CENTRAL NERVOUS SYSTEM (5): NEOPLASIA

Relevant Chapter 28 Robbins Problems: 5, 15, 18, 25, 35, 40, 42, 43, 45, 46, 58, 59, 60, 68

APPROVED

Neoplasia: Pathologic and Clinical Effects

- Mass Effects
- Seizures
- Focal Neurologic Deficits

Although you may have a benign tumor, its size and location can cause many symptoms (mass effects). Sometimes patients may have huge tumors, yet present with minimum symptoms.

mimicking a stroke

CNS Tumors tend to follow epidemiologic and anatomic patterns

- Intracerebral — aka intraaxial or intramedullary tumors
- Ventricular
- Posterior fossa ← most likely in children!
  - Cerebellum
  - Brainstem
  - Ventricular
- Spinal cord
- Meningeal — aka dural tumors
- Cranial Nerve/Nerve Root — similar to tumors of the peripheral nerves either intracranial or intraspinal

TUMORS

add "oma" !

- Glial cells
  - Astrocytomas
  - Oligodendrogliomas
  - Ependymomas
- Neurons
  - Gangliogliomas
  - Medulloblastomas
  - Neurocytomas
- Others
  - Schwannomas
  - Meningiomas

there is also a neurofibroma

CNS Tumors tend to follow epidemiologic and anatomic patterns

X axis = age
Y axis = location
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use this as a strategy for the most common tumors for age/ location

- Childhood locations:
  - Posterior fossa
- Childhood tumors:
  - Cerebellum
  - Brainstem
  - IV Ventricle

CNS Tumors tend to follow epidemiologic and anatomic patterns

- Young Adult Locations
  - Midline or periventricular
- Young Adults tumors (low grade)
  - Cerebellum
  - Brainstem
  - Hypothalamus
  - Temporal Lobes

CNS Tumors tend to follow epidemiologic and anatomic patterns

- Except Older Adult Tumors
  - Metastatic tumors
  - Parenchymal
  - Ventricular
  - Dural
  - Spinal Cord
    - Intramedullary
    - Extramedullary
  - Lymphoma

Older Adult brains are destroyed by metastatic tumors, especially when the lesions are multifocal or diffusely located in the brain

WHO Grading of Primary CNS Tumors

- Grade I - > 10 year survival untreated
- Grade II – 5 to 10 year
- Grade III – 3 – 5 year
- Grade IV - < 3 year

- Only a few CNS tumors have I –IV examples

Learn the WHO system! High grade tumor = very malignant (grades III and IV). Not all tumors have all grades ie oligodendroglioma only has grades II-III. Astrocytomas are one of the only brain tumors to encompass all four grades.

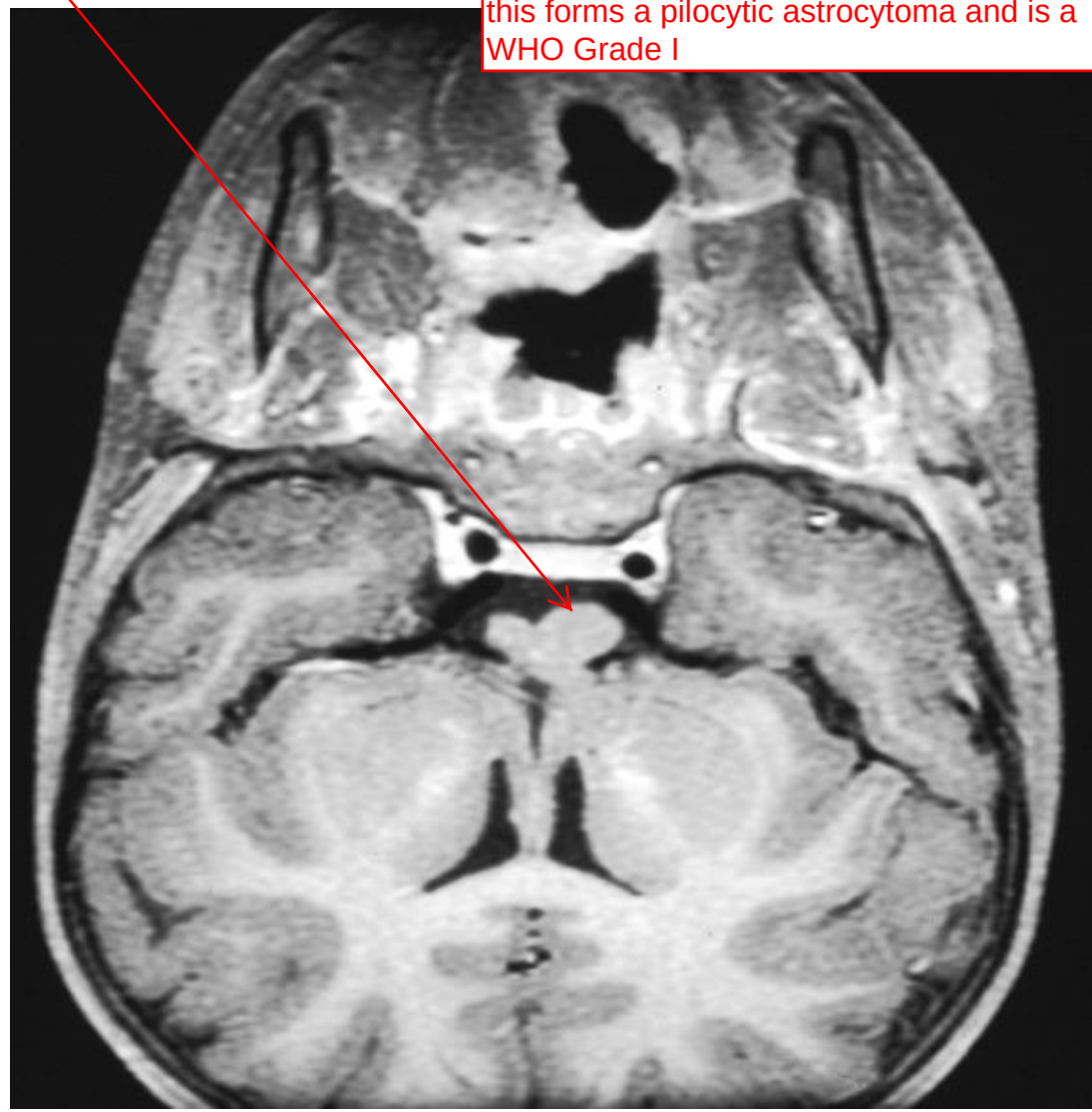
Parenchymal Tumors
- Gliomas

- Astrocytoma (Grades I-IV)
- Oligodendroglioma (Grades II-III)

Parenchymal tumor

Case 1

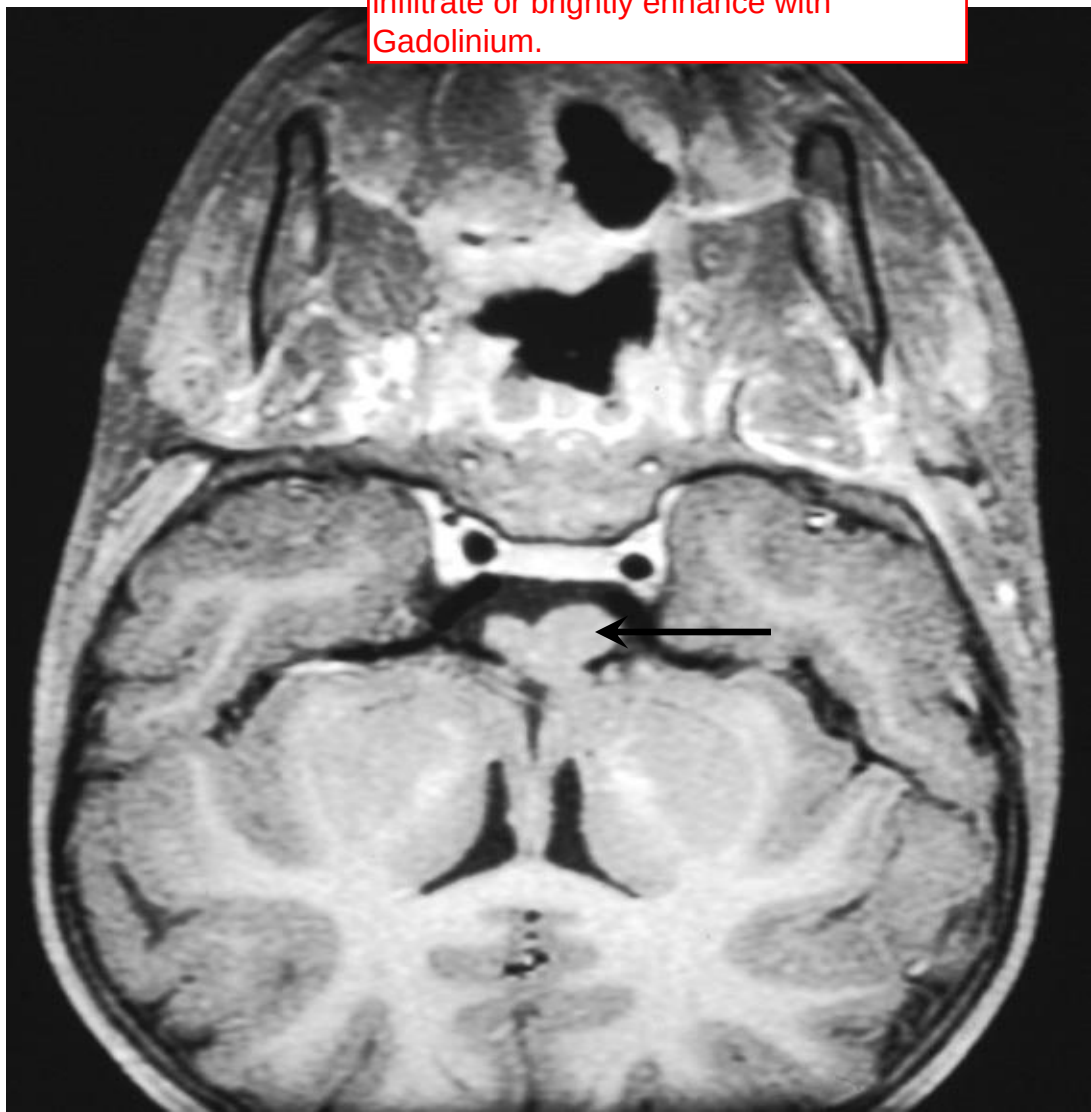
- 12 year old boy with family history of Neurofibromatosis Type 1 now with diminished vision in left eye.
- MRI scan performed



Pilocytic Astrocytoma

think MIDLINE. occurs in spinal cord, brainstem, cerebellum and optic nerve and periventricular (around the ventricles of the temporal lobes) locations. do not infiltrate or brightly enhance with Gadolinium.

- Pilocytic Astrocytomas (WHO Grade I)
- Occur in the optic nerves, cerebellum, brain stem, or temporal lobes
- Children and young adults
- Well circumscribed with little tendency to infiltrate
- Component of NF1

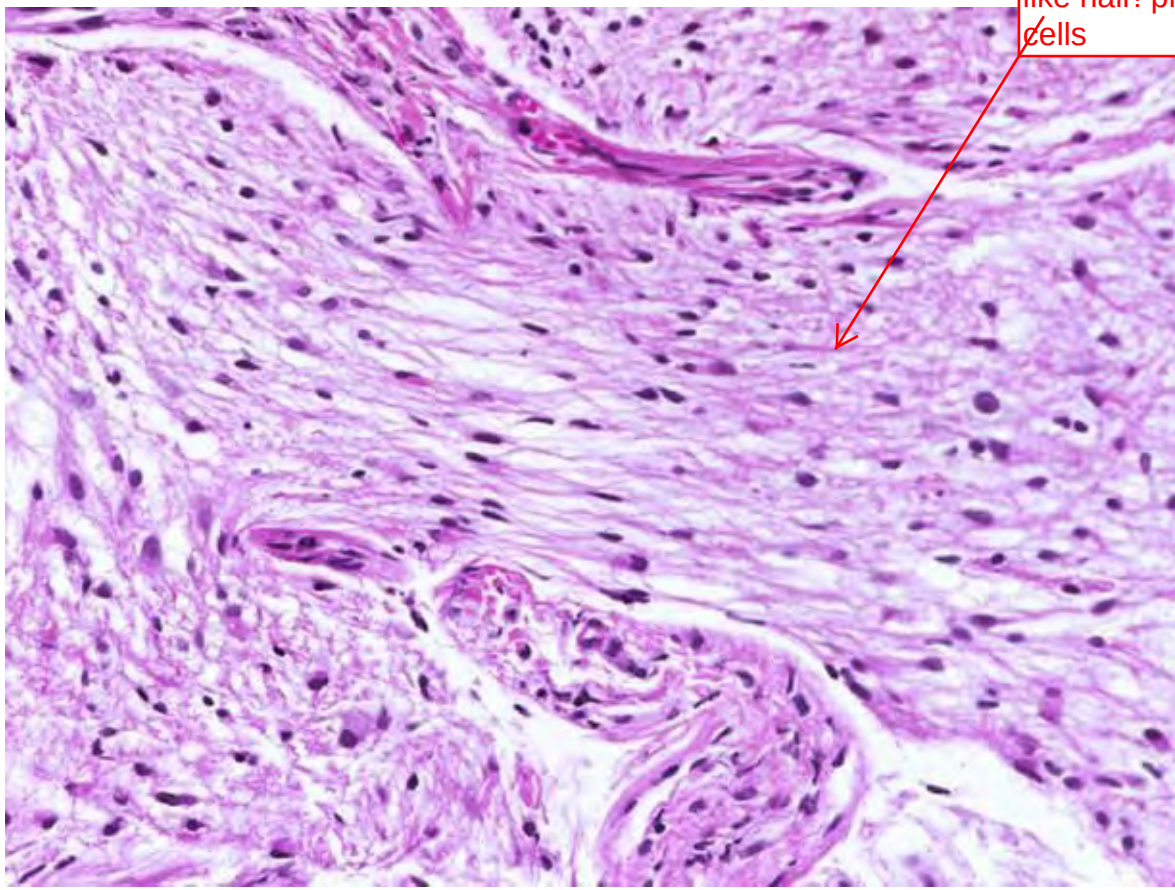


Pilocytic Astrocytoma

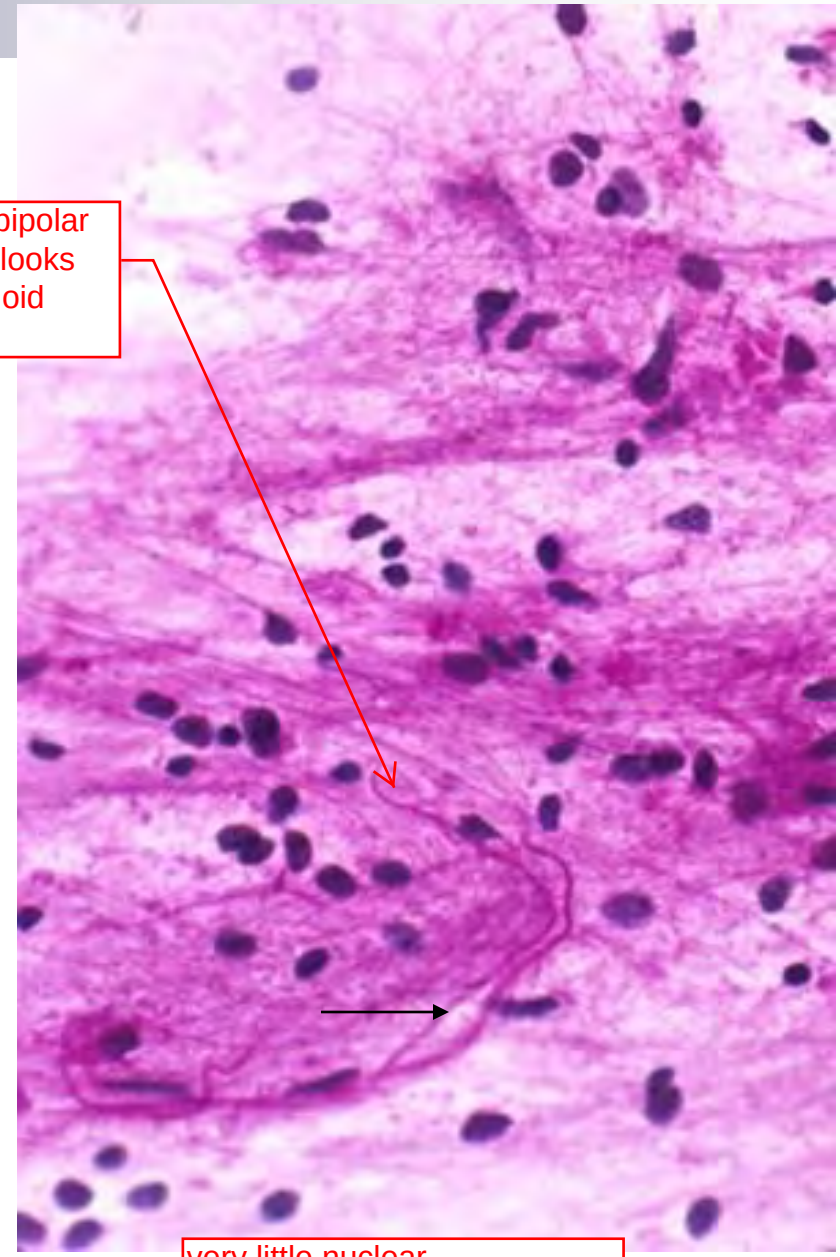
- Radiographically, the tumors are sharply circumscribed.
- The consequence of these characteristics is that tumors arising in the temporal lobe and cerebellum are frequently cured by surgical excision.
- Surgical excision of lesions in the optic chiasm and hypothalamus may produce unacceptable neurological deficit.

