

# CNS pathology

## Third year medical students

### lecture 10 CNS tumors/ 2

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FRCPath

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*Topics covered in this lecture:*

- Pilocytic astrocytoma*
- Oligodendroglioma*
- Ependymoma*
- Neuronal tumors*
- Medulloblastoma (embryonal/ premitive)*

# Pilocytic astrocytoma

- Relatively benign ( WHO grade 1) *\*Remember that grade 1 tumors are benign by definition*
- Occurs in children and young adults
- Mostly: in the cerebellum
- Can also involve: third ventricle, optic pathway, spinal cord and rarely cerebral hemispheres

# genetics

- They have different mutations than diffuse astrocytomas (no IDH mutation, and rarely TP53 mutation.)
- They have BRAF pathway mutations.. So targeted therapy with BRAF inhibitors can help in treatment, especially in cases where the tumor is not resectable.

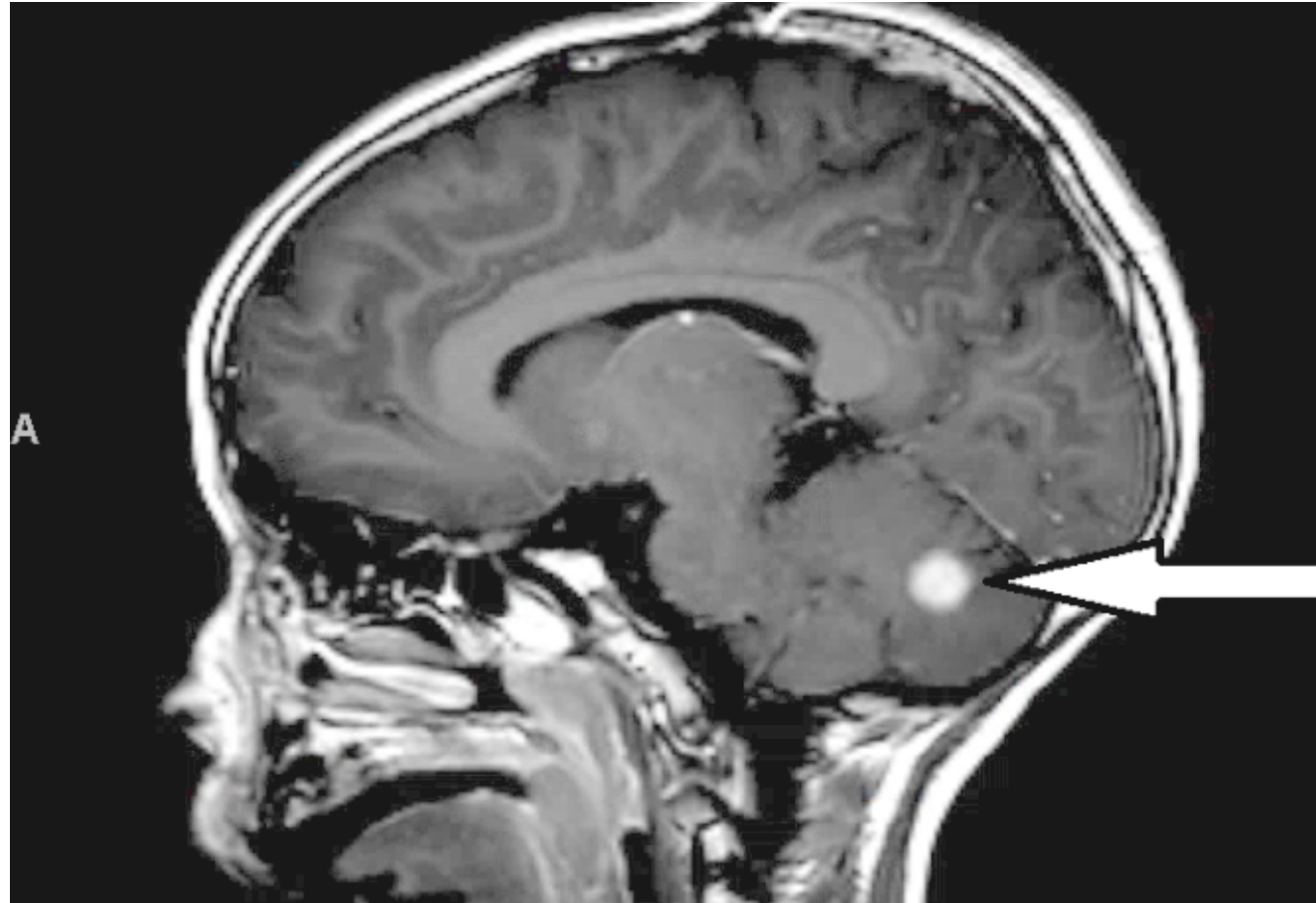
# morphology

- Solid and **cystic** components (*goes with the name- Pilo**CYTIC***)
- If solid it is usually well defined

## **Microscopically:**

- bipolar cells with long GFAP positive processes
- Rosenthal fibers
- eosinophilic granular bodies
- microcysts
- mitosis and necrosis are rare (*it's grade 1*)

Note the well circumscribed lesion in the  
cerebellum



*Well-  
circumscribed  
lesion*

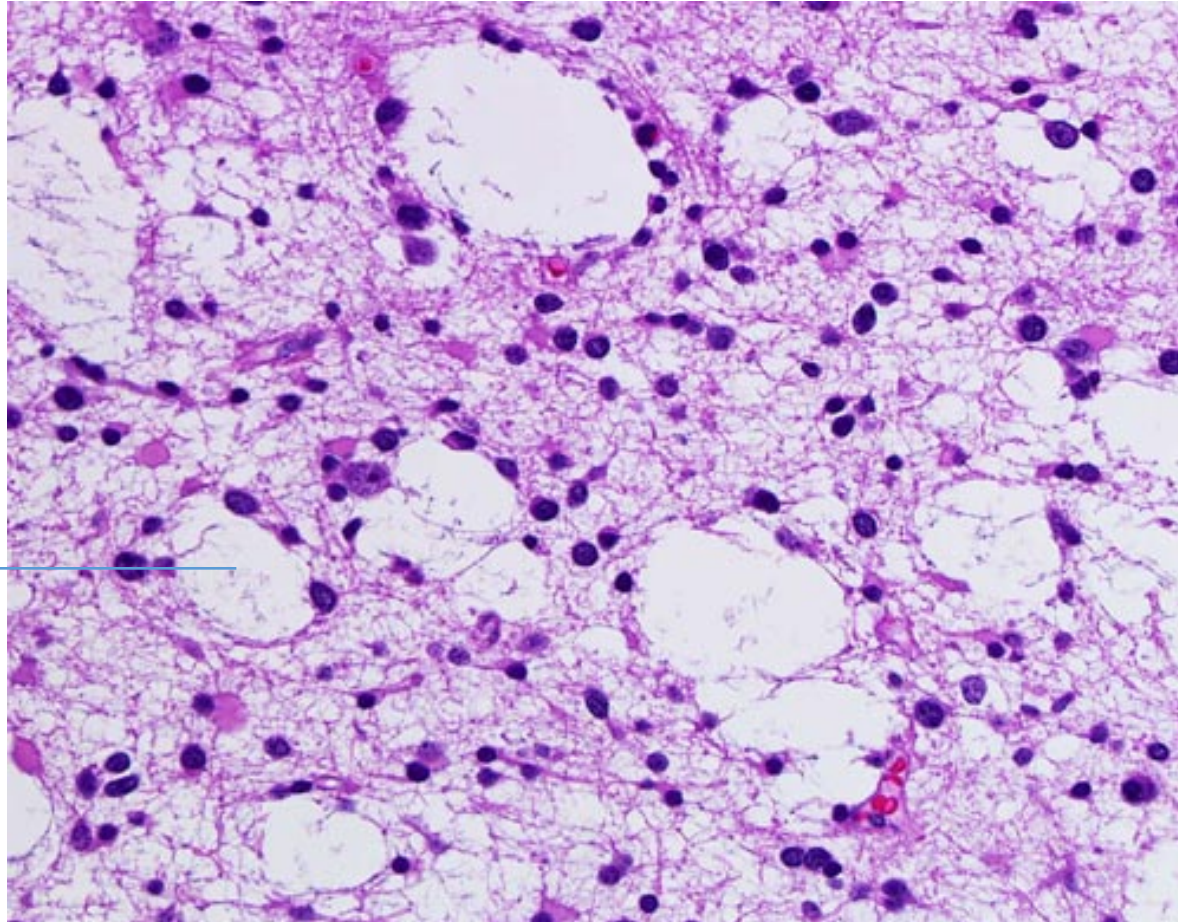
Pilocytic astro: this example is mainly cystic but has also a solid component



