CNS pathology
Third year medical students

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2018

Lecture 12: CNS tumours 2/3

Pilocytic astrocytoma

- Relatively **benign** (WHO grade 1)
- 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 were the tumor is not resectable.

morphology

- Solid and cystic components
- If solid it is usually well defined

Microscopically:

-bipolar cells with long GFAP positive processes

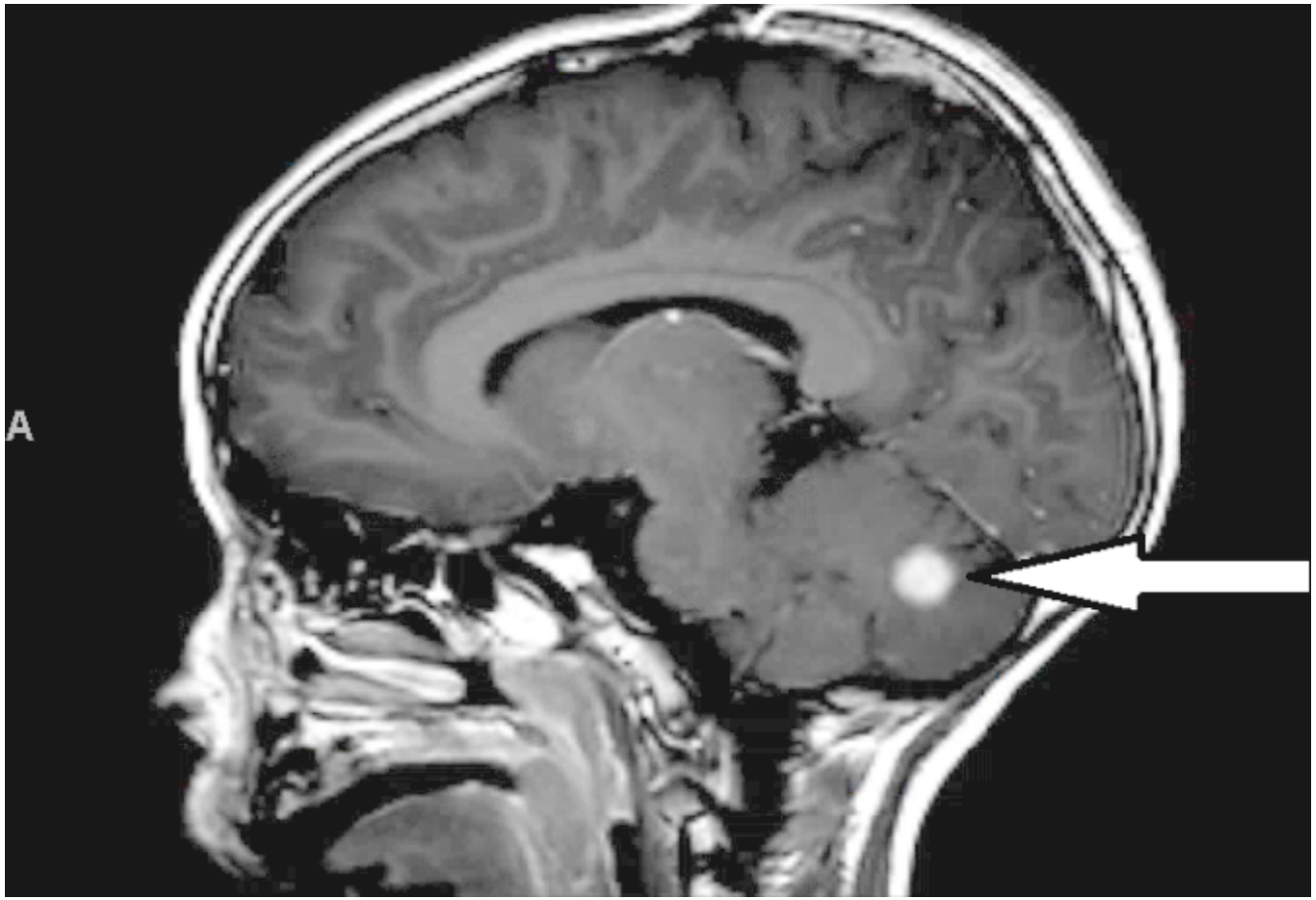
-Rosenthal fibers

-eosinophilic granular bodies

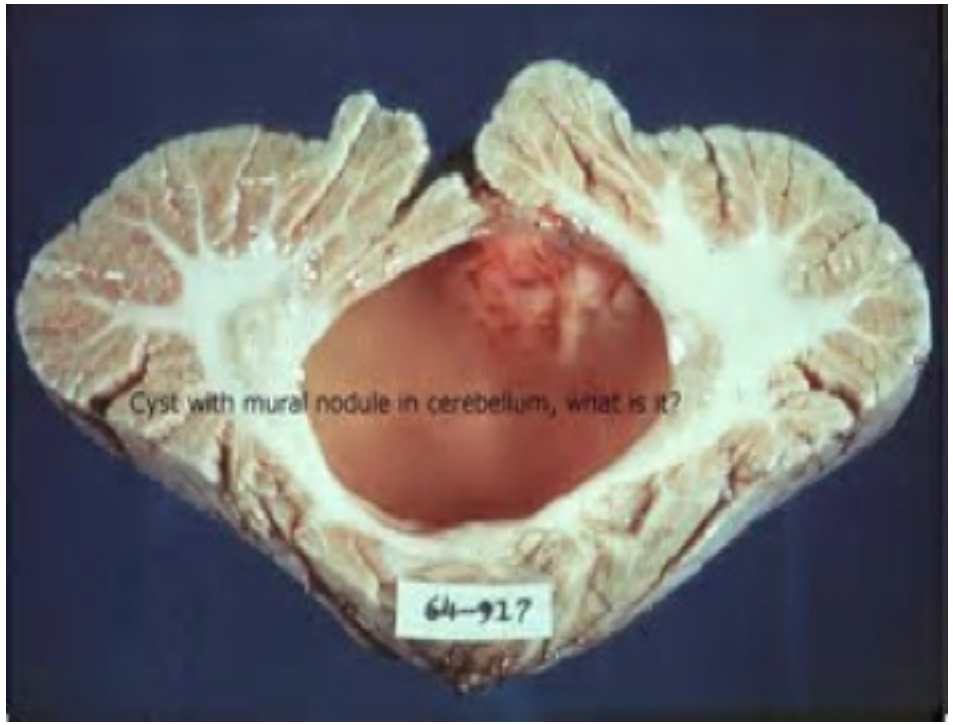
-microcysts

-mitosis and necrosis are rare

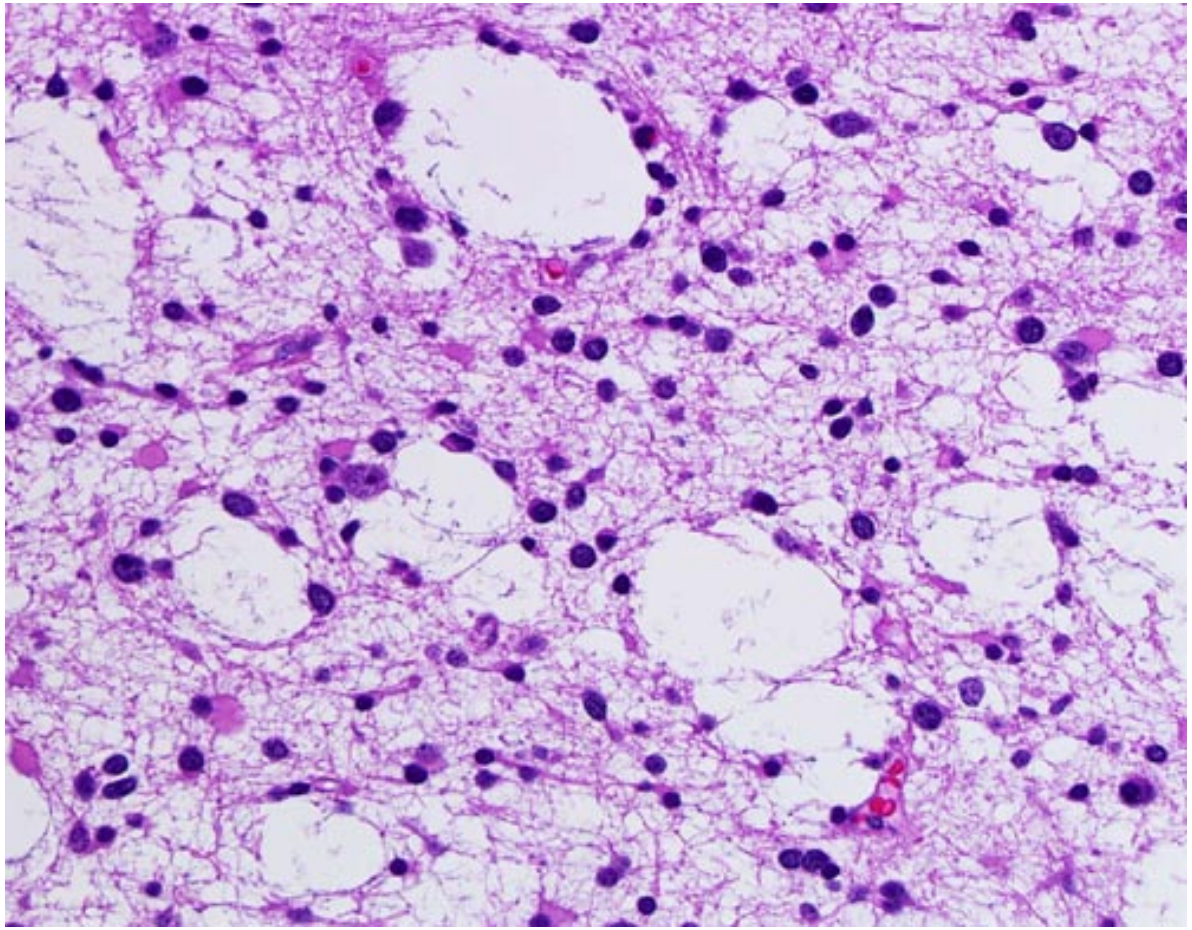
Note the well circumscribed lesion in the cerebellum