have to consider the location/ histology! you do not want to remove this benign tumor if in the process you will destroy parts of the brain that would prevent the individual from functioning normally

- Pilocytic astrocytoma of the optic nerve



Skeins of hair-like processes



Pilocytic Astrocytoma

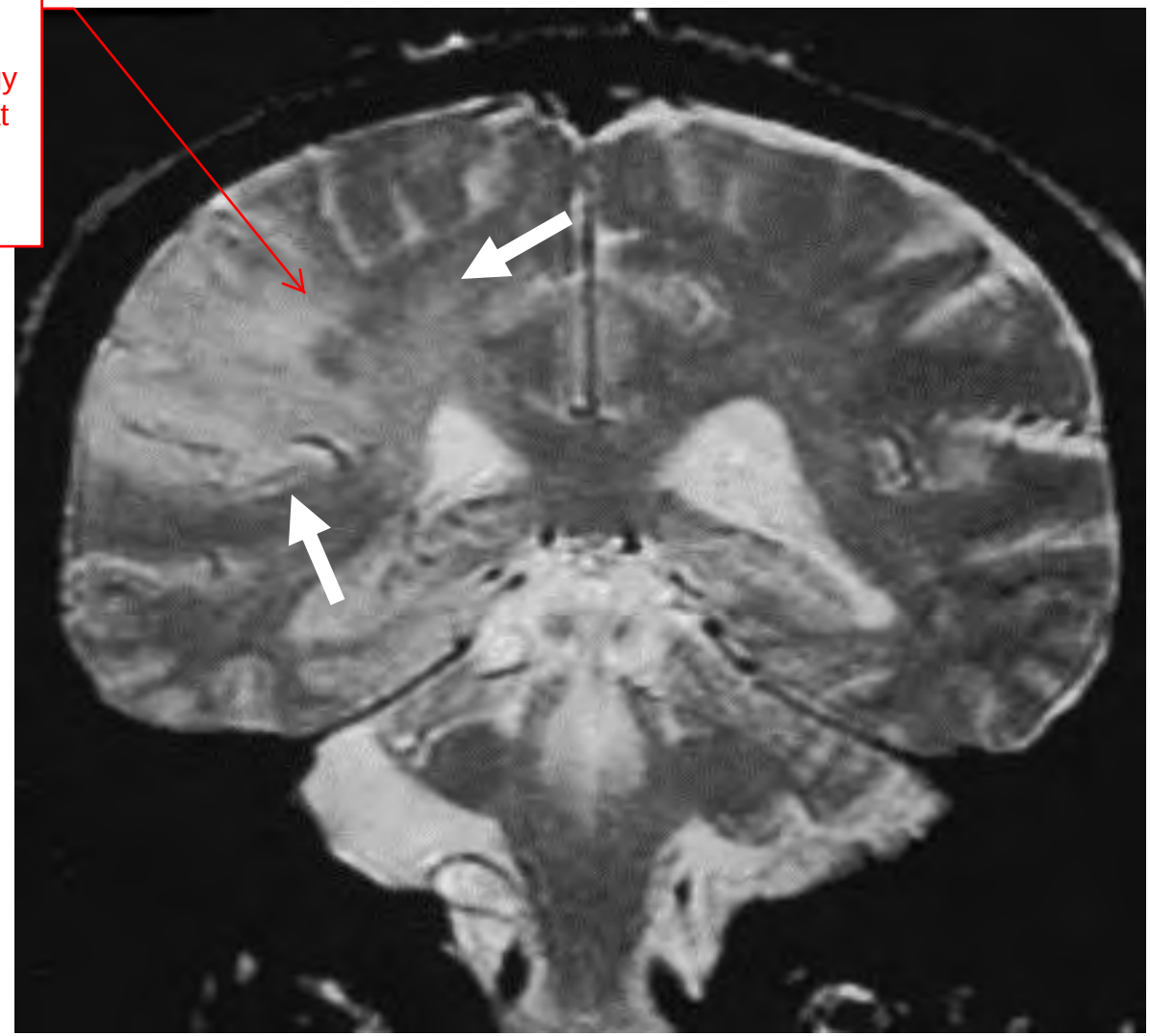
- Arise from a piloid astrocyte that is predominately located along the midline (spinal cord, brainstem, cerebellum, hypothalamus).
- These tumors show little invasiveness, are slowly growing, and show little tendency to become more malignant with time.

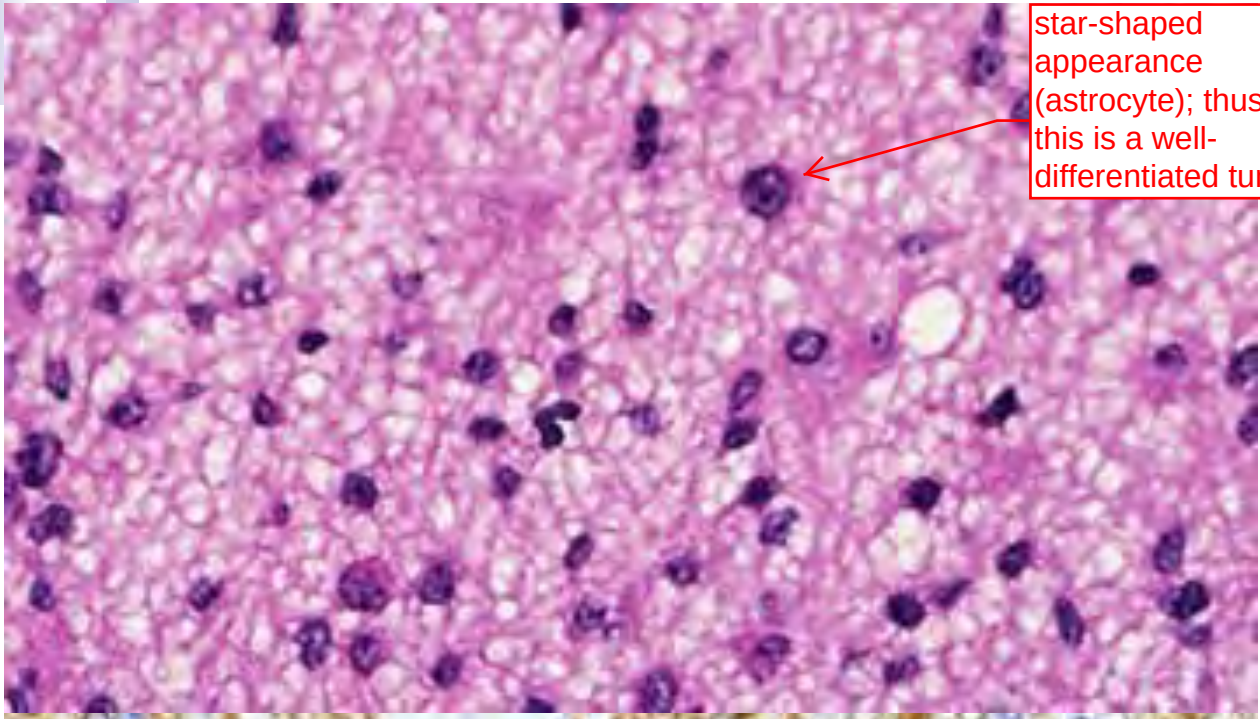
Astrocytic Tumors

- Circumscribed
  - Pilocytic Astrocytomas (WHO Grade I)
- Diffuse
  - Well Differentiated (Grade II)
  - Anaplastic Astrocytoma (Grade III)
  - Glioblastoma (Grade IV)

Case 2

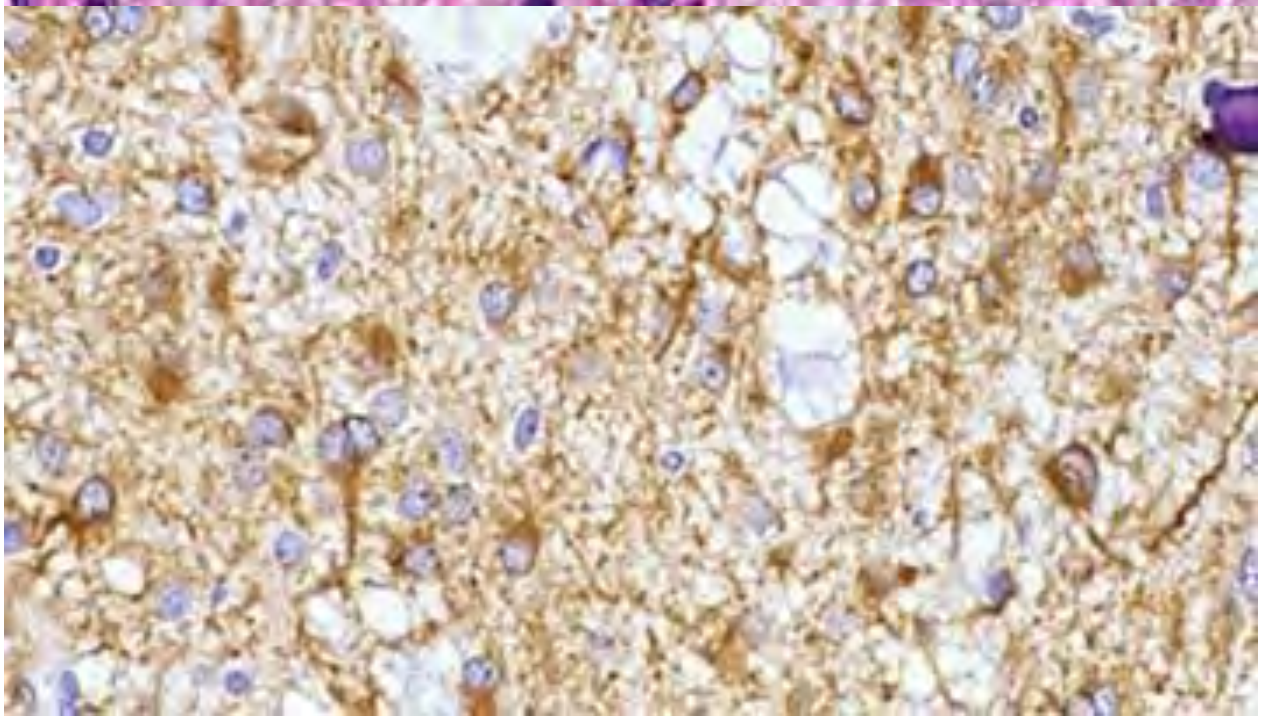
- 30 year old female who has chronic headaches and recently developed seizures





Diffuse Astrocytoma

- The lesion is an ill-defined area of well differentiated neoplastic cells that closely resemble normal fibrillary astrocytes.

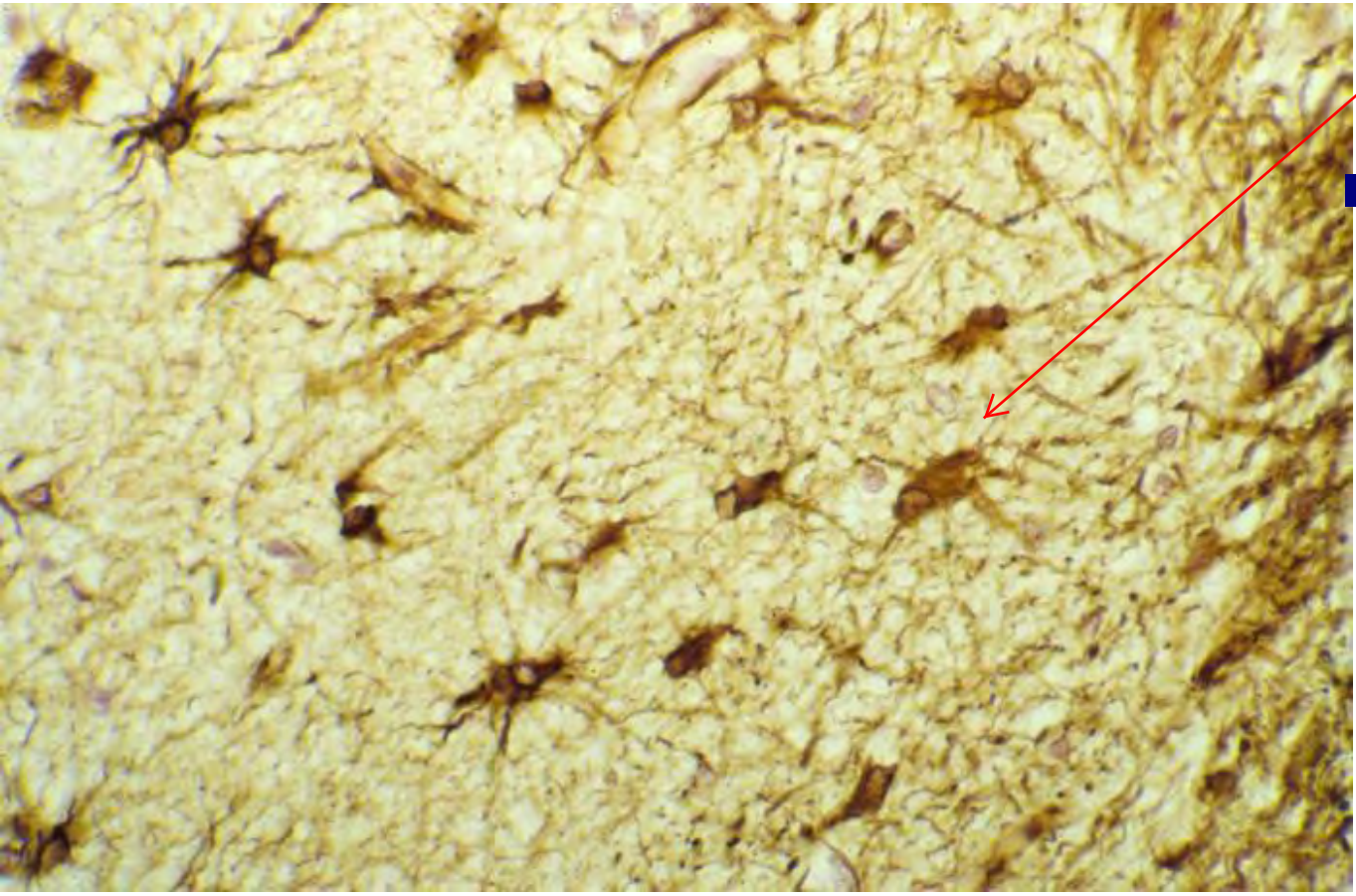


H&E

GFAP

glial fibrillary acid protein stain highlights the fibrillar processes found in the astrocyte

Fibrillary Astrocytoma



Reactive astrocytes

- Arise from the fibrillar, or stellate, astrocyte within the white matter of the brain and spinal cord.