# Pilocytic/ microcysts

Very important picture

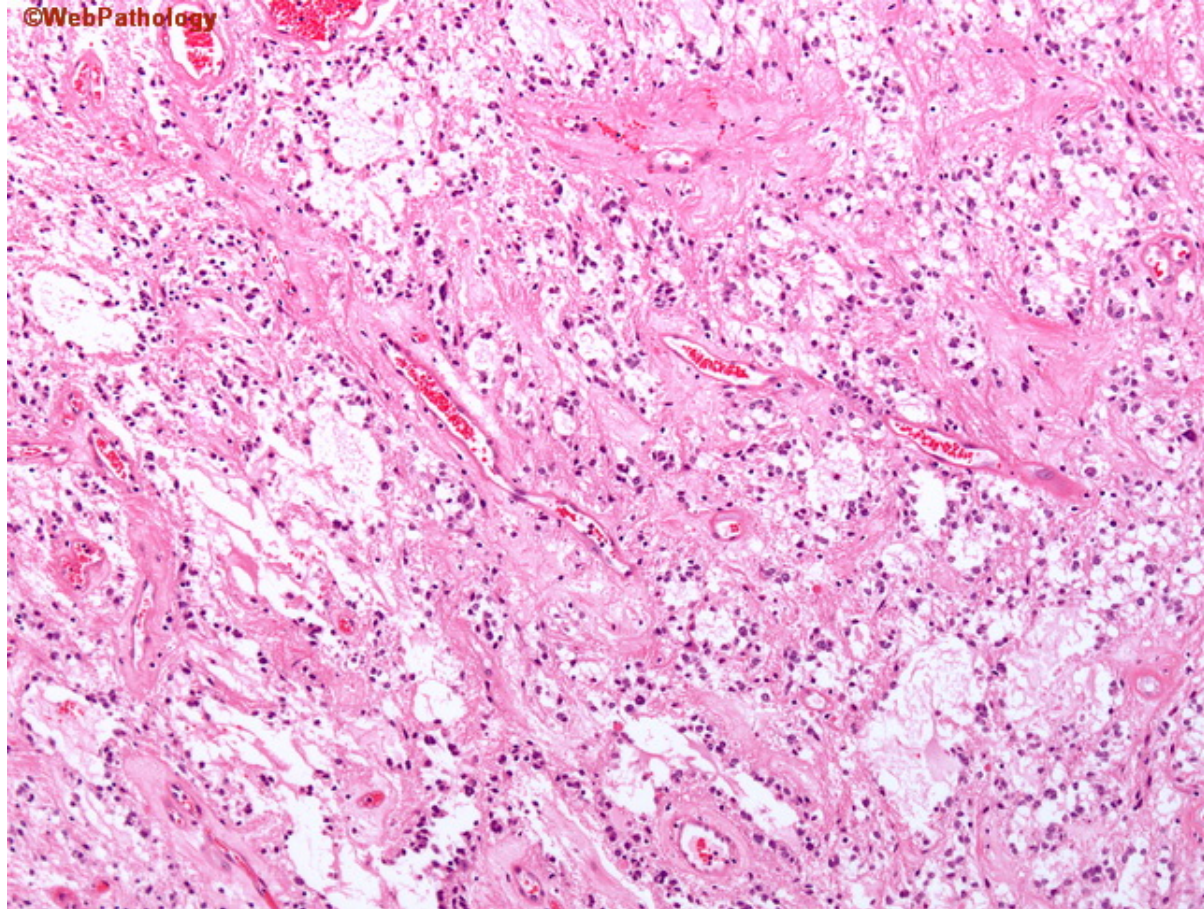
Cysts ←



*GFAP +ve*



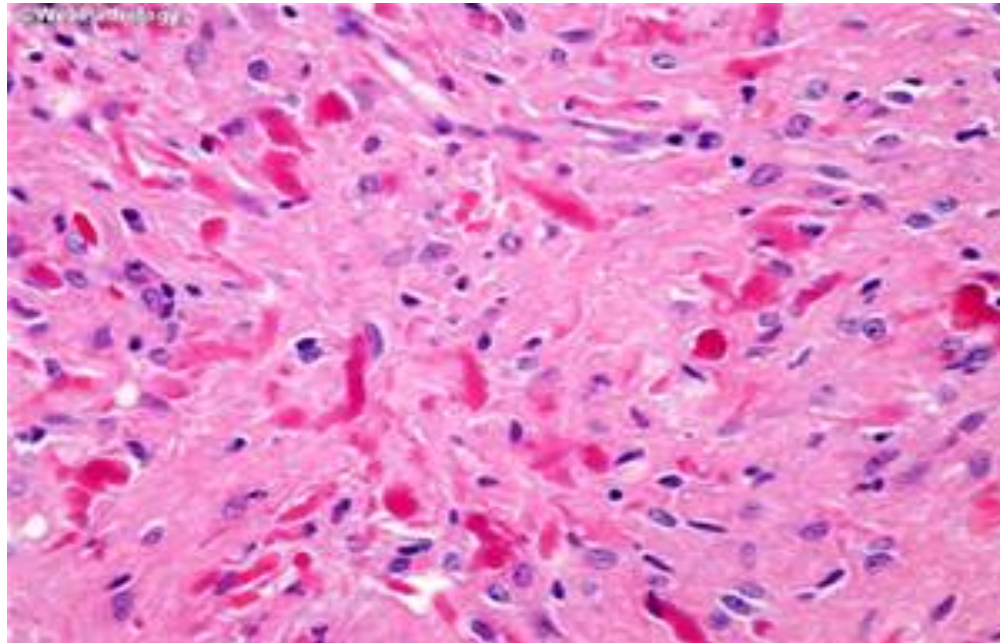
# Pilocytic astrocytoma





# Pilocytic astro

- **Rosenthal fibres**: thick ,elongated , eosinophilic protein aggregates seen in astrocytic processes.
- Note: Rosenthal fibres can also be seen with chronic gliosis.



*Rosenthal fibers are found in:*

*-Pilocytic astrocytoma*

*-Gliosis*

*REMEMBER: Pilocytic astrocytoma cells have BRAF mutation*

# behavior

- Slow growing tumors
- Can be treated by resection

# Oligodendroglioma- *Malignant*

- 5-15% of gliomas
- 40-50 years of age
- Cerebral hemispheres, mainly in the **white matter**. (*that's where oligodendrocytes are- remember that they form the myelin sheath*)
- **Better prognosis than astrocytoma of the same grade-** *except for a few ones; these were found to have p53/ BRAF mutation (mutations of astrocytoma; Better explained within the next few slides)*
- Well diff (WHO II): 10-20 years survival; with treatment
- Anaplastic (WHO III): 5-10 years survival; with treatment

# genetics

- IDH 1 and 2 mutations in 90% of cases. ( mutated tumors have better prognosis than wild type)

IMP.