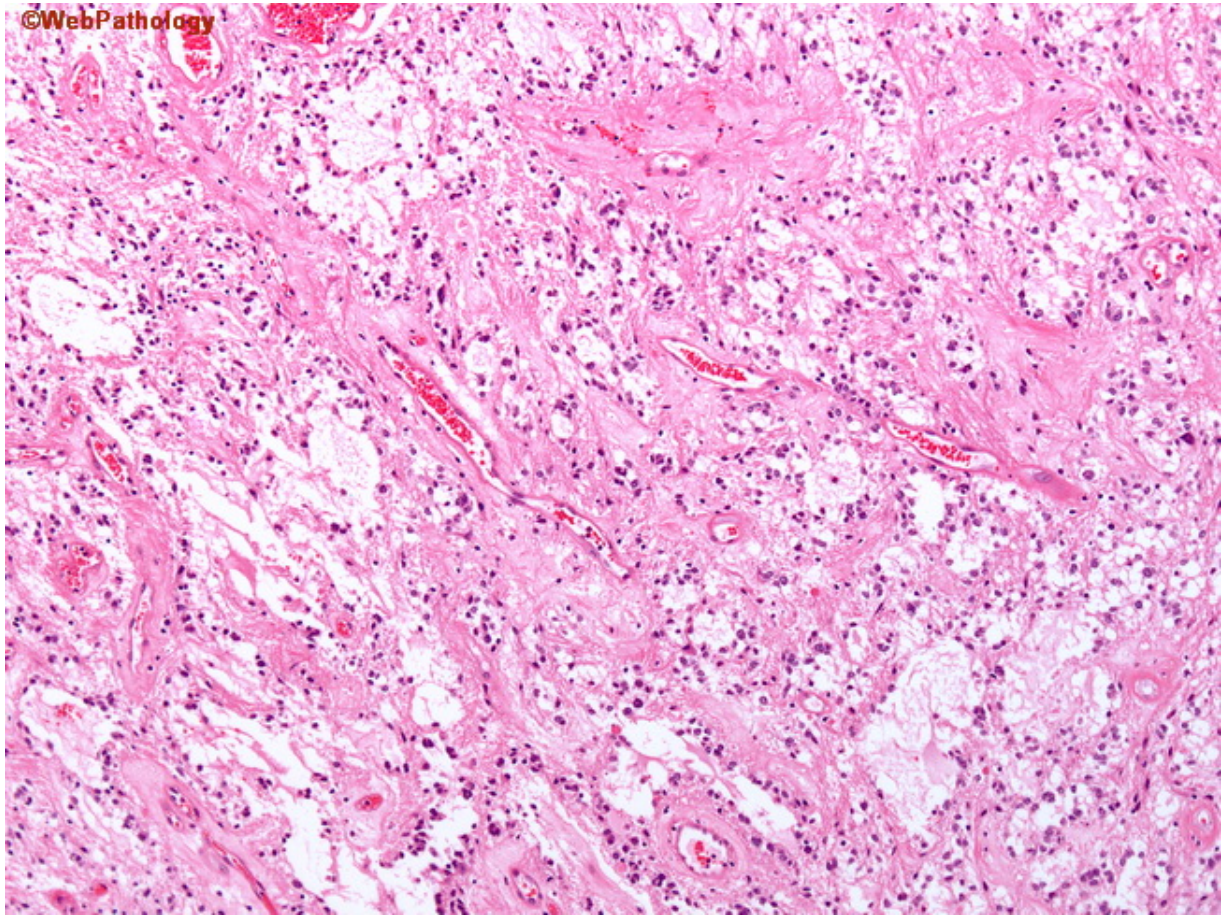
Pilocytic astro: this example is mainly cystic but has also a solid component