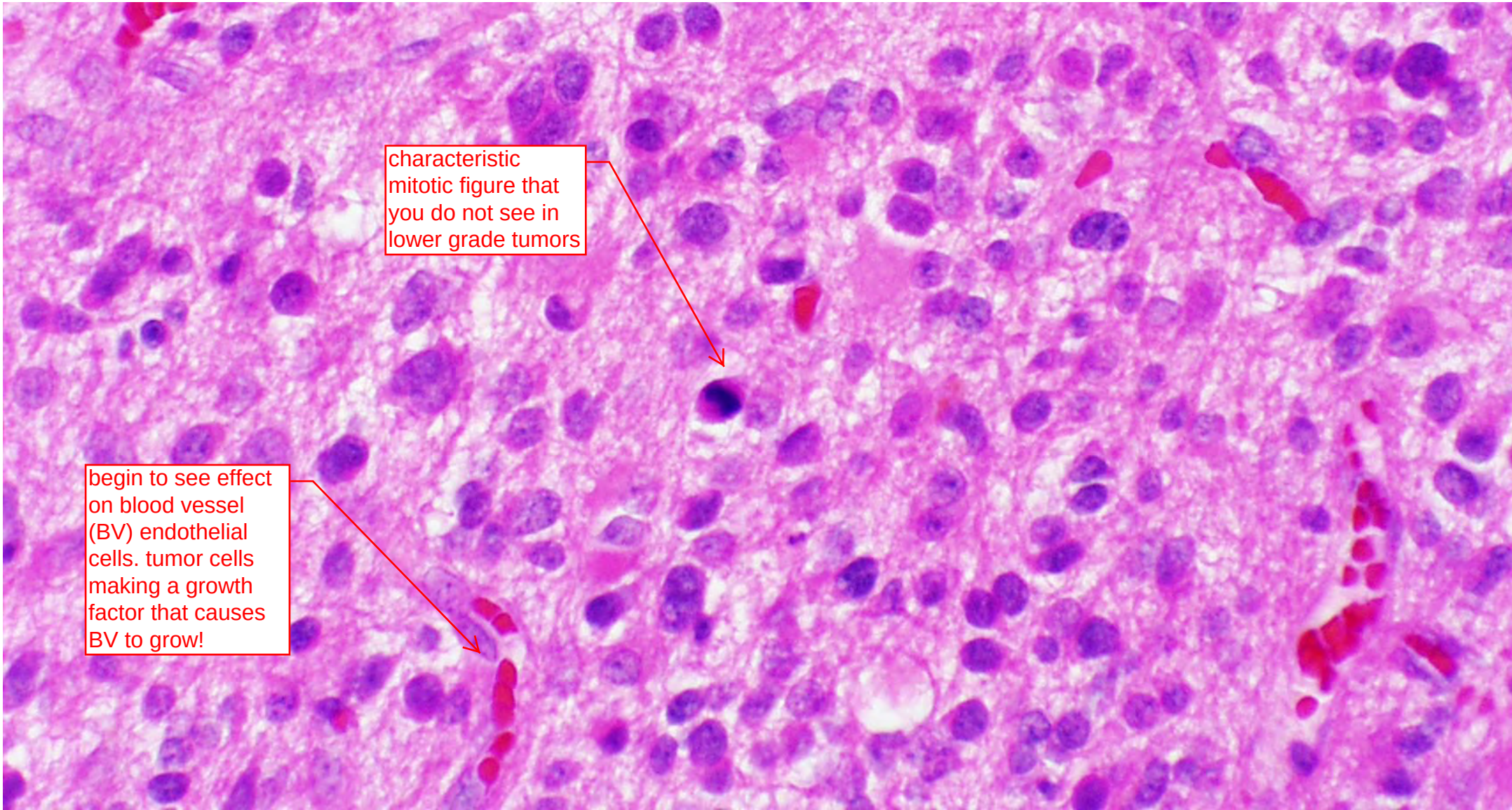
GFAP

Well-Differentiated Astrocytoma

has the ability to progress to a higher tumor grade (grade III and IV)

- In spite of the well differentiated nature of the lesion, the position of the tumor and its ill-defined diffuse growth pattern generally prevents complete resection.
- Prognosis is grim, survival usually only five to ten years
- Strong tendency for the lesions to progress in biologic malignancy in adults

Anaplastic Astrocytoma



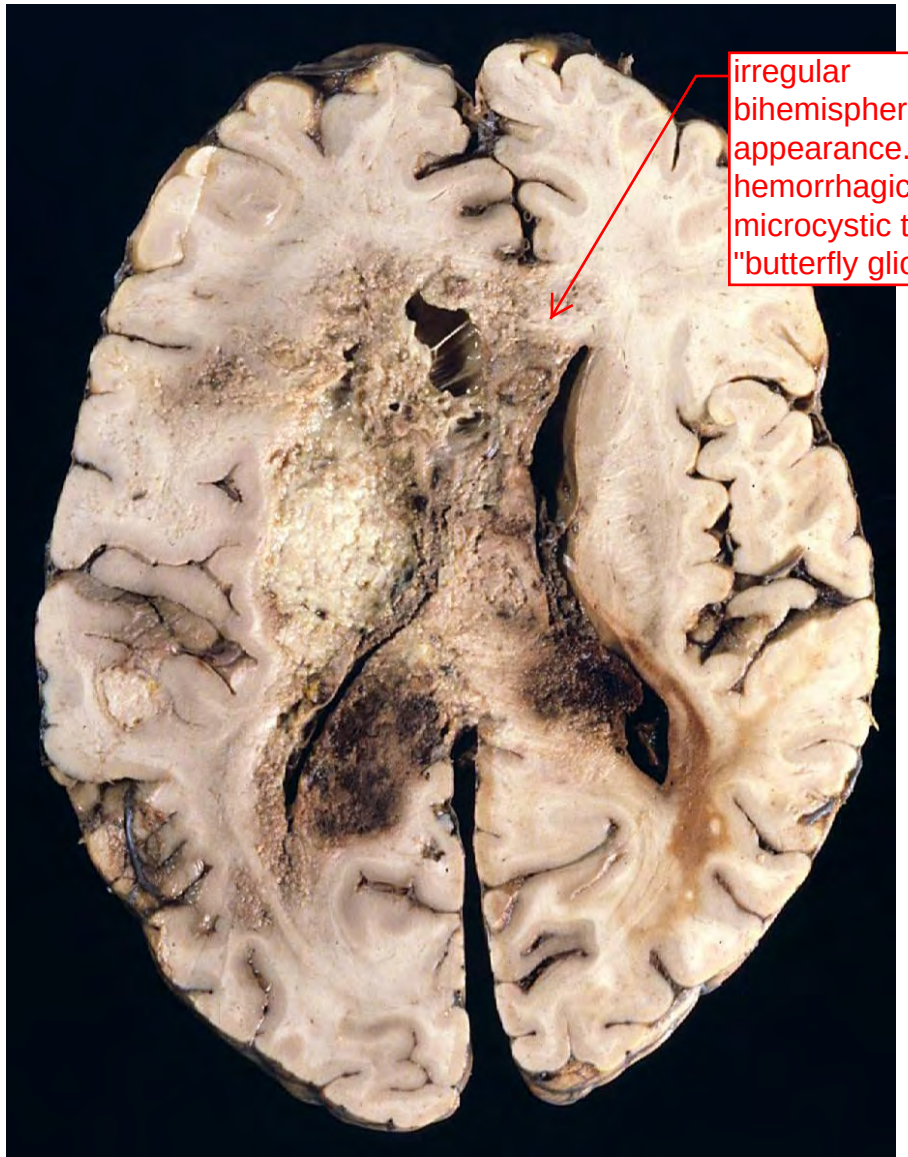
Anaplastic Astrocytoma (Grade III)

- Typically presents in fifth decade
- The neoplastic cells are more numerous, more pleomorphic, and more often found in mitotic division. Vascular proliferation may also be found.
- The survival is generally three to five years

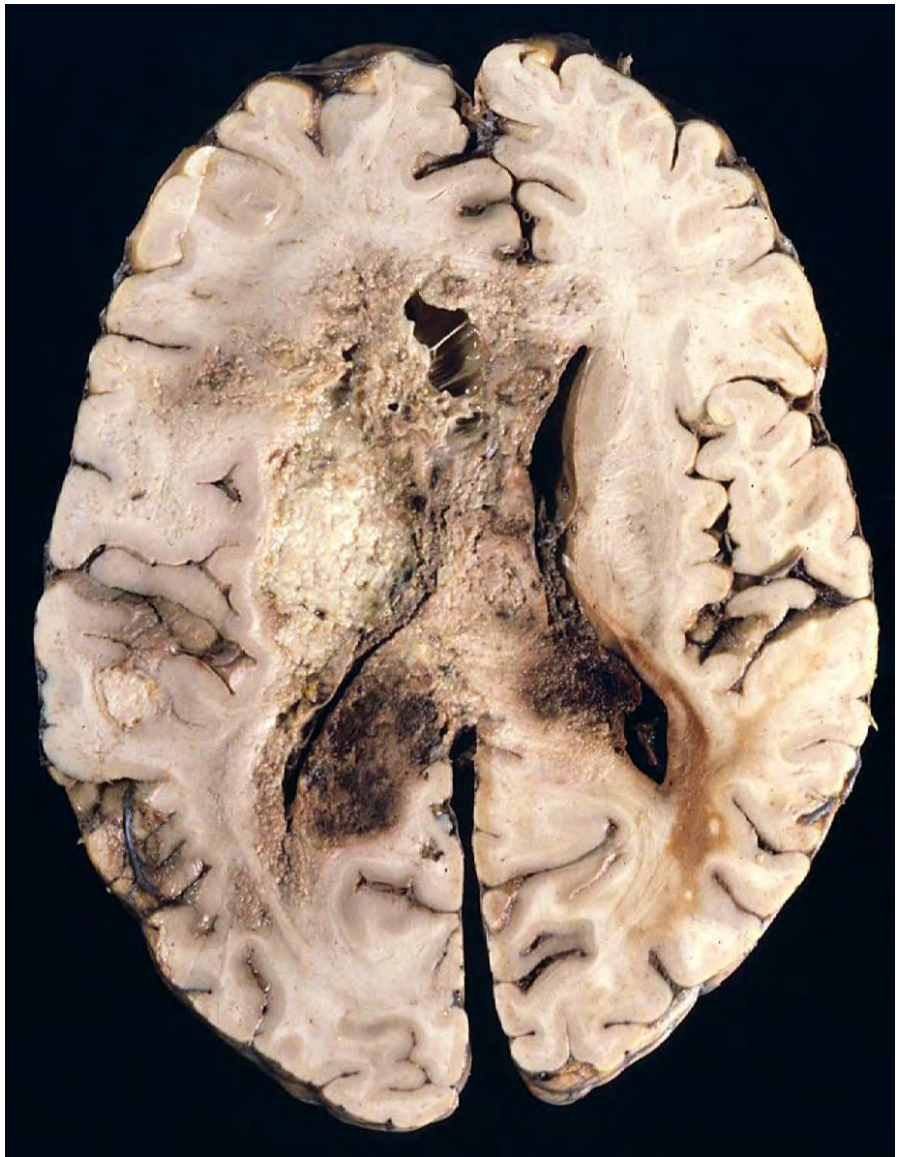
Case 3

GBM is most common primary brain tumor in CNS and it is also the most malignant. Patients over age 65 have an average survival of 4 months.

- 65 year old male develops mild weakness over period of two weeks then has a seizure. Decides to not pursue treatment and is dead in 3 months.



Glioblastoma

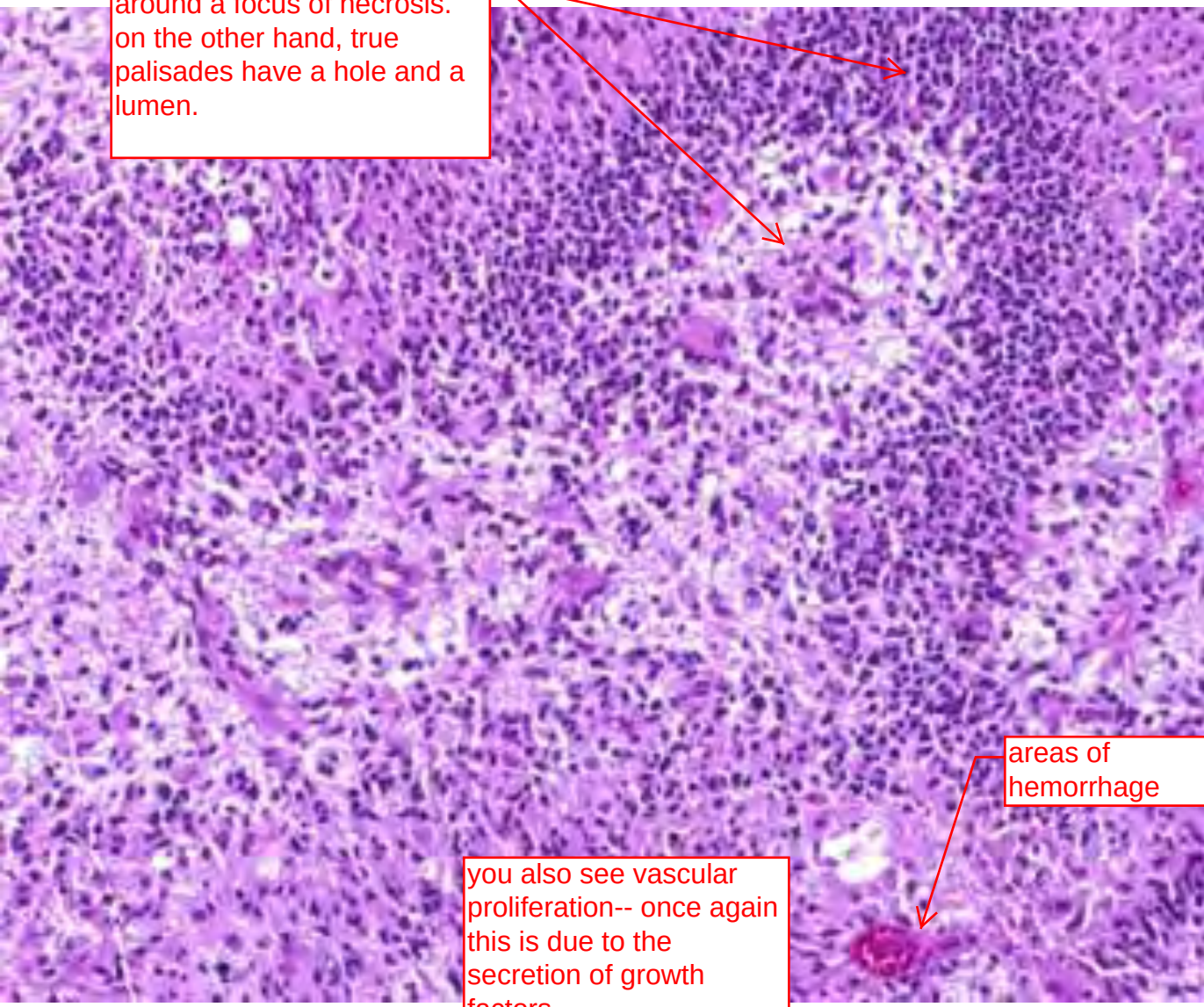


thus, a resection is not curative

- Infiltrative
- poorly circumscribed
- Necrotic
- Crosses the corpus callosum
  - “butterfly glioma”

Glioblastoma (Grade IV)

- Histologically it is usually a largely undifferentiated neoplasm with extensive necrosis and a distinctive proliferation of vascular cells ("endothelial proliferation").



Glioblastoma

5%

- There are two types of glioblastomas recognized
  - Secondary GBM progress from lower grade tumors
  - Primary GBM arise *de novo* with no preceding history

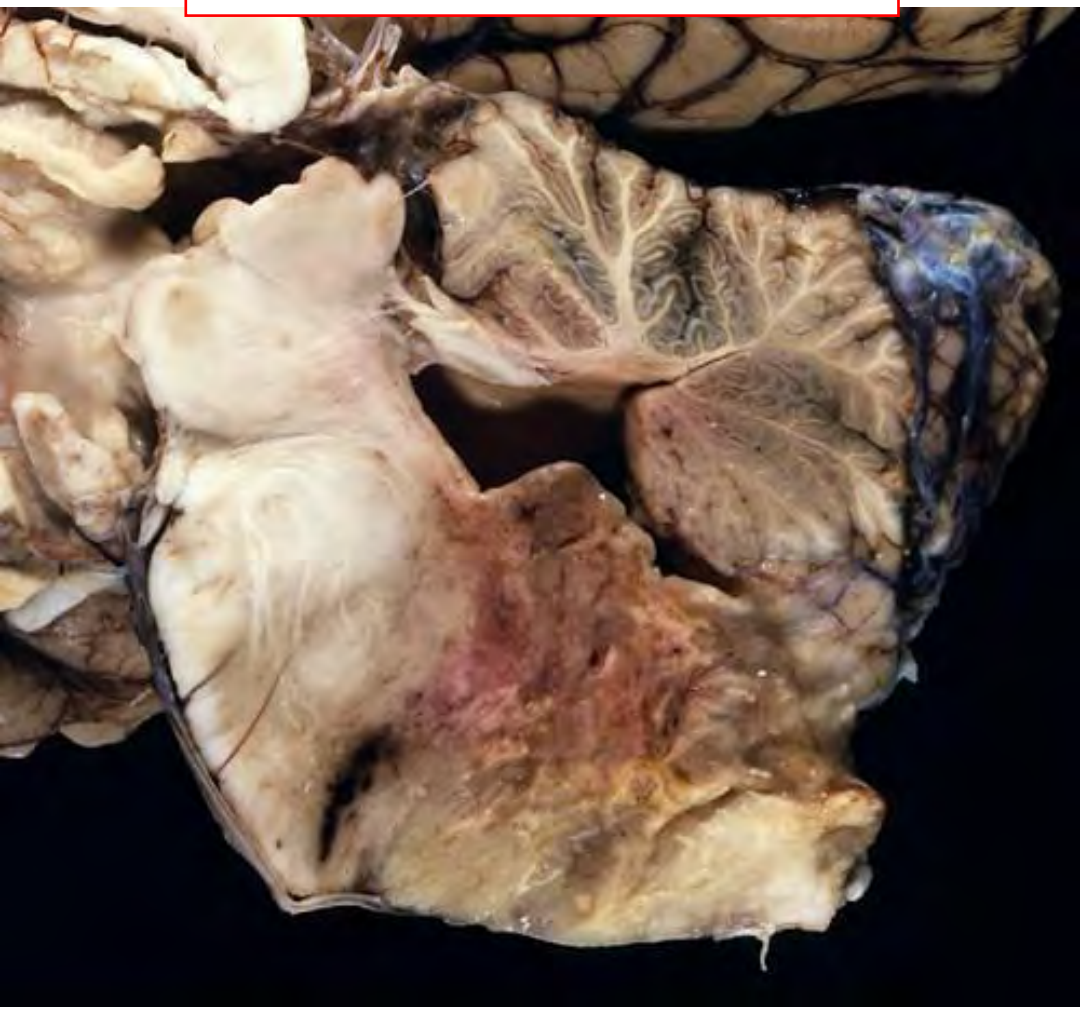
vast majority arise de novo

- There is mild prognostic benefit to having a secondary glioblastoma

big push to perform molecular tests on tumors to see if they are secondary

Case 4: 12 year old male with headaches, nausea and vomiting

GBM does affect children-- usually presents in the pons in children (this causes hydrocephalus)! Radiation and chemotherapy are only treatment options. Do not surgically resect in this location.



