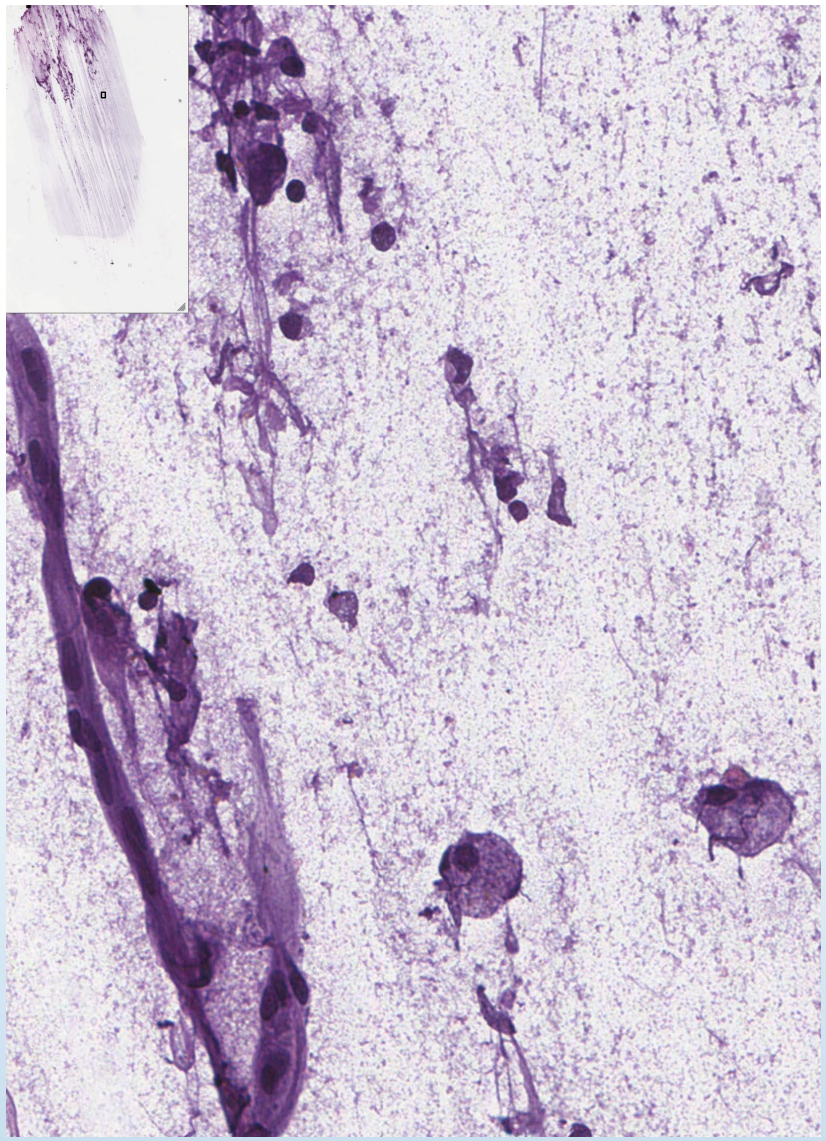
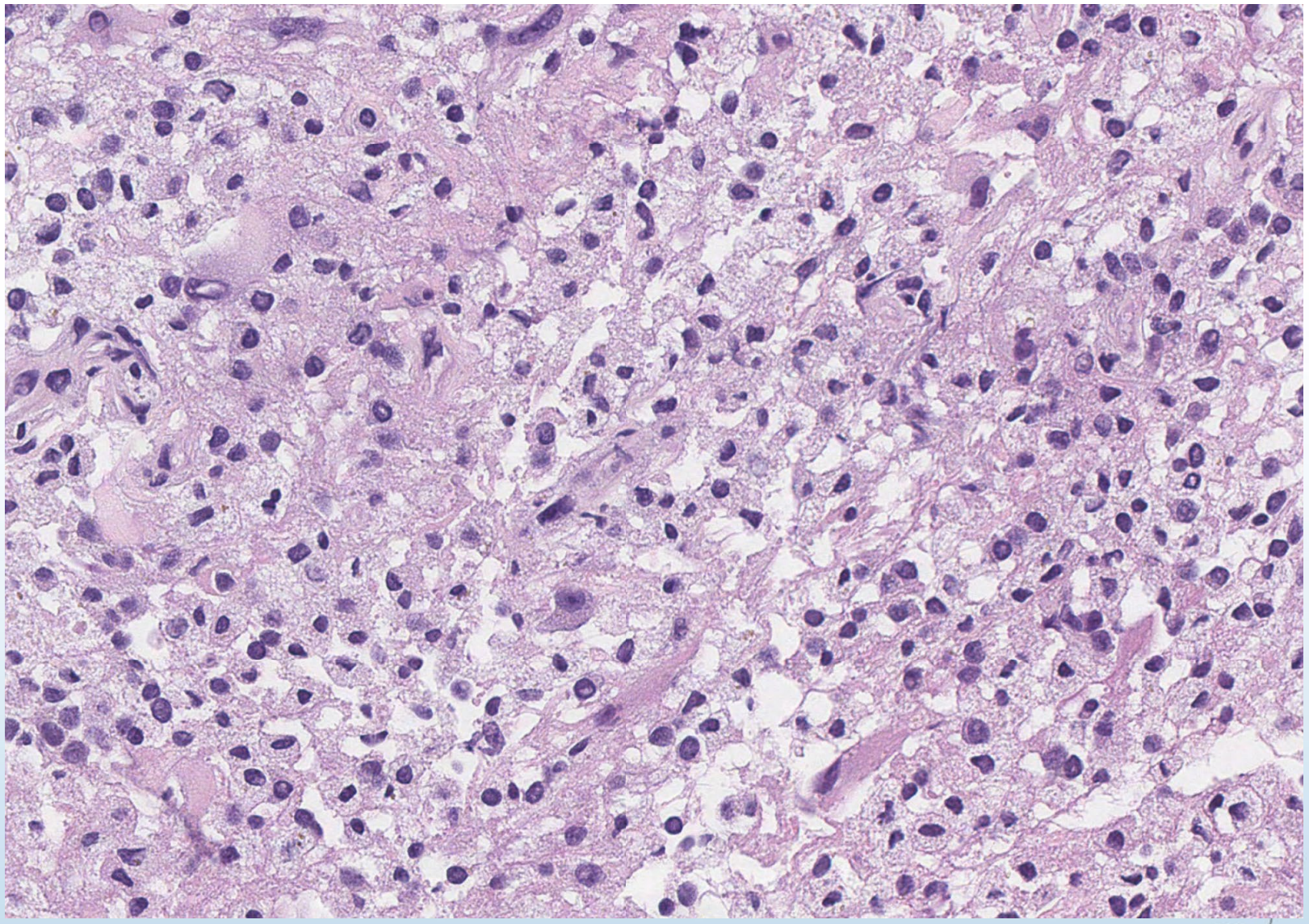
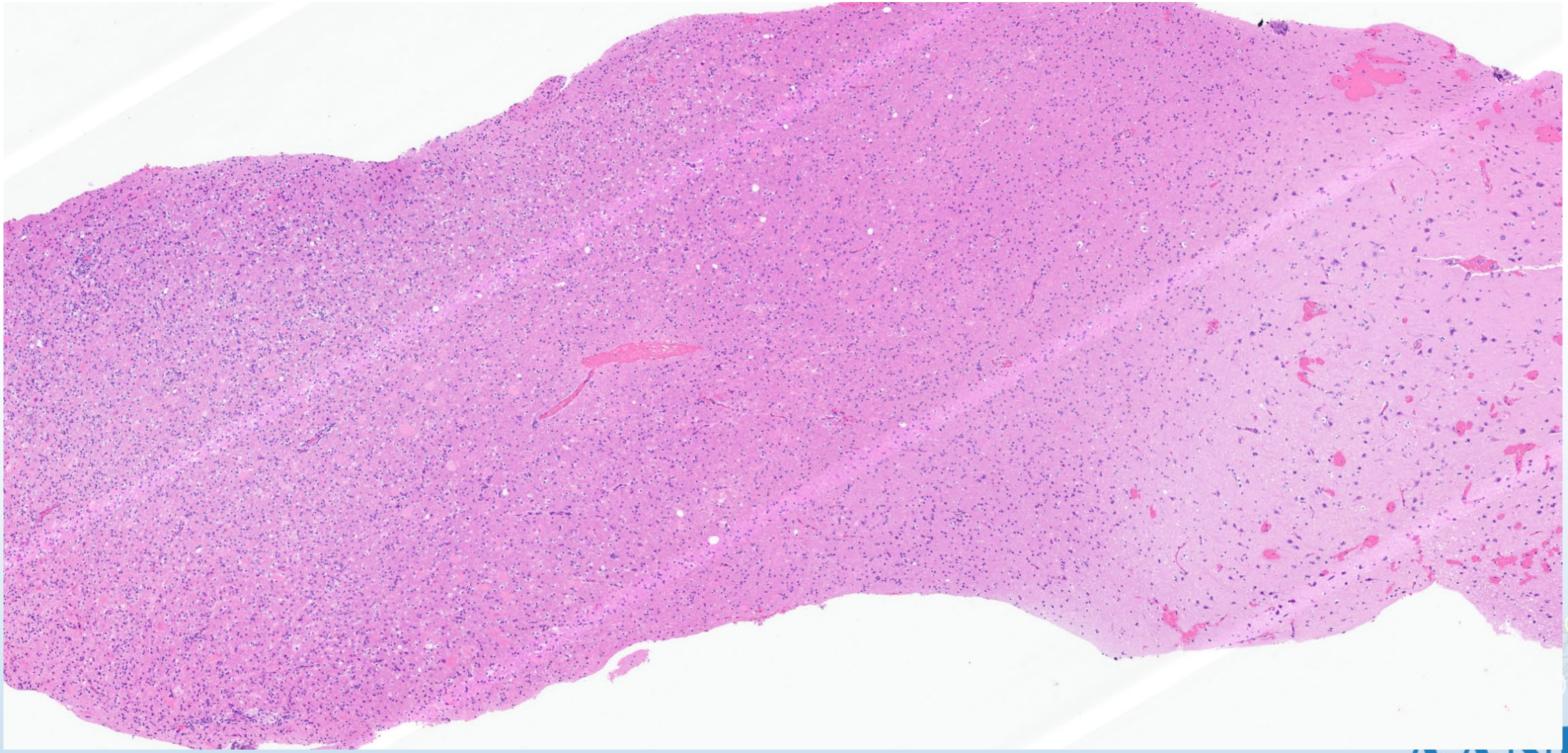
Demyelination

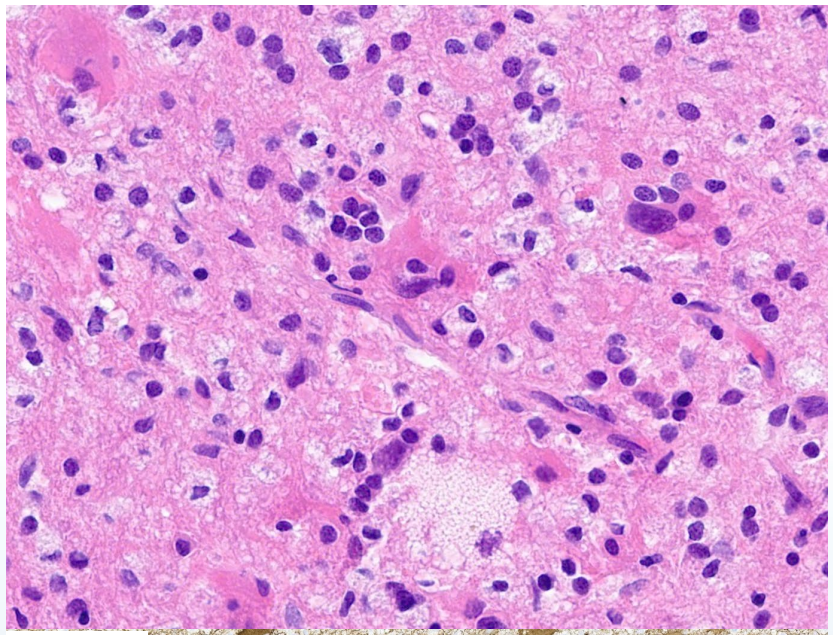


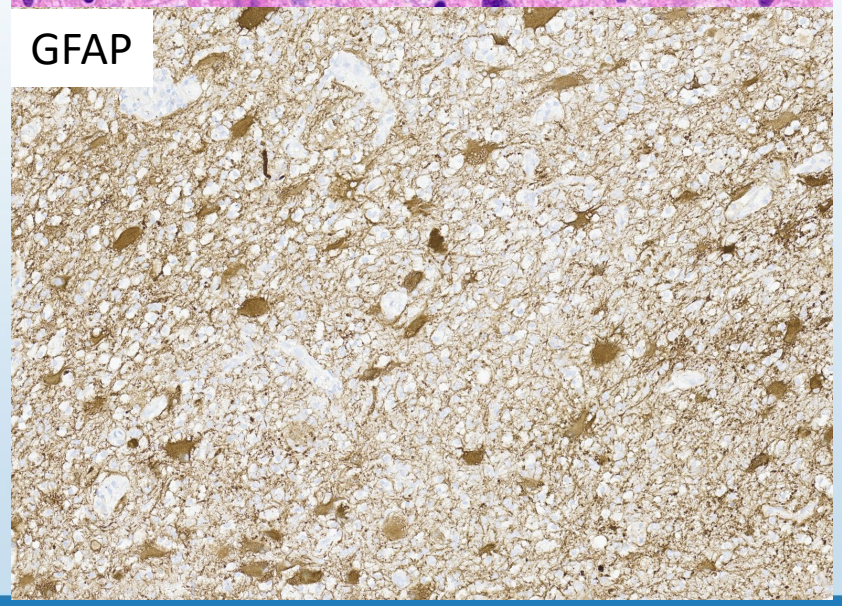


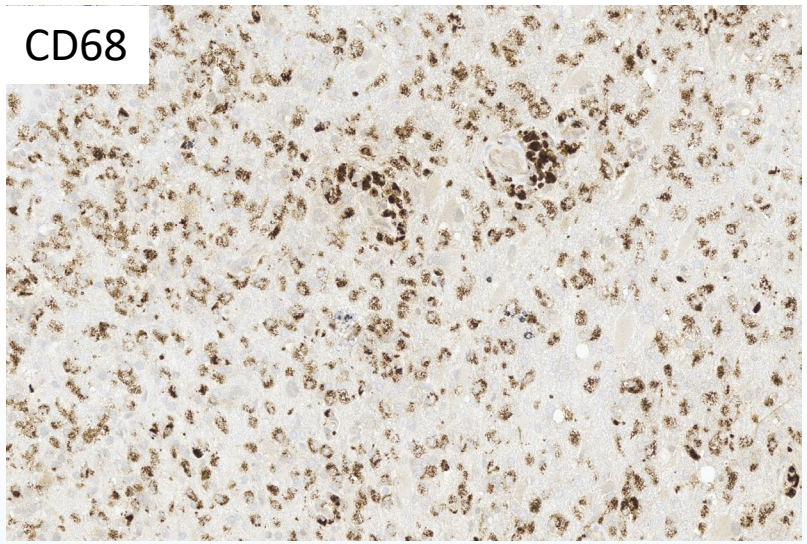
Demyelination

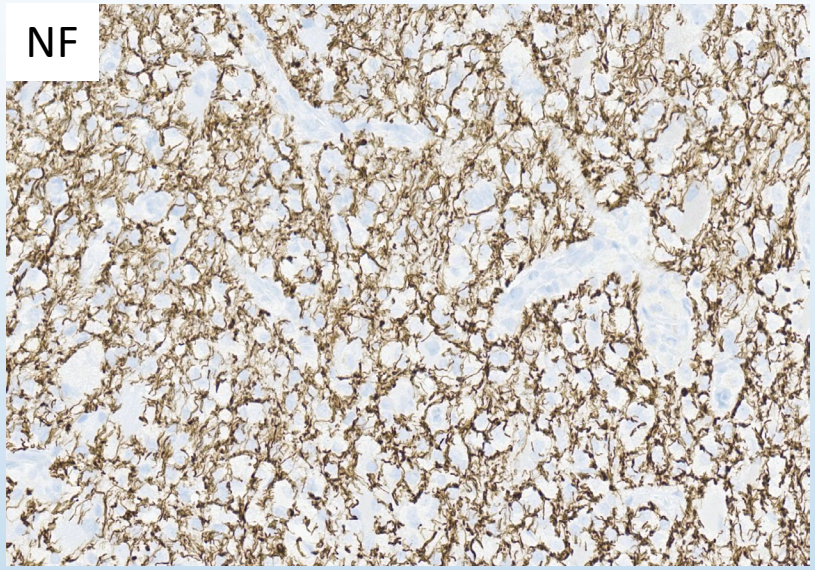


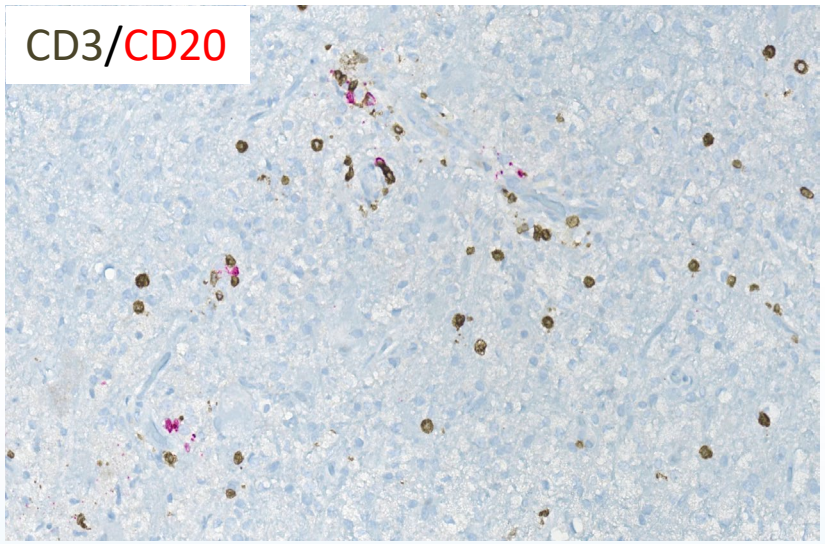
Demyelination

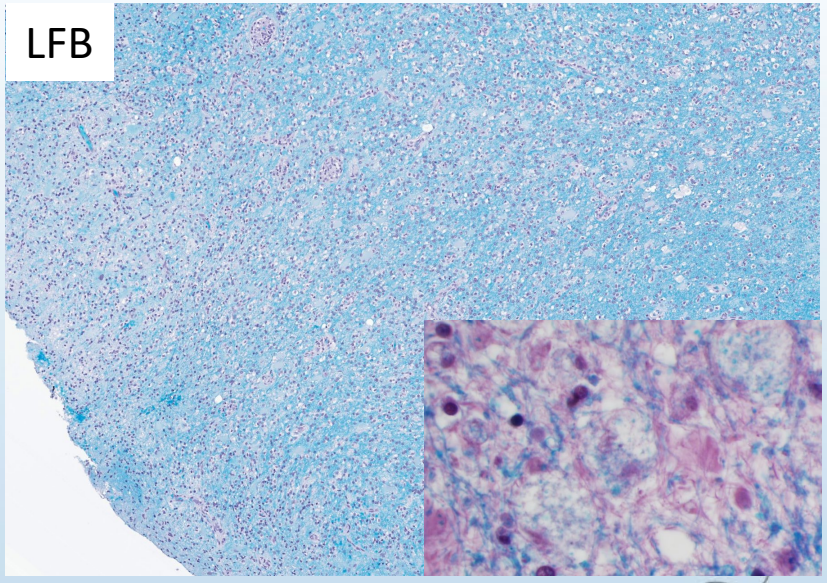




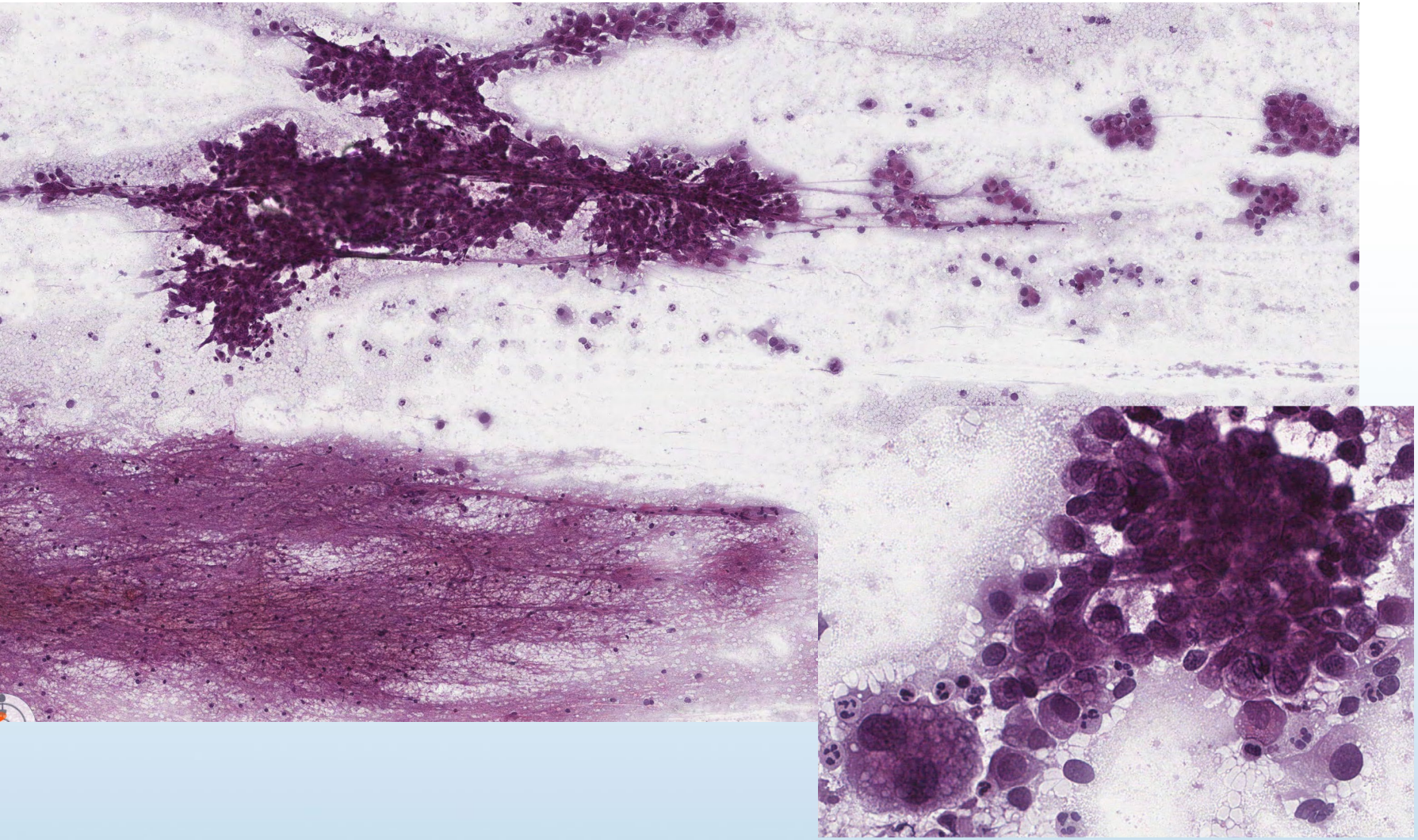


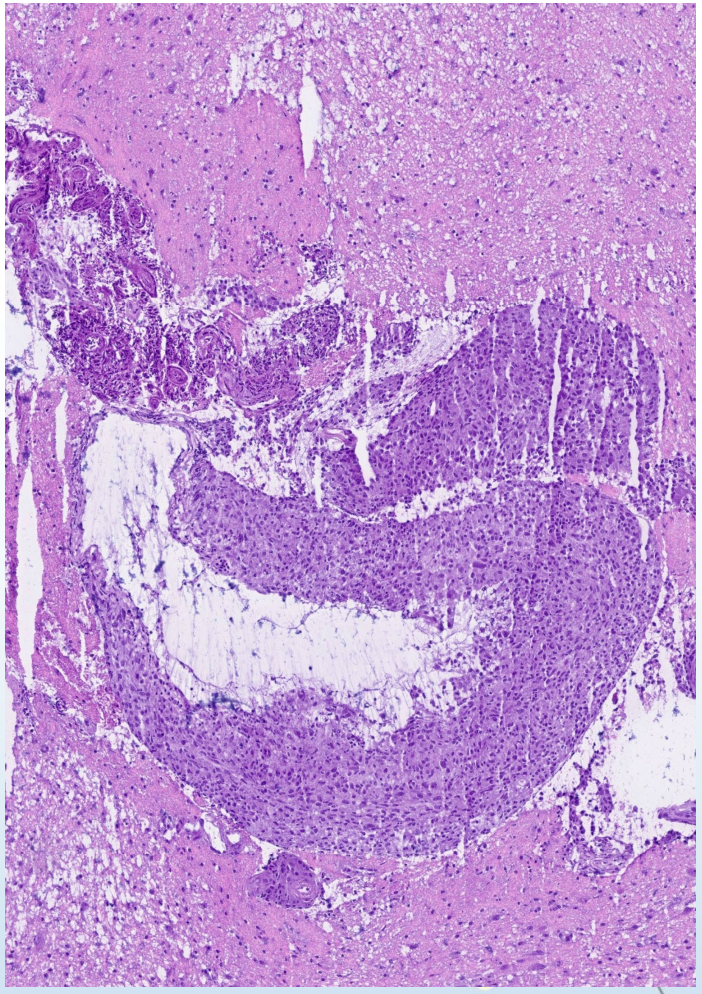






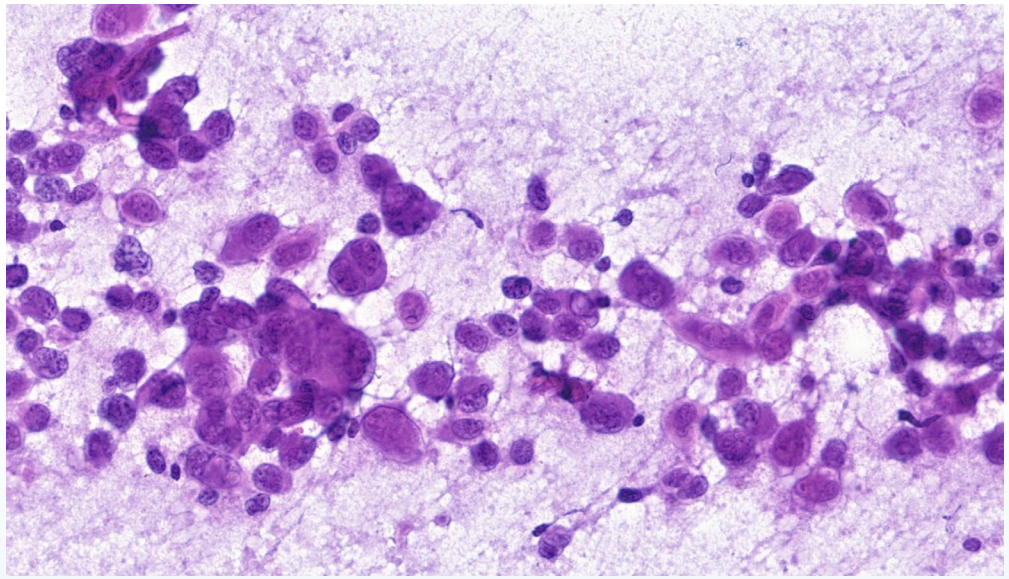
Metastasis (Carcinoma)