Pilocytic/ microcysts

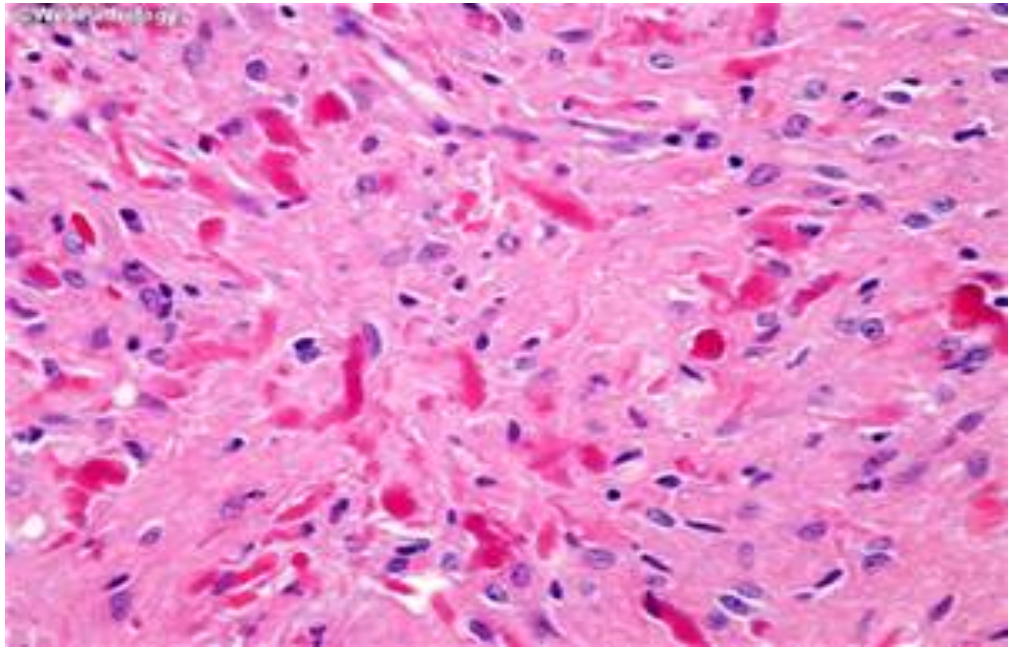


Pilocytic astrocytoma



Pilocytic astro

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



behaviour

- Slow growing tumors
- Can be treated by resection

oligodendroglioma

- 5-15% of gliomas
- 40-50 years of age
- Cerebral hemispheres, mainly in the **white matter.**
- Better prognosis than astrocytoma of the same grade
- 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)
- *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.

New WHO classification (2016)