- Most commonly found in the cerebral hemispheres of adults or brain stem, usually the pons, of children
- Causes hydrocephalus
- Diffusely infiltrative
- Glioblastoma of pons

Glioblastoma

- The most common primary brain tumor and also the most malignant.
- Typically occurs in adults over the age of 45, or in the brain stem of children.
- Components of Li-Fraumeni Syndrome and Polyposis Coli Syndromes

familial association with inc. risk of developing GBM

p53 mutation is a component of Li-Fraumeni Syndrome
Joe Fraumeni went to Duke!
Women with p53 mutation are likely to have breast cancer; men with this mutation more likely to develop GBM.

Glioblastoma

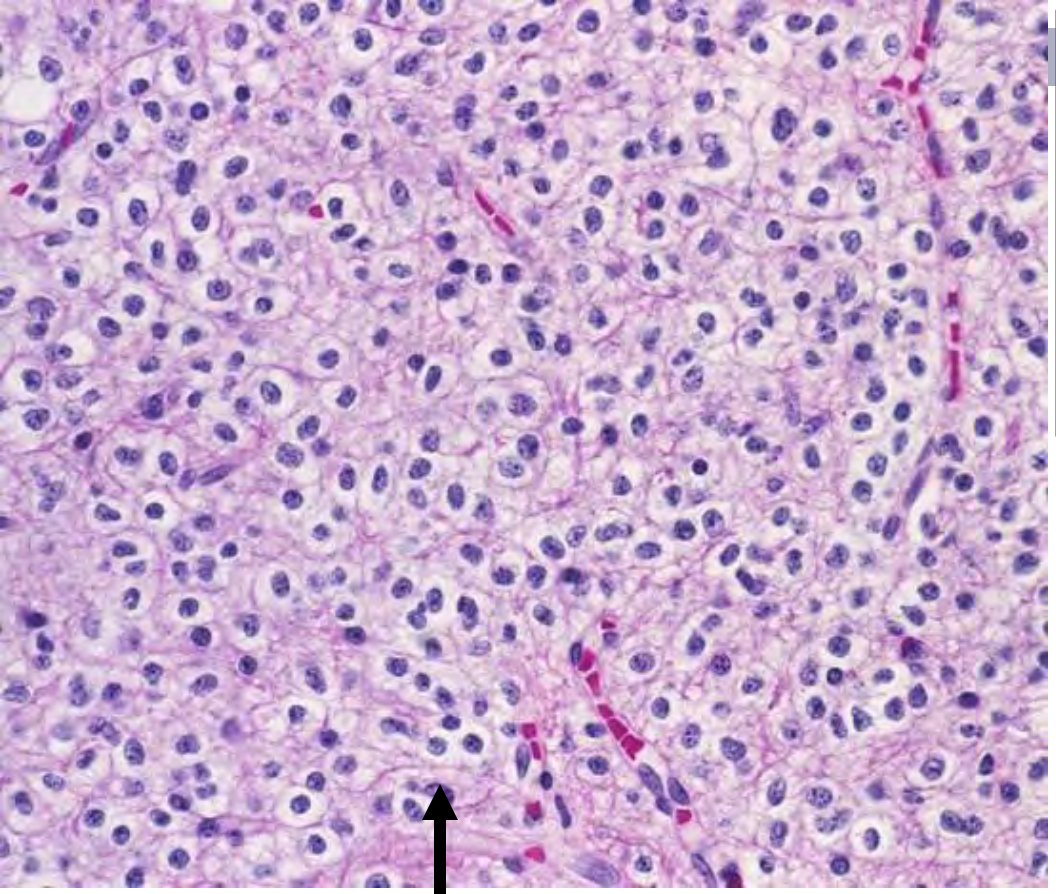
- The lesion is highly infiltrative and is rarely cured by surgery.
- To date, other therapeutic modalities such as radiation therapy or chemotherapy are effective only in retarding the progress of the disease but do not produce a cure
- The vast majority of patients are dead within two years of diagnosis.

only 5% live more than 5 years

- Case 5: 32 year old female with long history of seizures, recently becoming worse with little response to anti-epileptics. CT scan reveals a relatively well circumscribed, frontal lobe lesion with punctate microcalcifications in the gray and white matter. Biopsy was performed.

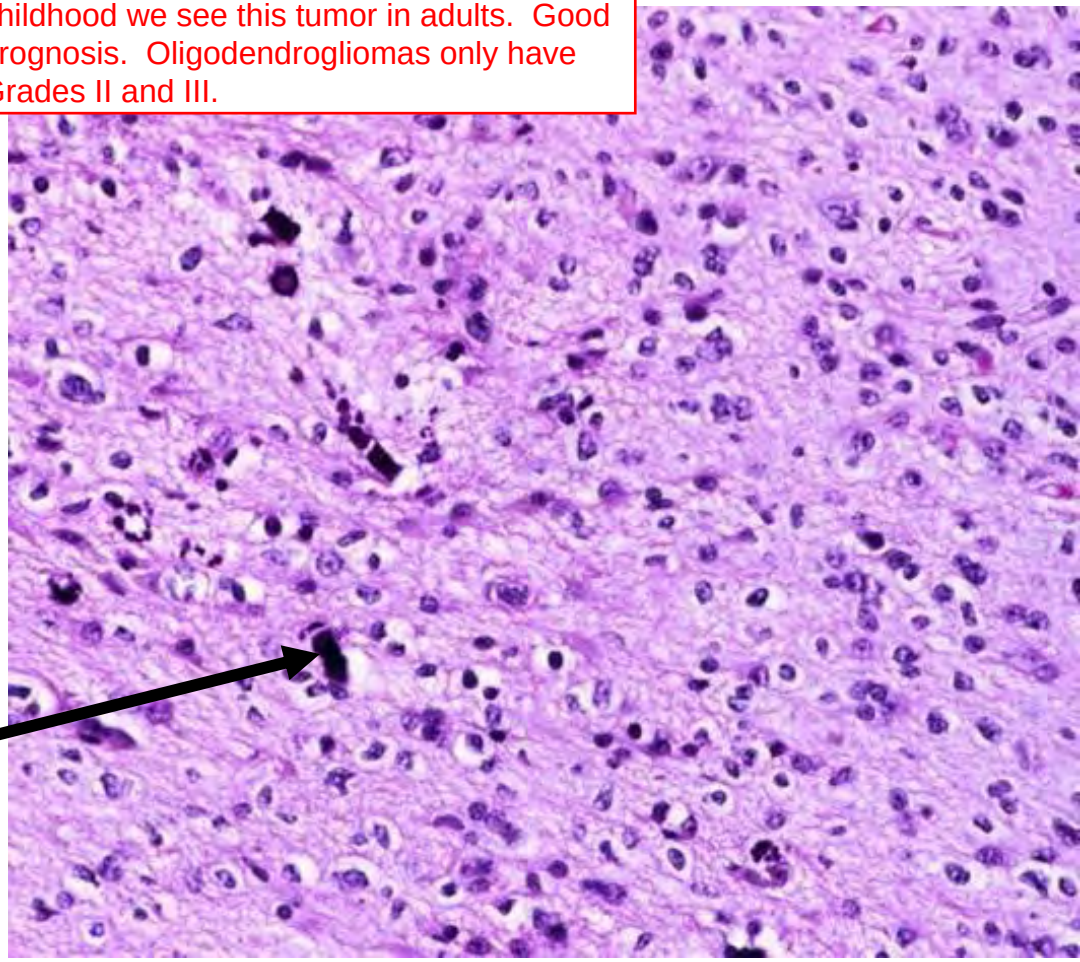
characteristic presentation!

Round, regular nuclear with a halo of clear cytoplasm--" fried egg" appearance. Oligodendrogliomas-- characteristic of long-seizure history and microcalcifications. They typically occur in frontal lobes. This stuff will show up on tests and we will occasionally see this in patients. Even though these individuals have a long history of seizures since childhood we see this tumor in adults. Good prognosis. Oligodendrogliomas only have Grades II and III.



“Fried egg” histology

Punctate microcalcifications



Oligodendroglioma

- Usually affects the frontal lobes of adults.
- Seizures are frequently present for many years prior to diagnosis, and attest to the slow growth of the neoplasm in its initial stages.
- Histologically there is a high incidence of calcification, high cellularity, and the presence of artifactual clear zones about nuclei (perinuclear halos) to produce the “Fried Egg” appearance.

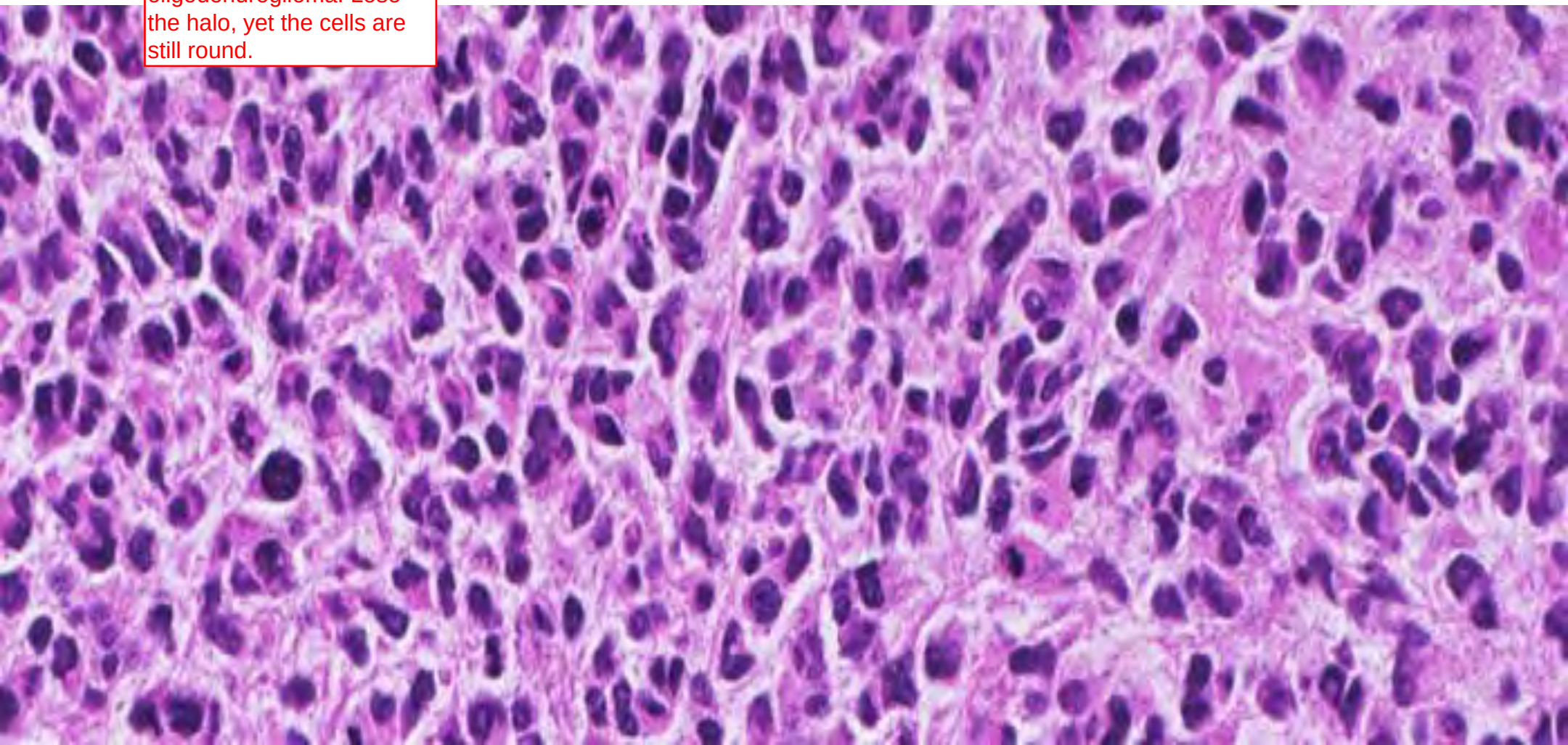
Oligodendroglioma (Grade II)

- Histologically resembles the oligodendrocyte
- Like the astrocytic tumors, these neoplasms can degenerate into more malignant forms.
- With newer therapies, even the anaplastic lesions are living longer than ten years after diagnosis.

attack the tumor with a biopsy-- favorable chemotherapeutic profile

Anaplastic Oligodendroglioma (Grade III)

More pleomorphic than the well-differentiated oligodendroglioma. Lose the halo, yet the cells are still round.



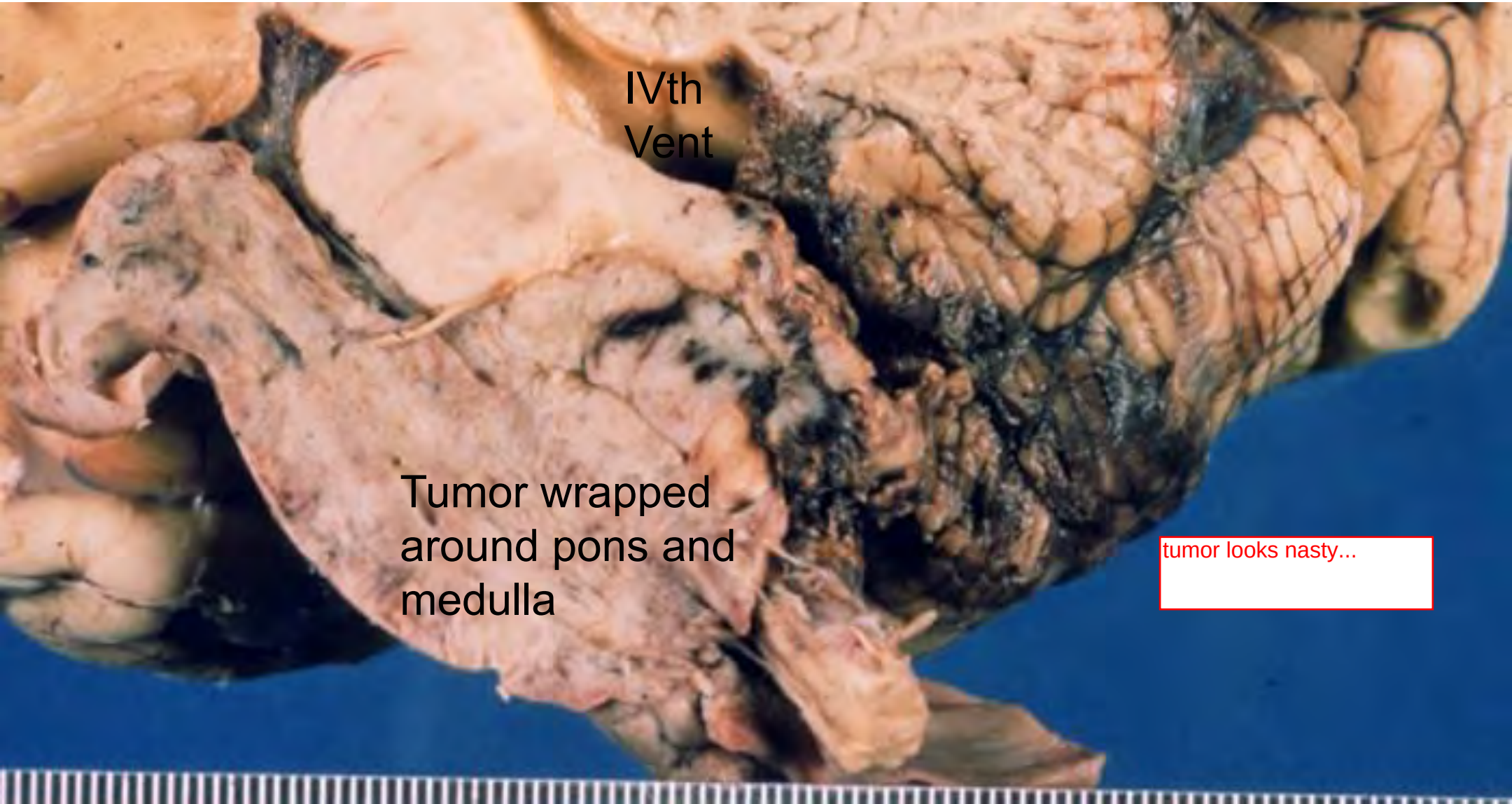
Intraventricular tumors
- Gliomas

We are leaving parenchymal tumors, going to discuss ventricular tumors.