→ Co-deletions of chromosomes 1p and 19q in 80%

- If the 1p, 19q mutation present: highly responsive to chemo and radiotherapy
- With the new WHO classification (2016) **the 1p , 19q co-deletion is essential to diagnose oligodendroglioma.**

*Extra slide*

## Progenitor

Remember that ALL gliomas originate from glial progenitor cells

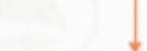


## IDH mutation

Remember that most of astrocytomas and oligodendrogliomas have IDH mutations



**P53/ BRAF mutation**



Astrocytoma

\*Bad prognosis 👎

OR

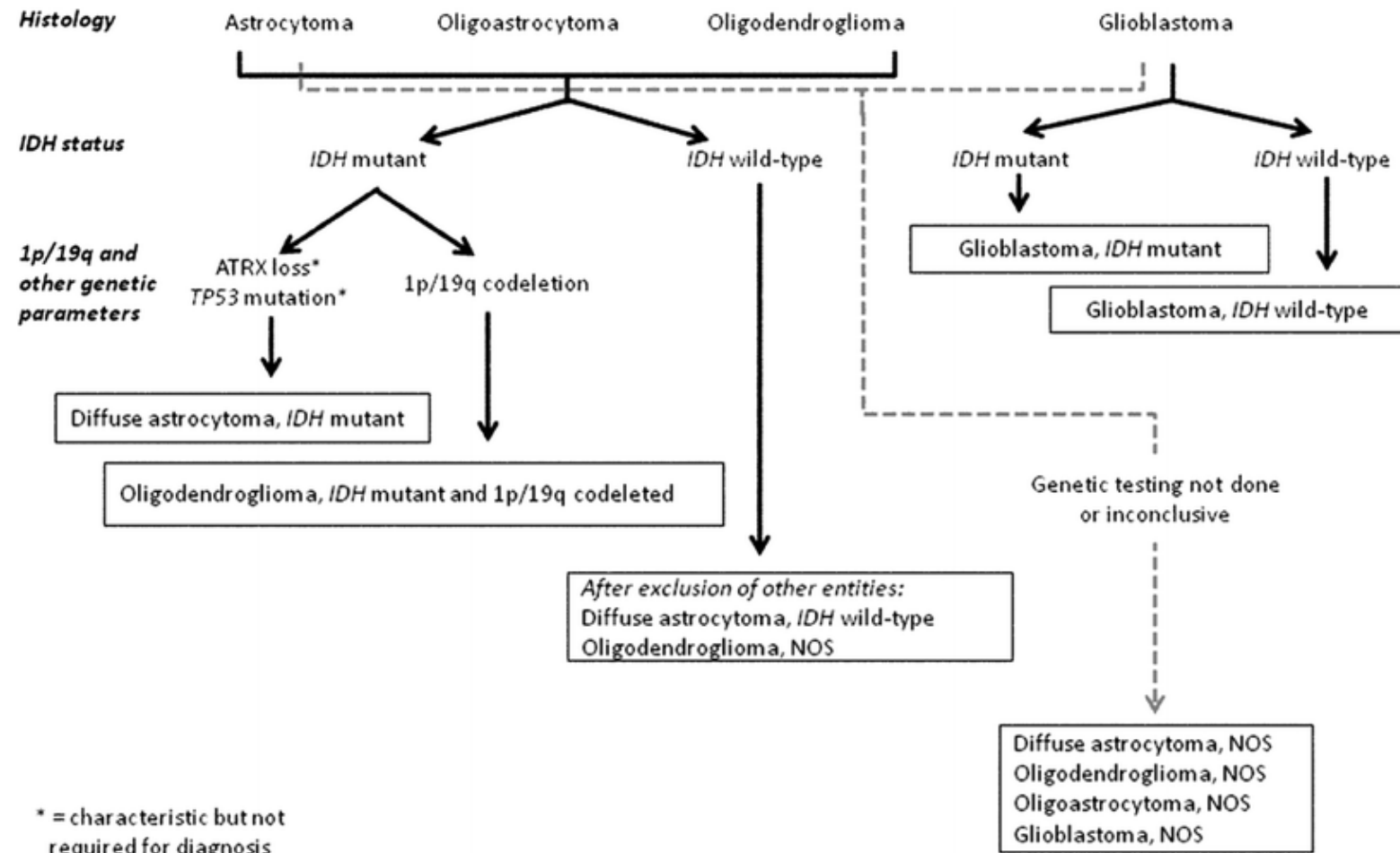
**CODELETION (1p19q)**



Oligodendroglioma

\*Good prognosis 👍

FYI





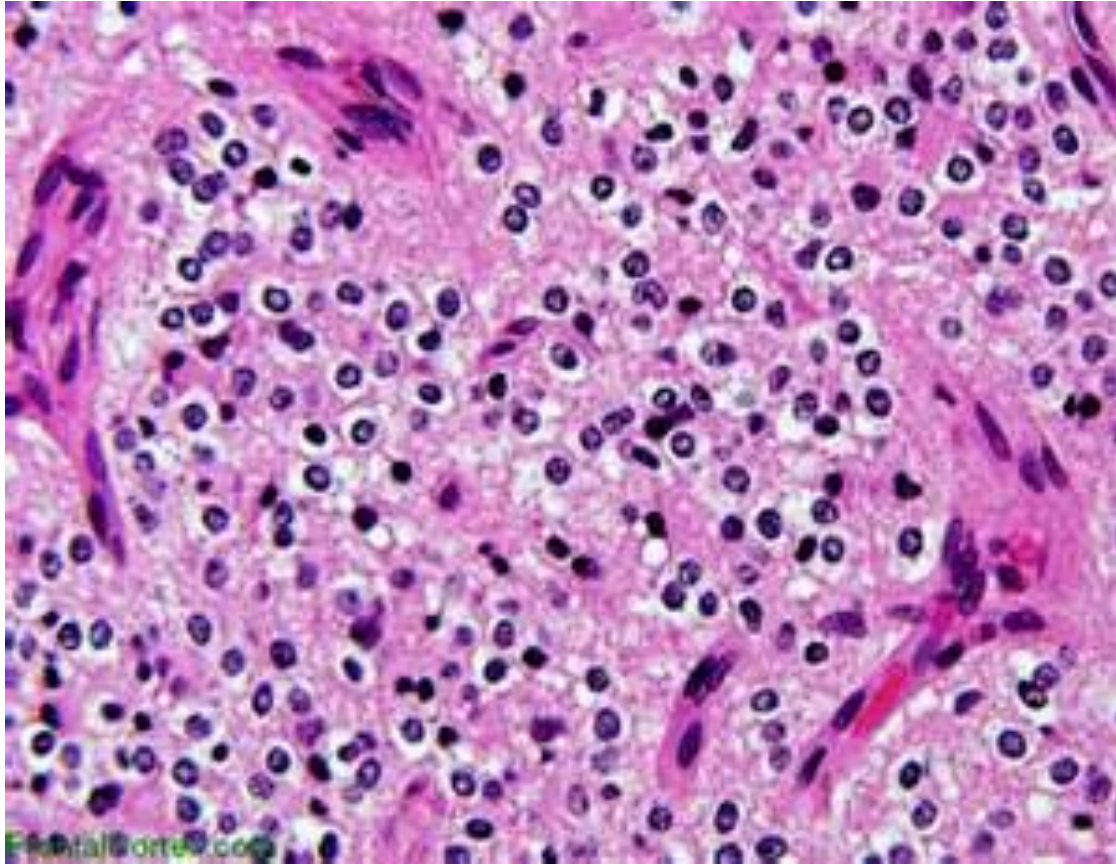
# New WHO classification (2016)

- Glial tumors with IDH mutation and no 1p,19q deletion are called astrocytomas regardless of their morphology.
- Glial tumors with IDH mutation and 1p,19q deletion are called oligodendrogliomas regardless of their morphology.
- This makes sense because with this definition ALL oligo will have a better prognosis than astro.