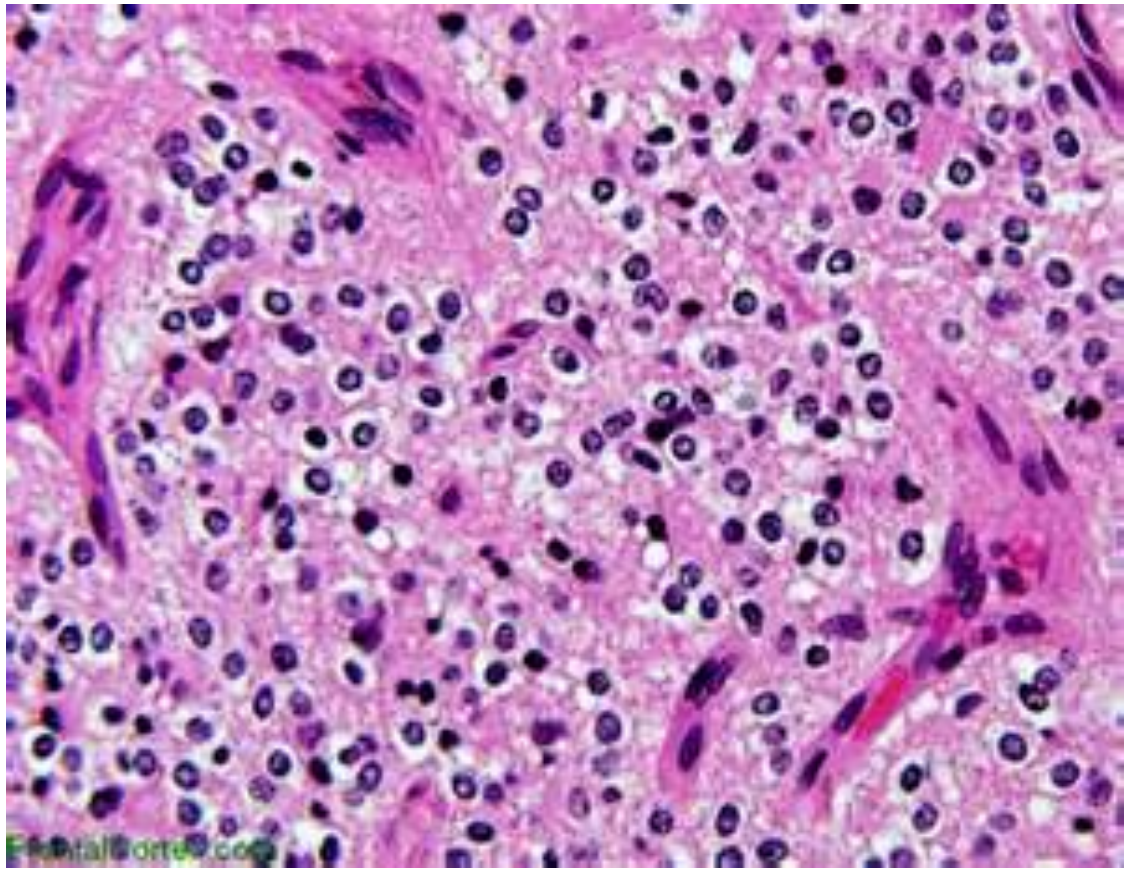
- Glial tumors with IDH mutation and no 1p,19q deletion are called astrocytomas regardless of their morphology.
- Glial tumors with IDH mutation and 1p,19q deletion are called oligodendrgliomas regardless of their morphology.

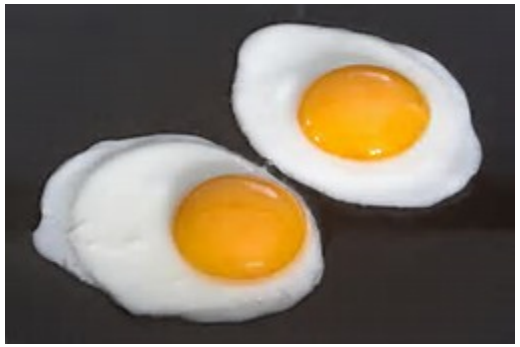
- This makes sense because with this definition ALL oligo will have a better prognosis than astro.