- Ependymoma (Grades I-III)
- Choroid Plexus Papilloma (Grades I-III)

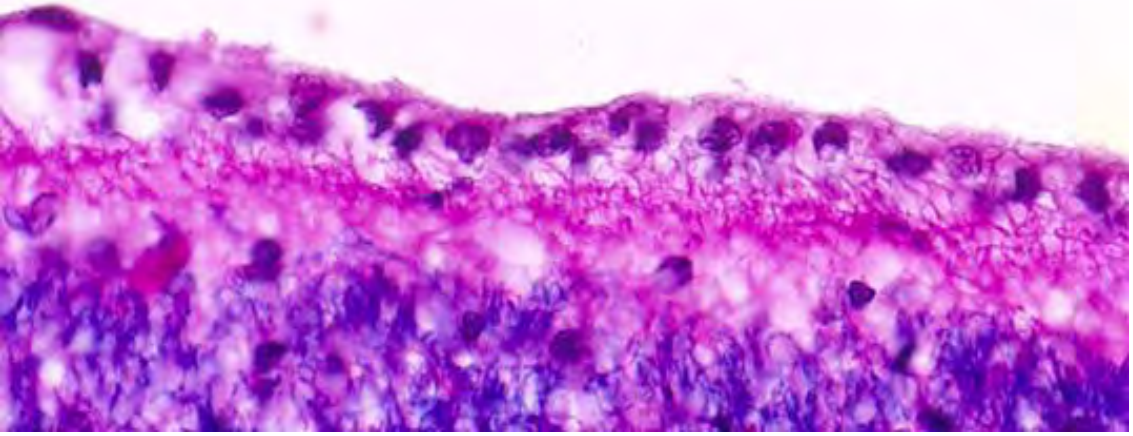
Case 6: 8 year old boy with headaches, nausea and vomiting.

these are posterior fossa (pons, medulla, cerebellum) symptoms

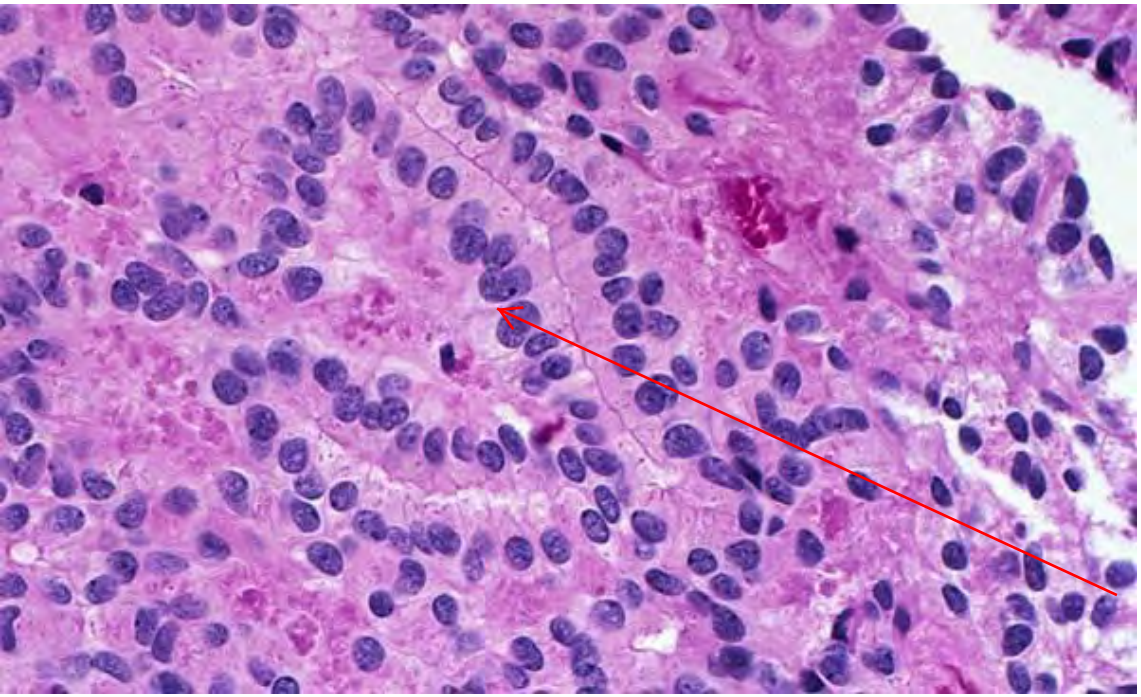


tumor looks nasty...

but histologically tumor looks well differentiated!



- Arise from the ependymal lining of the ventricular system or the remnants of the ependymal lining of the central canal within the spinal cord.



histologically, this tumor tends to recreate the cells that line the ventricles.

Ependymal rosettes mimic the ependymal lining of the ventricle

Ependymoma

- Intraventricular tumors
- Symptoms related to obstruction of flow of cerebrospinal fluid (hydrocephalus)

Ependymoma

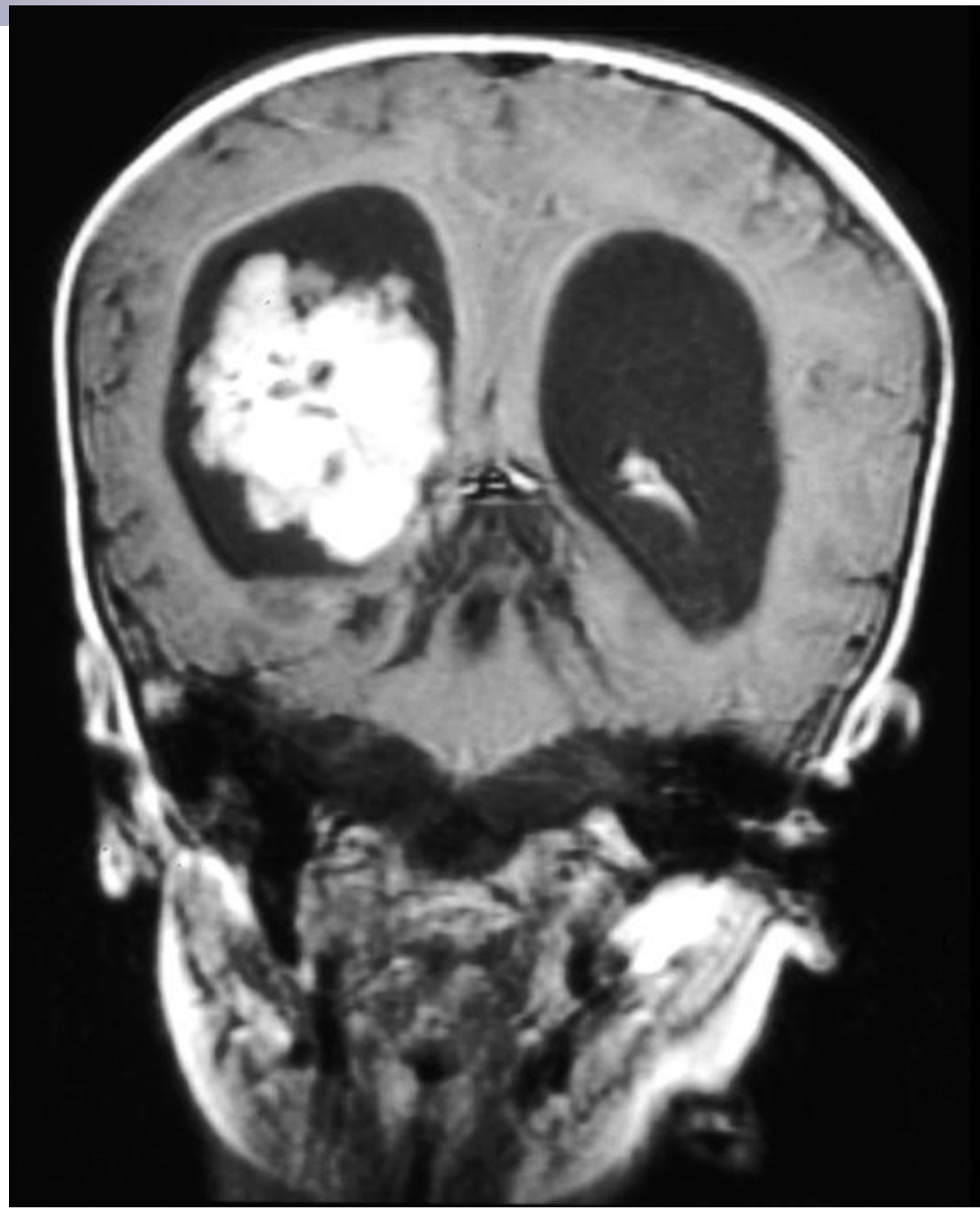
- Although the intracranial lesions are discrete and exophytic in nature, ependymomas are generally lethal lesions because of their position. They rarely can be totally excised and are refractory to radio- and chemotherapy.

But rarely can be cured! Cannot scrap this stuff off of the bottom of the ventricle- there are lots of cranial nerve nuclei in this area (IX, X, II) and this would neurologically devastate you. Grow slowly, but continue to progress.

Case 7

- 8 year old boy with chronic headaches, nausea and vomiting

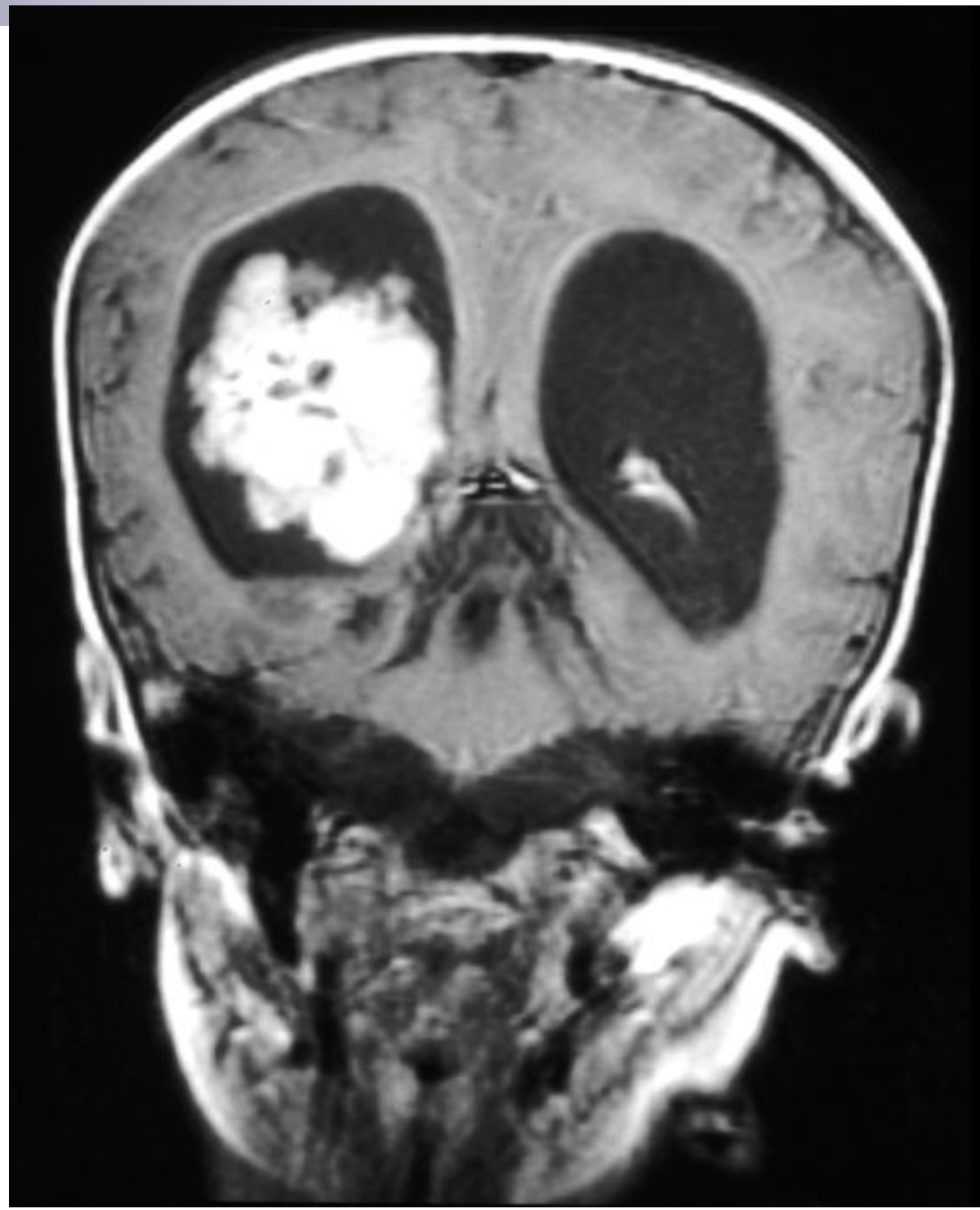
excessive production of CSF (hydrocephalus) from the califlower looking mass in the ventricle



Choroid Plexus Papilloma

- Able to produce cerebrospinal fluid resulting in hydrocephalus.
- Most frequently occur in children where the lateral ventricles are favored sites

In adults this tumor often arises in the 4th ventricle (posterior fossa).

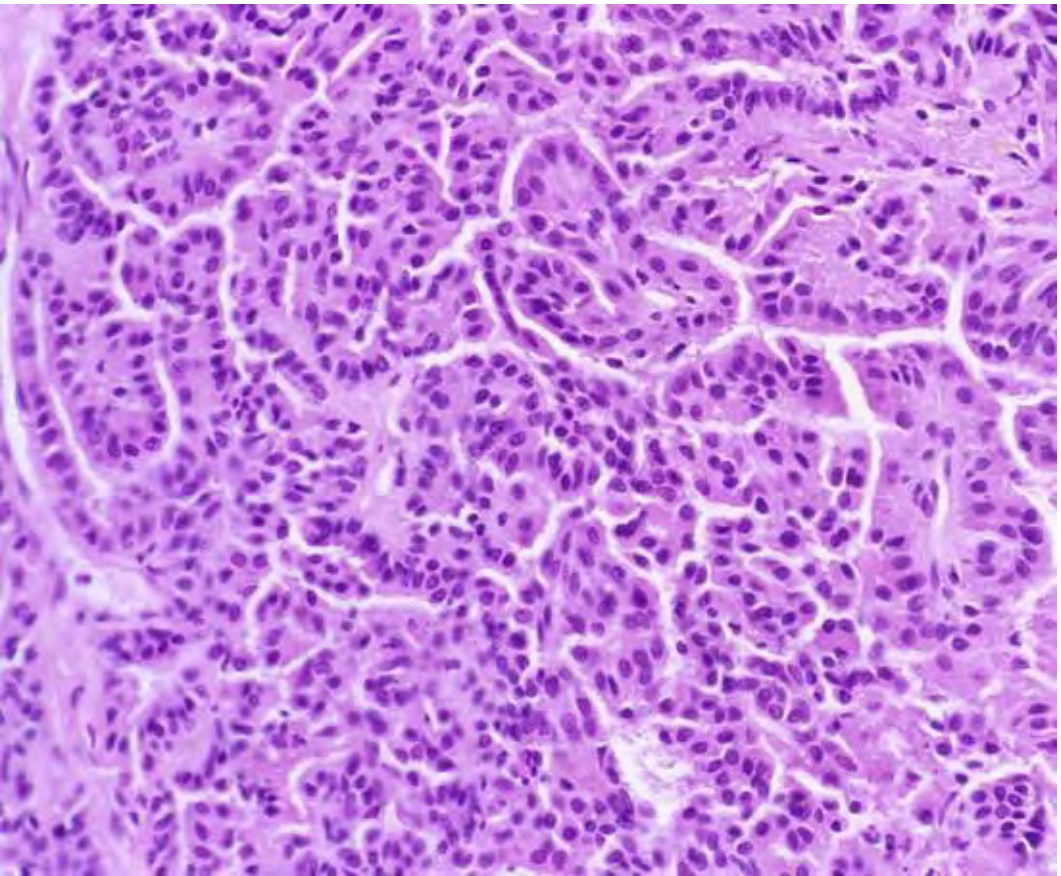


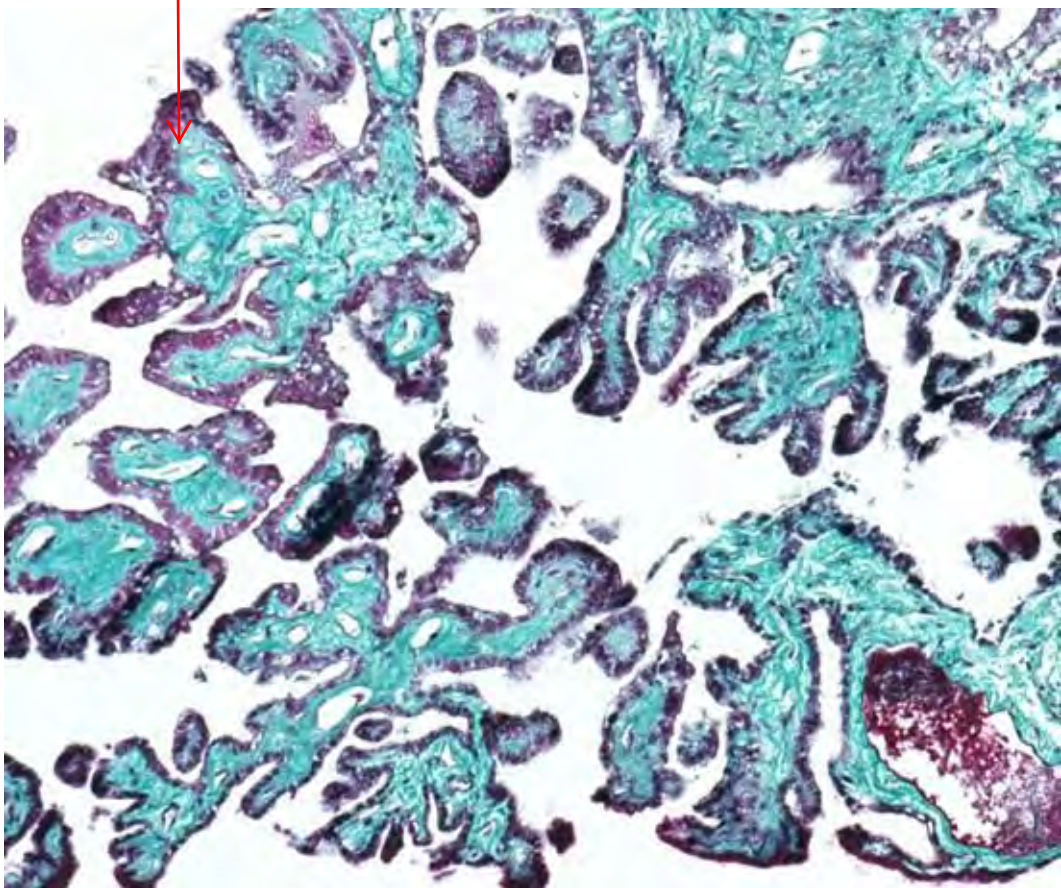
Choroid Plexus Papilloma

- Rare tumors
- Histologically resemble choroid plexus

trichrome stain: stains collagen green and tumor cells have a red appearance

Easy for surgeons to resect and cure. This tumor has a minor attachment to surrounding brain.