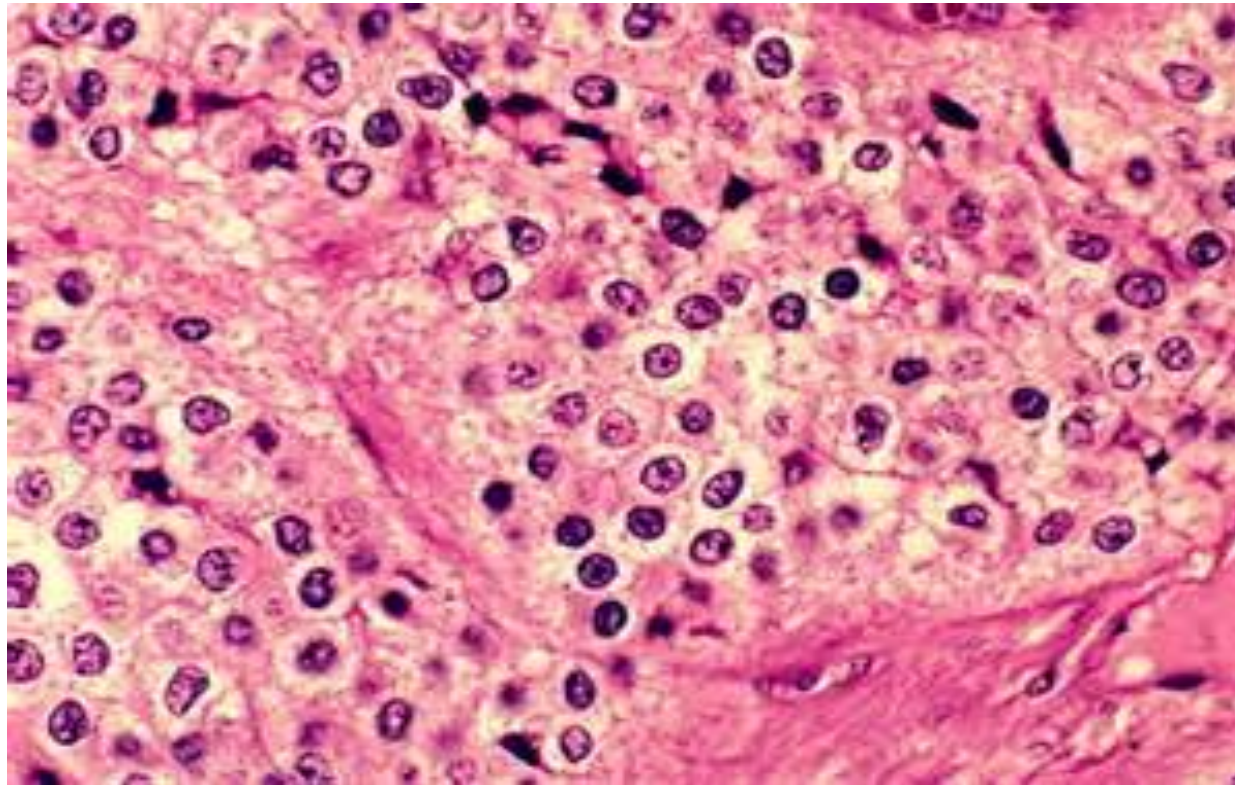
# morphology

- Infiltrative, gelatinous masses
- Can have cysts, haemorrhage or **calcifications**
- Micro: sheets of regular cells with spherical nuclei, granular chromatin, clear cytoplasm, rare mitoses
- Fried egg appearance of the cells.
- Anaplastic: more cellularity, more anaplasia and more mitosis....  
Poorer prognosis

oligodendroglioma;/ note the white halo around the nuclei giving the fried egg appearance