morphology of oligodendrogliomas

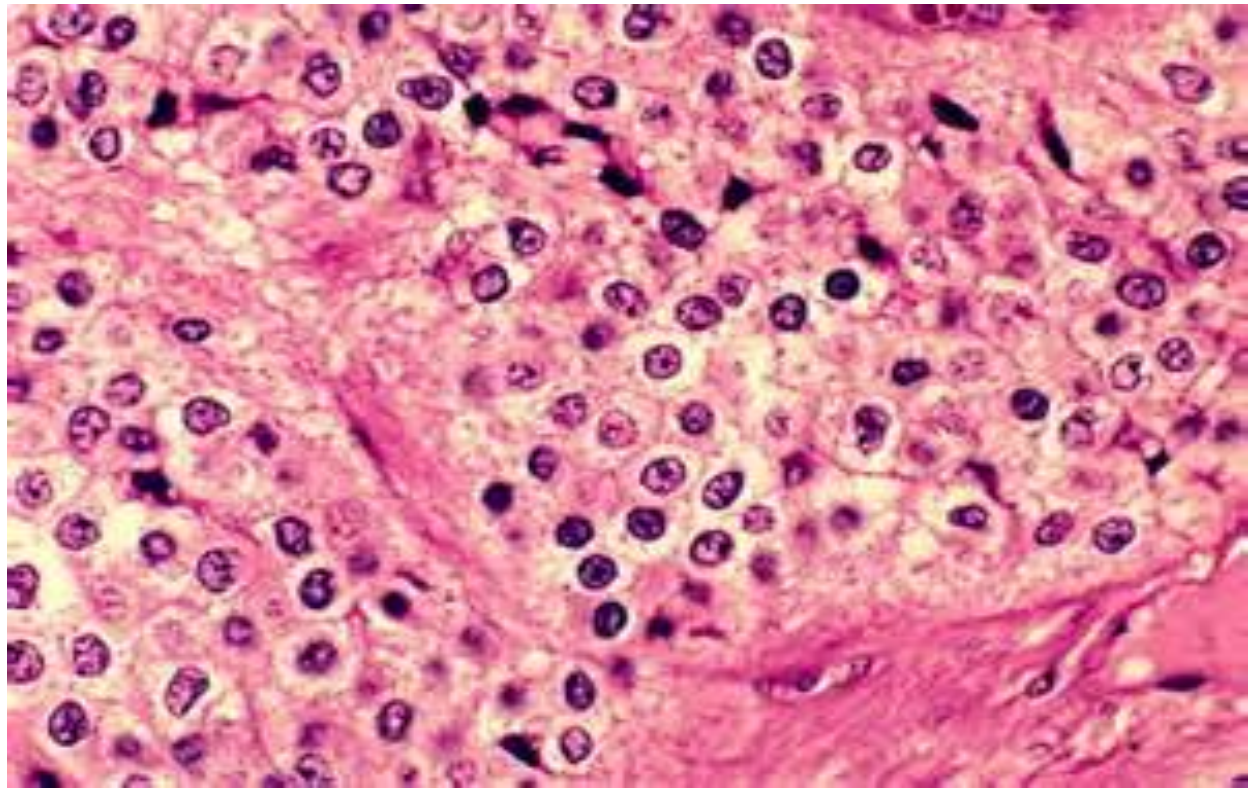
- Infiltrative, gelatinous masses
- Can have cysts, haemorrhage or calcifications
- Micro: sheets of regular cells with spherical nuclei, granular chromatin, clear cytoplasm, rare mitoses
- Fried egg appearance of the cells.
- Anaplastic: more cellularity, more anaplasia and more mitosis…. Poorer prognosis