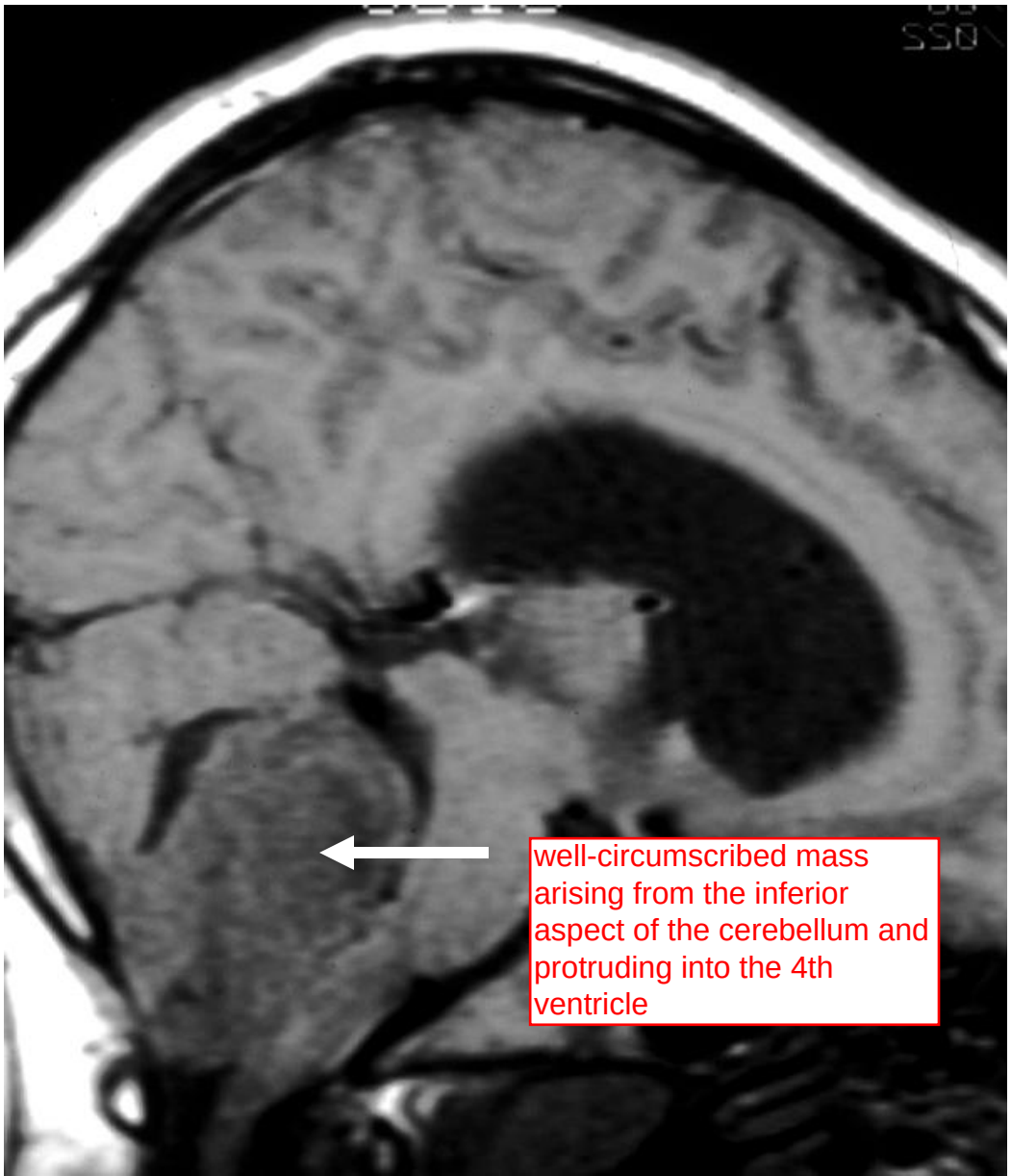


Choroid Plexus Papilloma

- Since many lesions are discrete with only minor attachment to the surrounding brain, surgical therapy is curative in many cases.

Malignant Cerebellar tumors of childhood

- embryonal tumors



Case 8

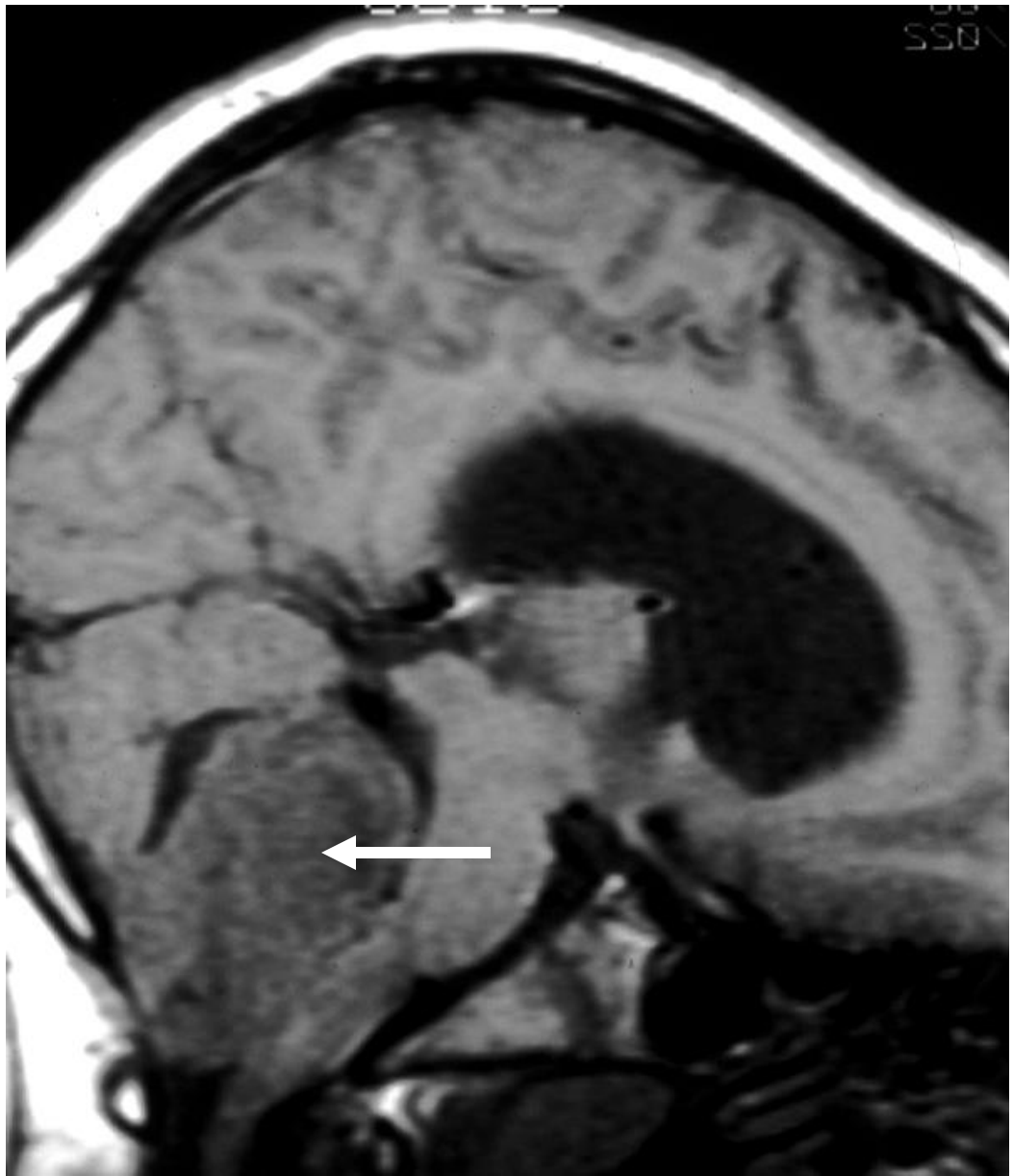
- 4 year old with somnolence, headaches, frequent nausea and vomiting

Embryonal Tumors

- Tumors composed of cells resembling embryonal cells that occasionally retain an ability for limited divergent differentiation
  - Medulloblastomas
  - Atypical Teratoid/Rhabdoid Tumors

two types of these tumors

ATRT- will not talk much about this

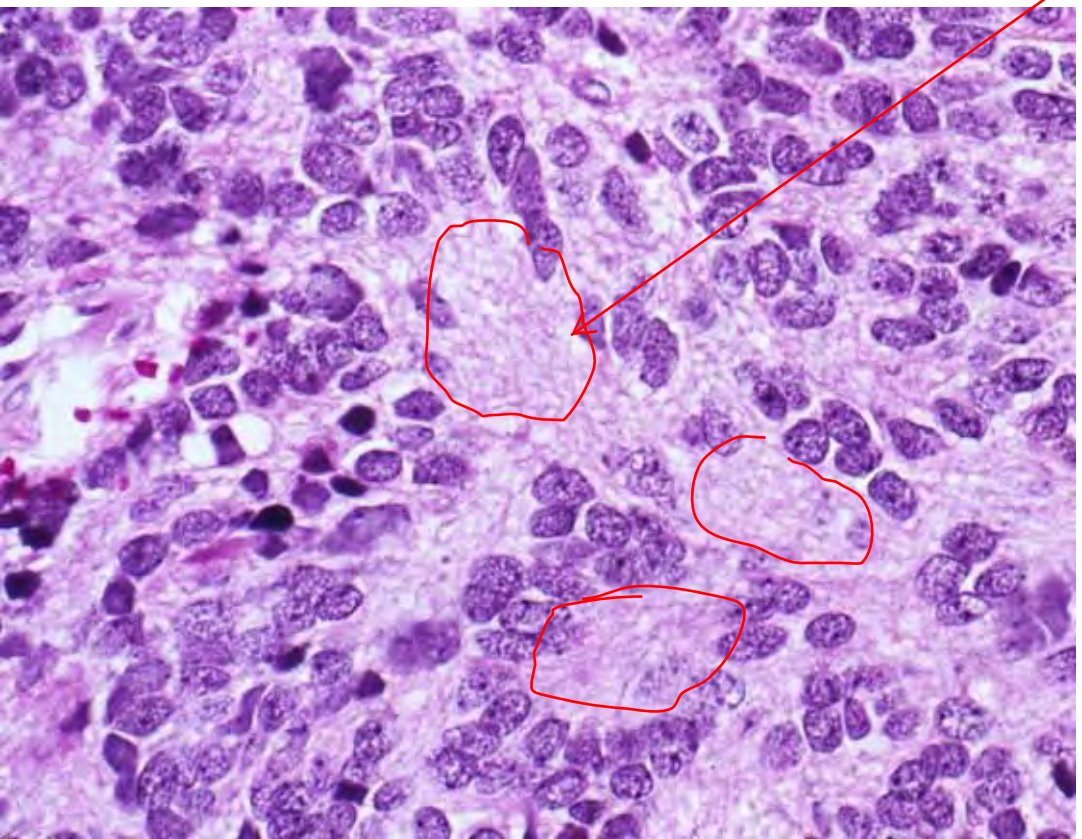


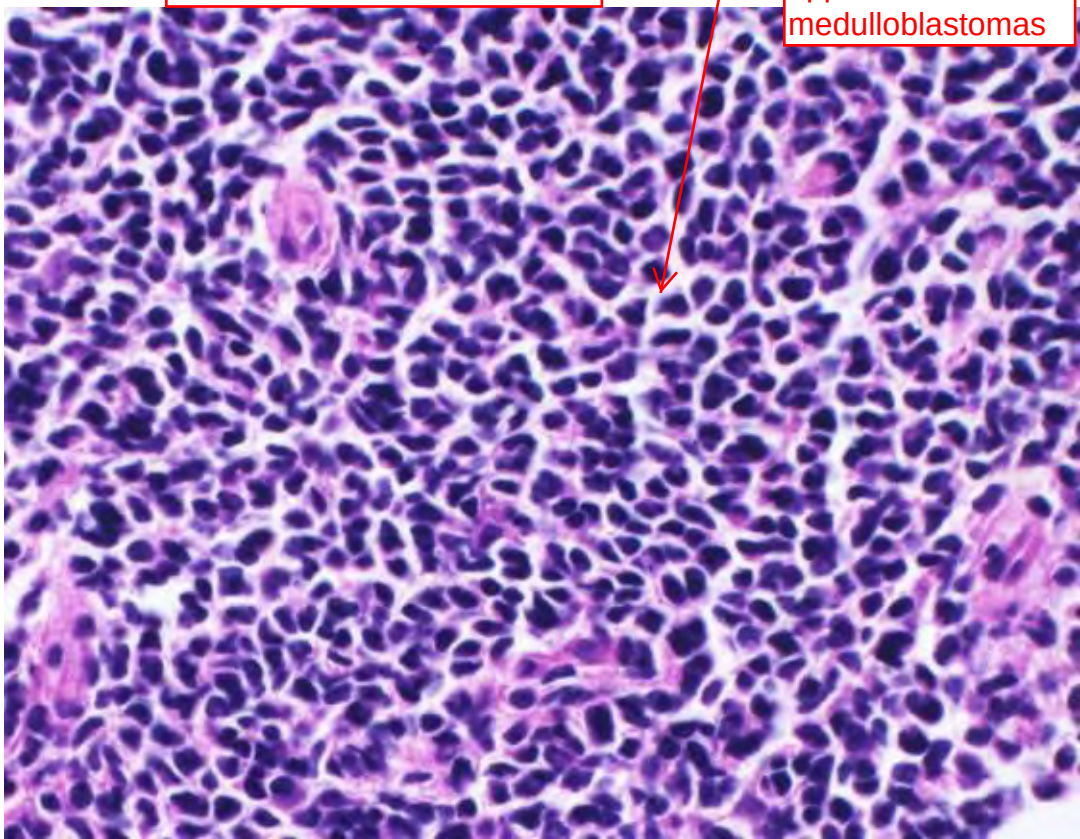
Medulloblastoma

by definition arises in the cerebellum!

- Tumor arising in the cerebellum and frequently protrudes into IV ventricle
- Most common solid tumor in children
- Occurs exclusively in the posterior fossa

- Cellular neoplasm of the cerebellum that usually occurs in children.
- Most tumors exhibit features of neurons
- “Homer Wright” rosettes





Embryonal Tumors of the CNS (Grade IV)

These tumors result in cranial/ spinal radiation. Lethal if left untreated.

- Notable features include their high incidence in children and their tendency to seed the neuraxis.
- The tumors are rapidly growing and lethal if left untreated.