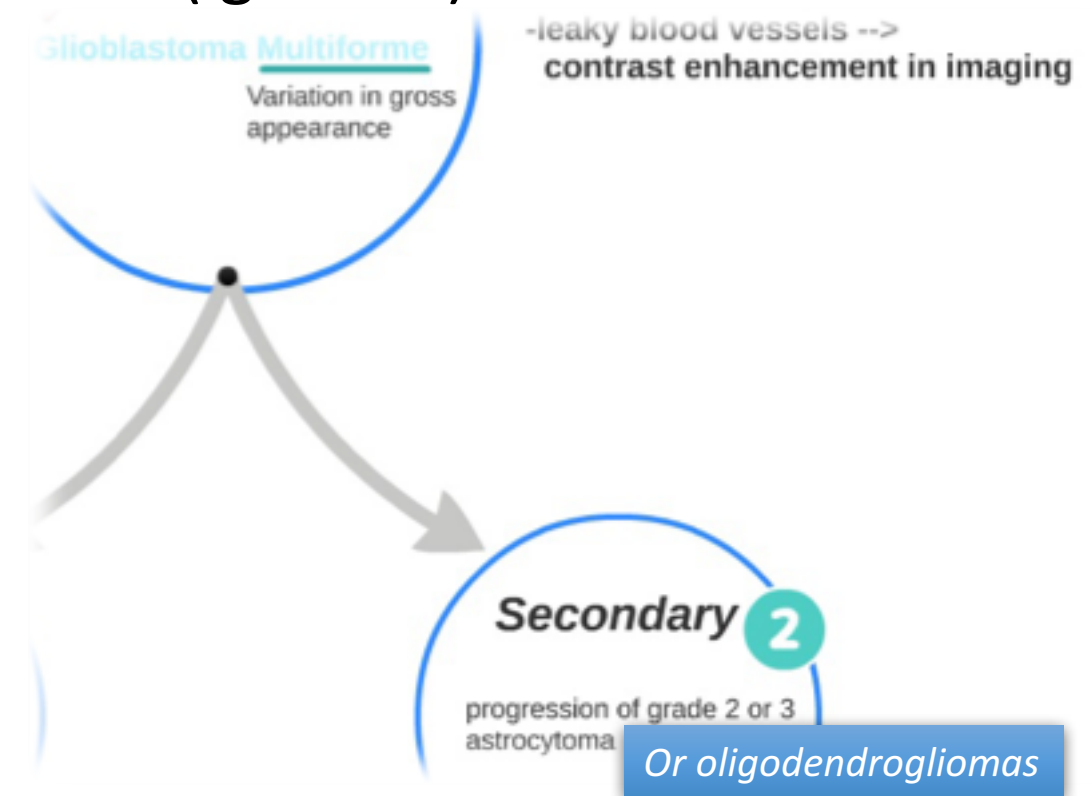


# Oligodendroglioma..



# WHO GRADING of oligodendroglioma

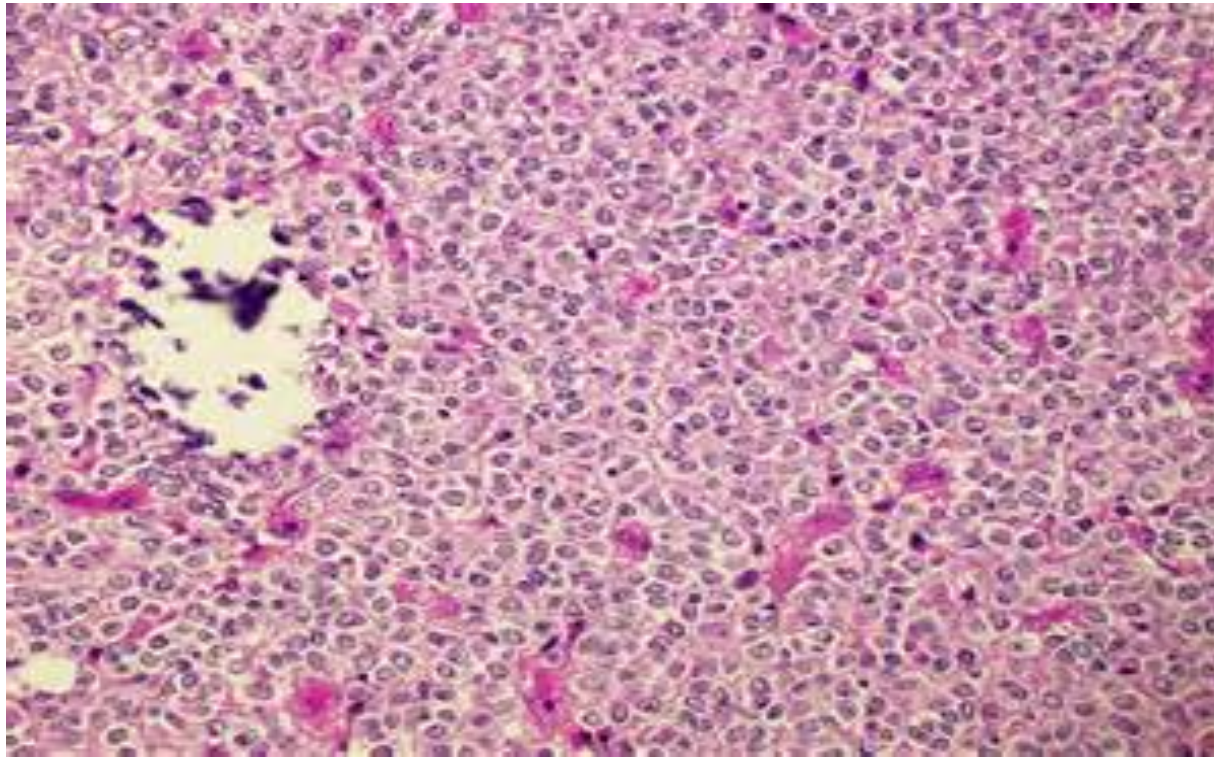
- Well differentiated is grade 2
- Anaplastic ( increased cellularity, pleomorphism and mitotic activity) is grade 3
- NOTE: OLIGO CAN PROGRESS TO GLIOBLASTOMA ( grade 4).
- NOTE: THERE IS NO WHO GRADE 1 OLIGO





# Anaplastic oligo (WHO grade 3)

- Dense cellularity





Adults: in spinal cord

Children: in 4<sup>th</sup> ventricle

## Ependymoma-Malignant/ Ependymal cells

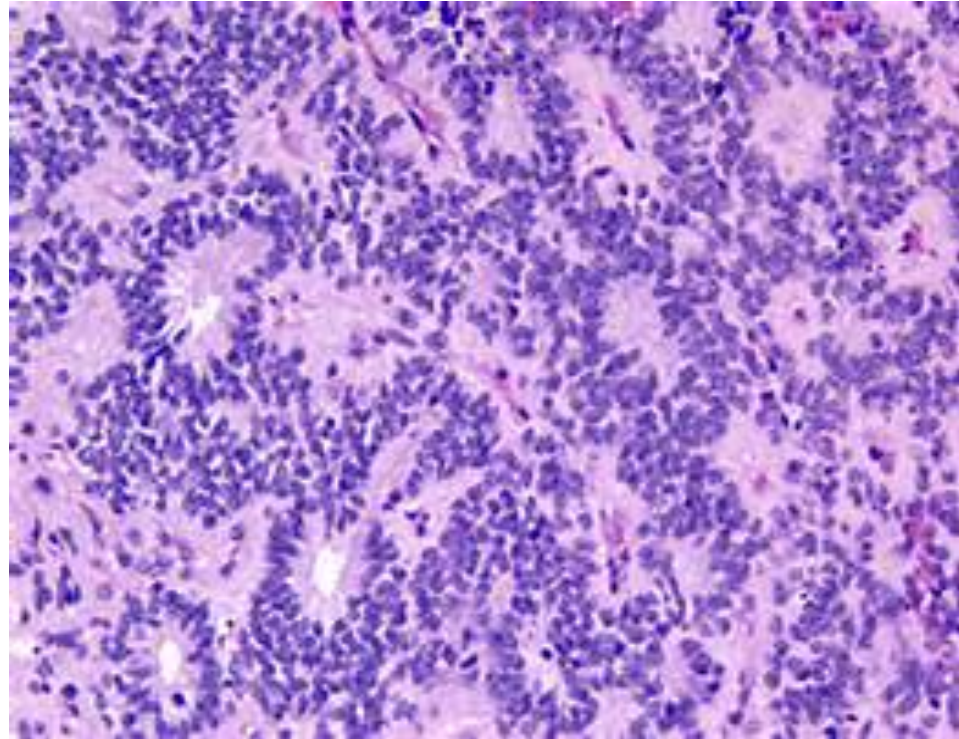
- Arise next to ventricles and central canal of spinal cord.
- If they occur **in first two decades of life**: mostly will arise near the **fourth ventricle** *Remember that children get their cns tumors below the tentorium*
- In adults : mostly in the spinal cord
- Prognosis is better if the tumour is resectable.
- Supratentorial and spinal cord tumours are more amenable to complete surgical resection, thus they have a better prognosis than posterior fossa tumors.

# morphology

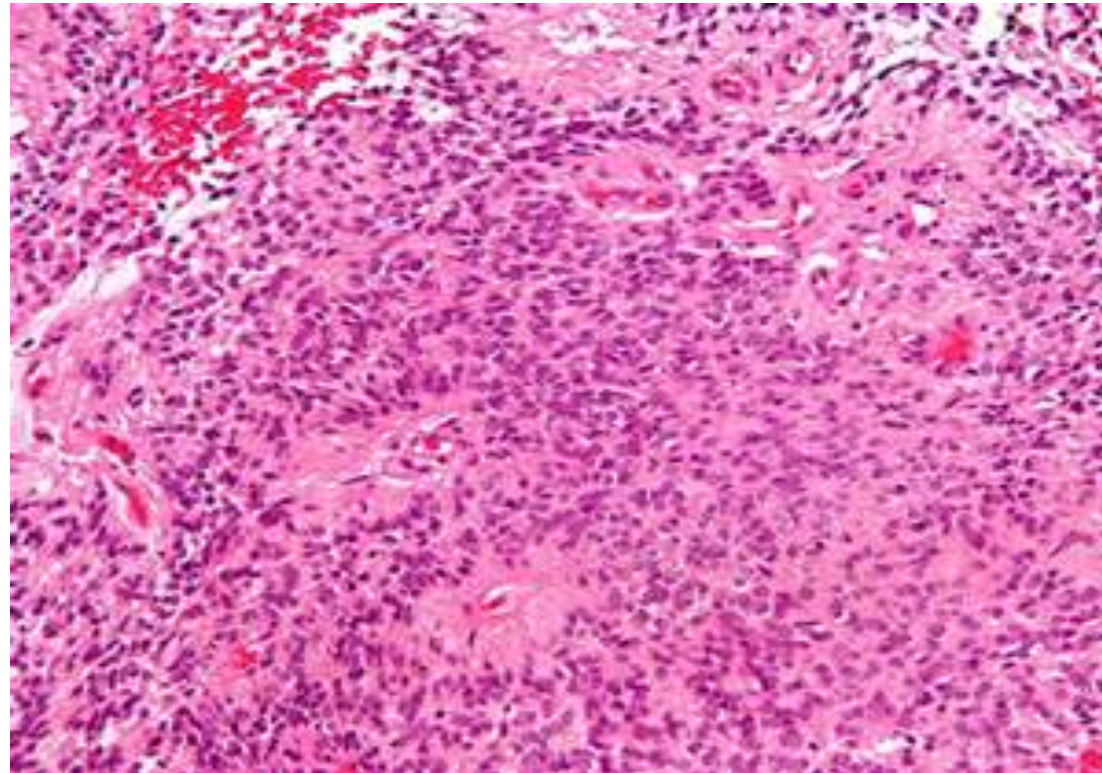
- Solid or papillary masses
- Regular round nuclei
- granular chromatin,
- dense fibrillary background ( GFAP POSITIVE). **Note that the fibrillary background is seen in all gliomas.**
- (1)**rosette formation** around canals and (2)**pseudo-rosette** around blood vessels (*perivascular*)
- Anaplastic ependymoma : cellular, mitosis, necrosis