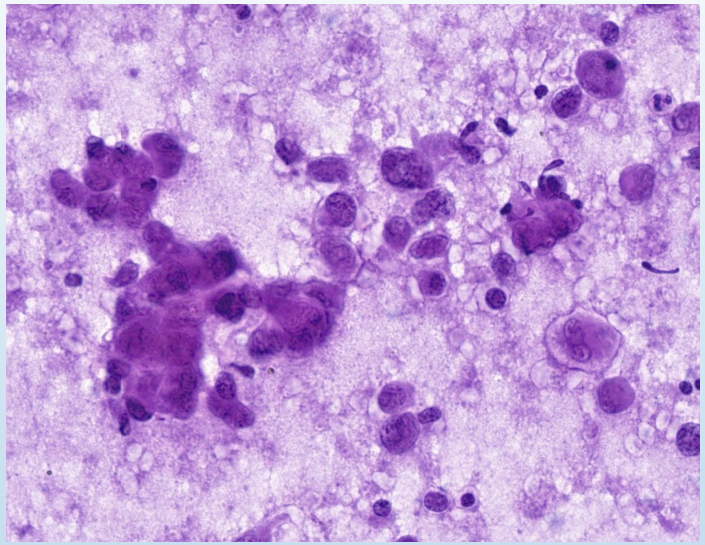


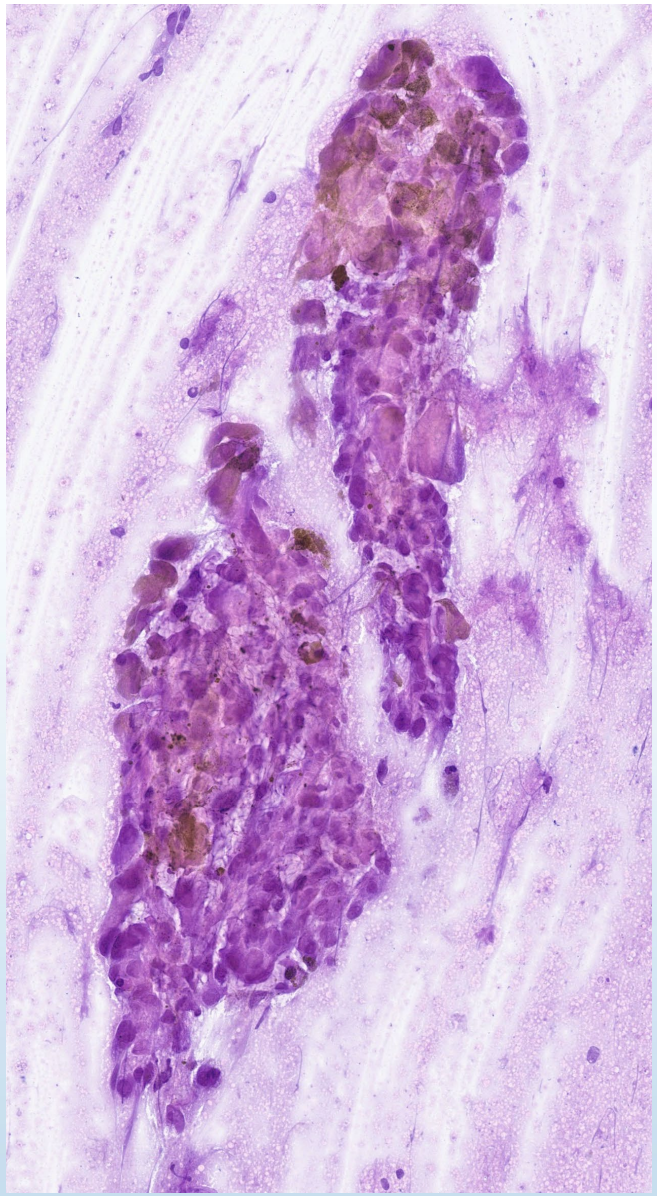


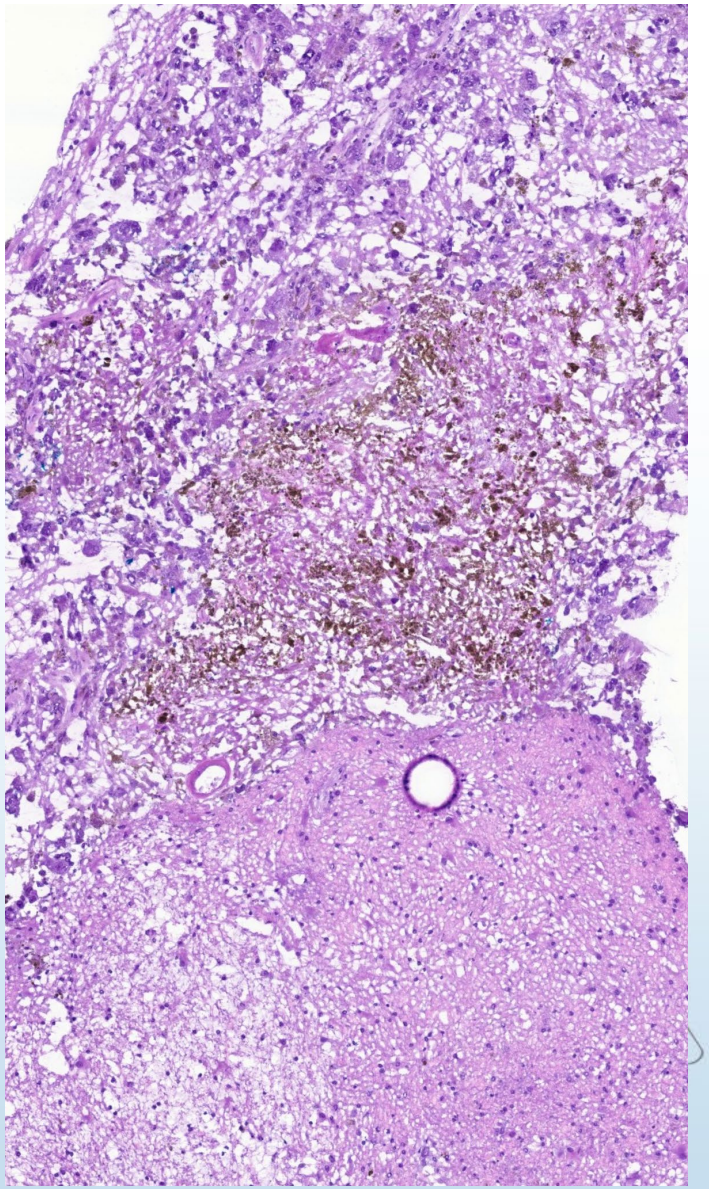
AANP

Metastasis (Melanoma)

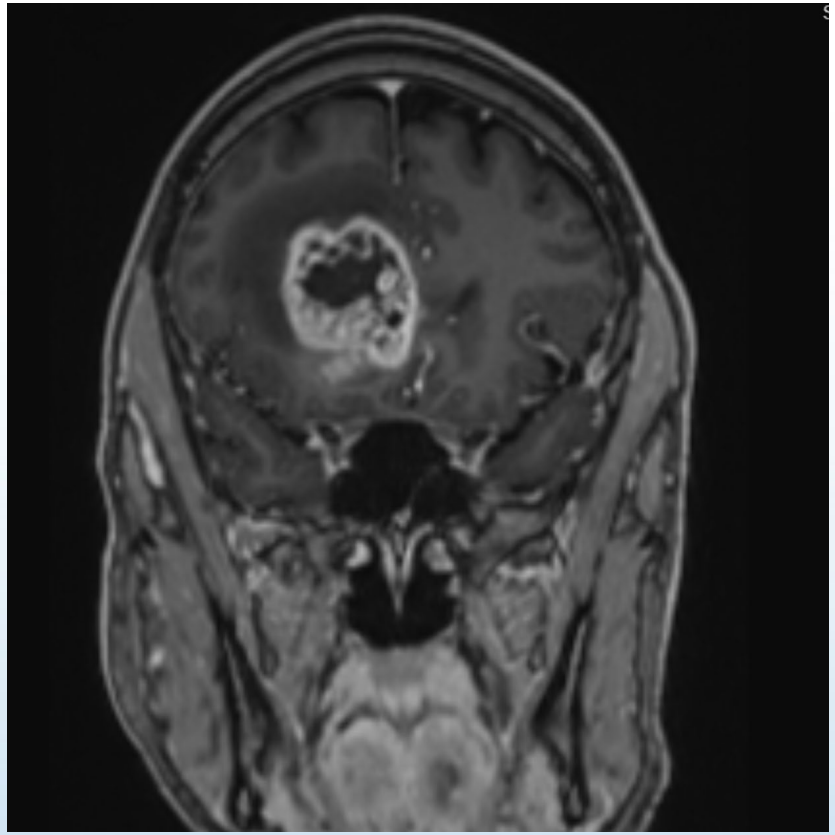








DDX by Radiologic Features: Rim Enhancing lesions



- Glioblastoma/HGG
- Lymphoma *
- Metastasis
- Demyelination *
- Infectious (Toxo, bacterial, fungal, abscess) #

* NOT a surgical lesion
# May need to send tissue for culture from the OR

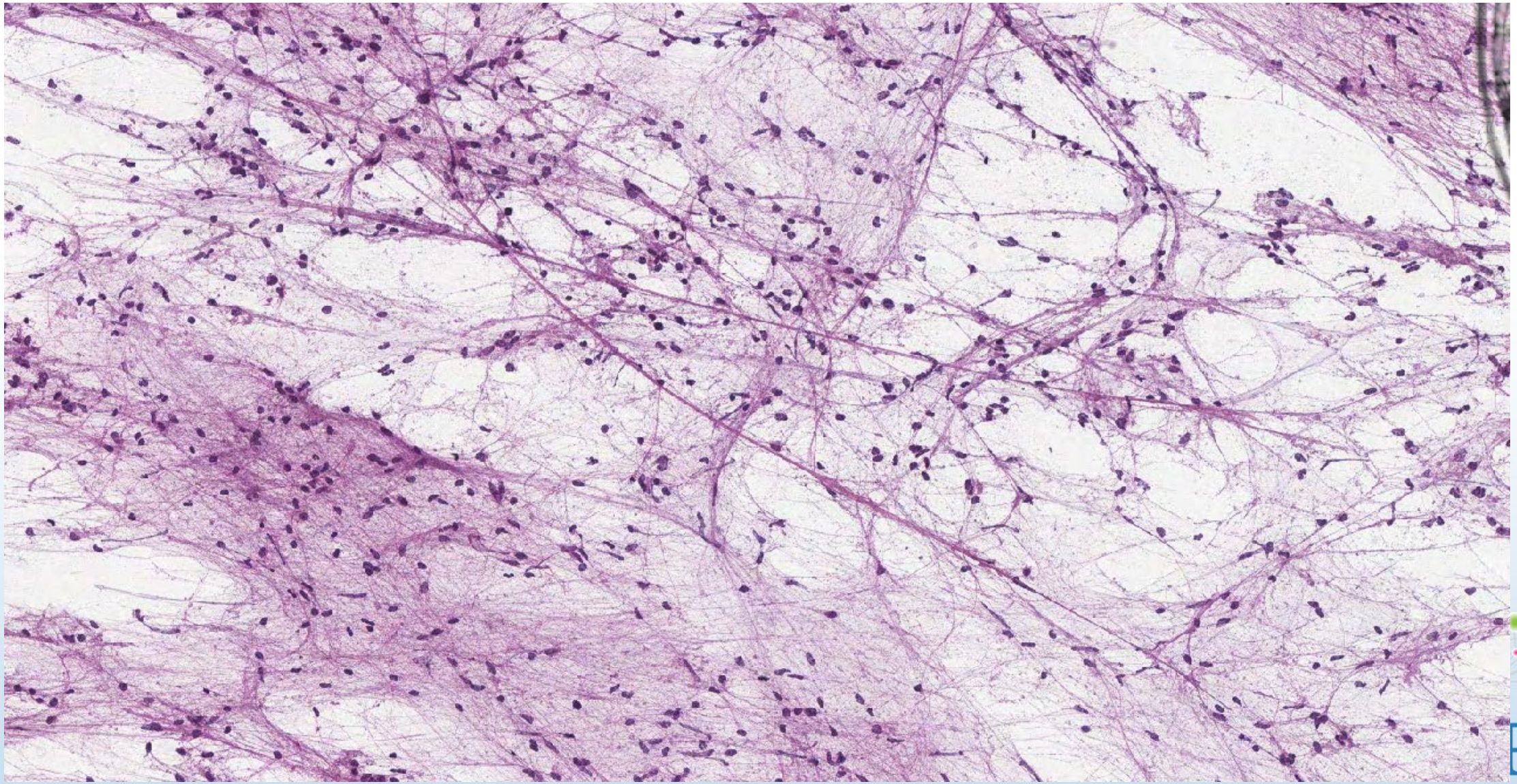
AANP

DDX by Radiologic Features: Cystic with a mural nodule

- Pilocytic Astrocytoma (PA)
- Hemangioblastoma (HGB)
- Ganglioglioma (GG)
- Pleomorphic Xanthoastrocytoma (PXA)

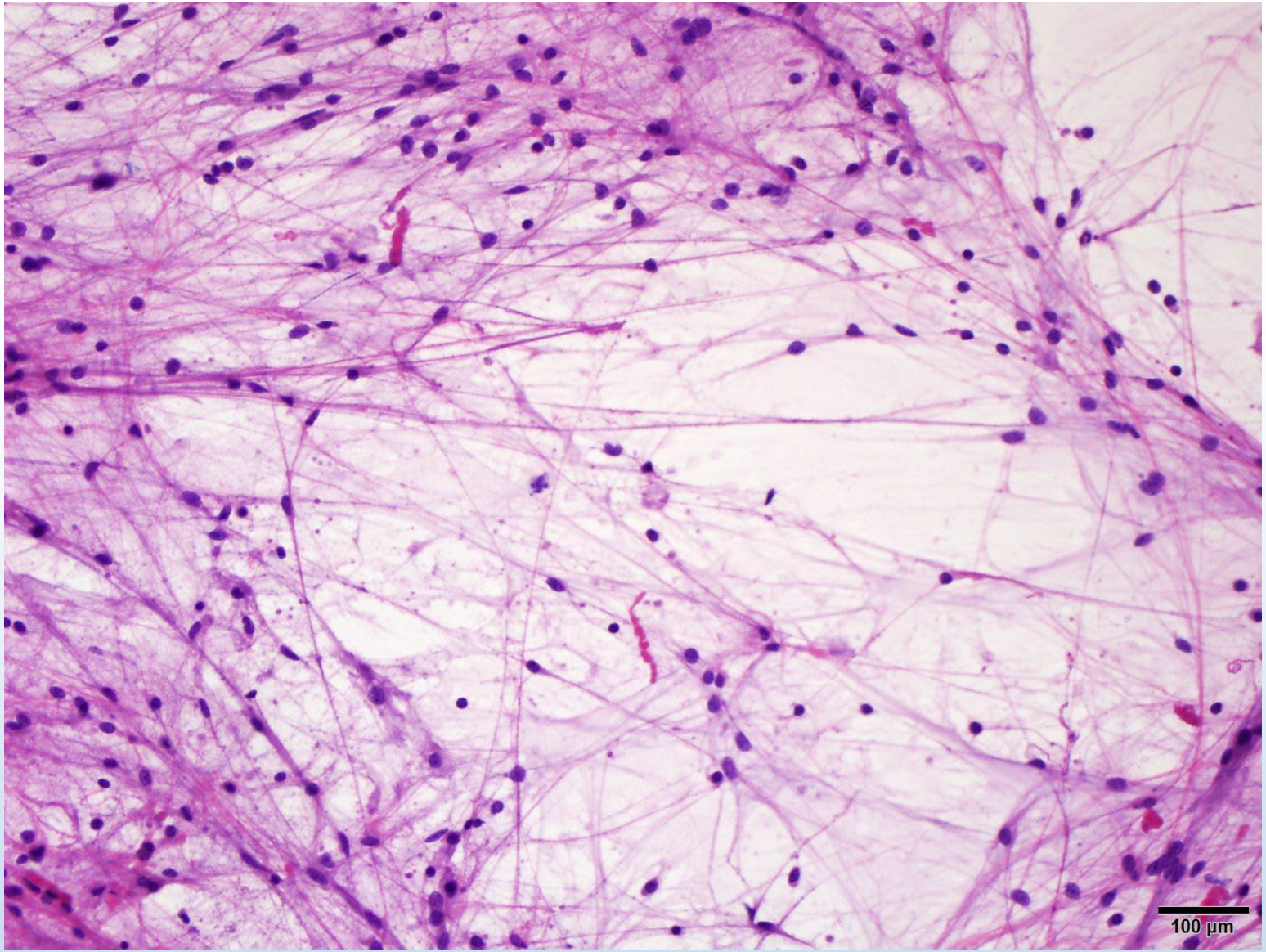
12-year-old with one month history of worsening headaches, nausea and vomiting