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





Oligodendroglioma..



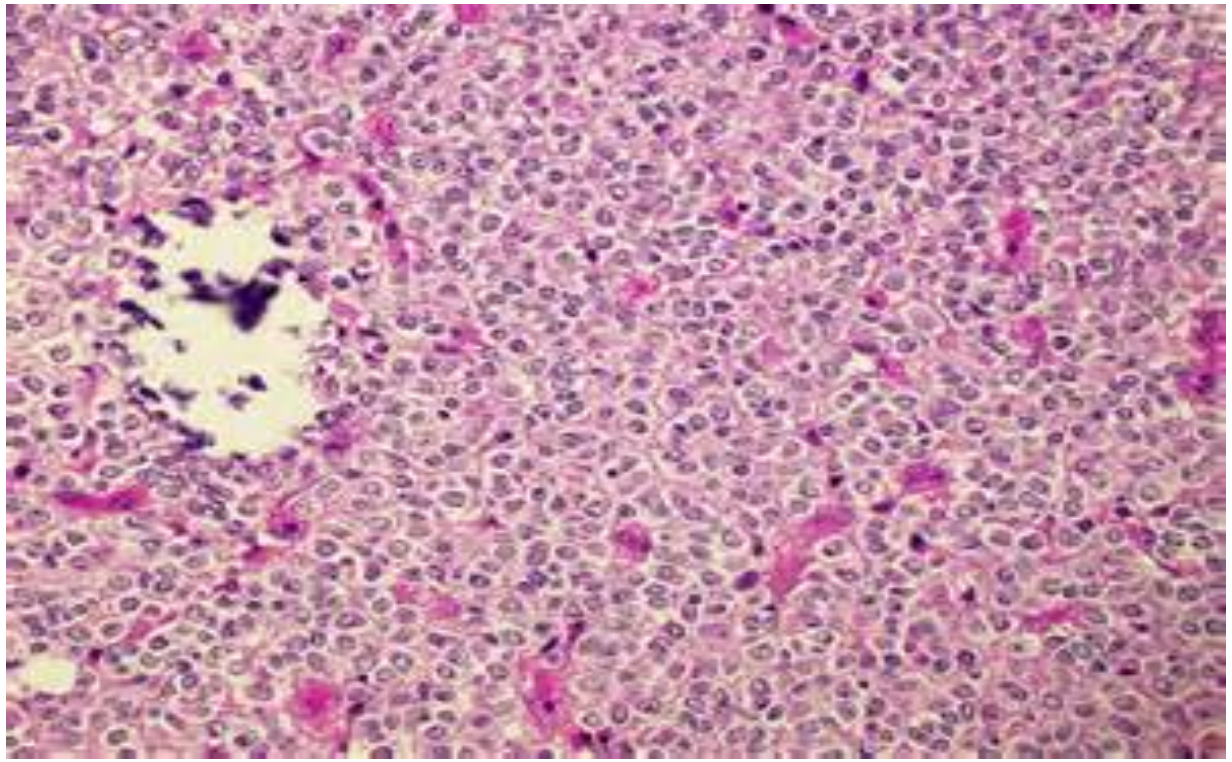
WHO GRADING of oligodendroglioma

- 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



Ependymoma

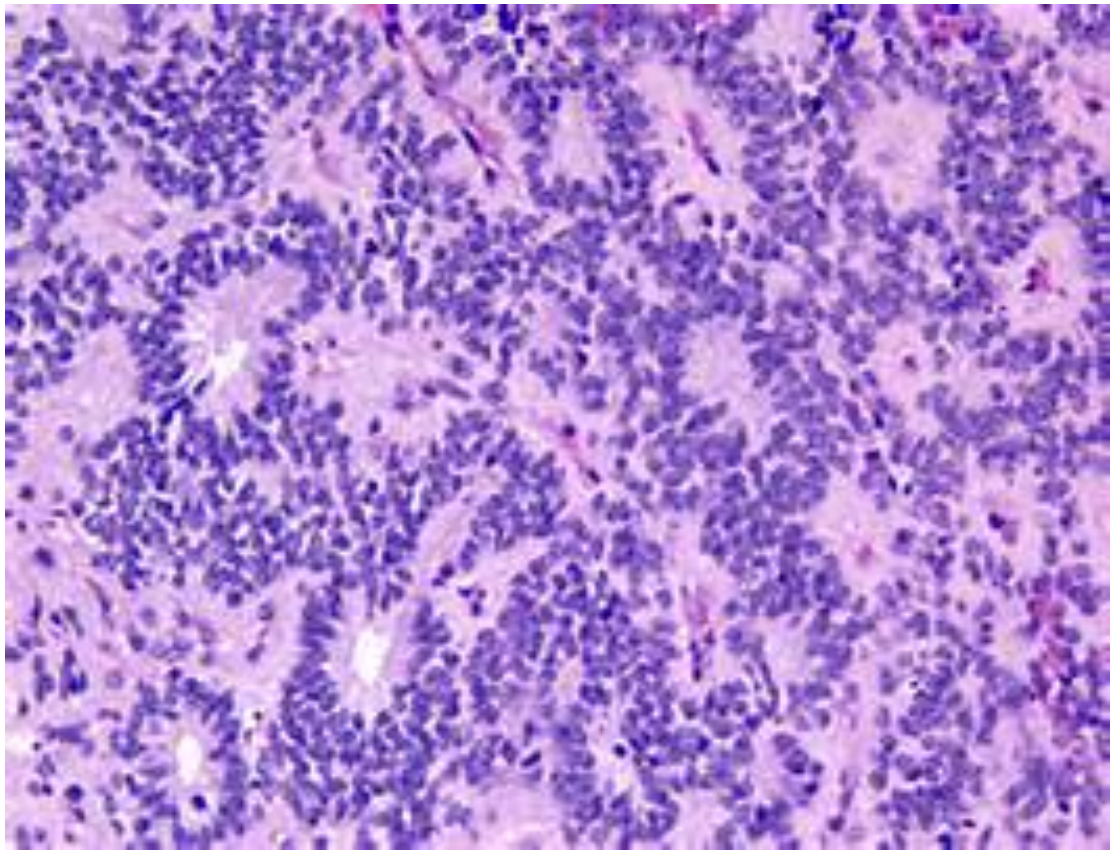
- Arise next to ventricles and central canal of spinal cord.
- If they occur in **first two decades of life: mostly will arise near the fourth ventricle**
- I**n adults : mostly in the spinal cord**

- 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.