# Ependymoma/ rosettes

note: true rosettes arise around canals



Ependymoma/ pseudorosettes, these arise around blood vessels



# Tumors related to the ependymal cells

- There are some tumors that occur below the ependymal lining or in association with the choroid plexus.
- These tumors include: choroid plexus papilloma, subependymoma and colloid cysts
- All the above are **benign!** And **rare.**
- However because of their location they cause clinical problems including hydrocephalus.
- Choroid plexus carcinoma can occur but is a rare tumor.

# Neuronal tumors

These are rare tumors that have neuronal differentiation.

- **Central neurocytoma**: low grade neoplasm within and adjacent to ventricular system.
- **ganglioglioma** : glial elements and mature appearing neurones.  
, usually slow growing but the glial element can progress

NOTE: I'M NOT going to ask you  
about these in the exam. Most likely  
you will not see a case in your career!



# Embryonal neoplasms

These are tumors of neuroectodermal origin.

- Primitive appearance that resembles the normal progenitor cells that are found in the developing CNS : small round cells, little cytoplasm
- Most common type of these tumors: medulloblastoma
- Medulloblastoma: 20% of pediatric brain tumors

# Medulloblastoma

- Occurs predominantly in children
- Exclusively in the cerebellum
- Highly malignant if untreated ( WHO grade 4)
- Radiosensitive
- Surgery + chemo + radio.. 5 year survival reaches 75%

# Medulloblastoma



**Presented By:**

Dr. Vandana

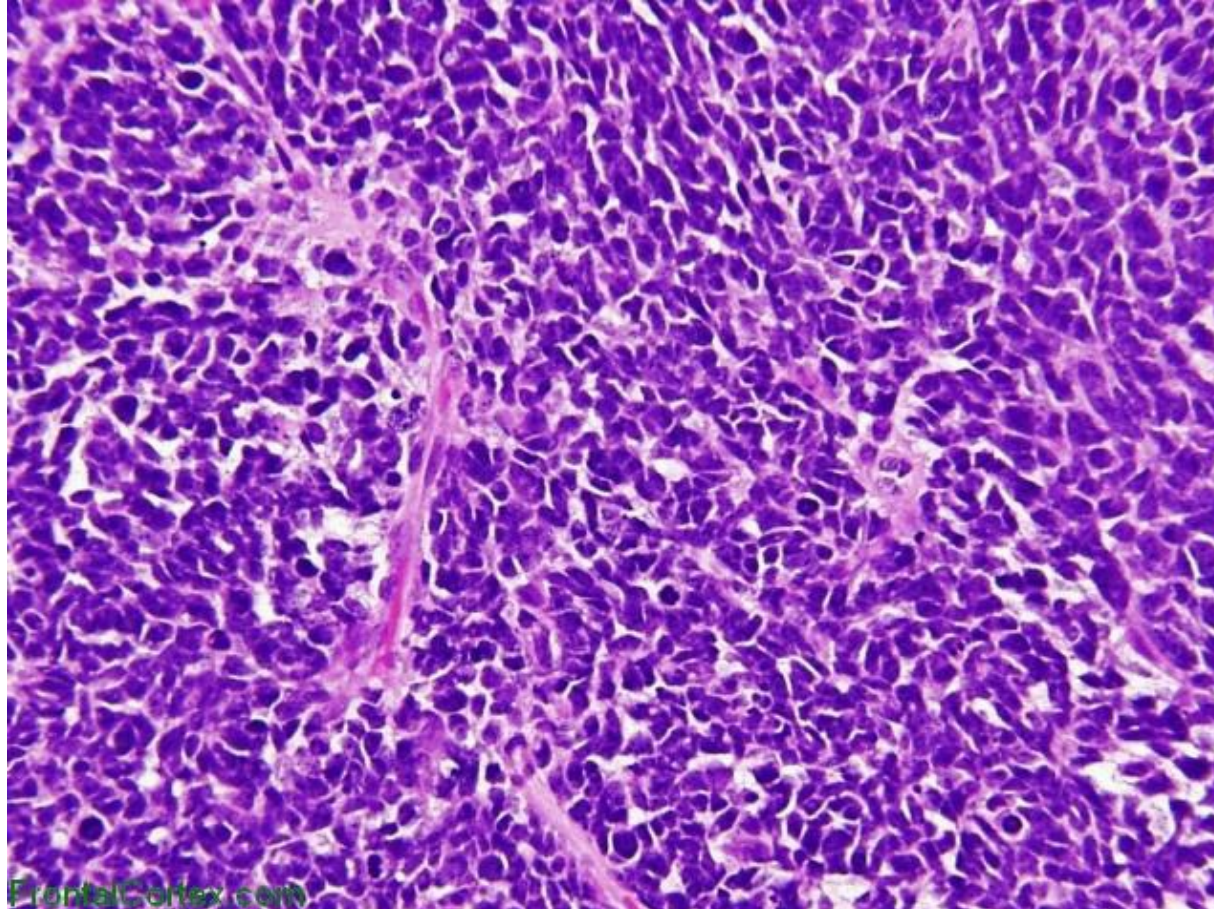
Deptt. of Radiotherapy

CSMMU, Lucknow

# Histology of medulloblastoma

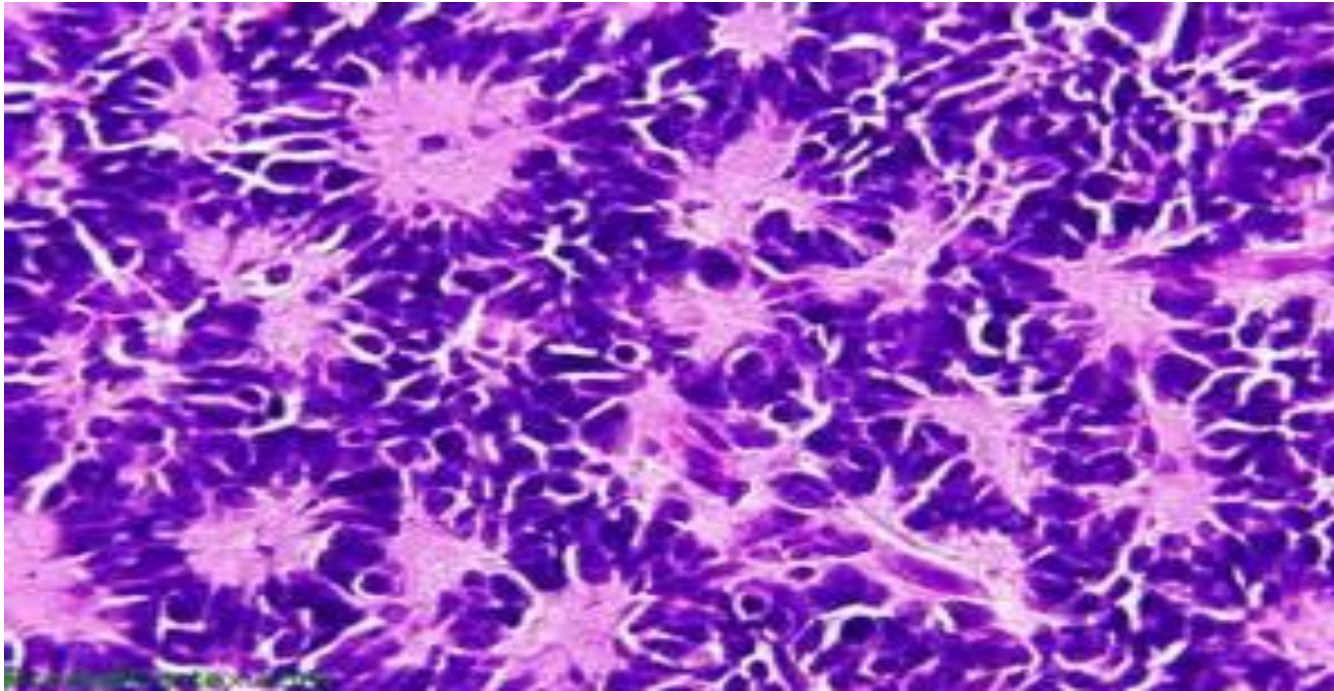
- (1) Highly cellular
- **Sheets of (2) small (3) blue cells** ( small, **rounded** hyperchromatic nuclei, scanty cytoplasm)
- **Many mitoses**
- **Homer Wright Rosettes** = primitive tumor cells surrounding central neuropil ( pink material formed by neuronal processes