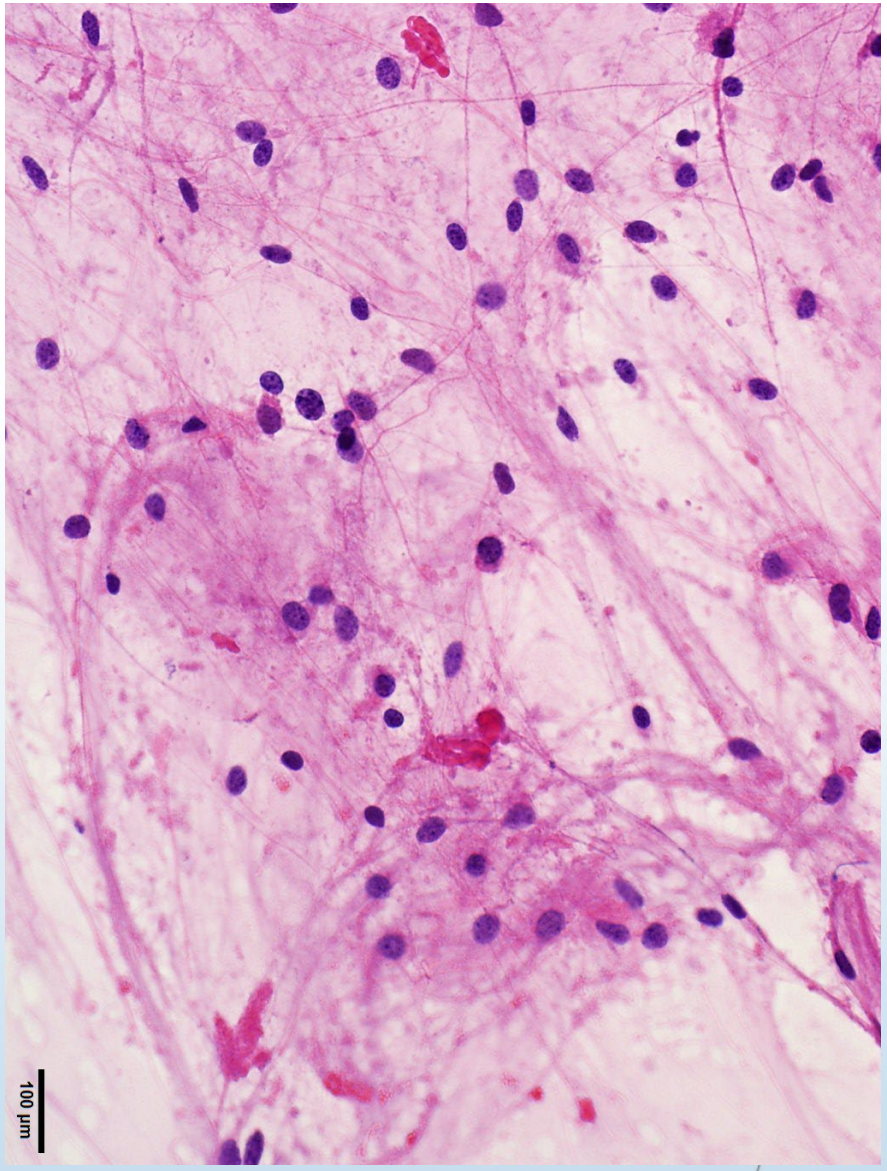
Smear Preparation



S2

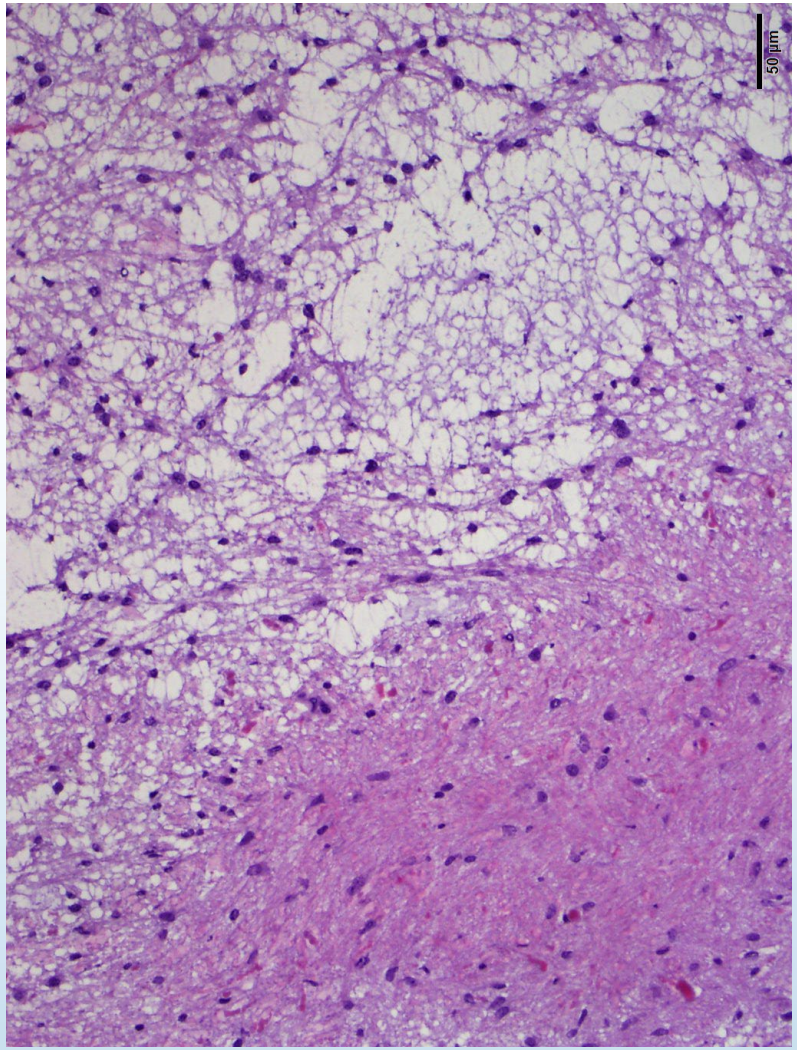
PA: Smear Preparation



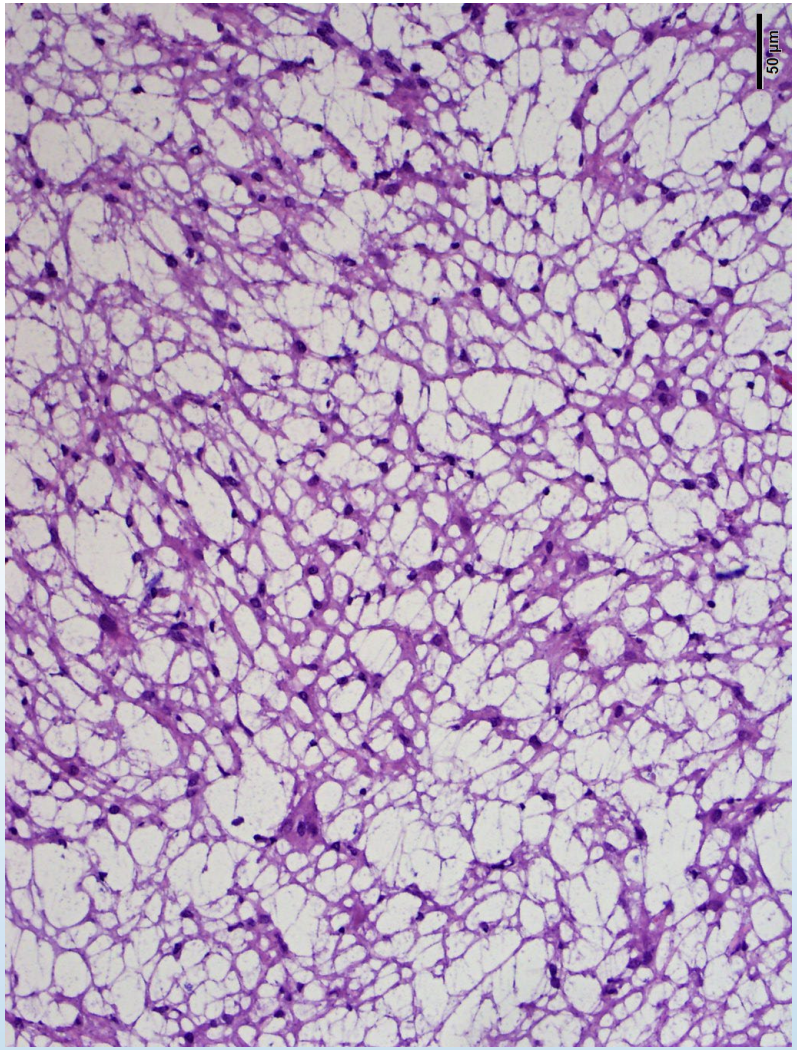


Glioma, most consistent with Pilocytic Astrocytoma

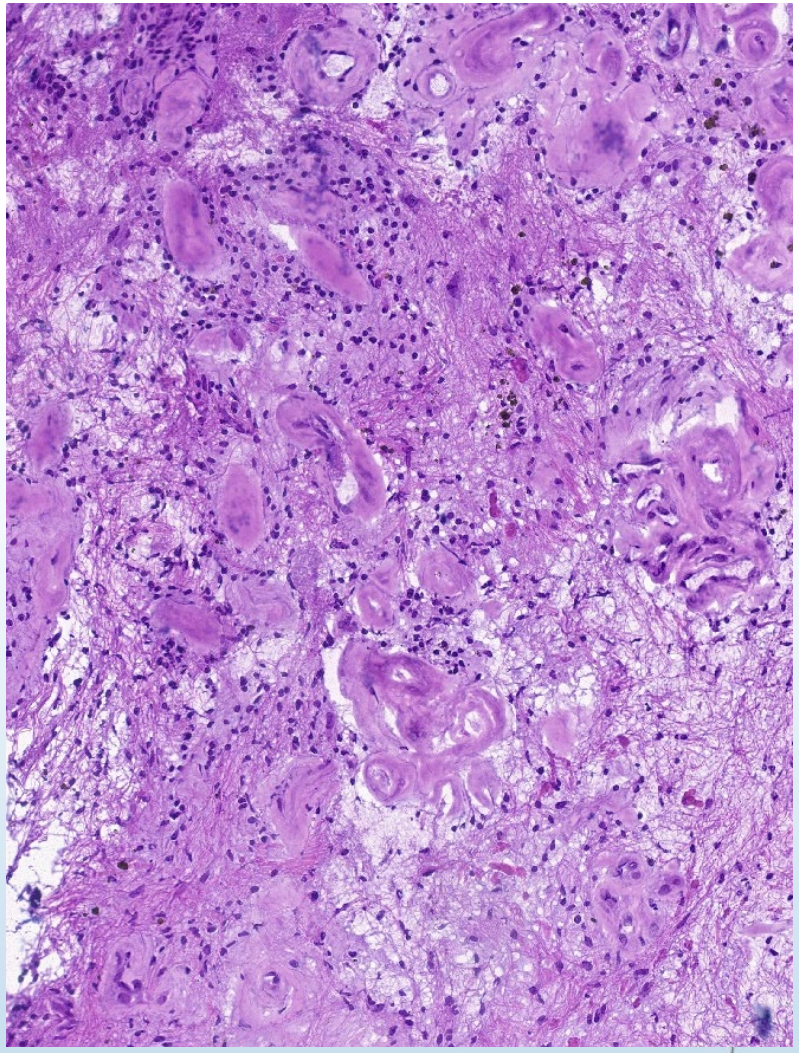
Biphasic Nature



Loose Areas

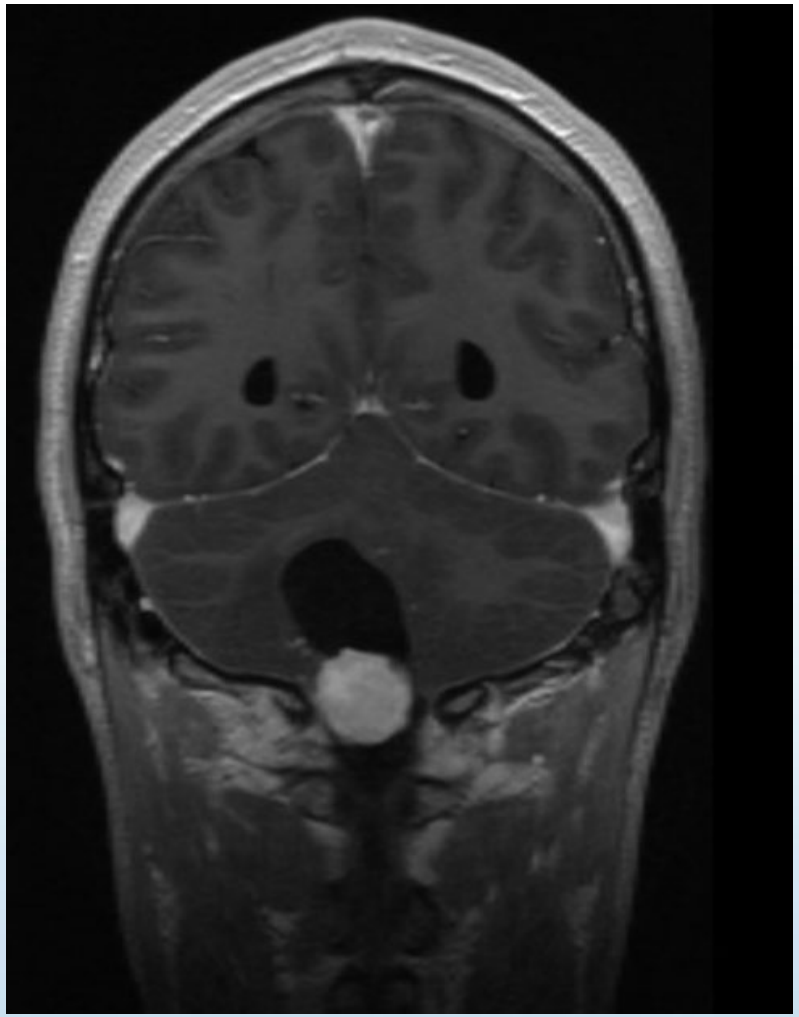


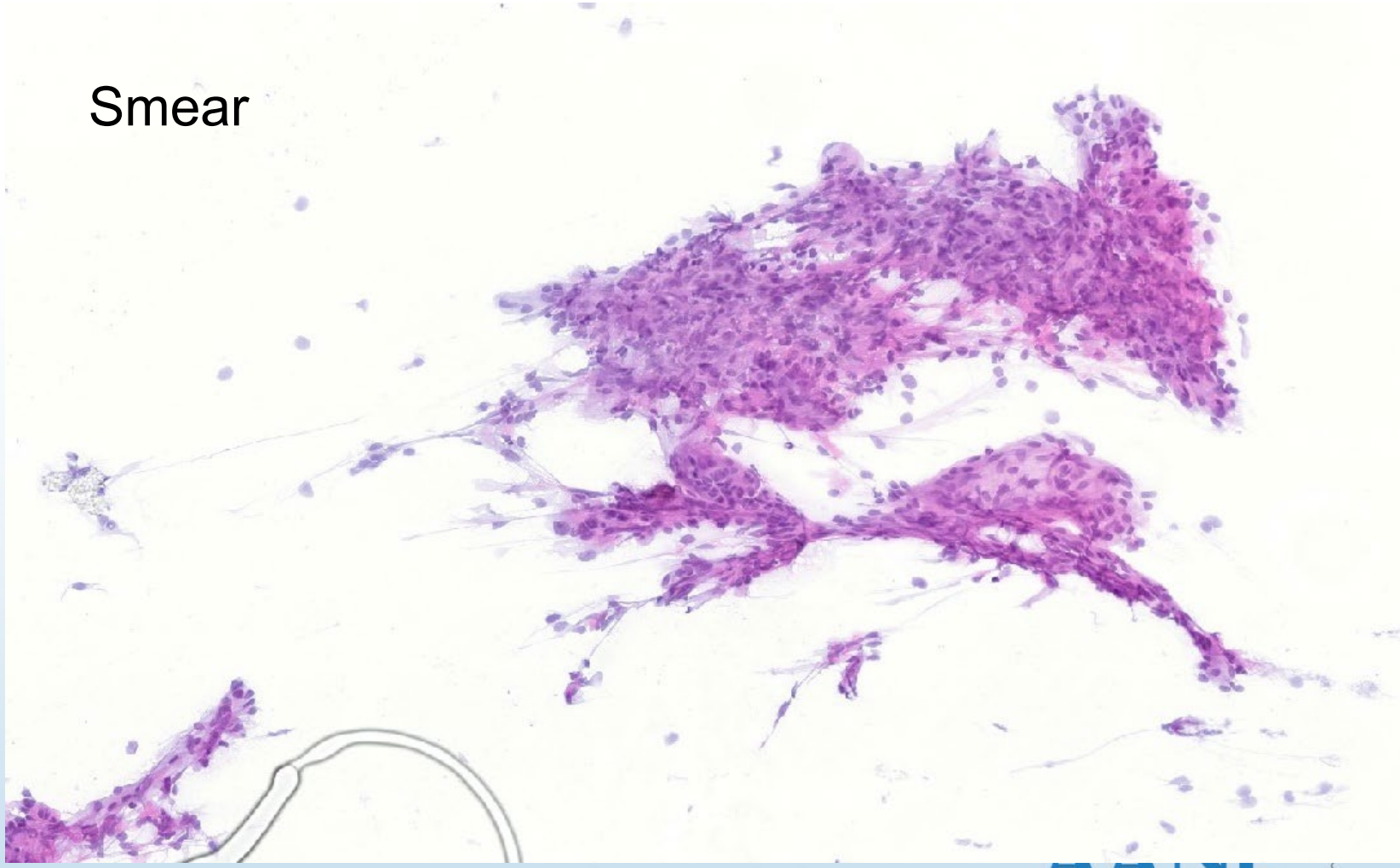
Hyalinized Vessels



Hemangioblastoma

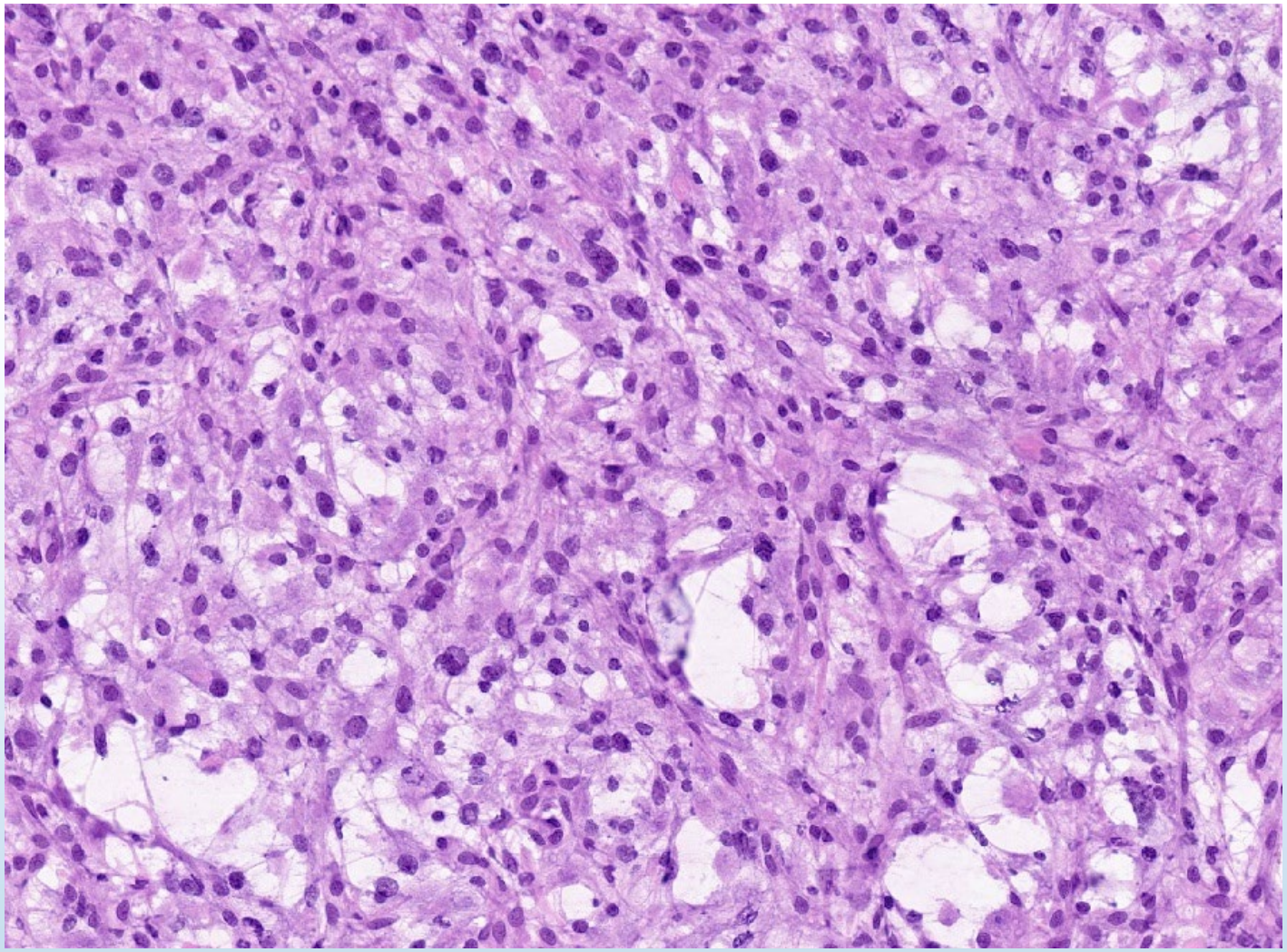
24-y.o. with inferior cerebellar cystic lesion with a mural enhancing nodule