Medulloblastoma

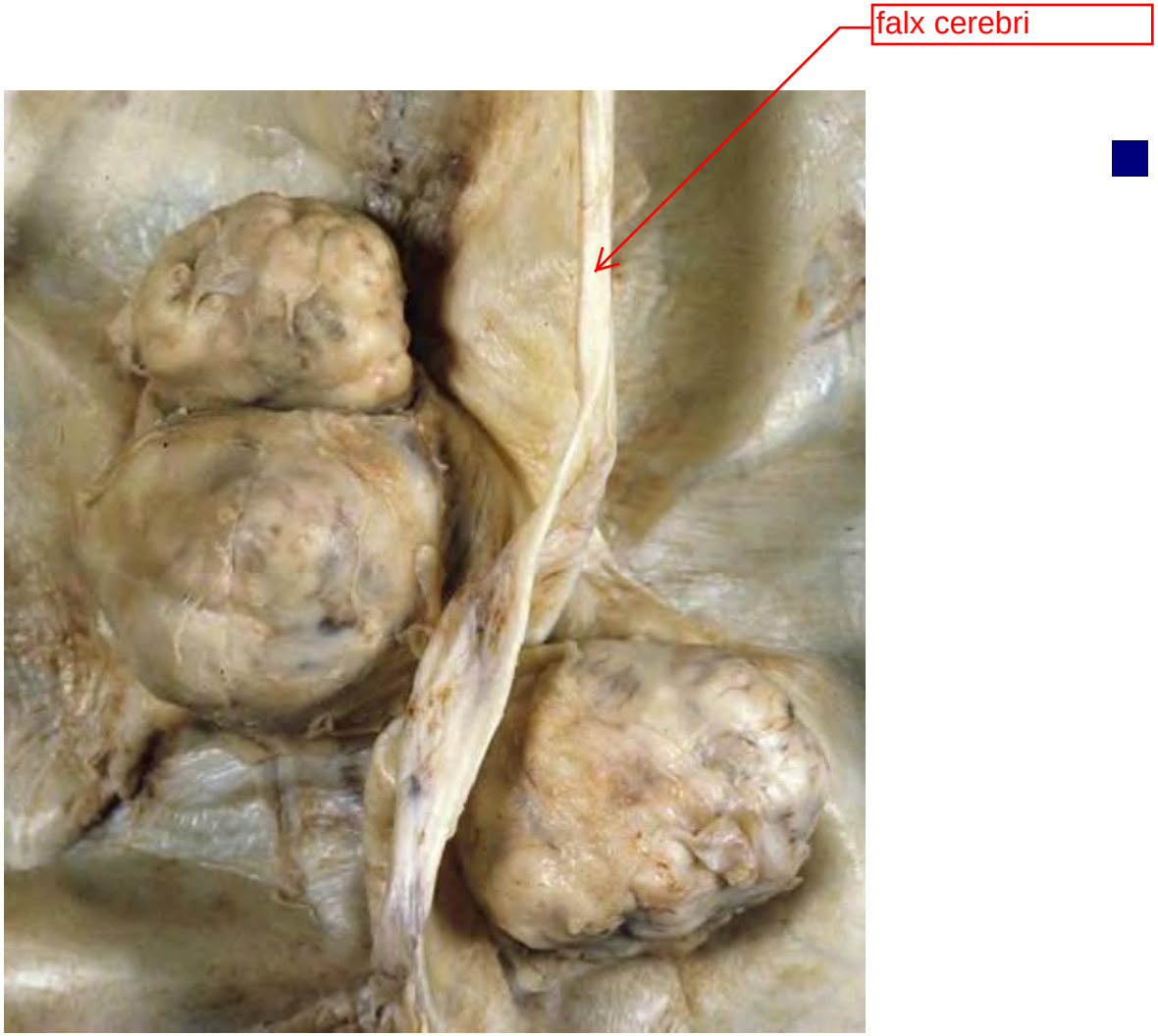
- The use of radiotherapy, especially when the entire neuraxis is included, has been associated with a cure rate of greater than fifty percent in many institutions.
- Chemotherapy has increased this cure rate to approximately 70%.

Dural Based tumors

- Meningiomas

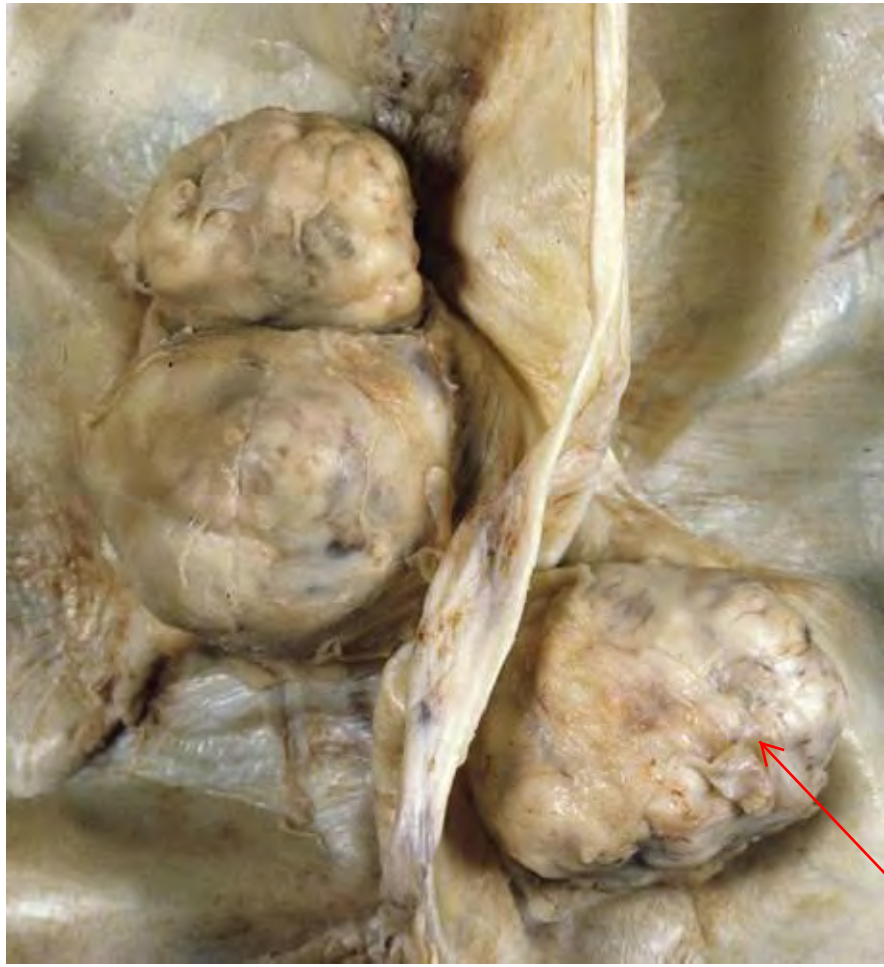
Intradural extramedullary tumors.
predominantly arising in women.

Case 9:



- 55 year old female with multilobular tumor attached to the dura

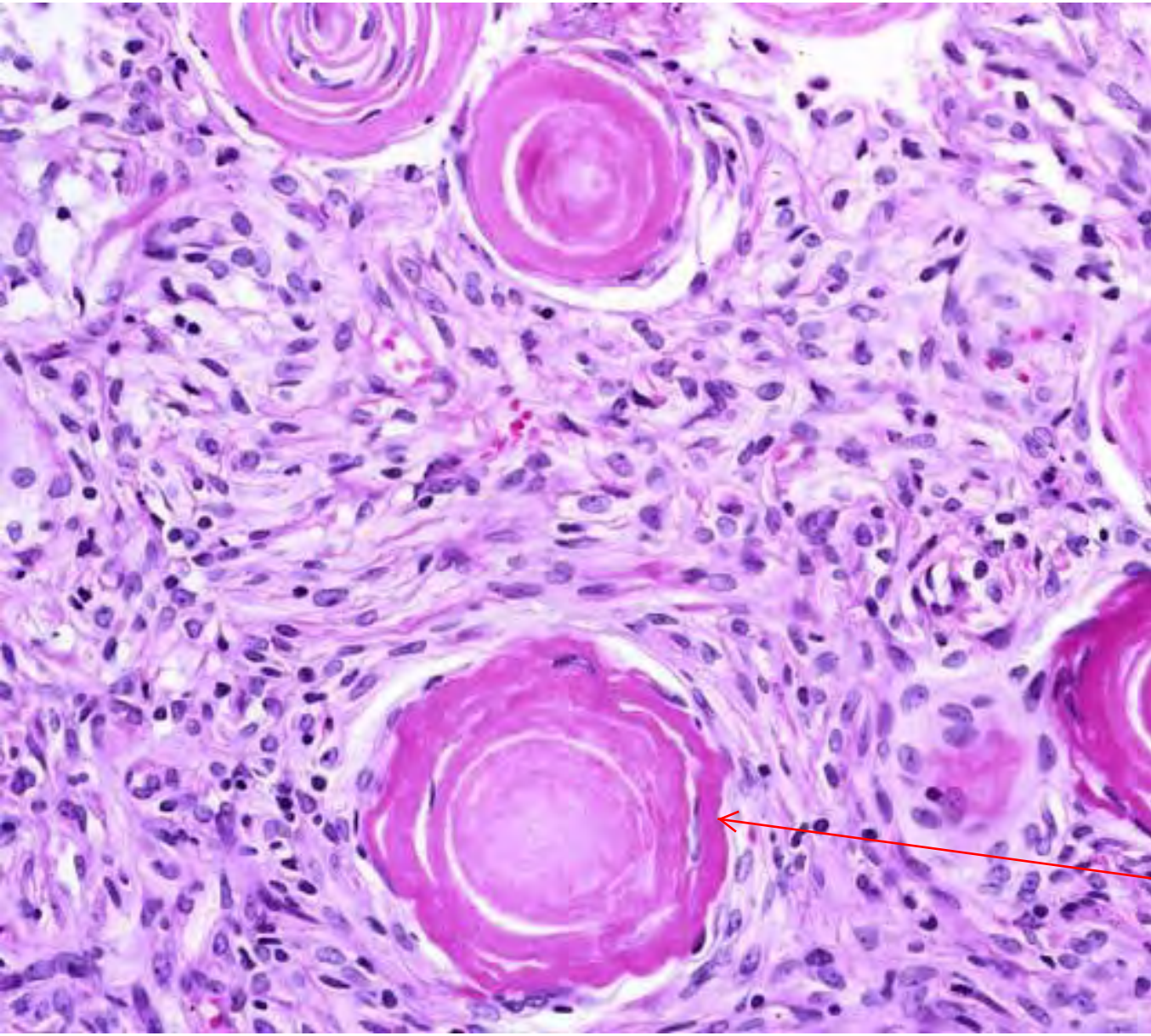
Meningioma



- It is the most common primary tumor of the meninges
- One of the most common of all intracranial neoplasms.

These tumors adhere to the dura, not attached to brain at all. so surgical resection is beneficial and

Meningioma (Grade I)



- Whorling spindle shaped cells often associated with psammoma body formation (“brain sand”)

Meningioma

- The neoplasm is more frequent in women
- In spinal cord M:F ratio is 1:8!!
- Most remain as discrete masses with a compressive rather than infiltrative relationship to the brain (benign)
- Component of NF2

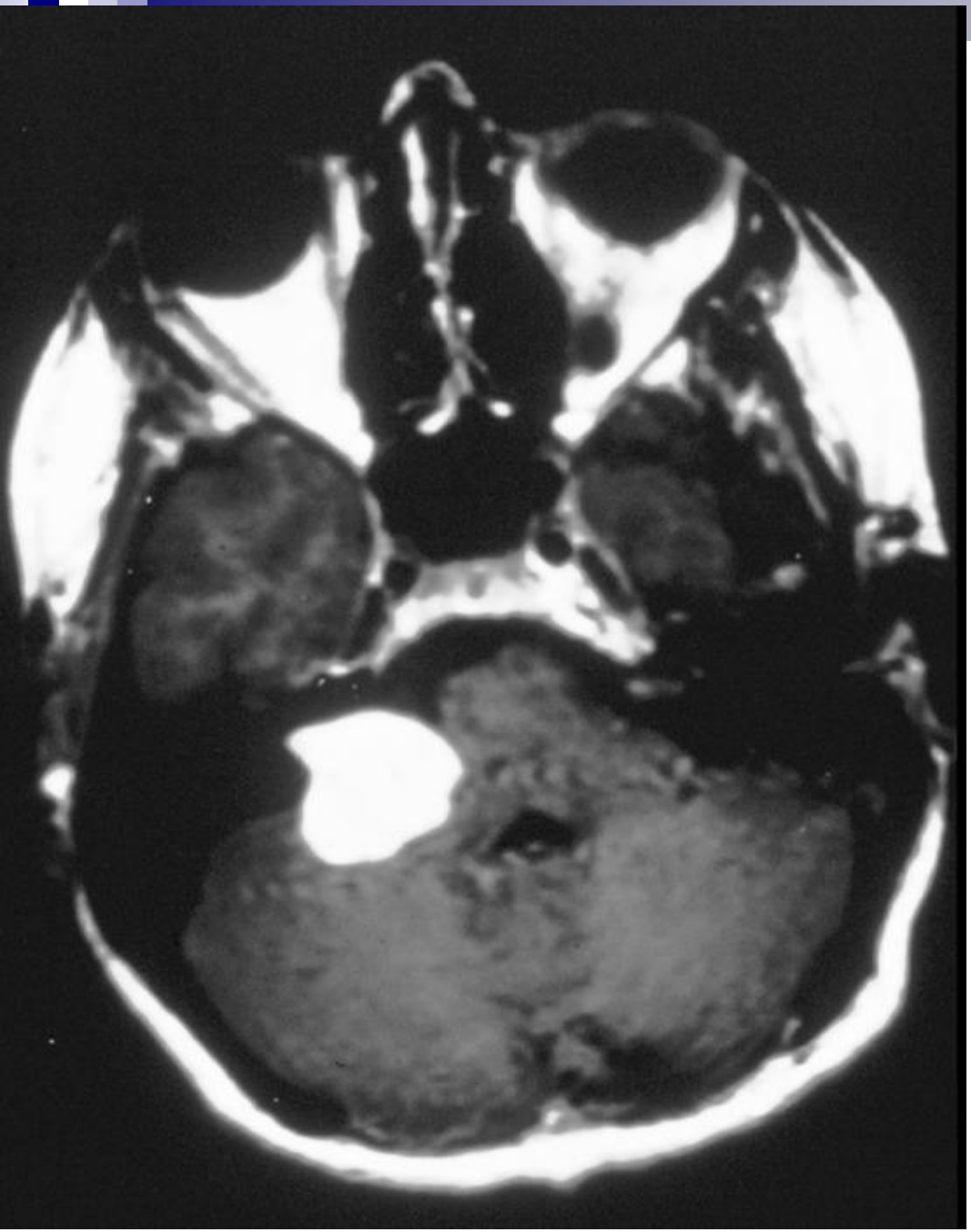
These tumors have an active progesterone receptor.

Common component of this familial brain tumor syndrome-- NF2 is associated with both meningiomas and schwannomas.

Cranial Nerves/Nerve Roots

- Schwannomas

Remember: Schwann cells myelinate nerve cells.



Acoustic Schwannoma

- Any of the cranial nerves (with the obvious exception of CN 1 and 2), are potential sites
- Acoustic „Neuroma" CP angle tumor (CN VIII)

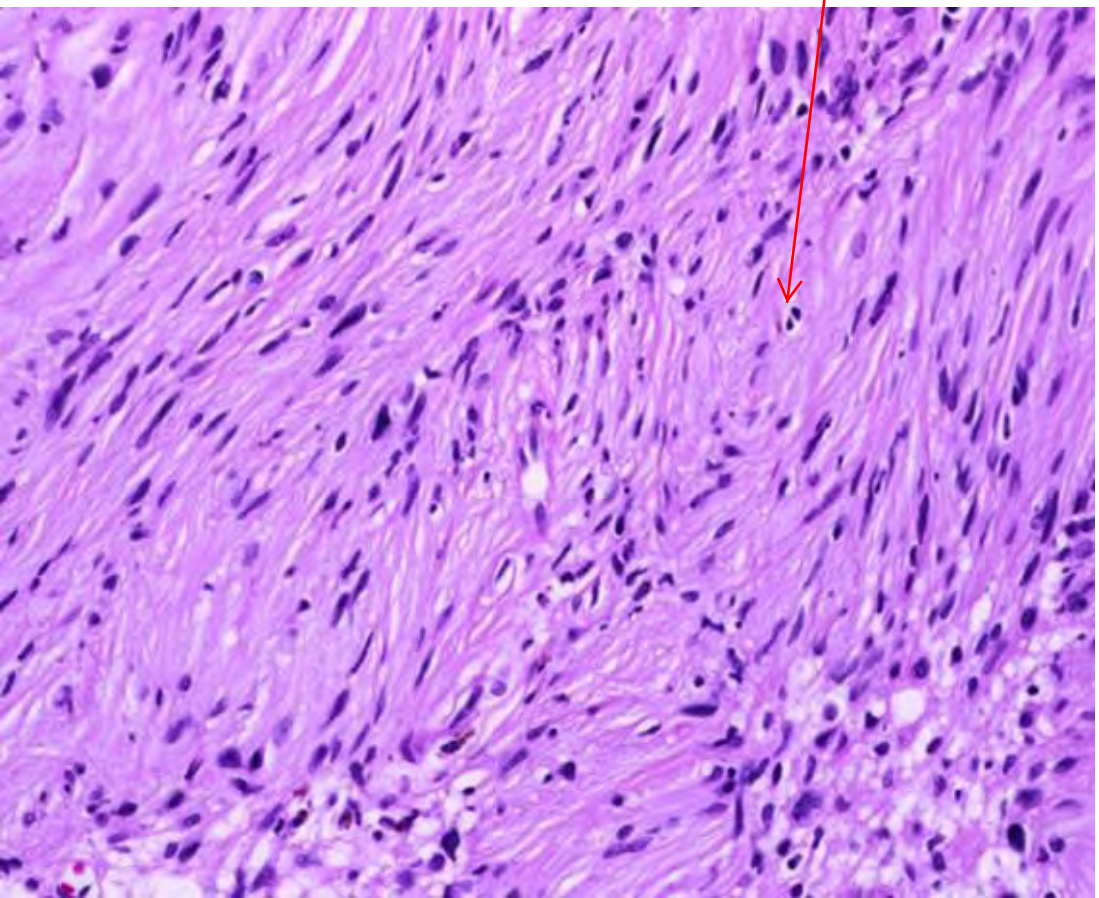
These tumors usually forms at the cerebellar pontine angle. usually arises on CNVIII.