# medulloblastoma

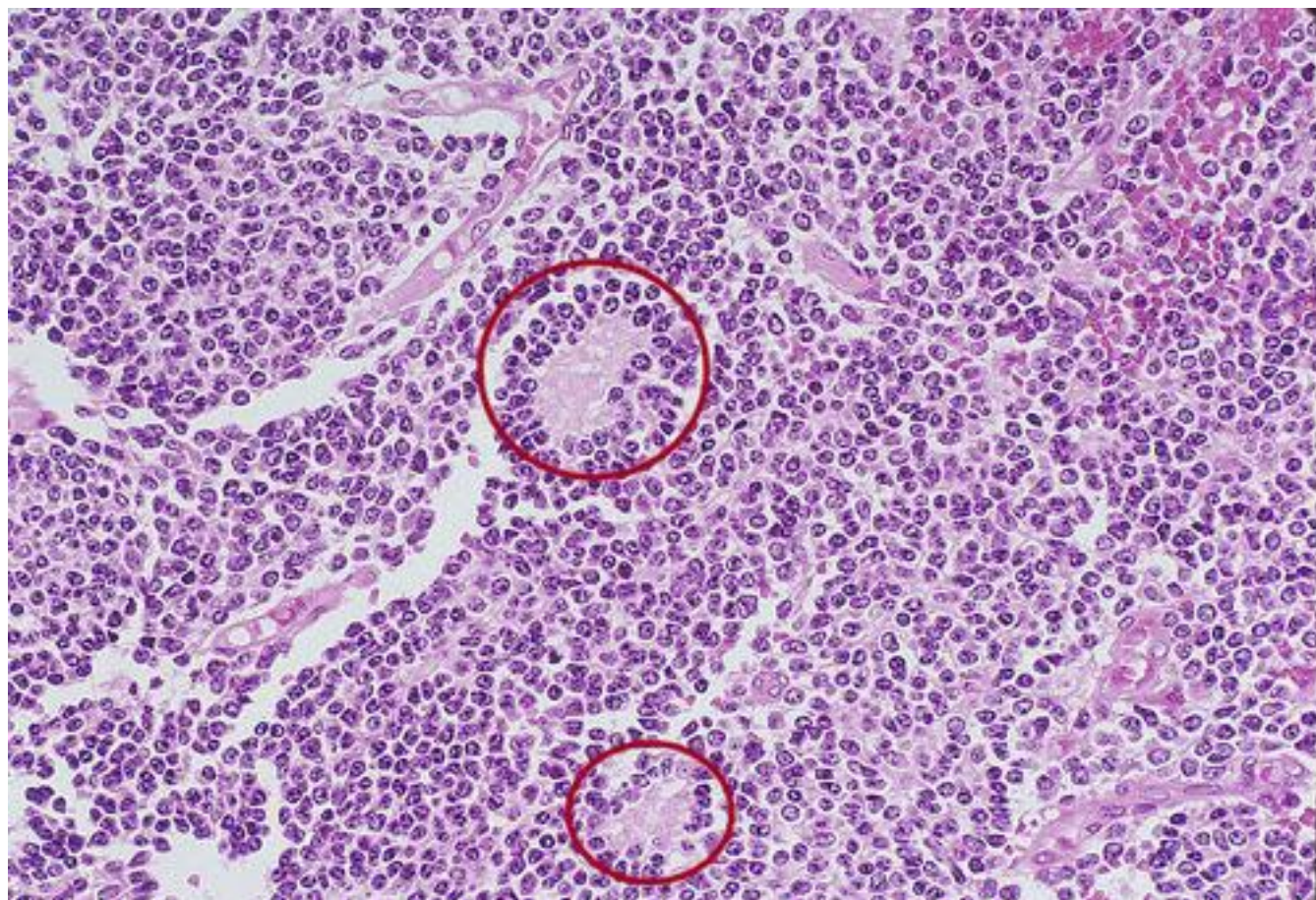




# Homer Wright Rosettes





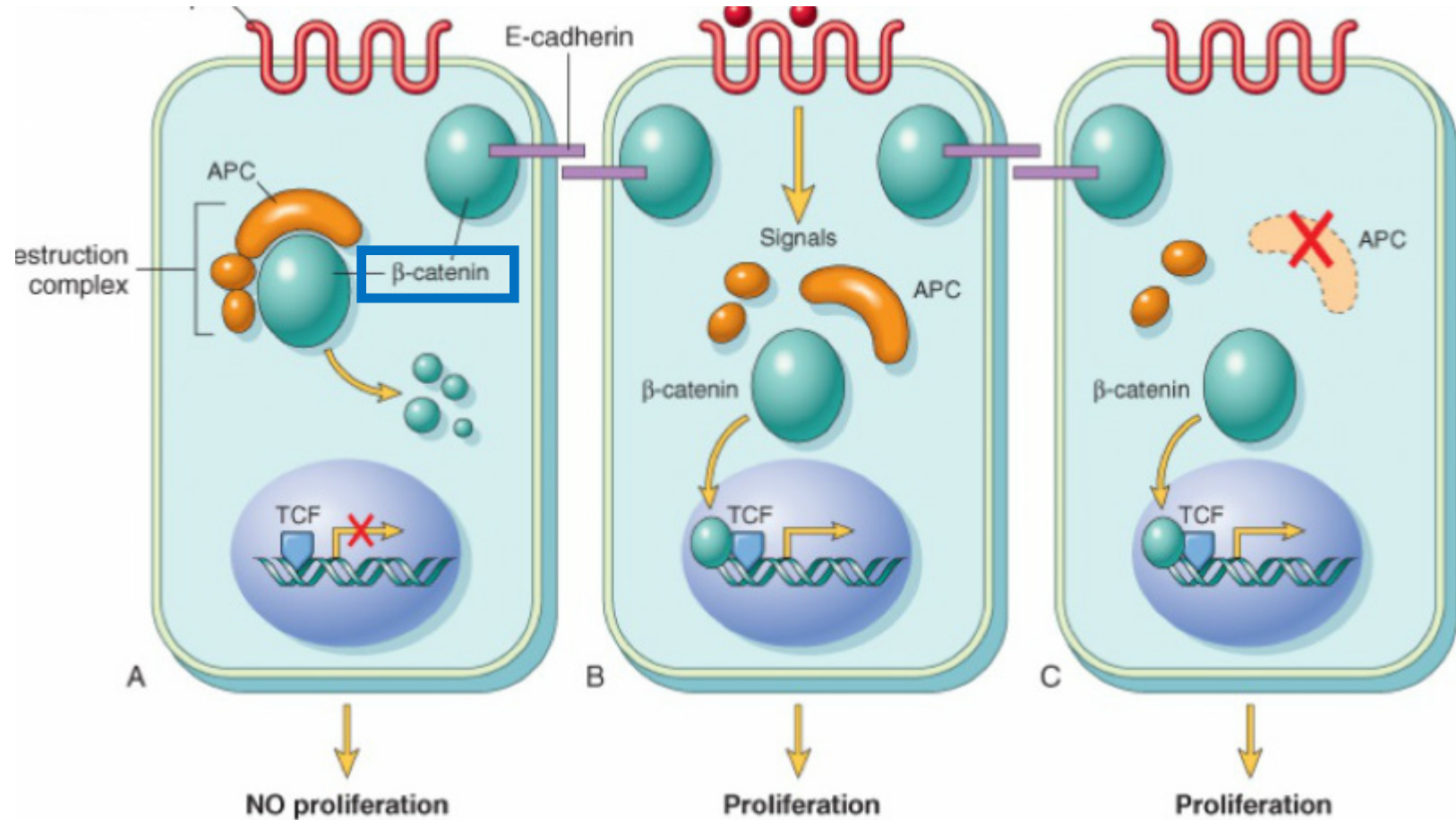


# genetics

- MYC amplification: poor prognosis
- WNT signaling pathway mutations: better prognosis
- These can help in developing new therapies... because it is better to avoid radiotherapy in young patients

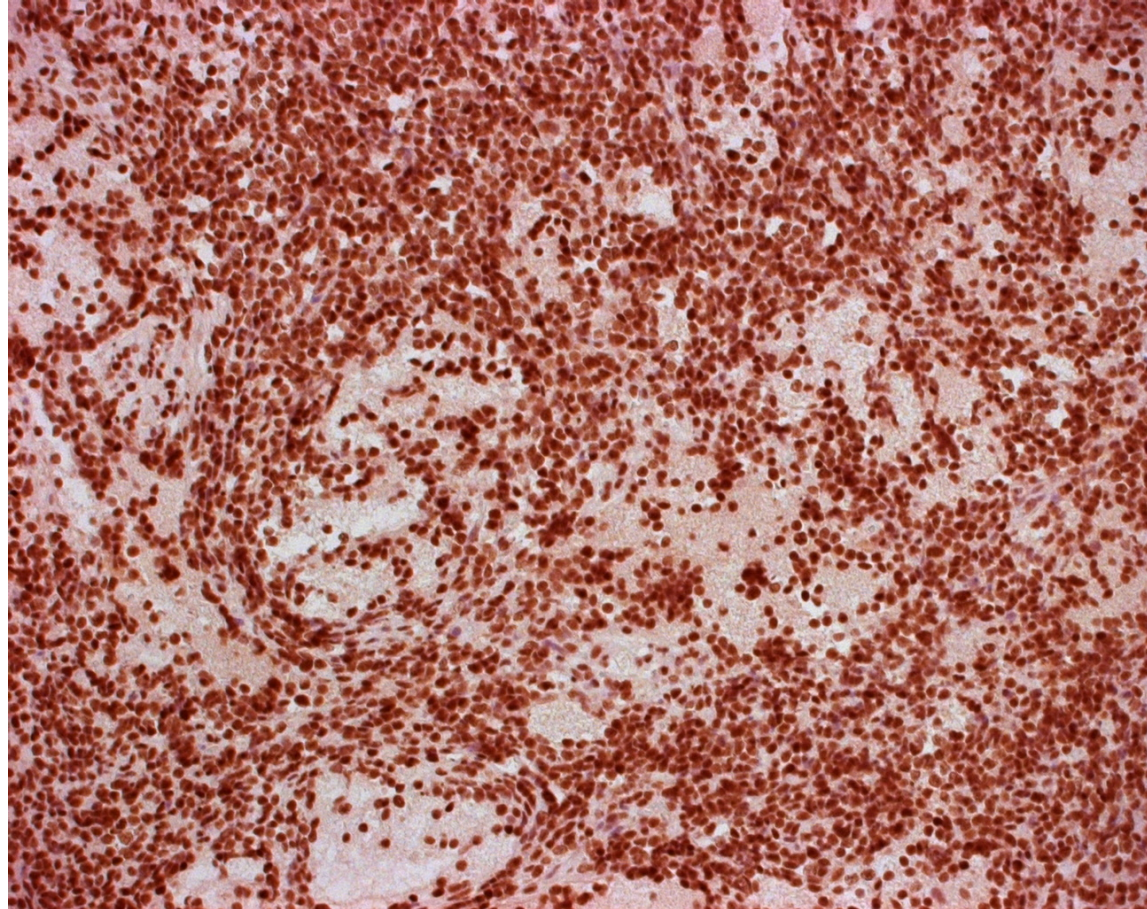
# WNT signaling pathway

*When WNT is there  
Beta catenin is in the  
nucleus,  
When WNT is not here;  
Beta catenin is in the  
cytoplasm*





Beta catenin stain/ if positive then the medulloblastoma has WNT signaling mutation: better prognosis..



*We do not have a stain that stains WNT directly so we stain for  $\beta$ -catenin as an indirect way to measure WNT*

- Activating mutations in beta-catenin in approximately 10% of medulloblastoma represent the WNT subtype.
- The identification of nuclear beta-catenin has been demonstrated to be nearly 100% specific and sensitive for the presence of mutation and makes it possible to reliably identify WNT pathway tumors using routine immunohistochemistry.

Remember that when beta catenin is in the nucleus That means WNT is upregulated→ cancer.

# Treatment of medulloblastoma

- Medulloblastoma therapy, including craniospinal radiation and multiagent chemotherapy, results in **significant long term toxicity** for many disease survivors, including neurocognitive impairment, neuropathy, endocrinopathy, impaired bone growth, impaired motor function, hearing loss, and secondary malignancy.
- These side effects are closely related to **dose of radiation** therapy and **age at diagnosis, the earlier the age, the worse the neurologic toxicity for the developing brain**