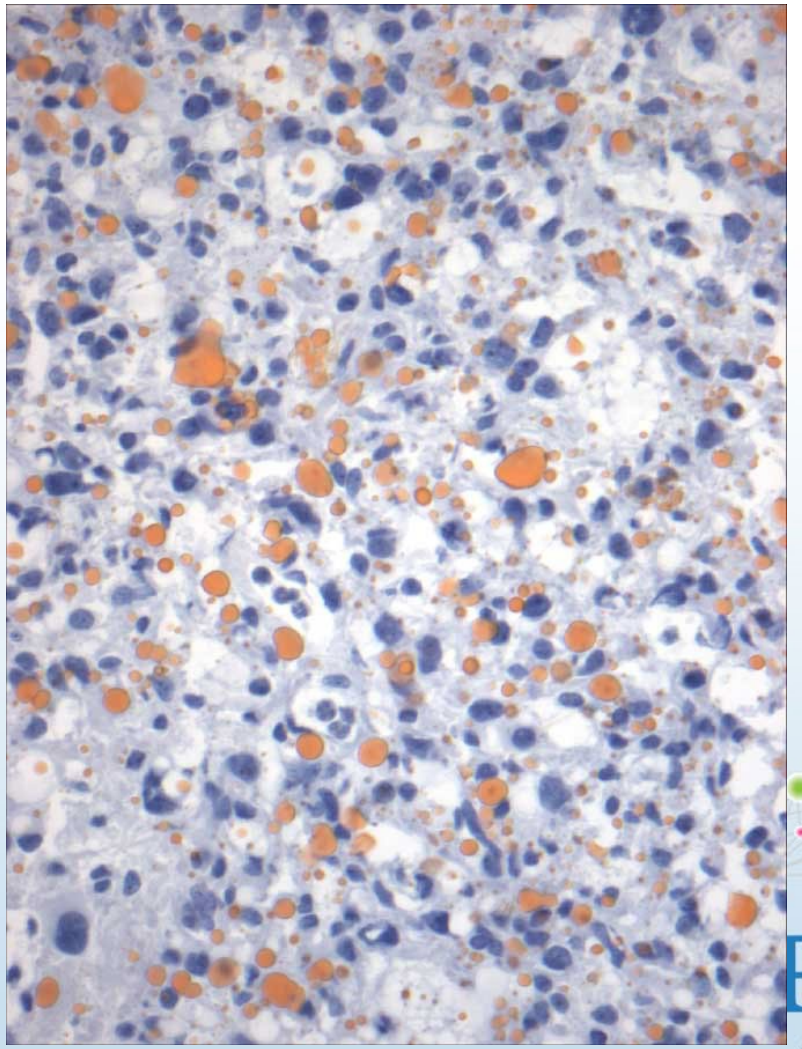


Hemangioblastoma

Frozen Section

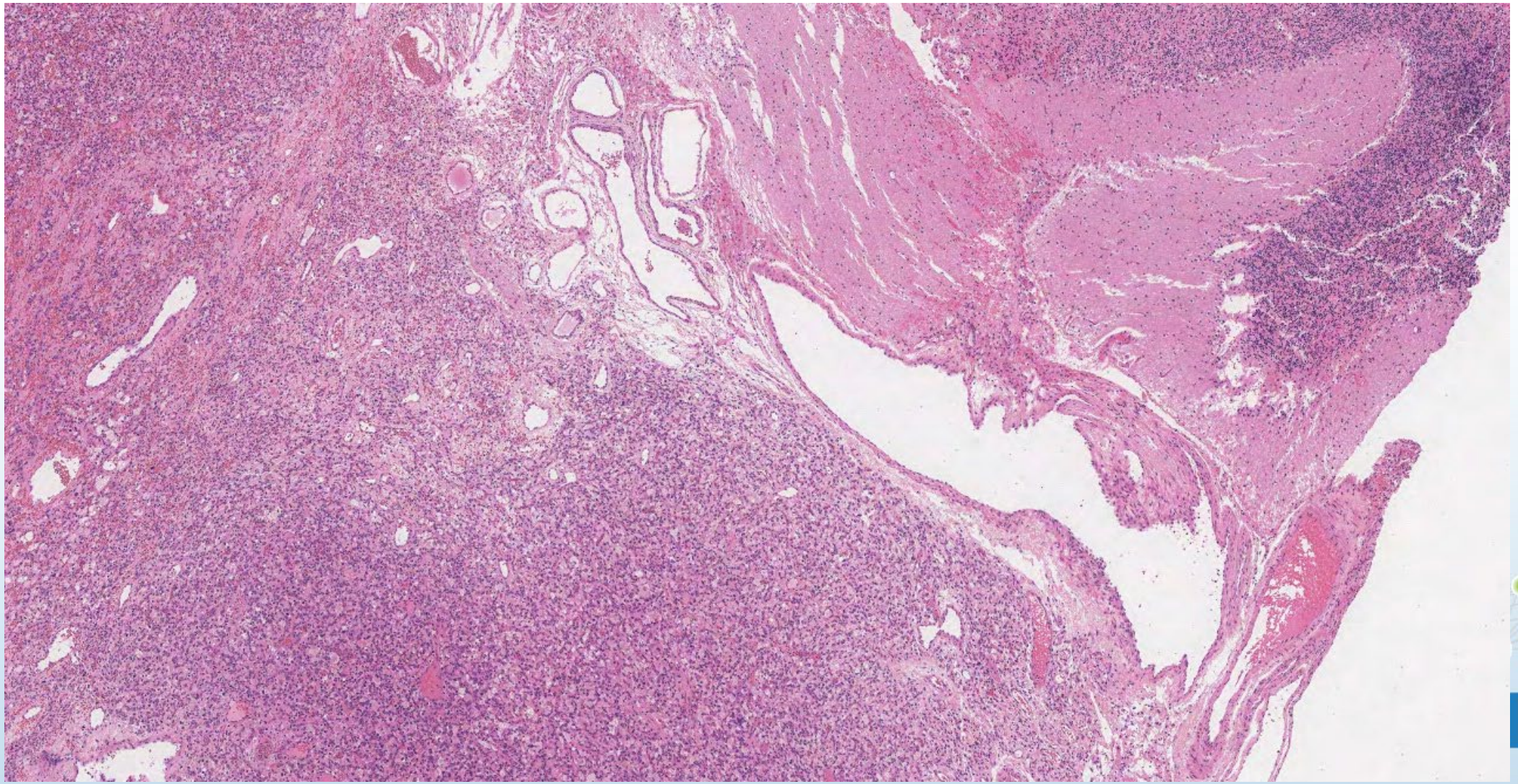


Oil Red O



Hemangioblastoma

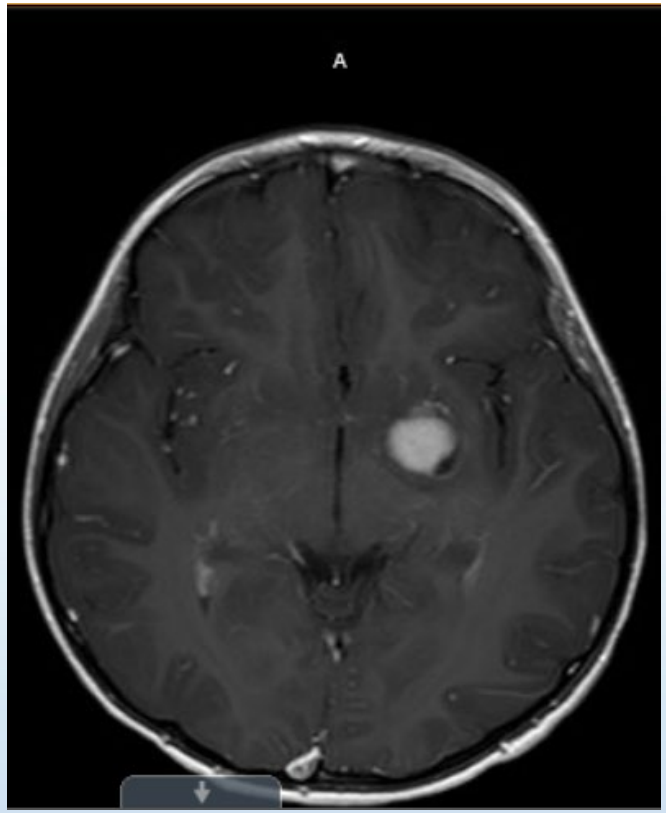
Permanent Section

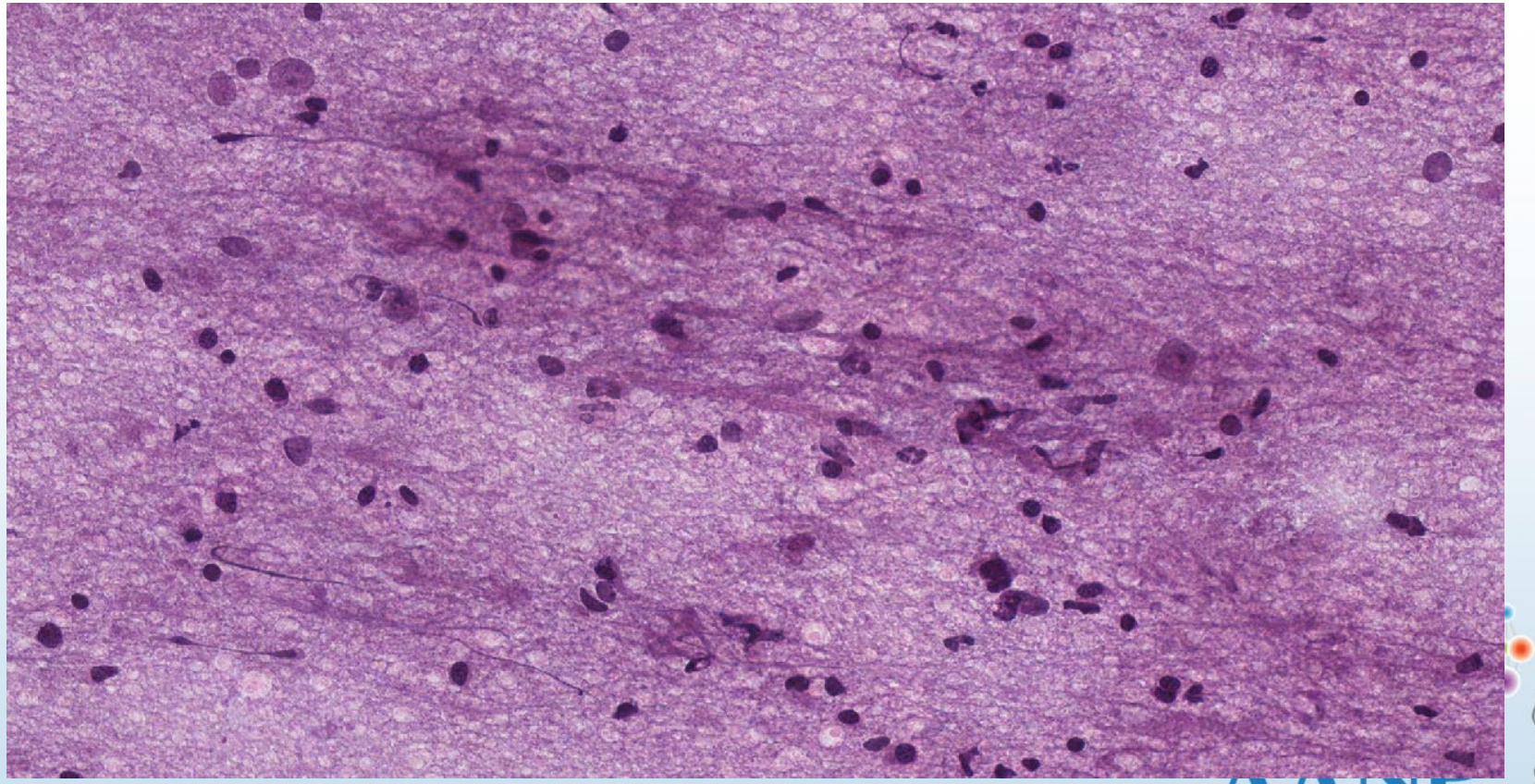


Ganglioglioma

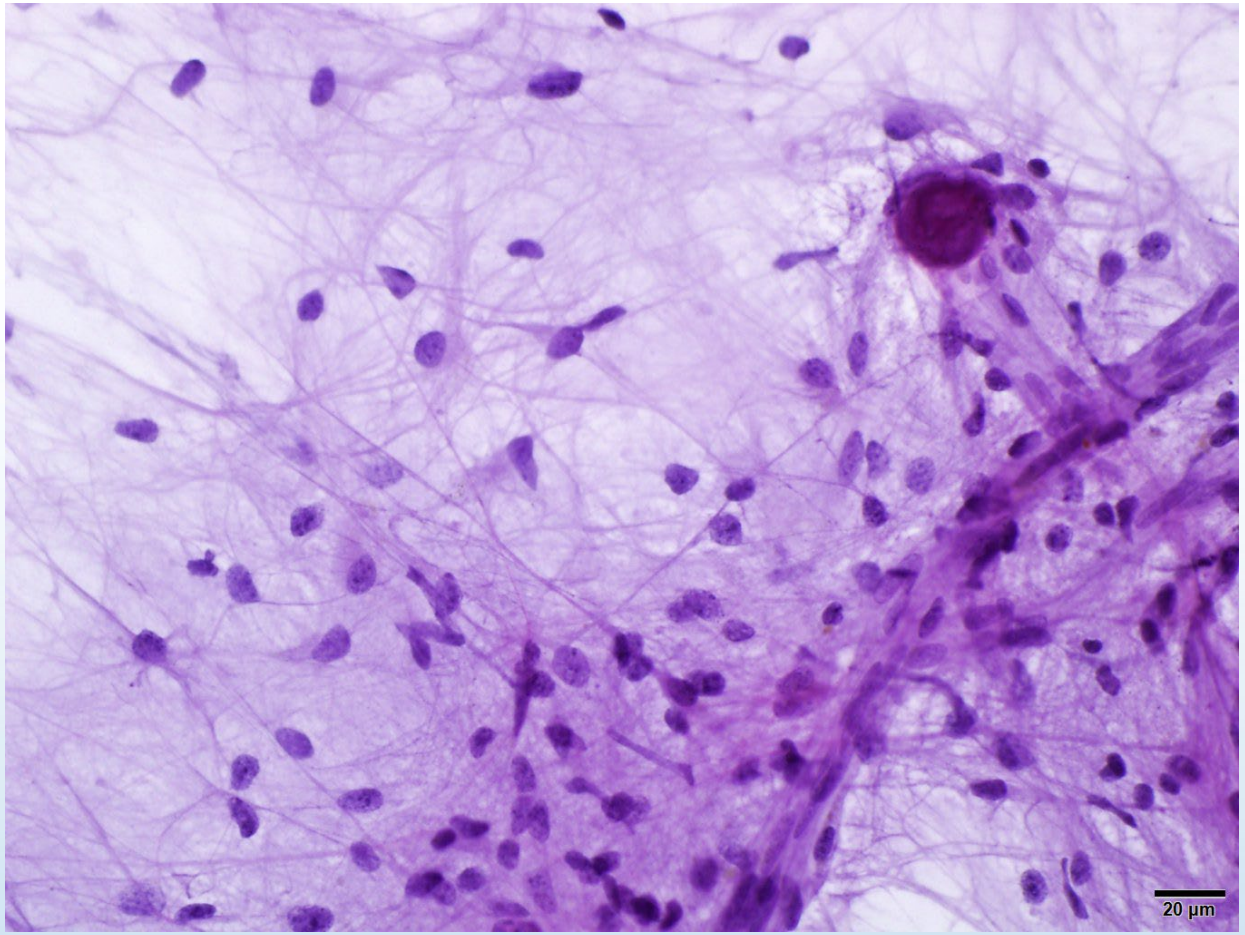
23-year-old male with history of seizures since age 9

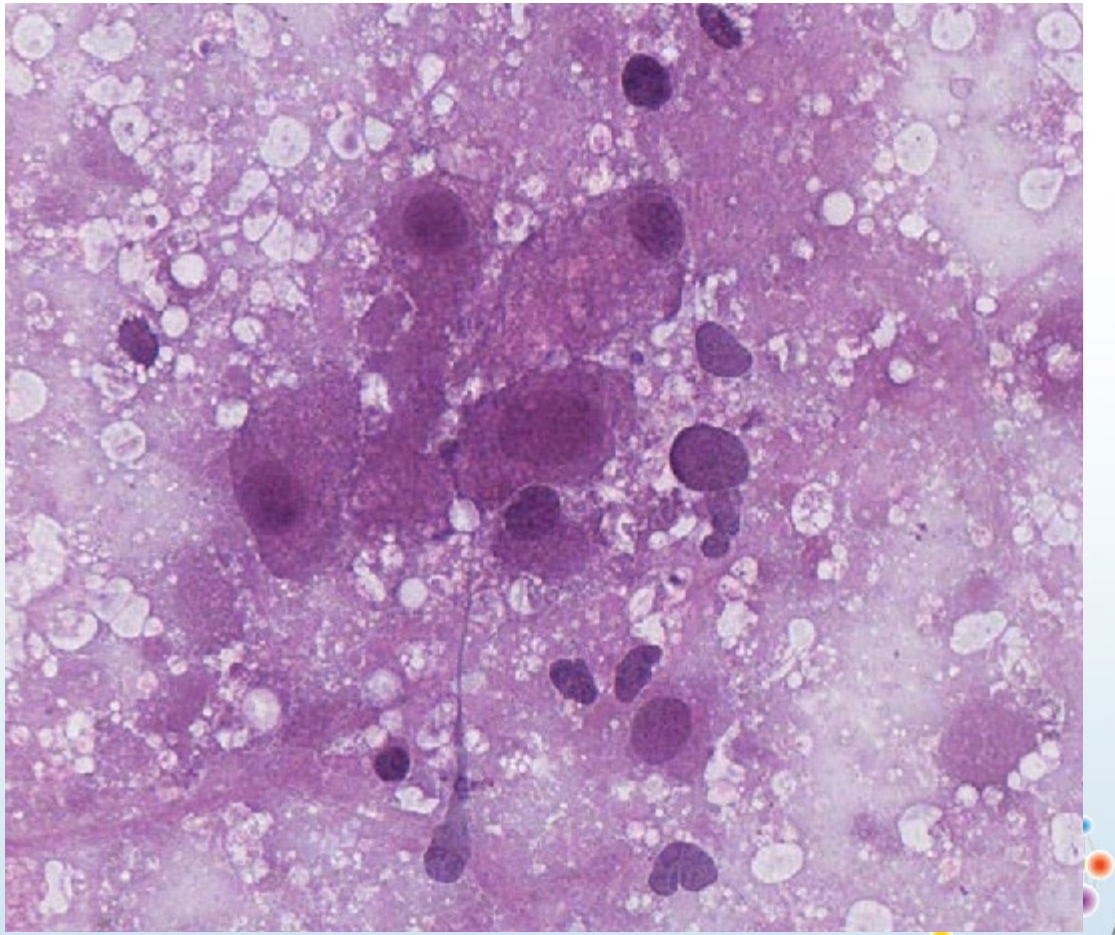
Post-Contrast



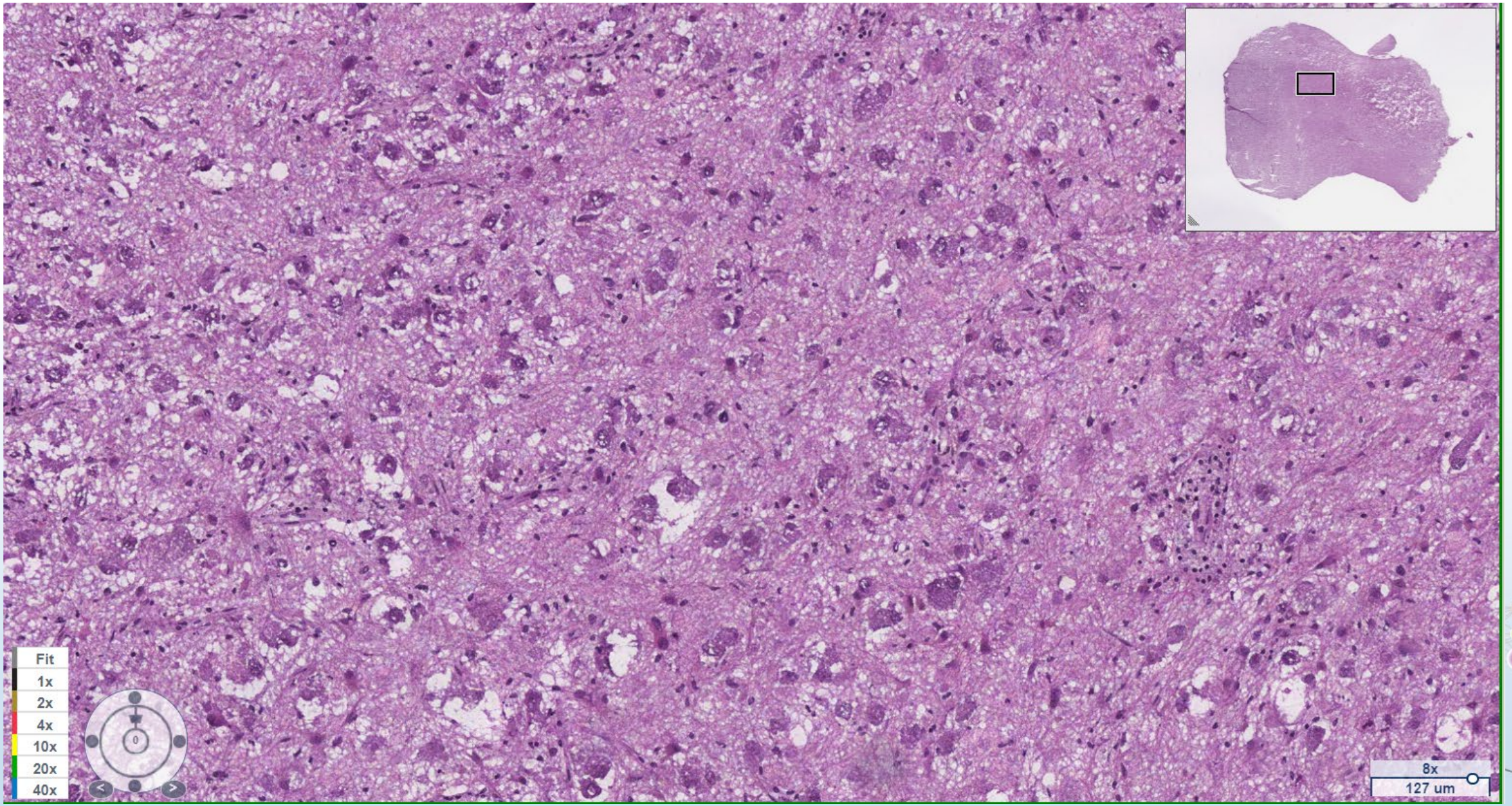


Ganglioglioma



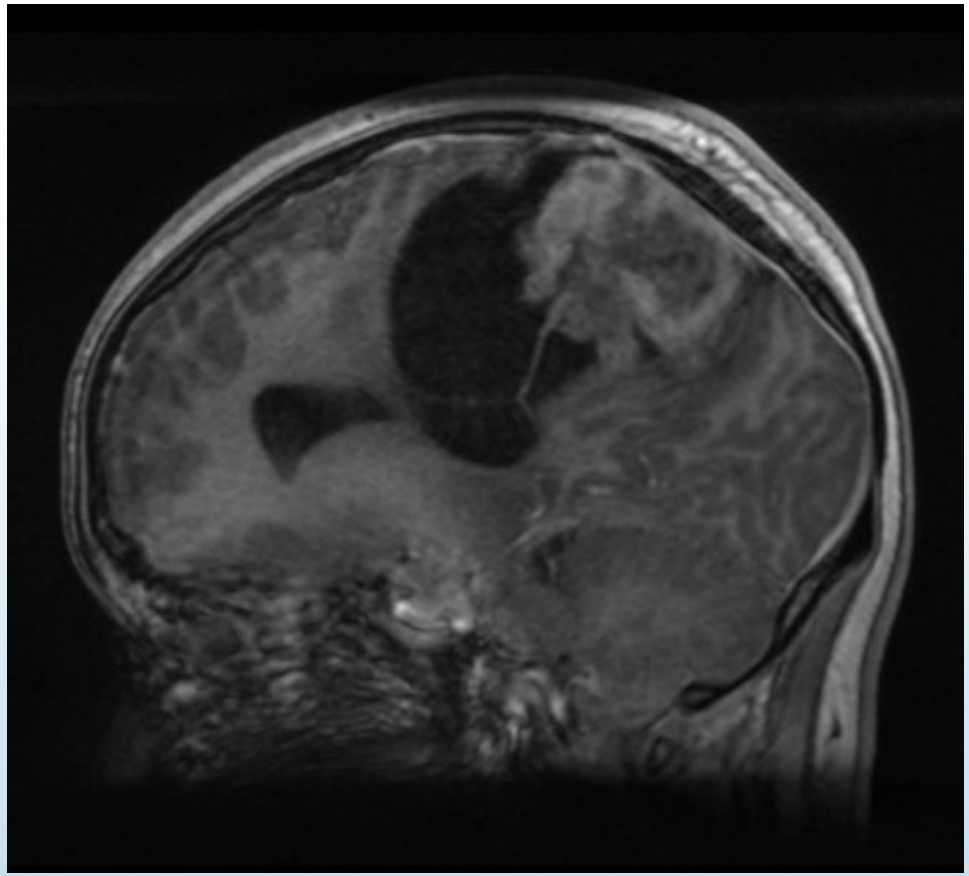


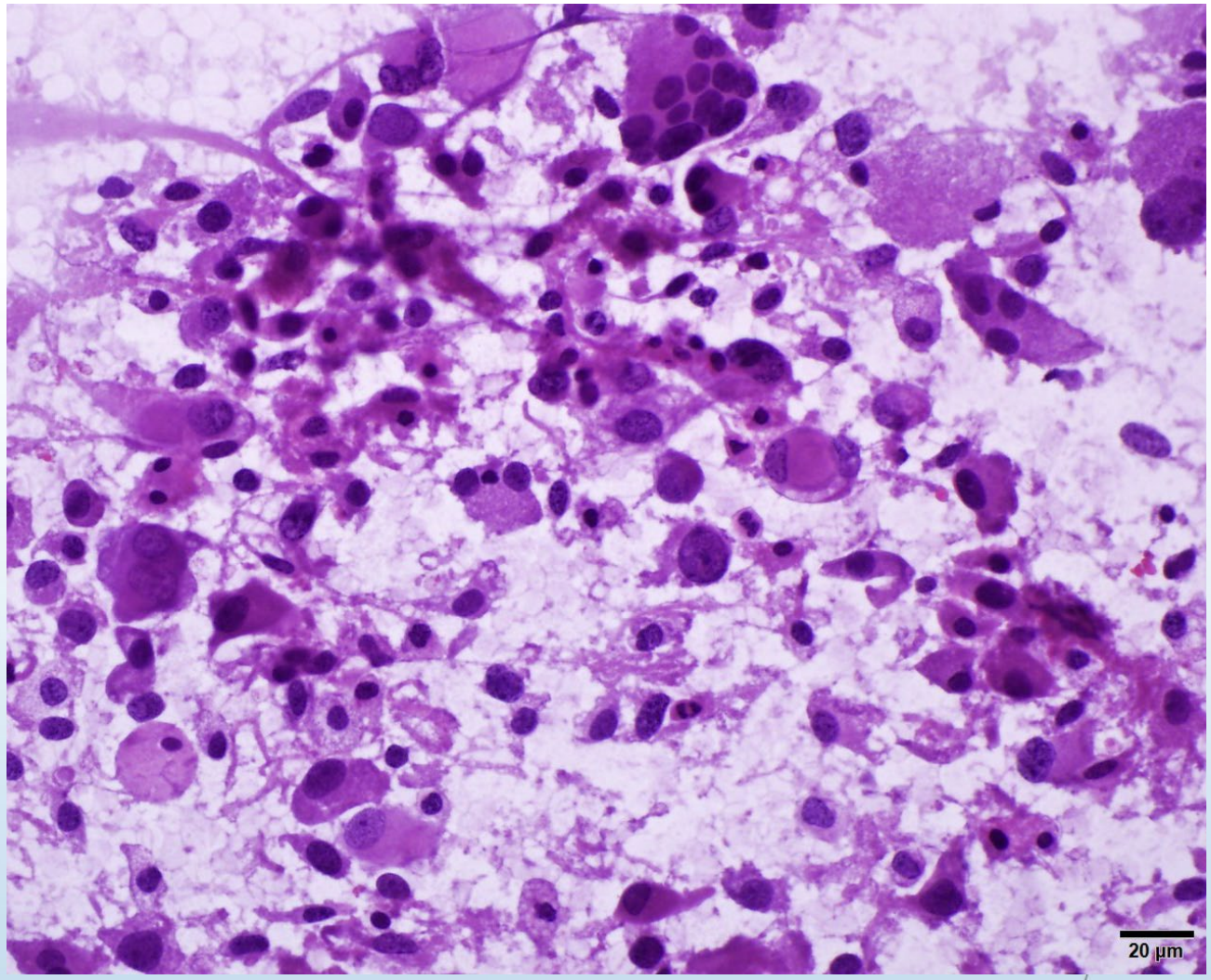
Ganglioglioma Frozen Section



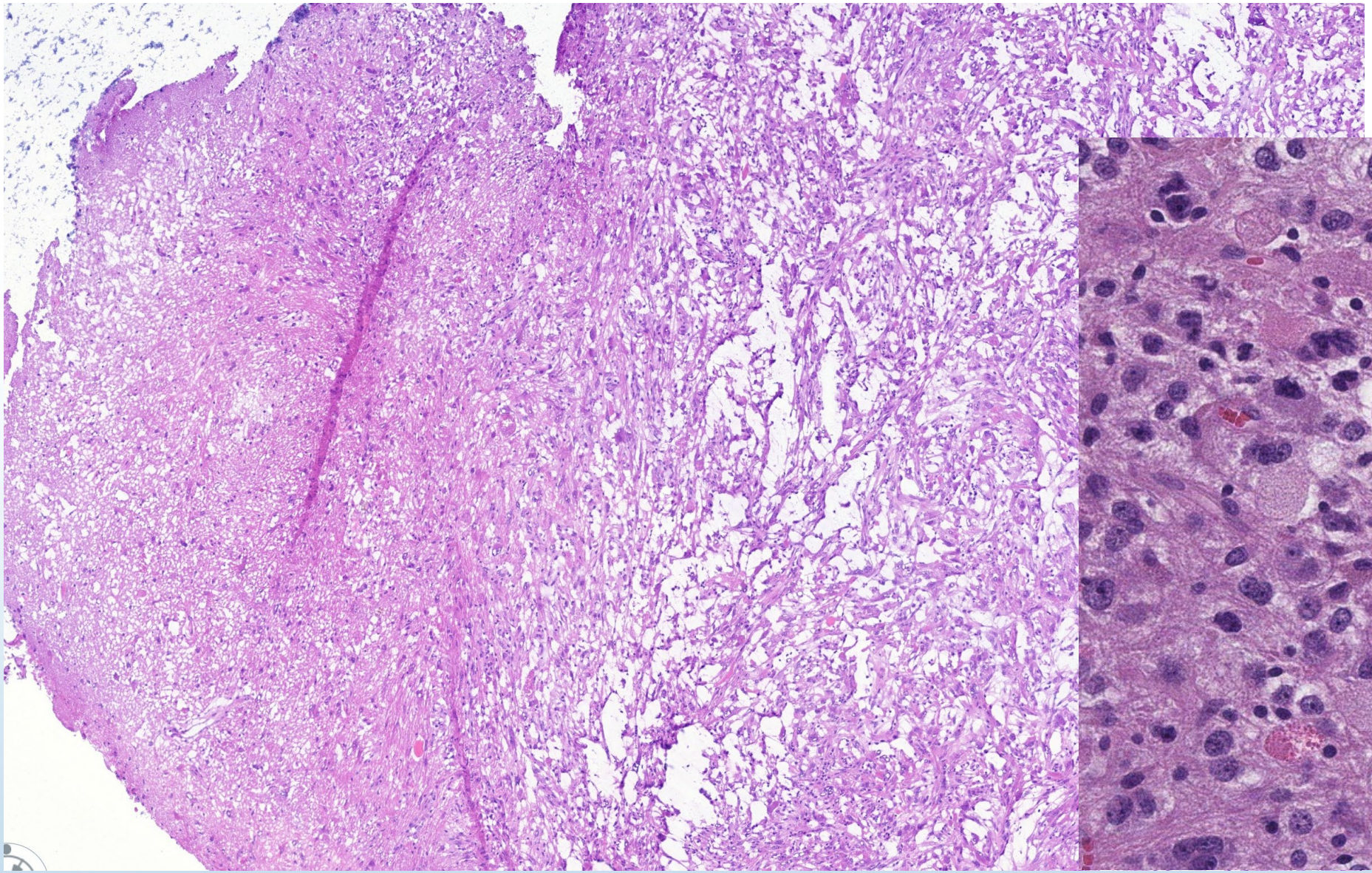
Pleomorphic Xanthoastrocytoma

13-year-old with chronic headaches and focal seizure activity, now with numbness and weakness of lower extremities.