Schwannoma

According to Robbins (pg 1340), tumors show a mixture of two growth patterns, Antoni A and Antoni B. **Antoni A** is characterized by elongated cells with cytoplasmic processes which are arranged in fasicles in areas of moderate cellularity and scant stromal matrix. **Antoni B** pattern of growth, the tumor is less densely cellular and there is a loose meshwork of cells, microcysts and myxoid stroma.

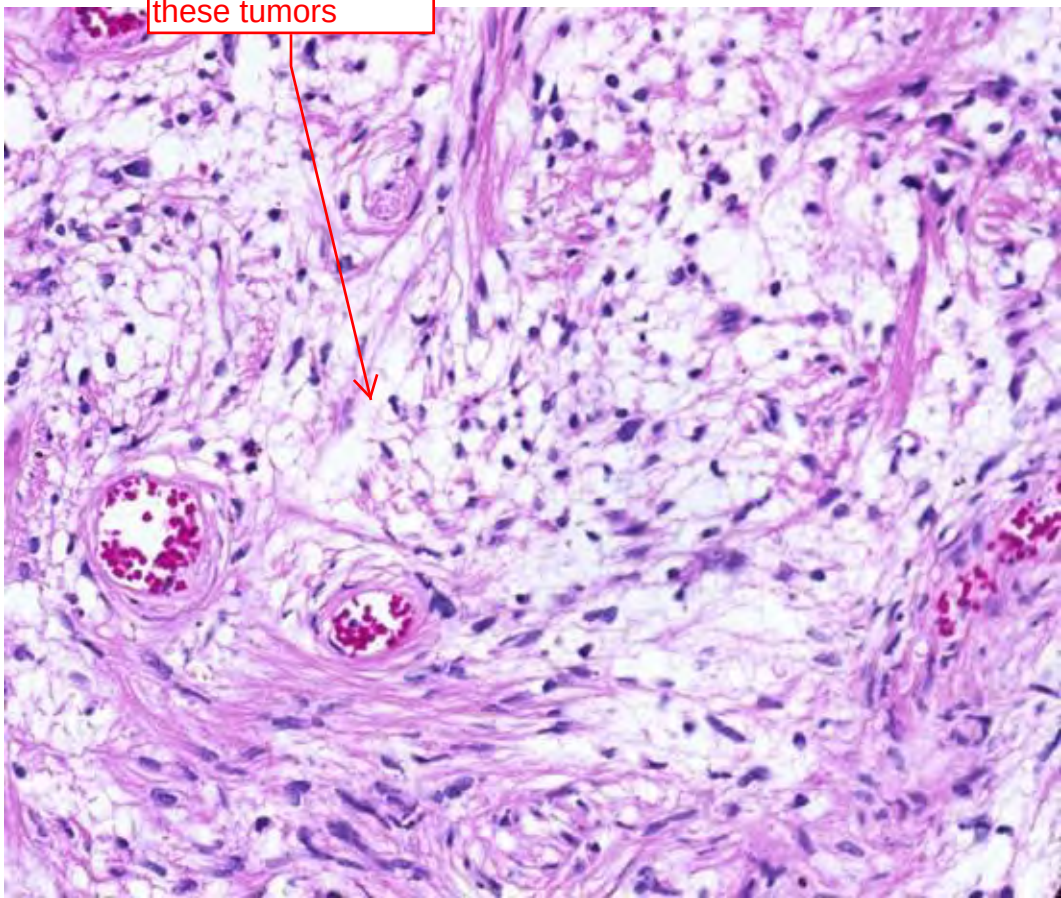
- Antoni A: compact

These are elongated cells. in compact areas.



Antoni B:

also there are loose areas in these tumors



Acoustic Schwannoma

- Schwannomas are almost always histologically benign, although the size and location of the lesion can present surgical problems.
- Component of NF2

again, location is key for treatment.

Tumors of the Cortical Gray/White Junction

- parenchyma of the cerebrum and of the cerebellum
- metastases

Cerebellum has plenty of gray/white junction

Metastatic Neoplasms

yet, not primary to the brain

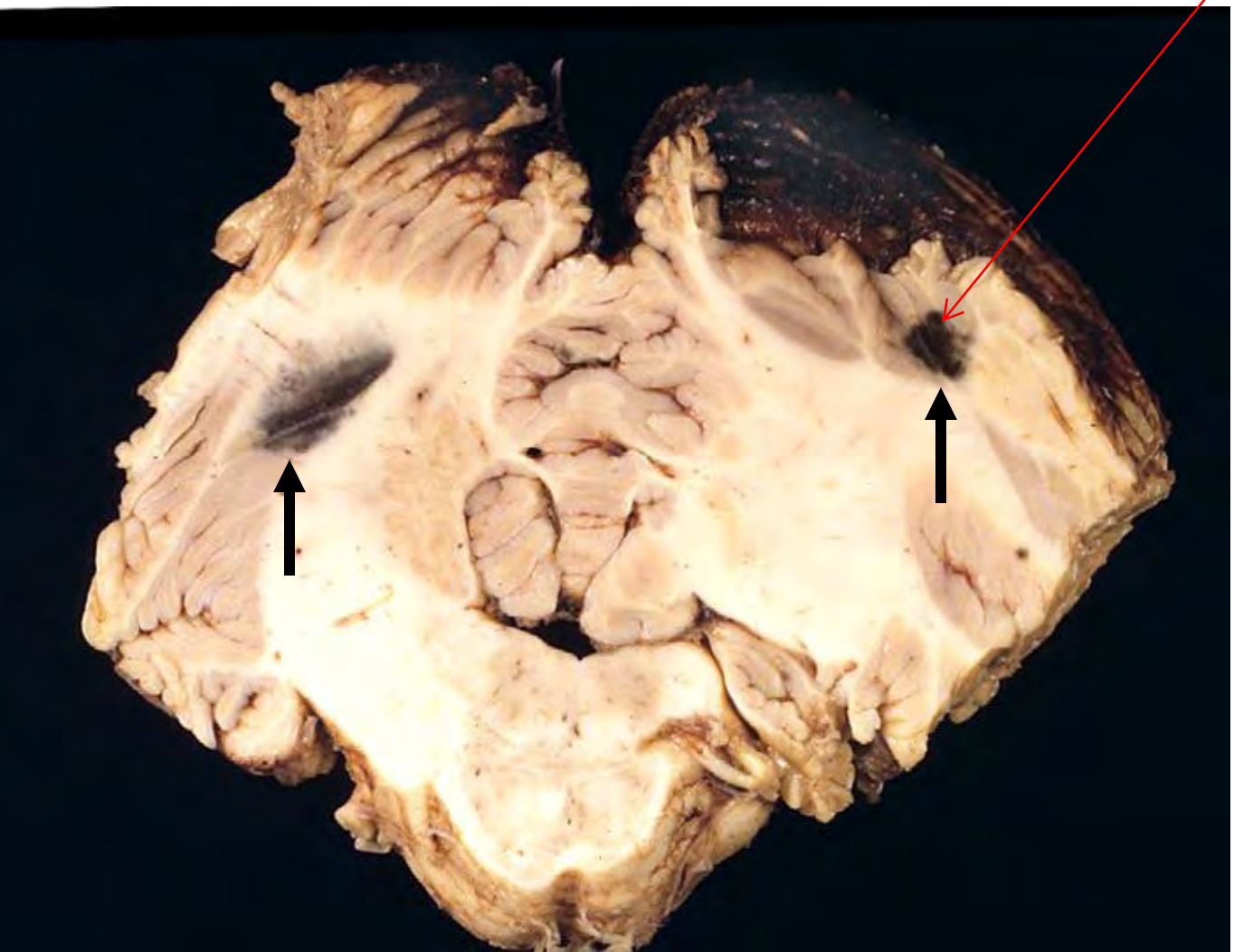
- In a practical sense, the metastatic neoplasms represent the most common form of malignant brain tumor
- The majority of metastases to the brain originate via the lungs where the neoplastic cells gain access to the systemic circulation via the pulmonary vein

if a patient has a brain tumor, do a chest xray!

There are lots of small BV at the gray/ white junction. Thus, metastatic neoplasms commonly end up at this junction and occlude these small BV.

Metastatic Neoplasms

pigmented tumor! common location to find metastatic melanoma



- Characteristic location is Gray-White junction
- Most commonly associated with a lung mass

Metastatic melanoma

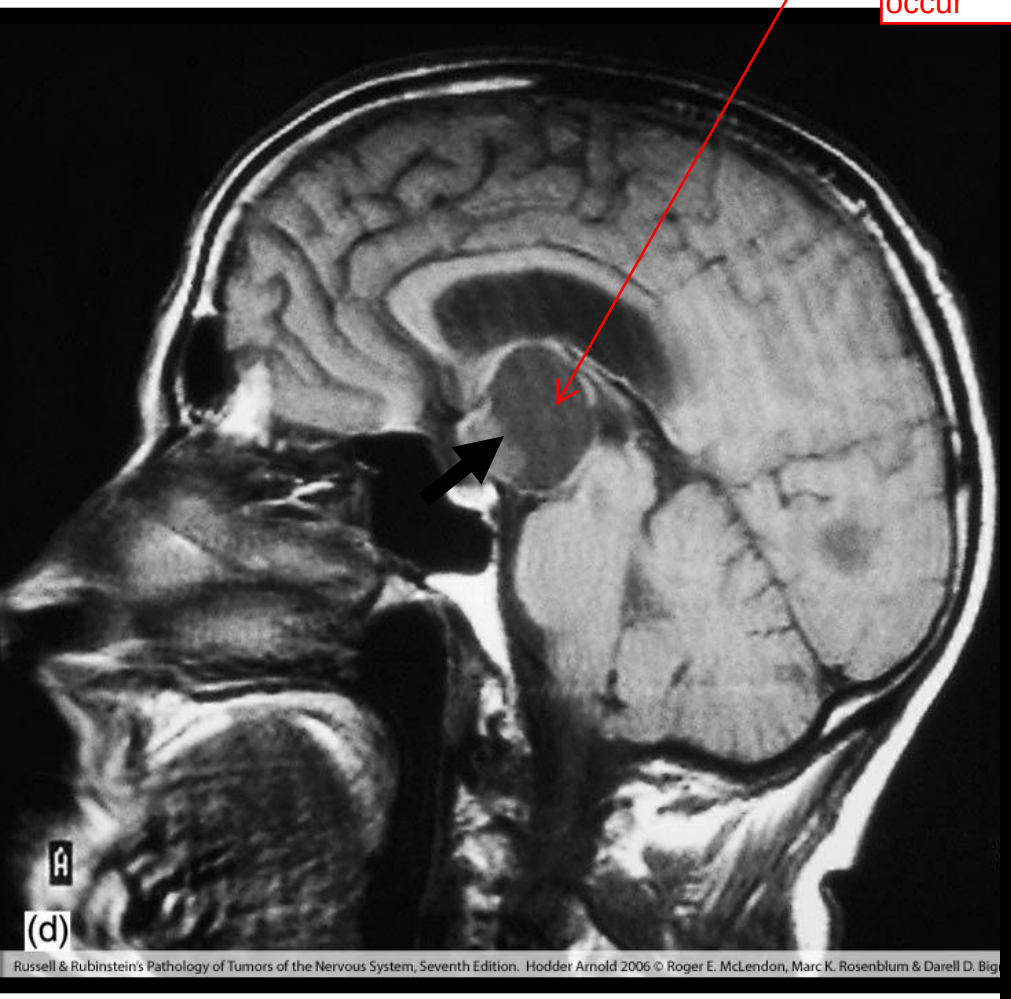
Tumors of maldevelopment

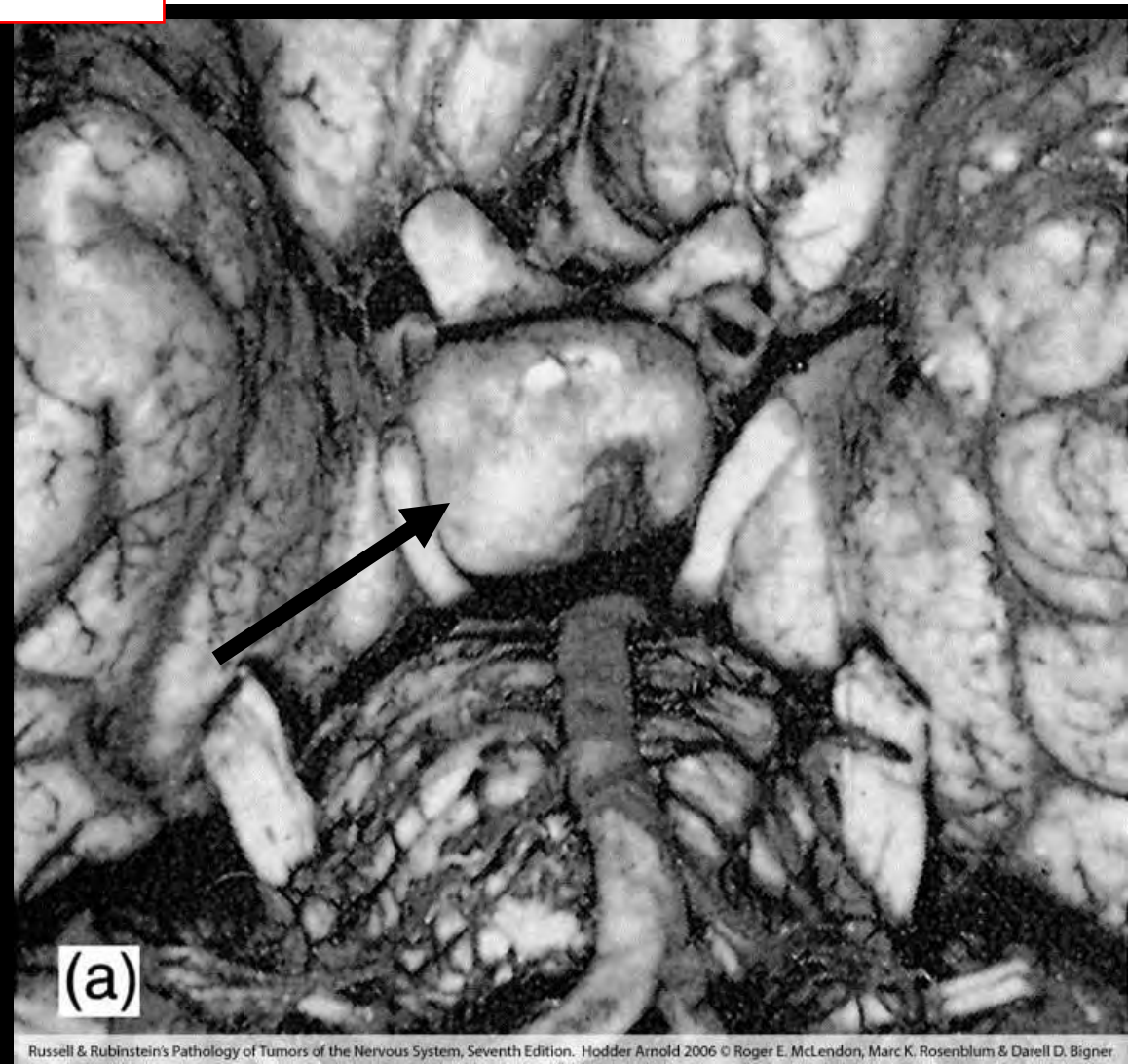
- predominately of children

Tumors can migrate and cause a mass effect in the brain.

Case 8: 22 year old with visual problems and pituitary insufficiency

Tumor arising in the sella turica. Visual problems occur





Craniopharyngioma

- An epithelial neoplasm derived from the primitive Rathke‟s pouch (precursor to anterior pituitary) which is derived from the primitive mouth pore
- It typically occurs in children as a calcified cystic mass producing endocrine deficiency states such as diabetes insipidus but can be found in adults as old as 65 years.

Tumors Related to Maldevelopment

- Craniopharyngioma - derived from primitive stomodeum remnants involved in formation of anterior pituitary
- Rathke's cleft cyst - same as 1)
- Dermoid cysts - ectodermally committed cells folded into CNS during closure of neural tube
- Teratomas - abnormal migration of primitive germ cells along midline sites.

Dermoid cyst has air shafts, sebaceous glands, will secrete a fluid. This is how you distinguish from the epidermoid cyst that does not produce fluid and shows up in adults

Nugget: WHO grading is based on the natural history of an untreated neoplasm