- The long-term survival of patients with WNT tumors is excellent, exceeding 90%.
- Also, WNT tumors arise exclusively in an older age group of children over the age of three years.

- The rest of the slides in this lecture are FYI.. And to stimulate you to think!
- Happy reading !

# Palliative care of patients

- Palliative care: Aim is to **relieve symptoms and side effects** caused by cancer or its treatment. Palliative care helps a child with cancer **live as comfortably as possible. It also addresses the psychological, social, and spiritual needs of the child and family.**

- Palliative care focuses on preventing, managing, and relieving the symptoms of cancer and the side effects of cancer treatment.
- It also provides comprehensive support to people living with cancer and their family, friends, and caregivers.
- Anyone, regardless of age or type and stage of cancer may receive palliative care before, after, and during treatment.
- Talking about palliative care soon after a cancer diagnosis helps patients better understand their prognosis and goals of treatment, clarify their expectations, and maintain their quality of life

# The goals of palliative care include:

- Treating symptoms, including pain, nausea, breathlessness, insomnia, and other physical issues caused by cancer or its treatment
- Making sure patients and caregivers understand the diagnosis and goals of treatment
- Providing guidance for making treatment decisions
- Working with the patient's other doctors and providing referrals to other health care providers as needed
- Providing support for the patient's emotional and social needs, spiritual needs or concerns, and practical needs
- Providing support for caregivers, and other family members and friends