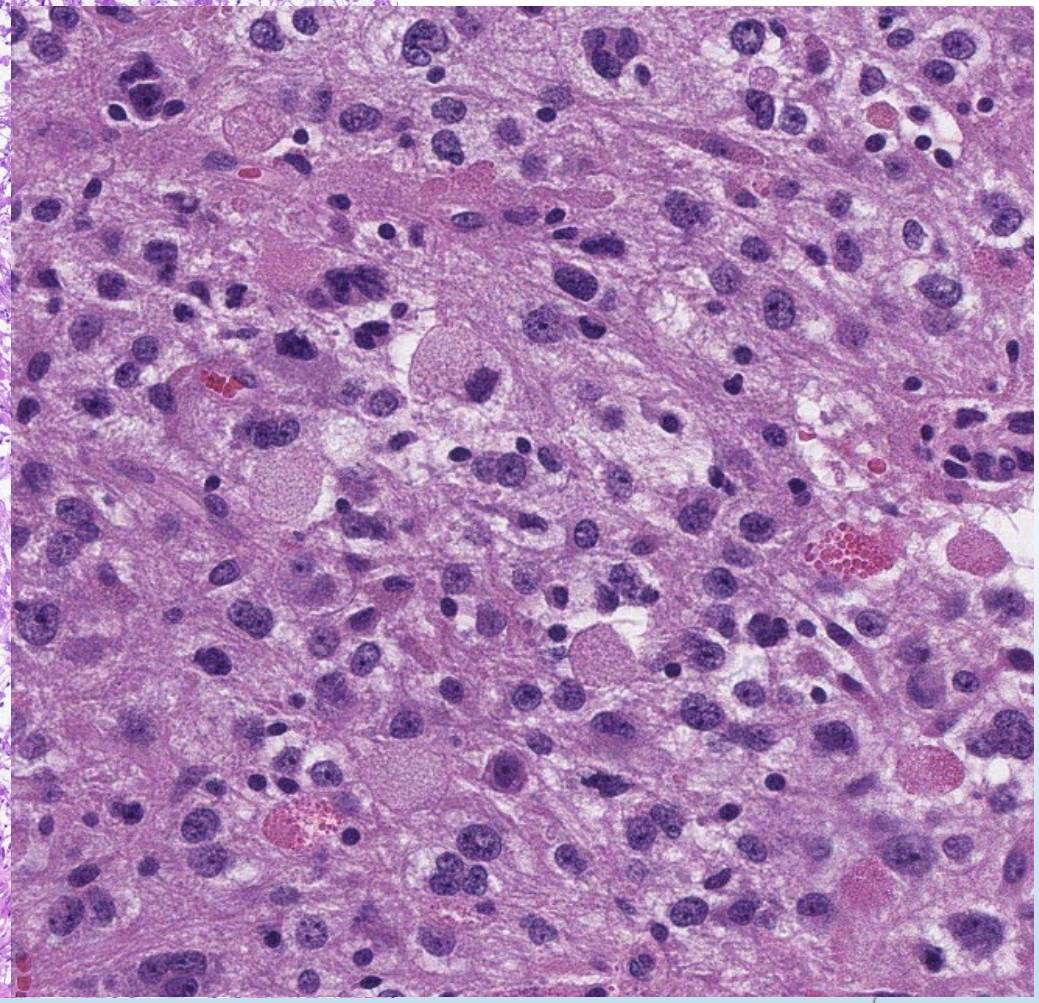




Pleomorphic Xanthoastrocytoma



Lipidized cells and EGBs

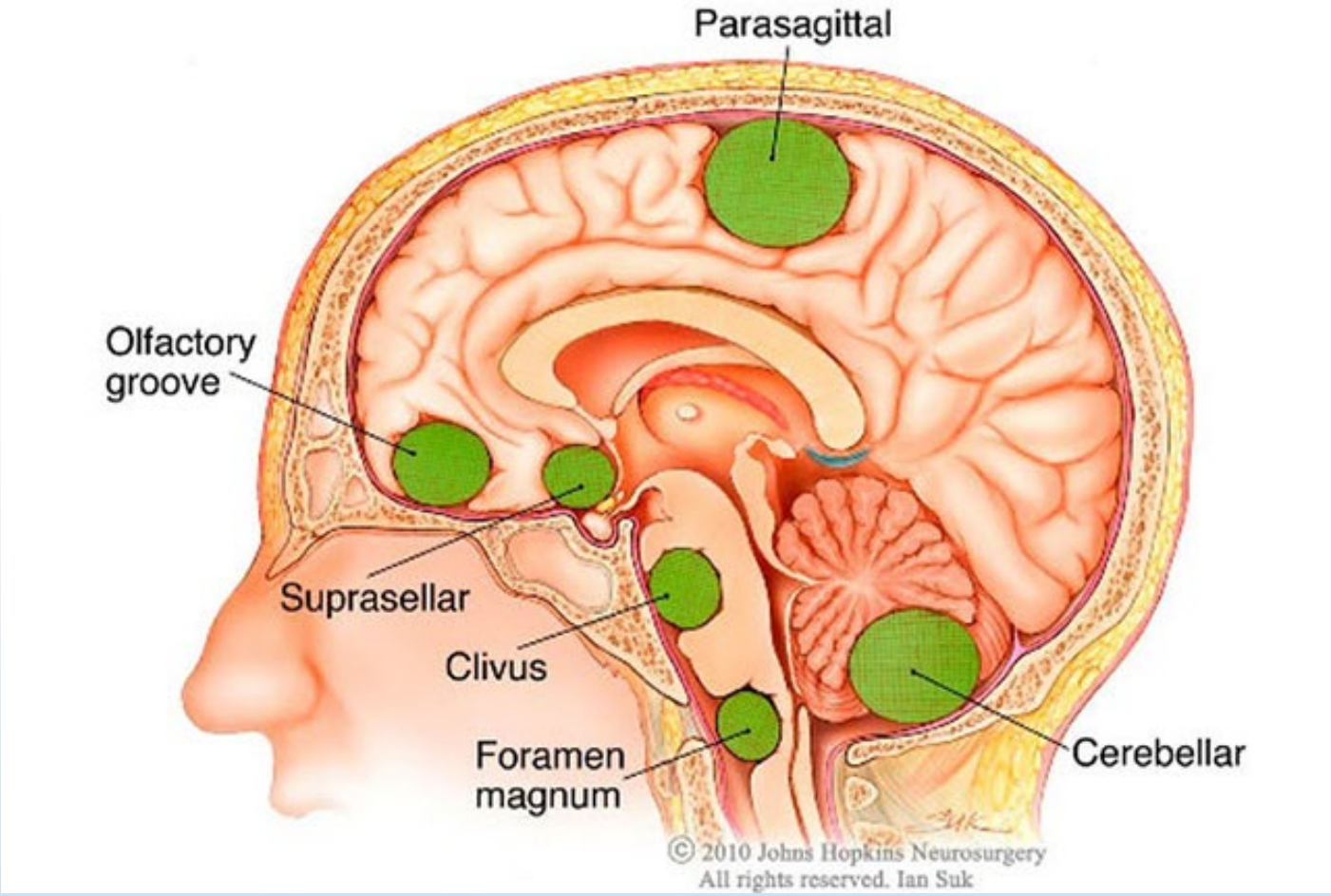


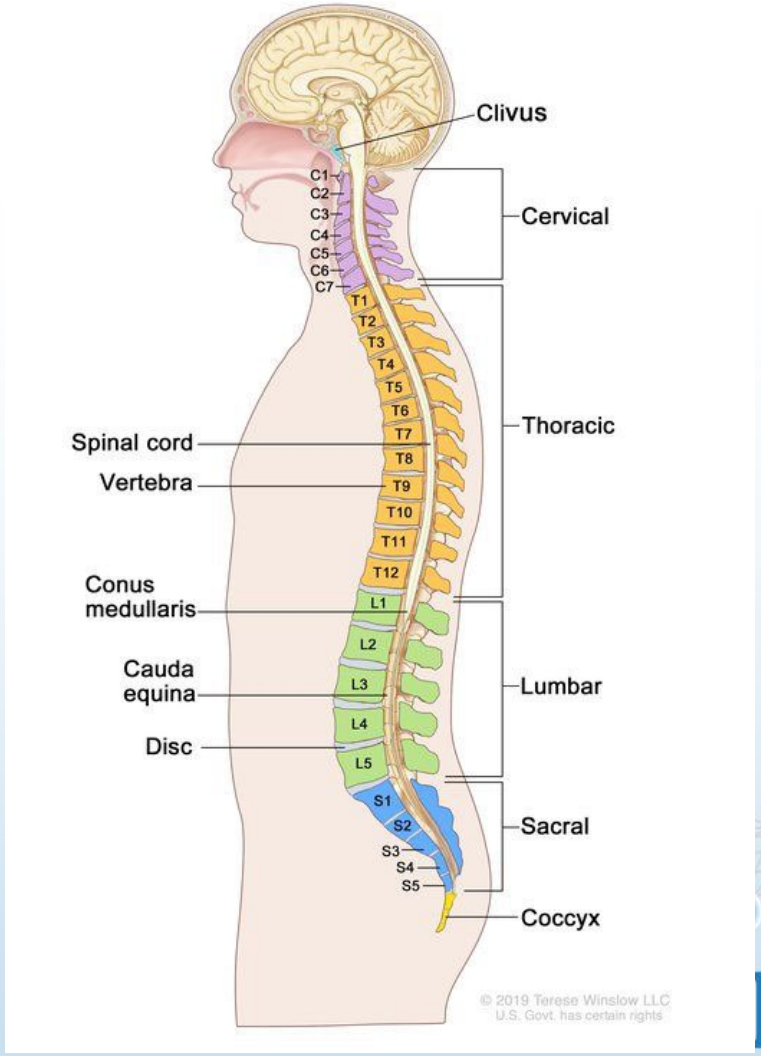
DDX by Radiologic Features: Cystic with a mural nodule

- Pilocytic Astrocytoma (PA)
- Hemangioblastoma (HGB)
- Ganglioglioma (GG)
- Pleomorphic Xanthoastrocytoma (PXA)

AANP

Differential Diagnosis by Location

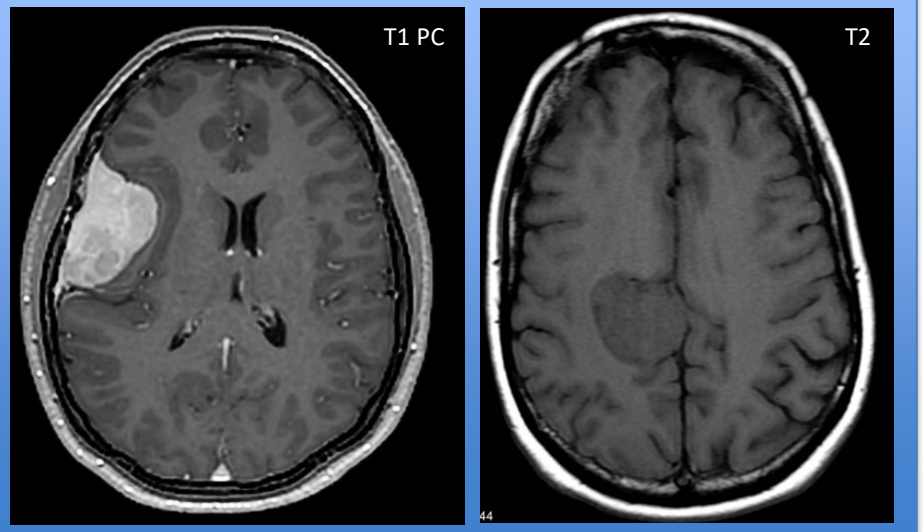




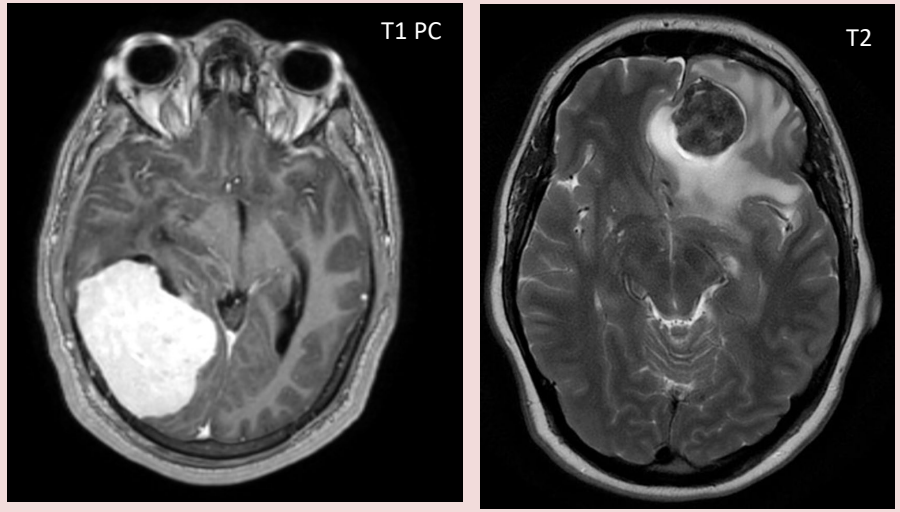
Dural base lesions

- Meningioma
- Solitary Fibrous Tumor
- Metastasis
- Lymphomas
- Sarcomas

Meningioma



Solitary Fibrous Tumor

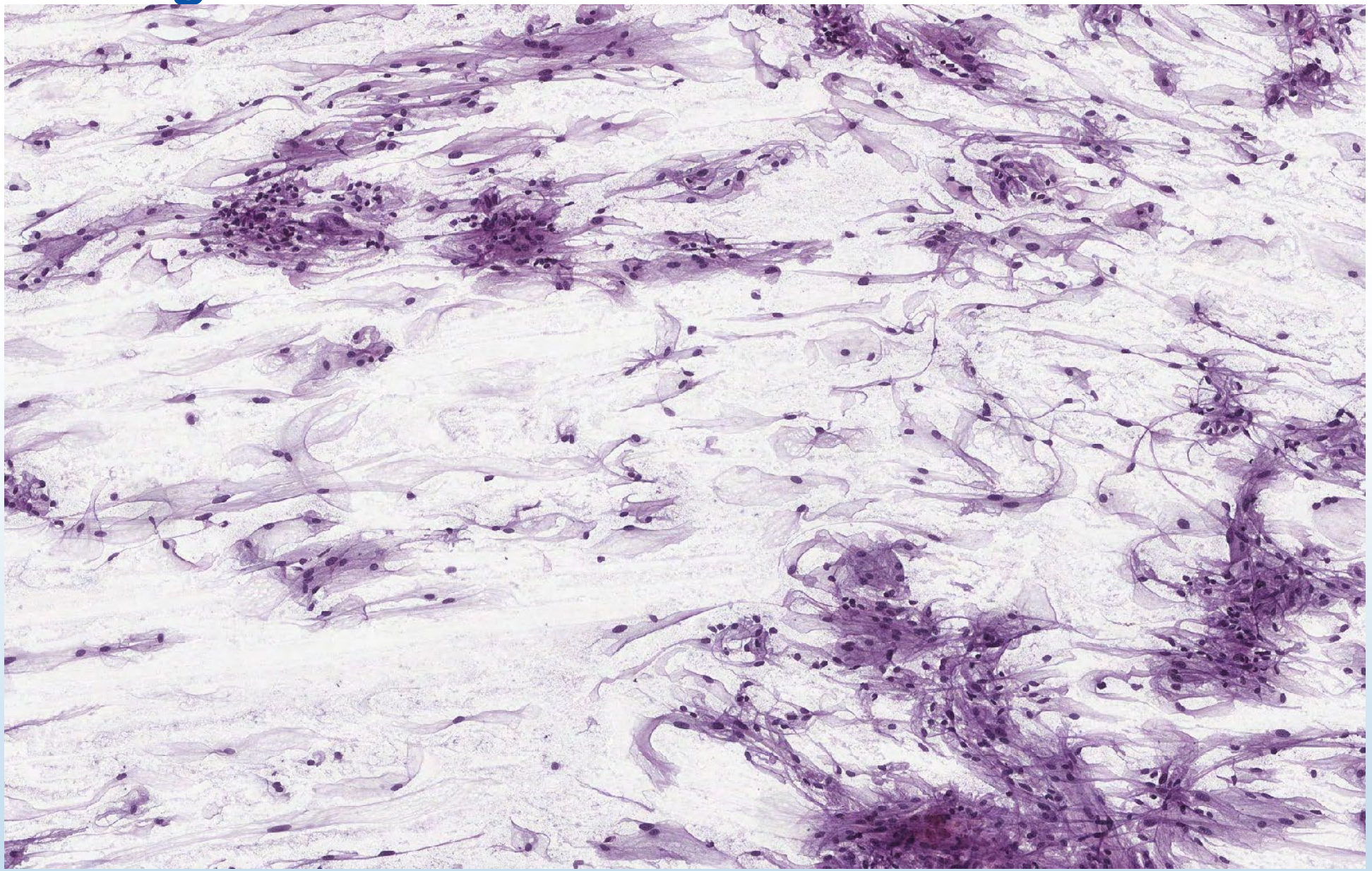


- Less evident dural tail
- “yin-yang” pattern in T2
- Often have flow voids

AANP

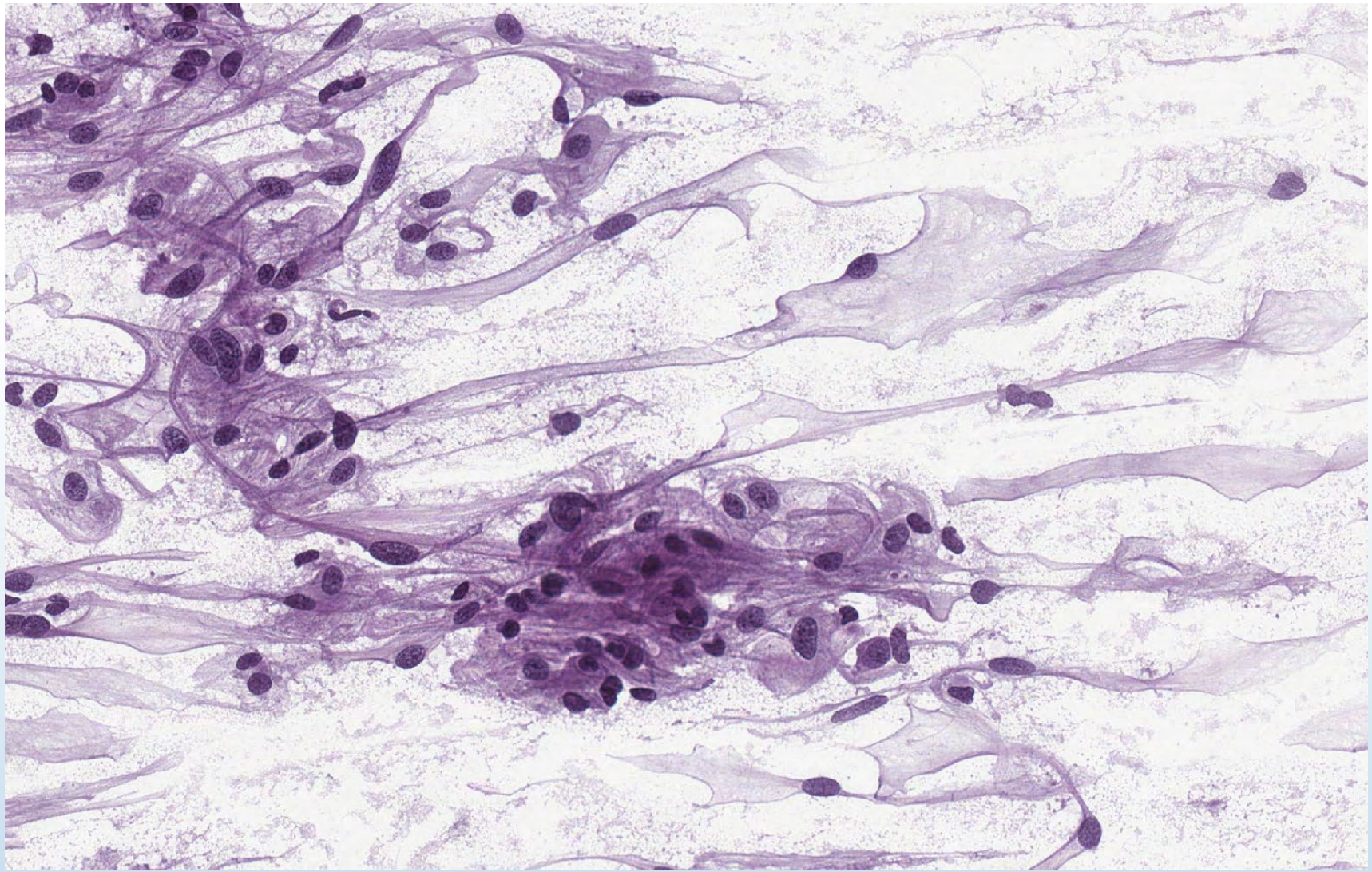
Radiopedia.org

Meningioma

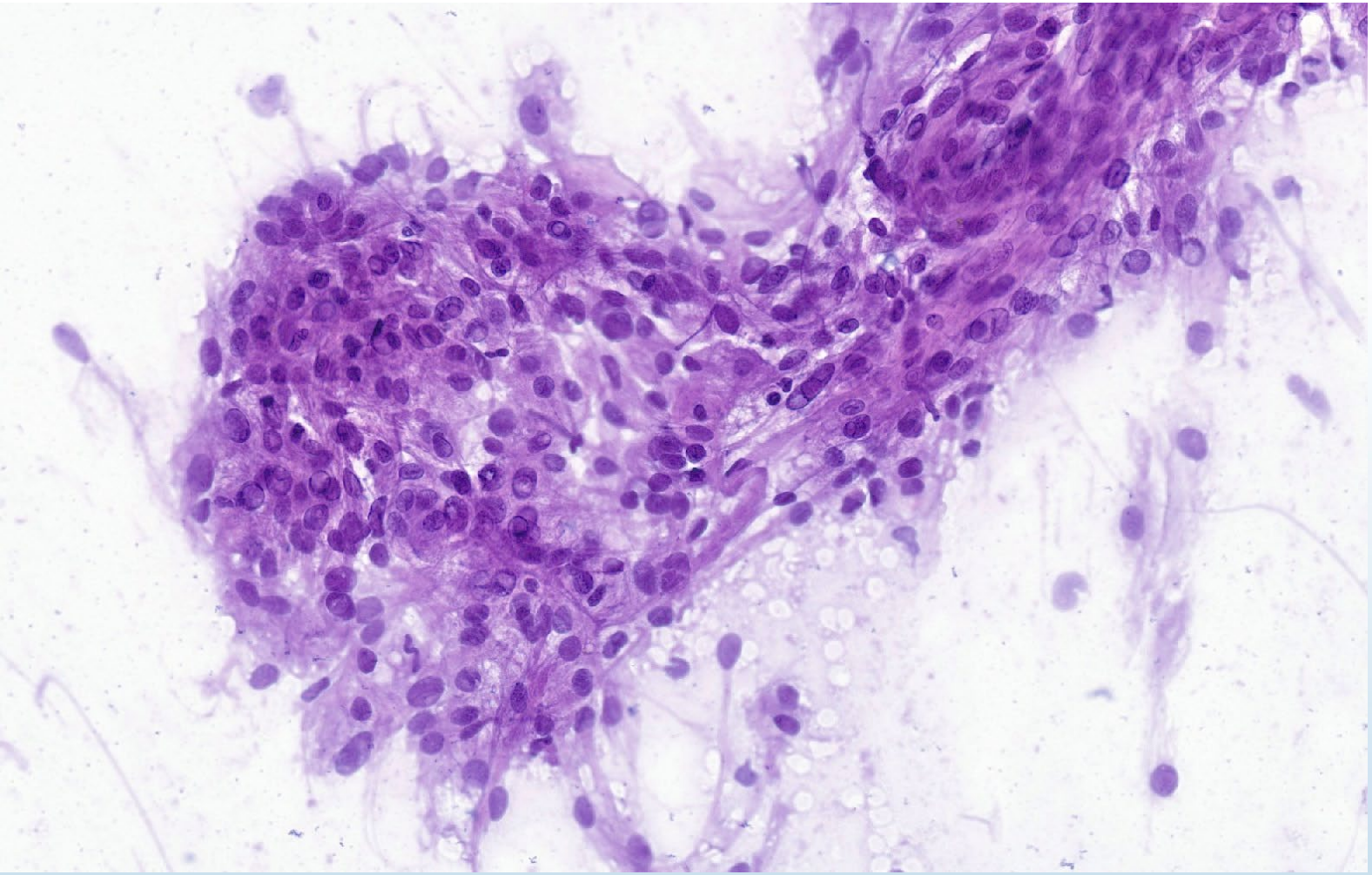


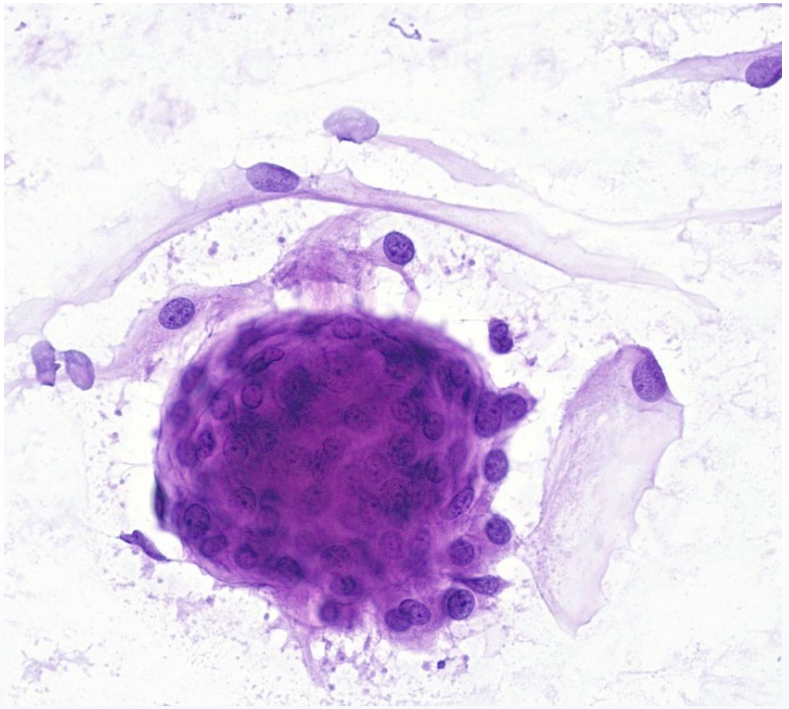
Smear

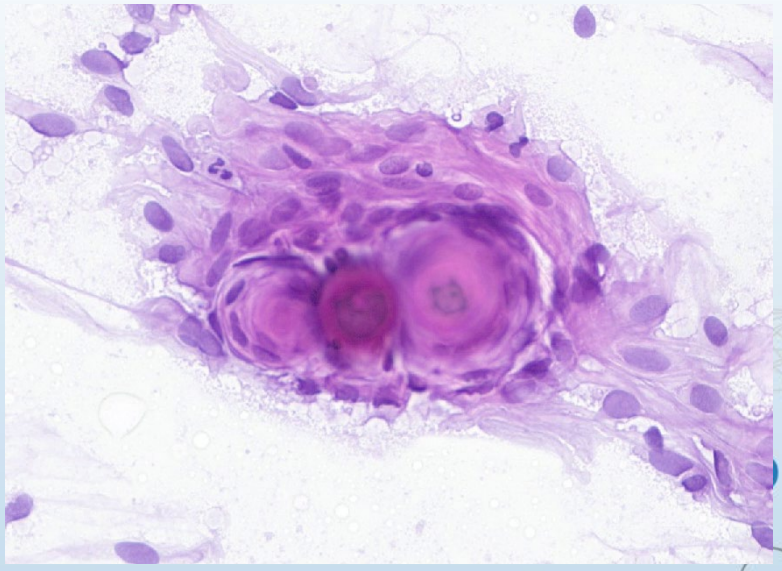
Meningioma



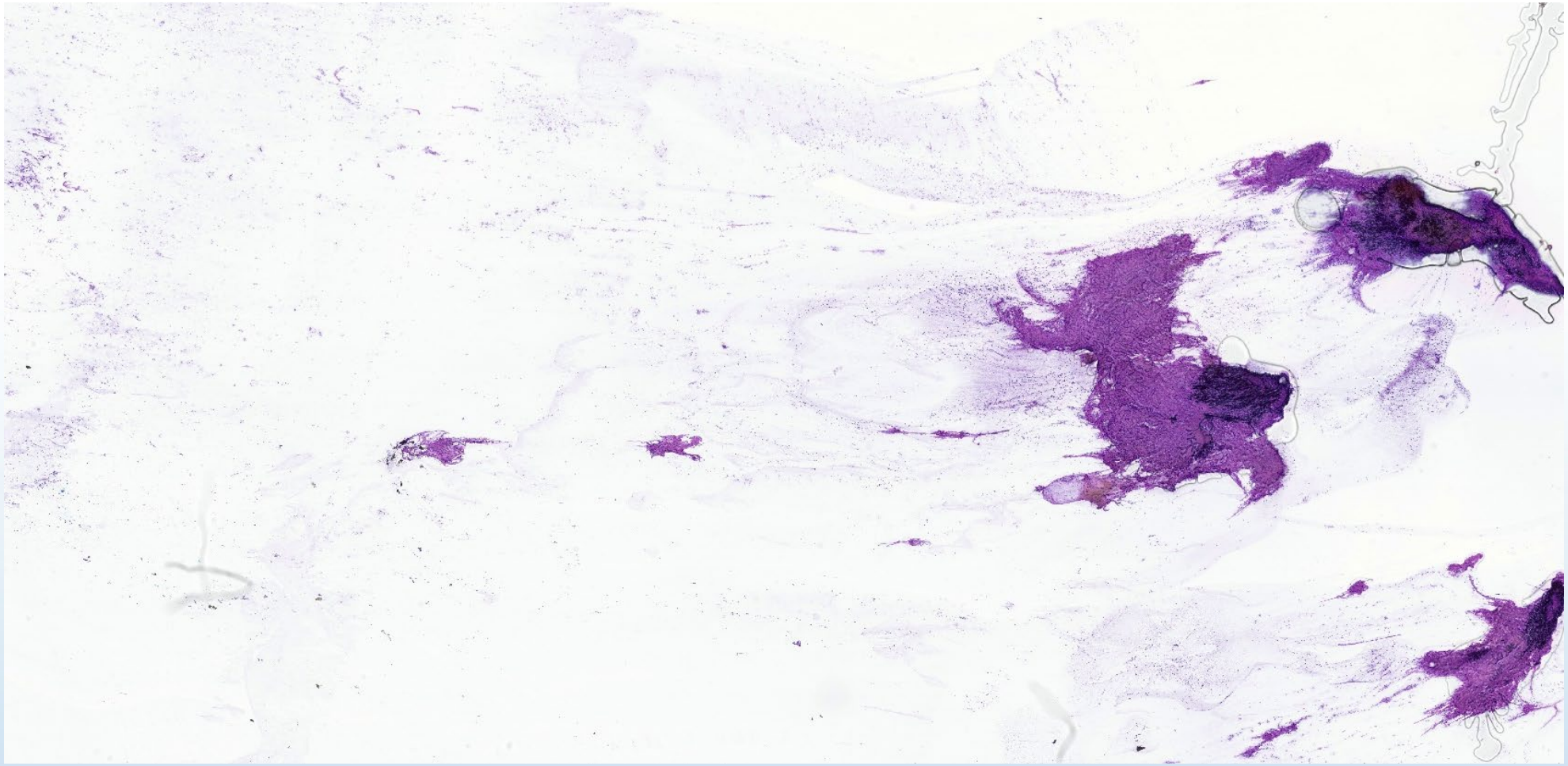
Meningioma







Solitary Fibrous Tumor

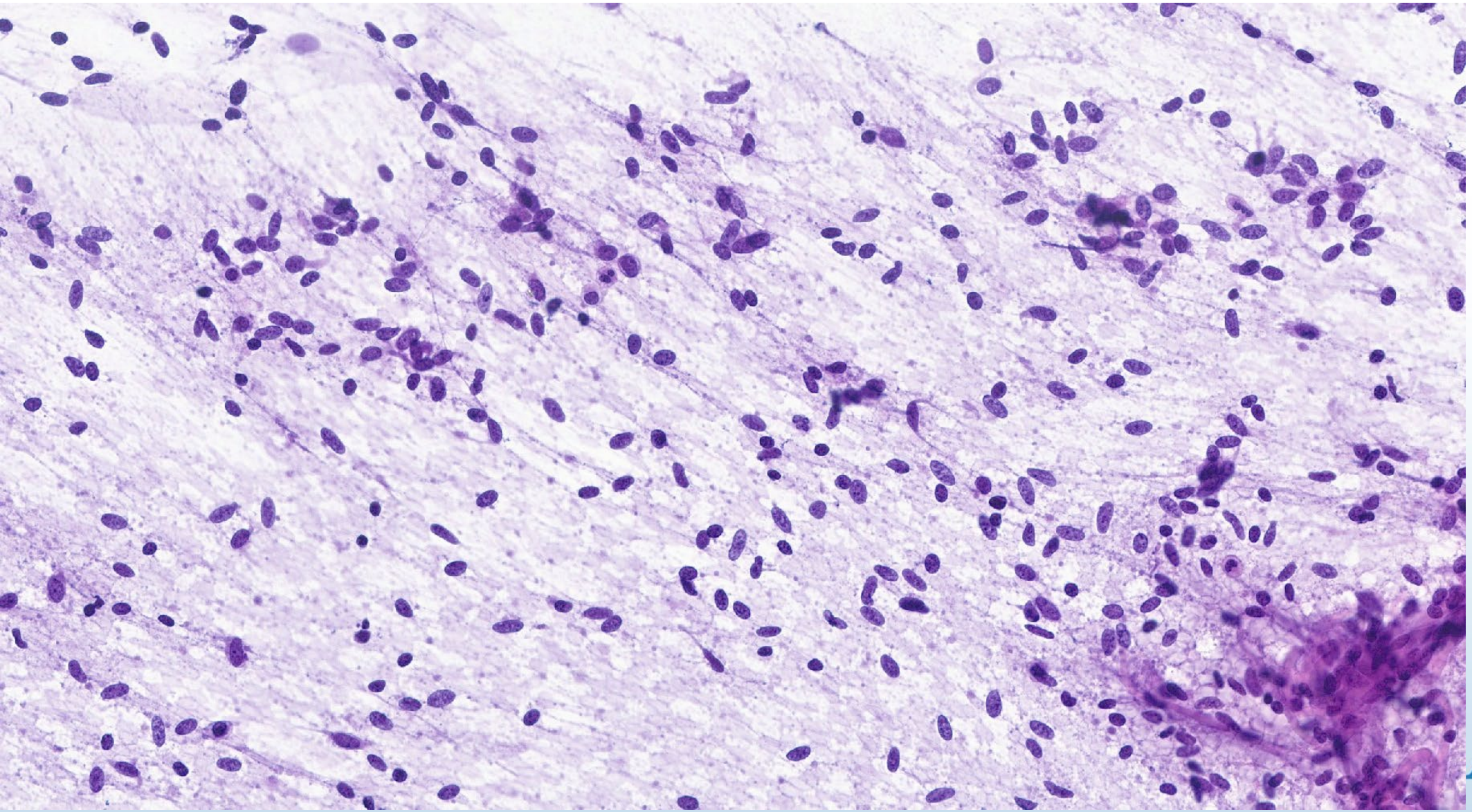


Smear

Solitary Fibrous Tumor

Smear

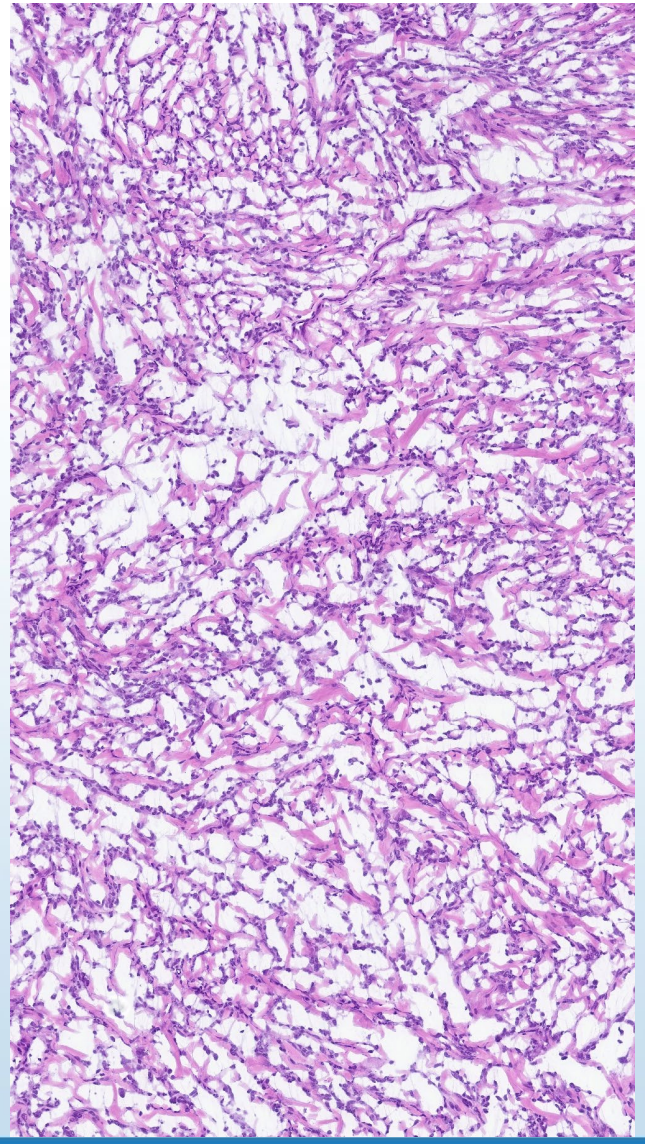
Solitary Fibrous Tumor



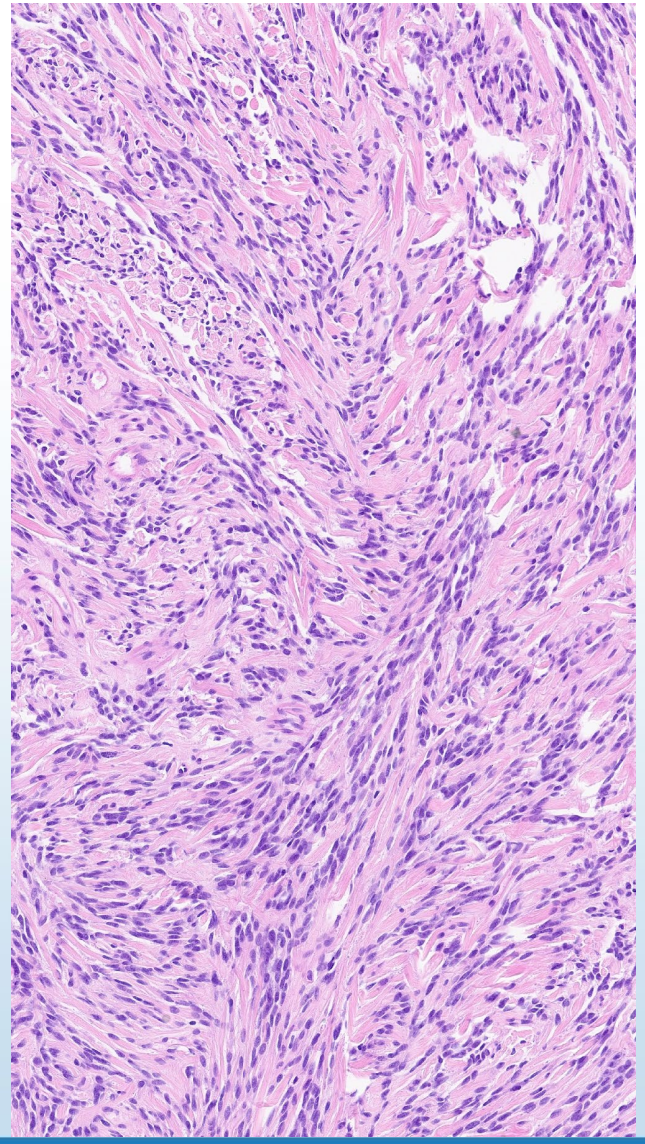
Smear

Solitary Fibrous Tumor

Frozen



FFPE



STAT6

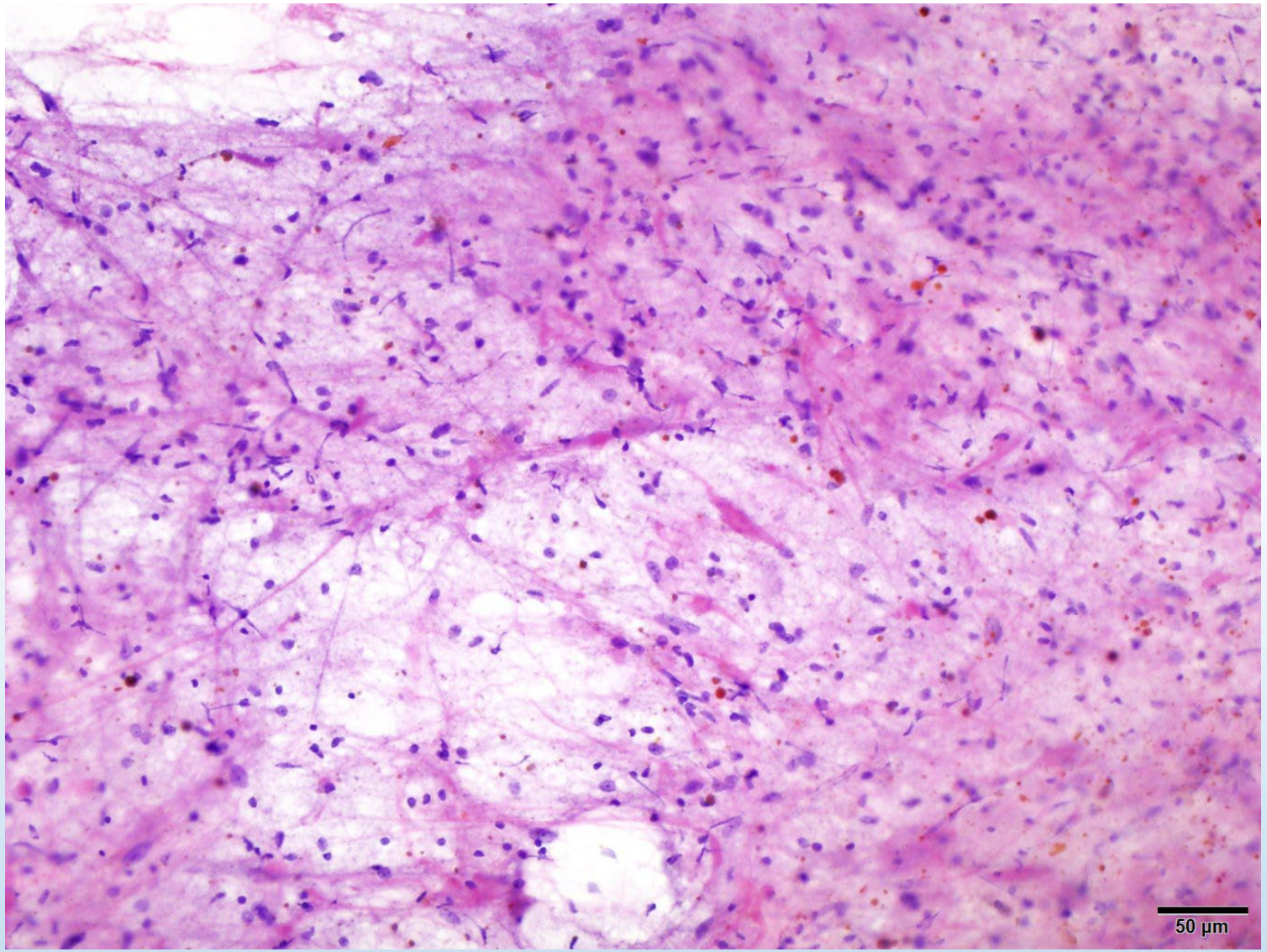
VIRTUAL SLIDE

- 55-year-old woman with intermittent left-hand numbness, weakness of left lower extremities and imbalance when walking, progressing for the last year.

- MRI shows a T2 hyperintense intramedullary lesion with possible enhancement at the C4-C6 region

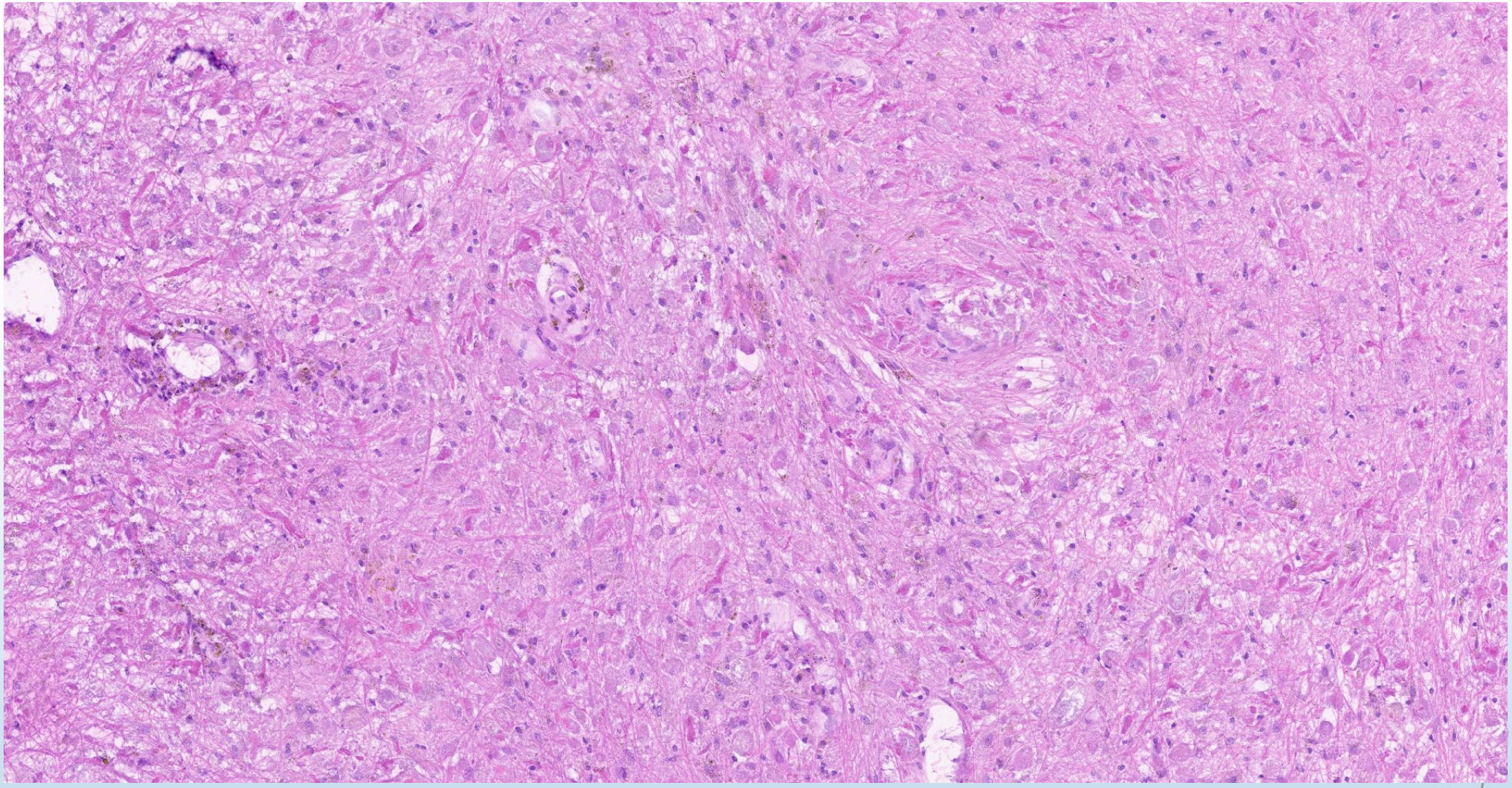
VIRTUAL SLIDE

Smear



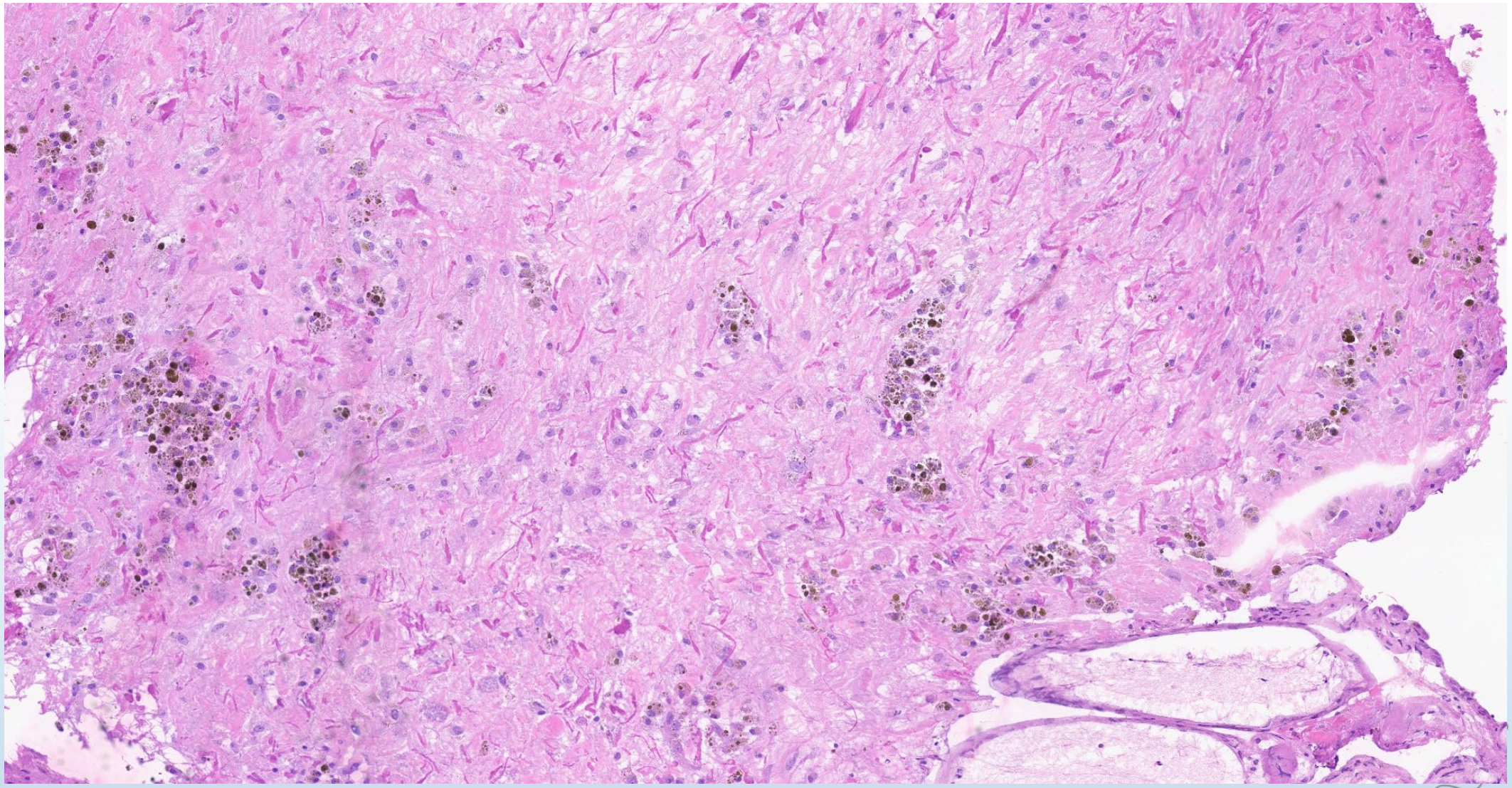
VIRTUAL SLIDE

Frozen Section

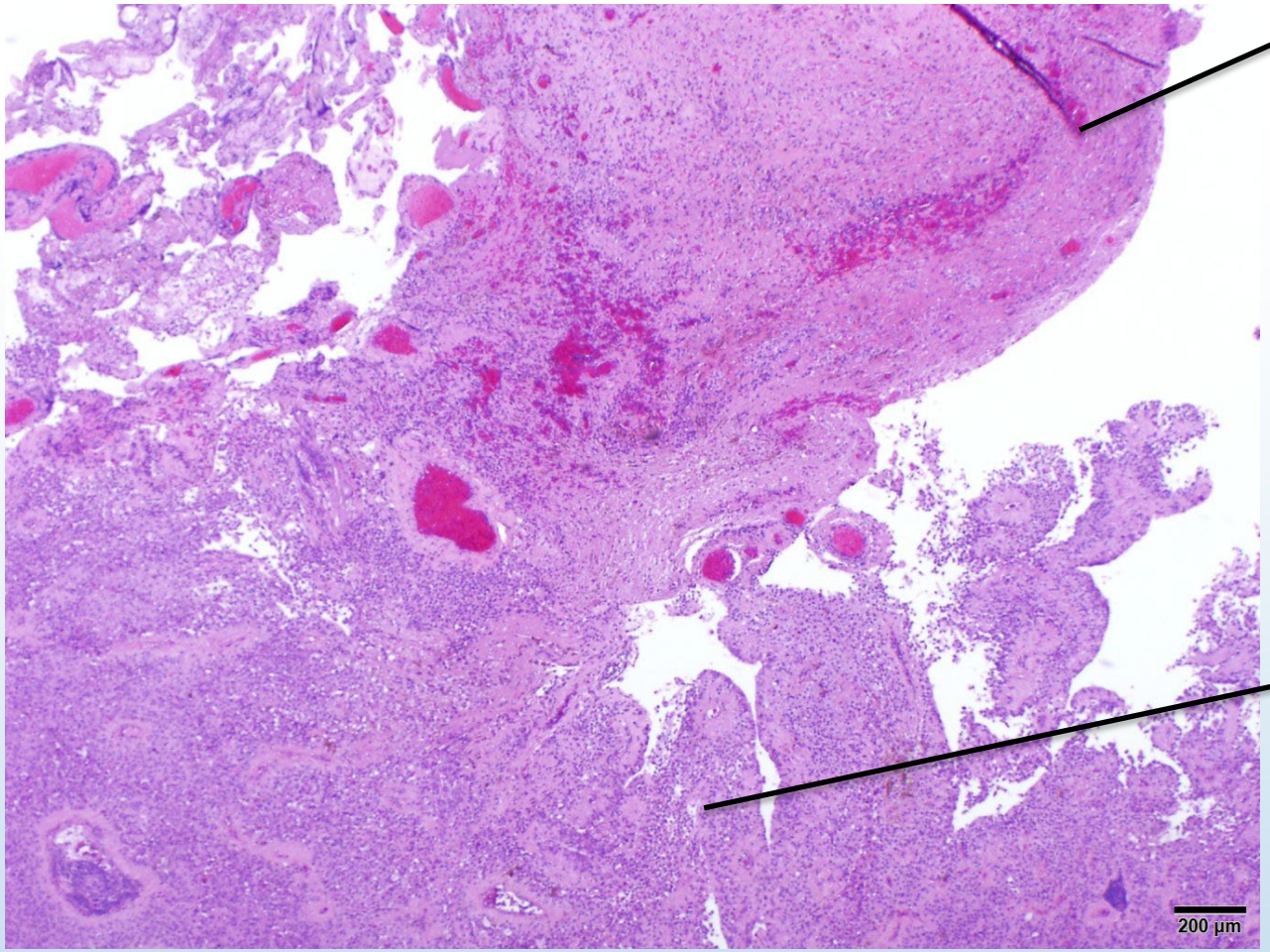


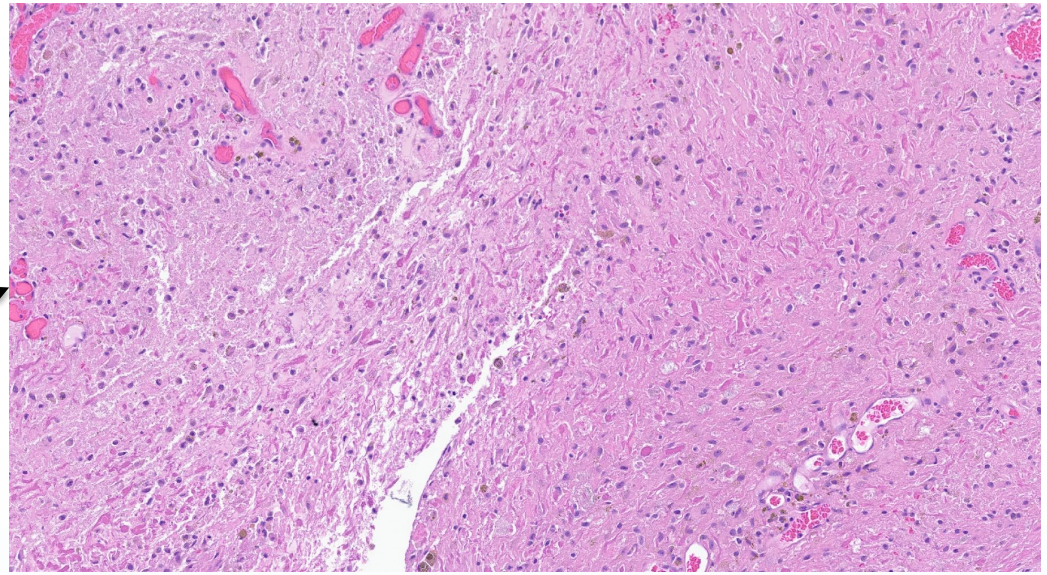
VIRTUAL SLIDE

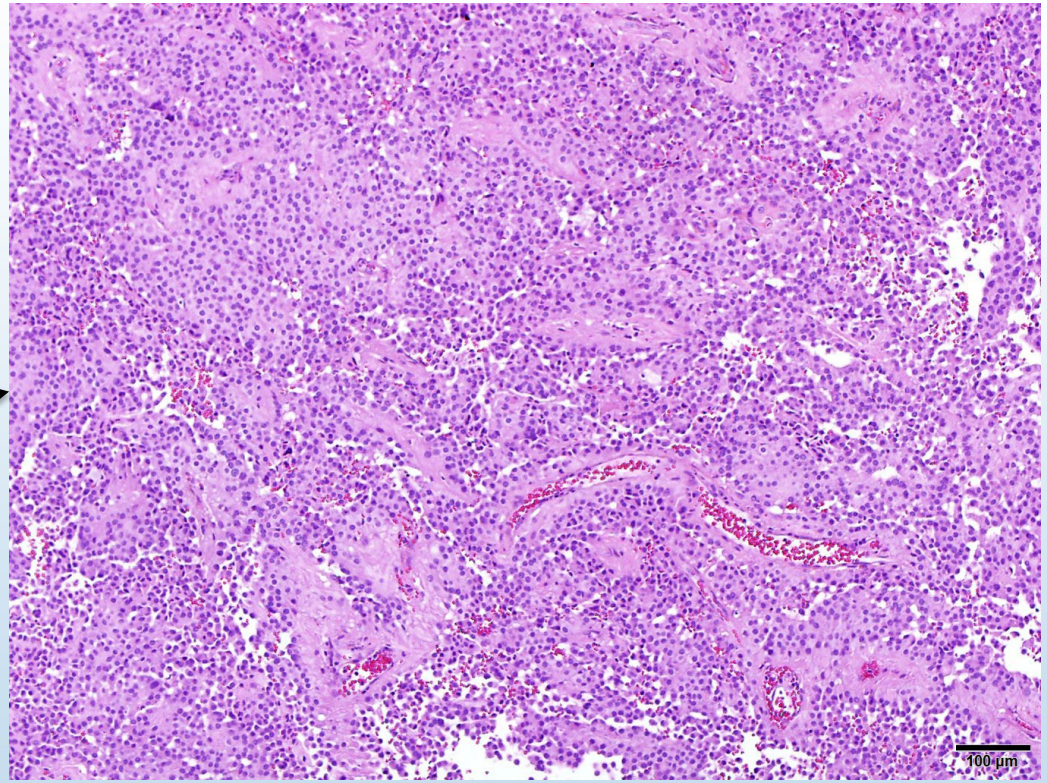
Frozen Section



Case for Virtual slide

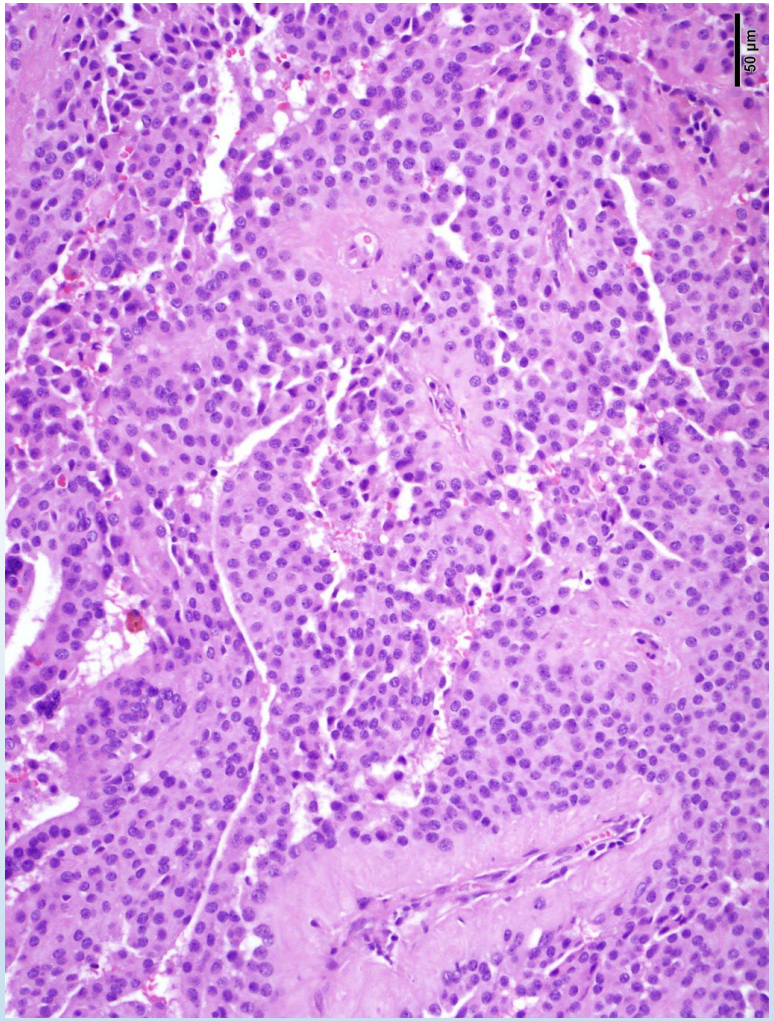




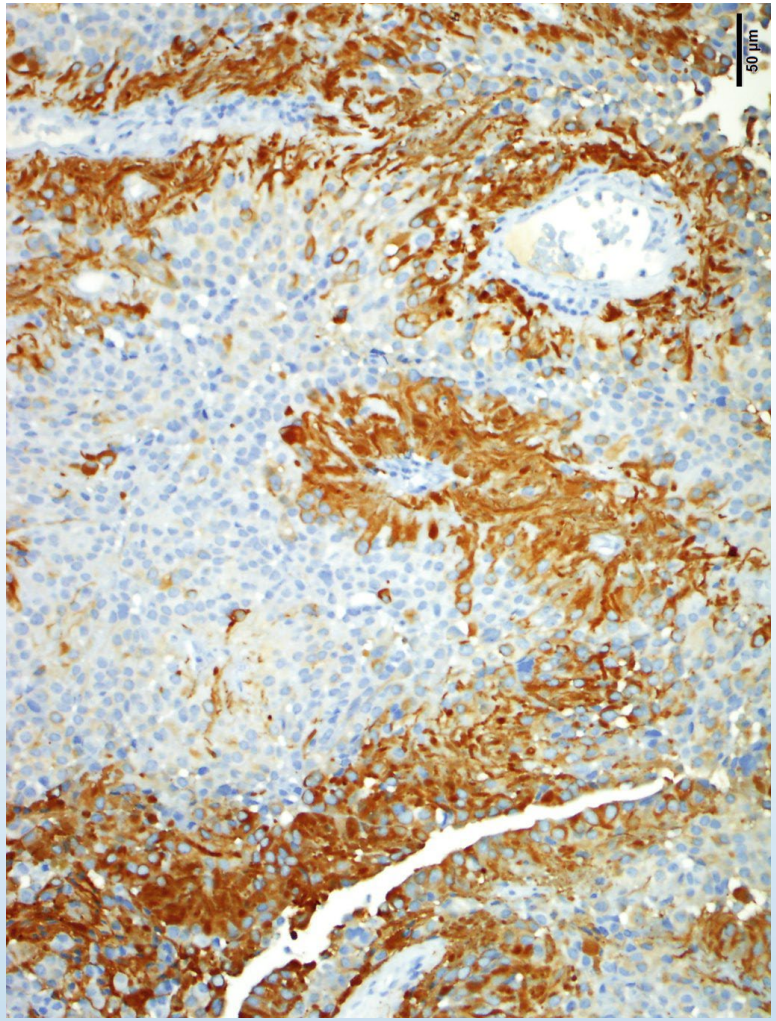


Case for Virtual slide

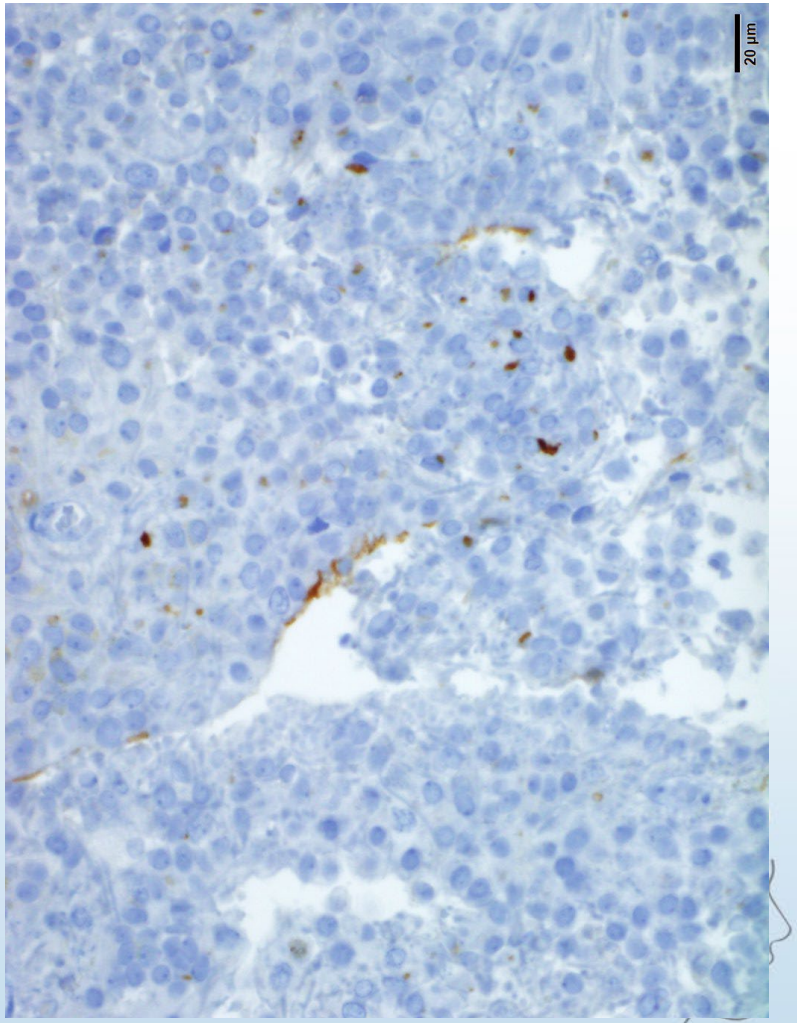
DX: Spinal Ependymoma



GFAP



EMA



Pitfalls to be aware of

Rosenthal Fibers (Piloid gliosis), around:

- Ependymoma (spinal)
- Vascular malformations (spinal)
- Pineal cyst
- Craniopharyngiomas
- Hemangioblastoma
- Third ventricle in Chordoid Gliomas
- Chronic glial scar (malformation, trauma, ischemia, epilepsy)

Macrophage rich lesion

- Infectious
- Demyelination
- Infarct
- Histiocytic lesion
- Renal cell carcinoma, clear cell type

Prominent inflammatory infiltrate

- Infectious
- Histiocytic lesion
- Germ cell tumor
- Recent tumor ablation (e.g. LITT, radiosurgery)

Differential Diagnosis by Anatomical Location

- Cerebello-pontine angle (CPA)
- Tectum/quadrigeminal plate/pineal region
- Sellar and suprasellar regions
- Thalamus
- Intraventricular
- Spinal Lesions
- Skull

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Cerebello-Pontine Angle Lesions

SAME C

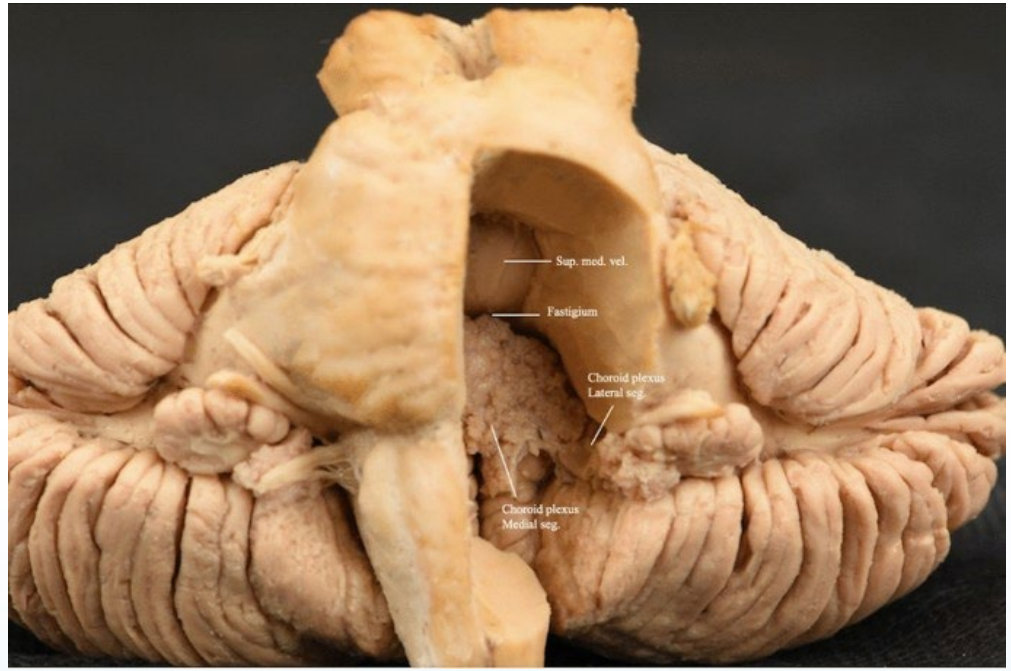
Schwannomas (8th >>> 5th CN)

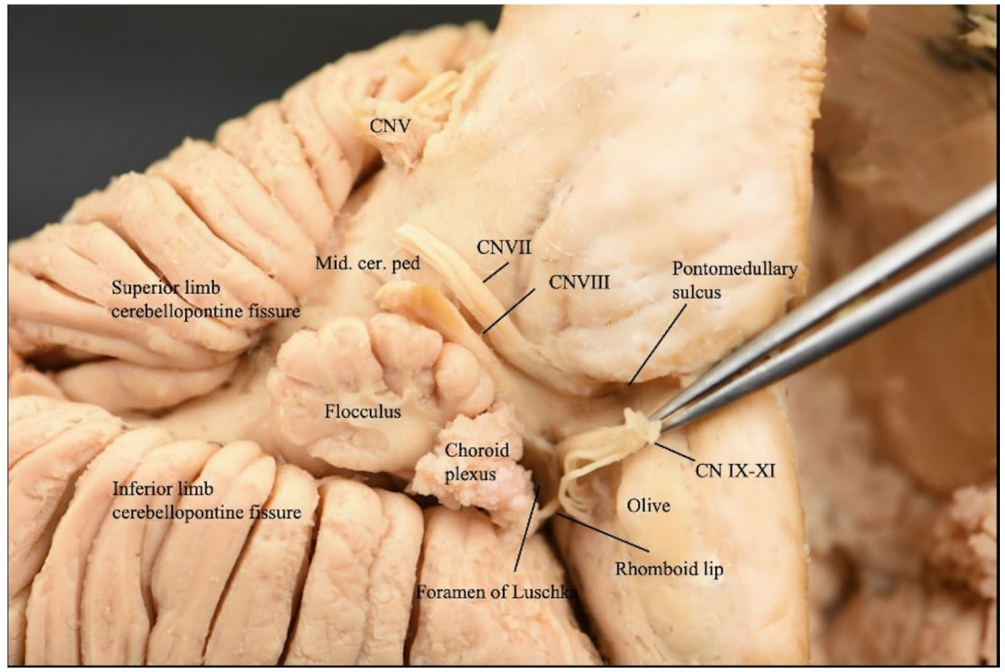
Arachnoid cysts, **A**neurisms

Meningiomas, **M**esenchymal T, **M**etastasis

Ependymomas, **E**pidermoid Cyst

Choroid Plexus Tumors

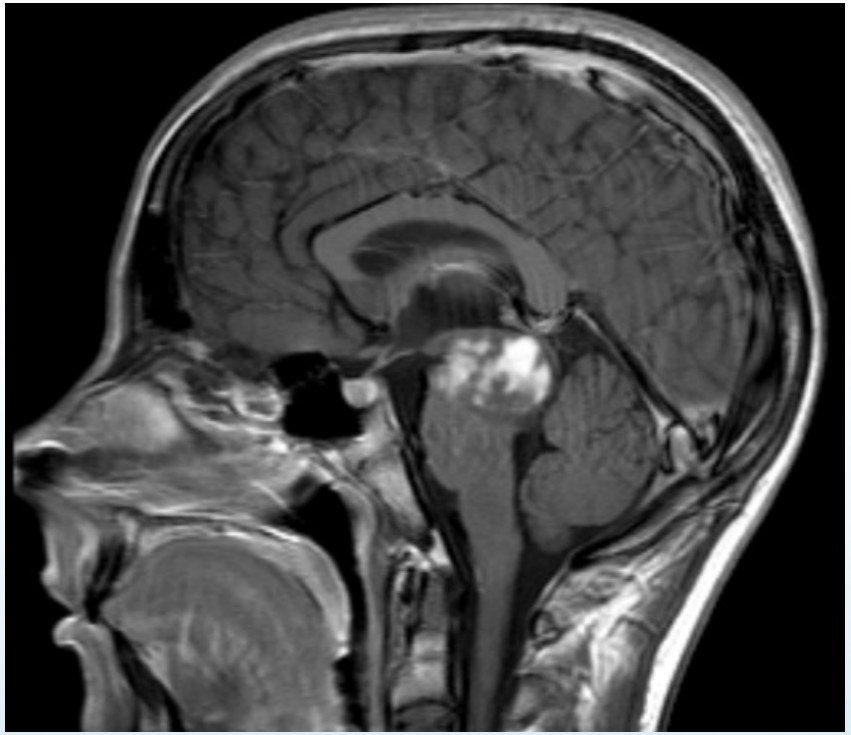


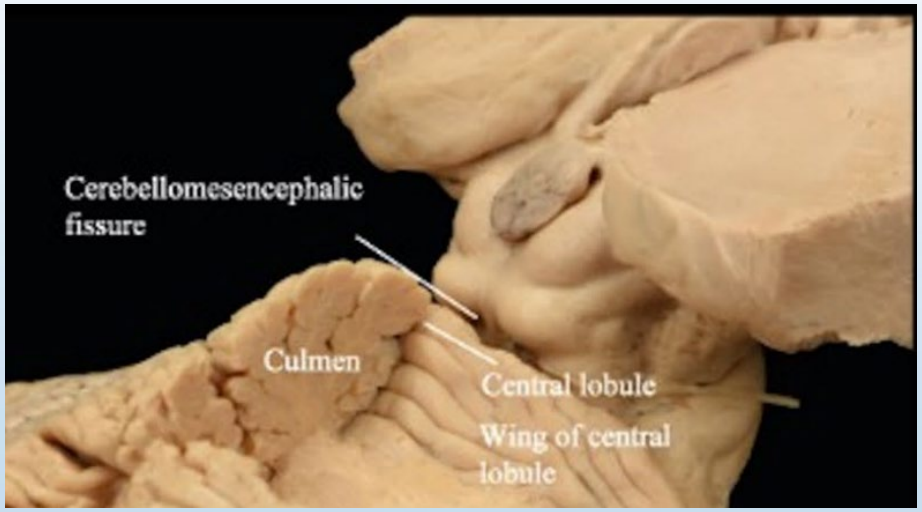


Formentin C, et al. Childs Nerv Syst. 2024
PMID: 37999790.

Tectal/Quadrigeminal plate/Pineal Region Lesions

- Midline gliomas
- Pilocytic astrocytoma
- Pineal Tumors
- Germ Cell Tumors
- RFGNT (4th V)
- Meningiomas
- Choroid plexus tumors
- Metastasis





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PMID: 37999790.

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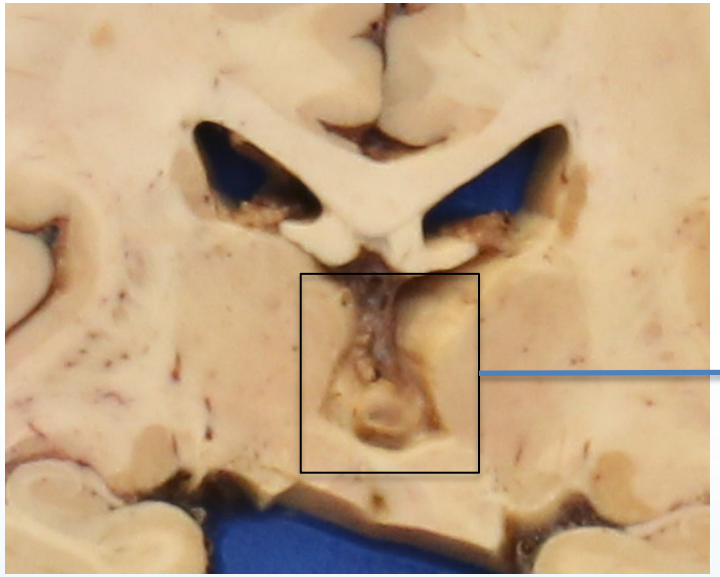
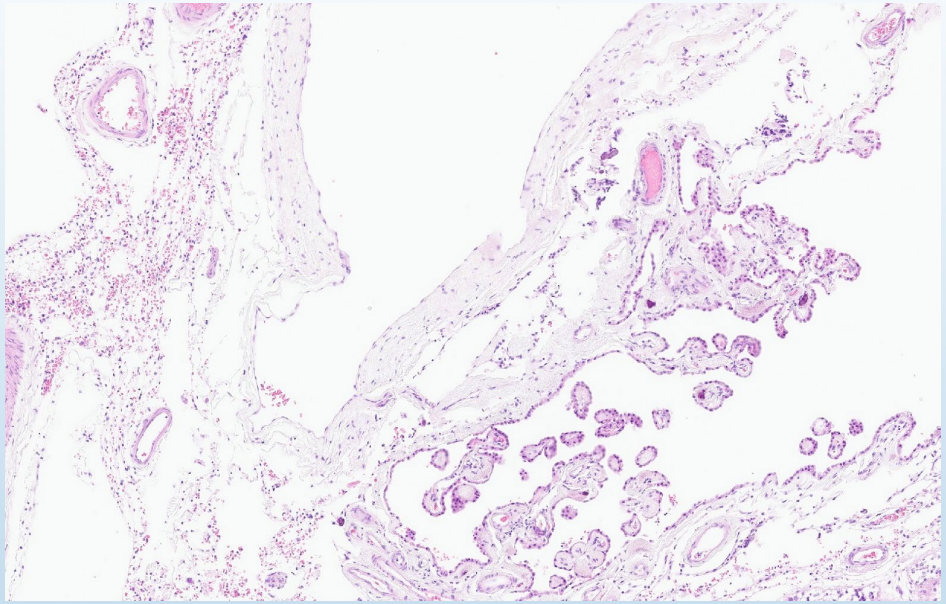
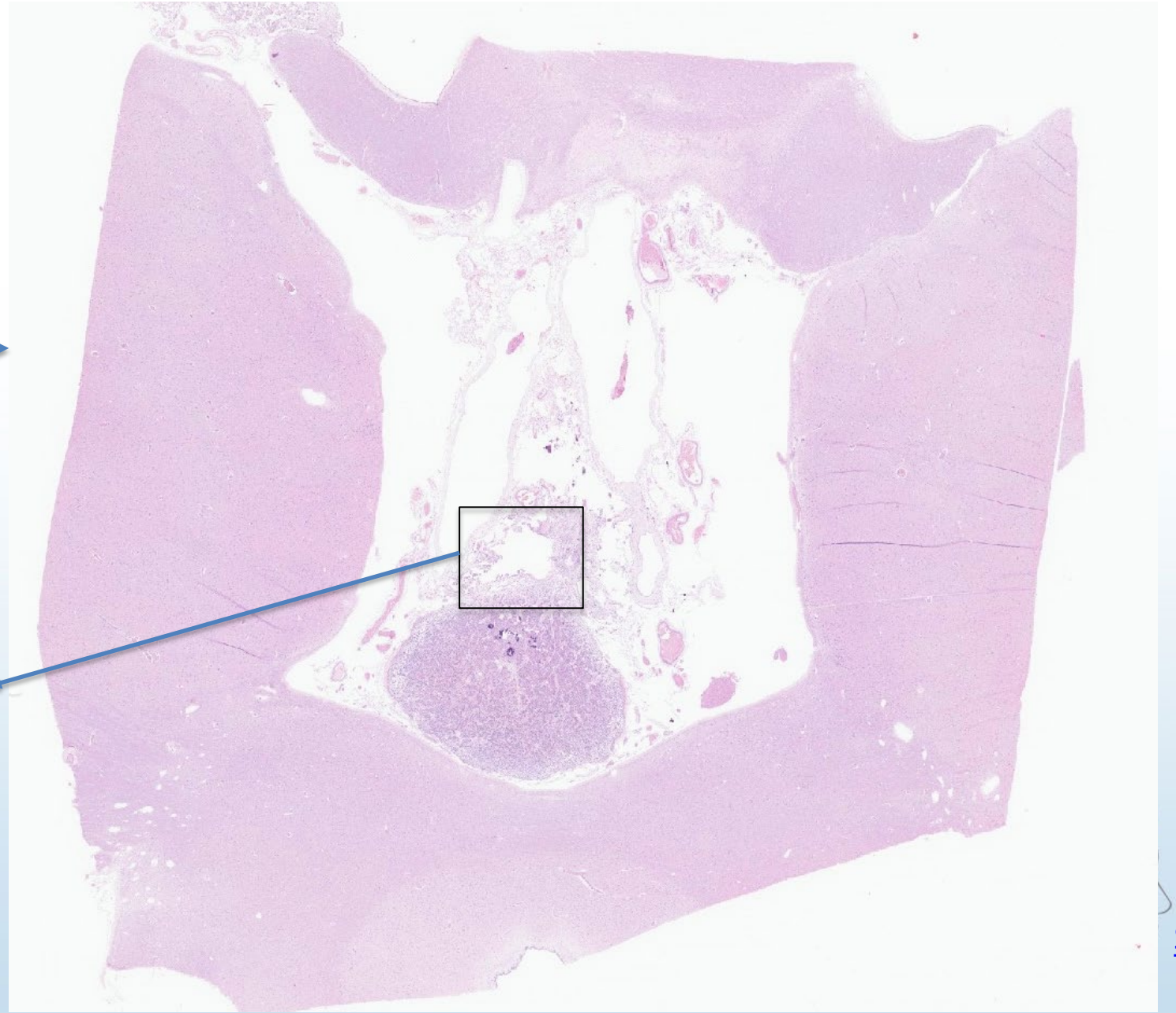
Tectal/Pineal Region

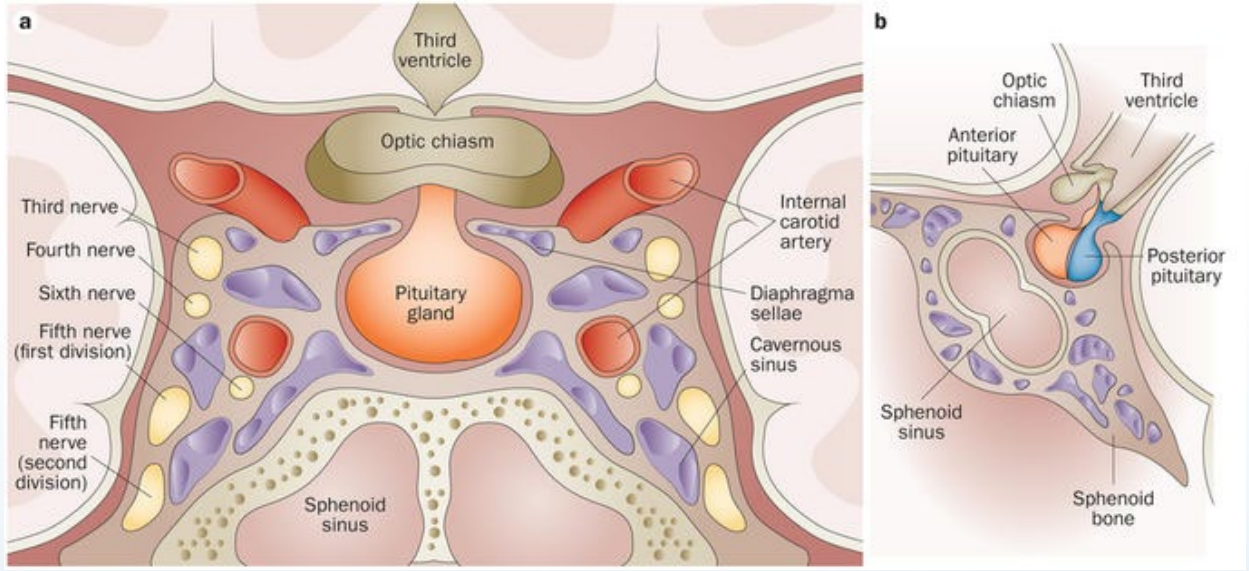






Sellar and Suprasellar Regions Lesions

- Pituitary tumors (anterior or rarely posterior)
- Rathke's cleft cysts
- Craniopharyngioma
- Germ Cell Tumors
- Metastasis
- Histiocytic Lesions
- Inflammatory
- Hematopoietic neoplasm
- Epidermal inclusion Cysts
- Mesenchymal Tumors (Chordoma, chondrosarcoma, etc.)



Classic clinical presentation: Blurry vision, headaches, bitemporal hemianopsia
Check for pituitary hormone levels
Check for germ cell markers in CSF
Age (e.g.: Child/YA Germ cell tumor)

Thalamic Region Lesions

High grade glioma	Rim enhancing Adult or pediatric
DLBCL	Rim enhancing Older Adult Check for immune suppression, primary, infectious or iatrogenic (drugs, post transplant)
Pilocytic astrocytoma	Cystic with a mural nodule Children or young adults
Germ cell tumors	Occasionally arise in the midline Children and Young adults Check CSF markers
Toxoplasma	Largely necrotic Immunosuppression
Hemorrhagic infarcts	Older adults, may mimic tumors

S

Intraventricular lesions

- Choroid Plexus Tumors
- Ependymal tumors
- Central neurocytoma (septum)
- Primitive Neuroectodermal Tumors (e.g. AT/RT)
- Intraventricular Meningiomas
- Myxoid Glioneuronal Tumor
- Metastasis
- Infections

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Spinal lesions

Intradural Intra-axial

- Ependymal
- PA
- Infiltrating gliomas
- PNST
- Hemangioblastoma
- Transverse myelitis
- Demyelination
- Infarct
- Metastasis
- Lymphomas

Intradural Extra-axial

- Meningioma
- PNST
- Chordoma, other Mesenchymal Tumors
- Histiocytic lesions
- Metastasis
- Lymphoma

Extradural-Extra-axial

- PNST
- Metastasis
- Lymphomas
- Ganglioneuromas
- Neuroblastomas
- Soft Tissue tumors

AANP S

Spinal lesions

Lower Spinal Cord/Conus Medullaris/Filum terminale/Cauda Equina

- Peripheral Nerve Sheath tumors(Schw, NF, Hybrid, Perineurioma, MPNST)
- Meningioma (Clear cell)
- Ependymoma (Classic or MPE)
- Gliomas (PA or infiltrative)
- Cauda equina NECT (Previously known as paraganglioma of the SC)

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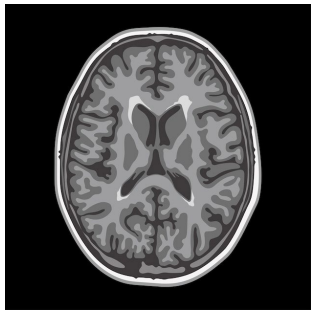
Skull

- LCH (Children) or other histiocytosis
- Plasmacytoma
- Hemangioma
- Meningioma
- SFT
- Metastasis

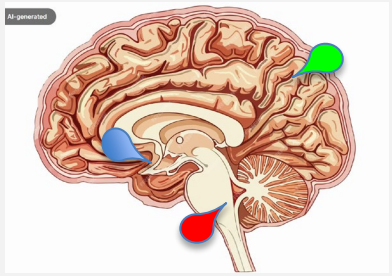
Summary

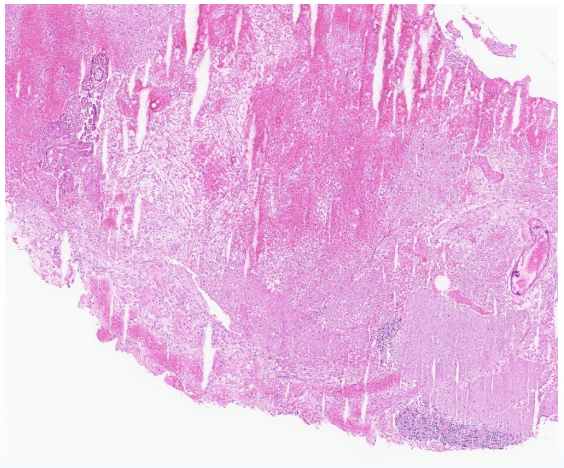
Review clinical history prior to IOC

- Age
- Main clinical presentation
- Radiologic findings

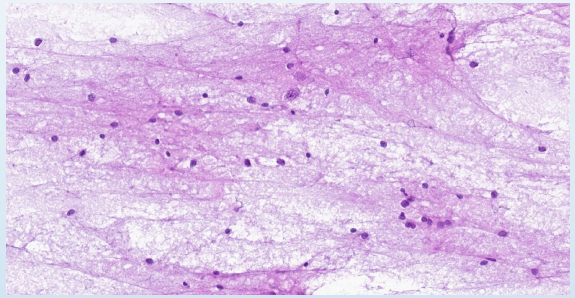


Location, Location , Location!



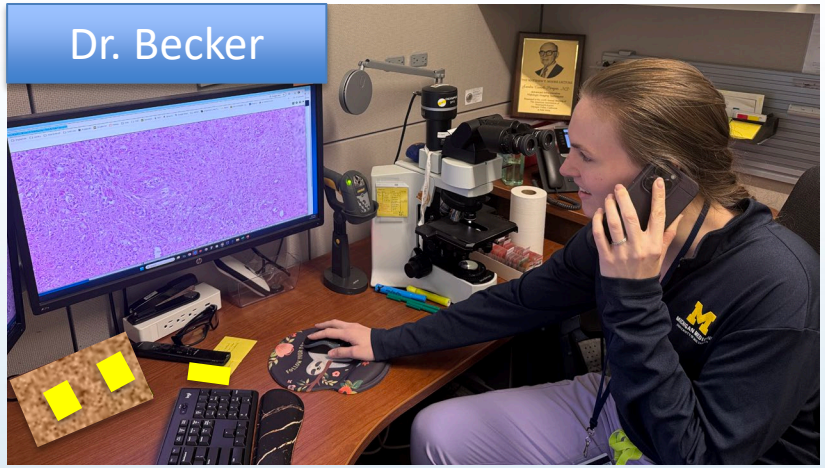


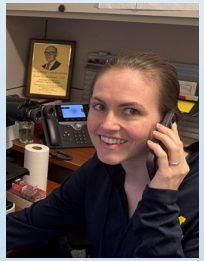
Formulate a DDX



- Report only what you see
- Are you answering the clinical question?
- Do you need more tissue?

Dr. Becker





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