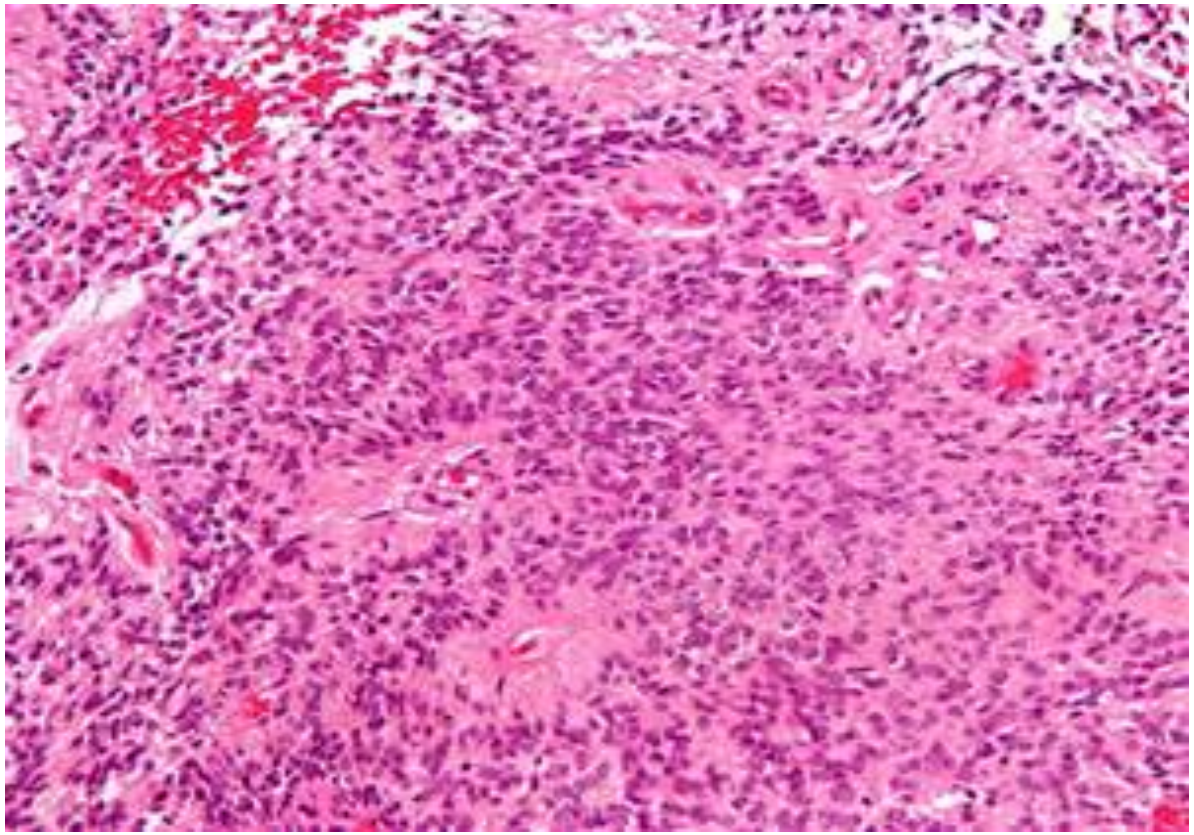
morphology

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

Ependymoma/ rosettes
note: true rosettes arise around canals



Ependymoma/ pseudorossetes, 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

Embryonal neoplasms

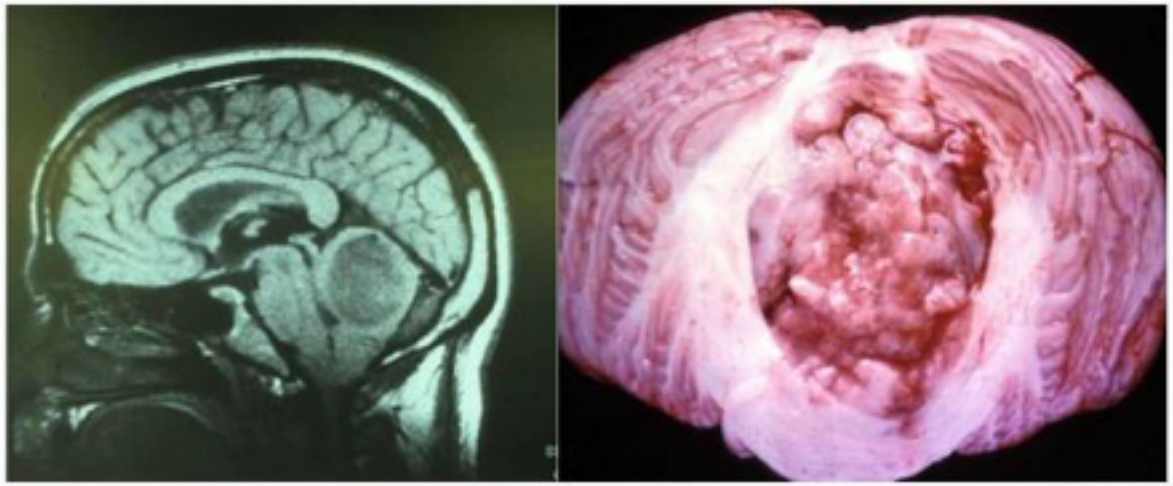
These are tumors of neuroectodermal origin.

- 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
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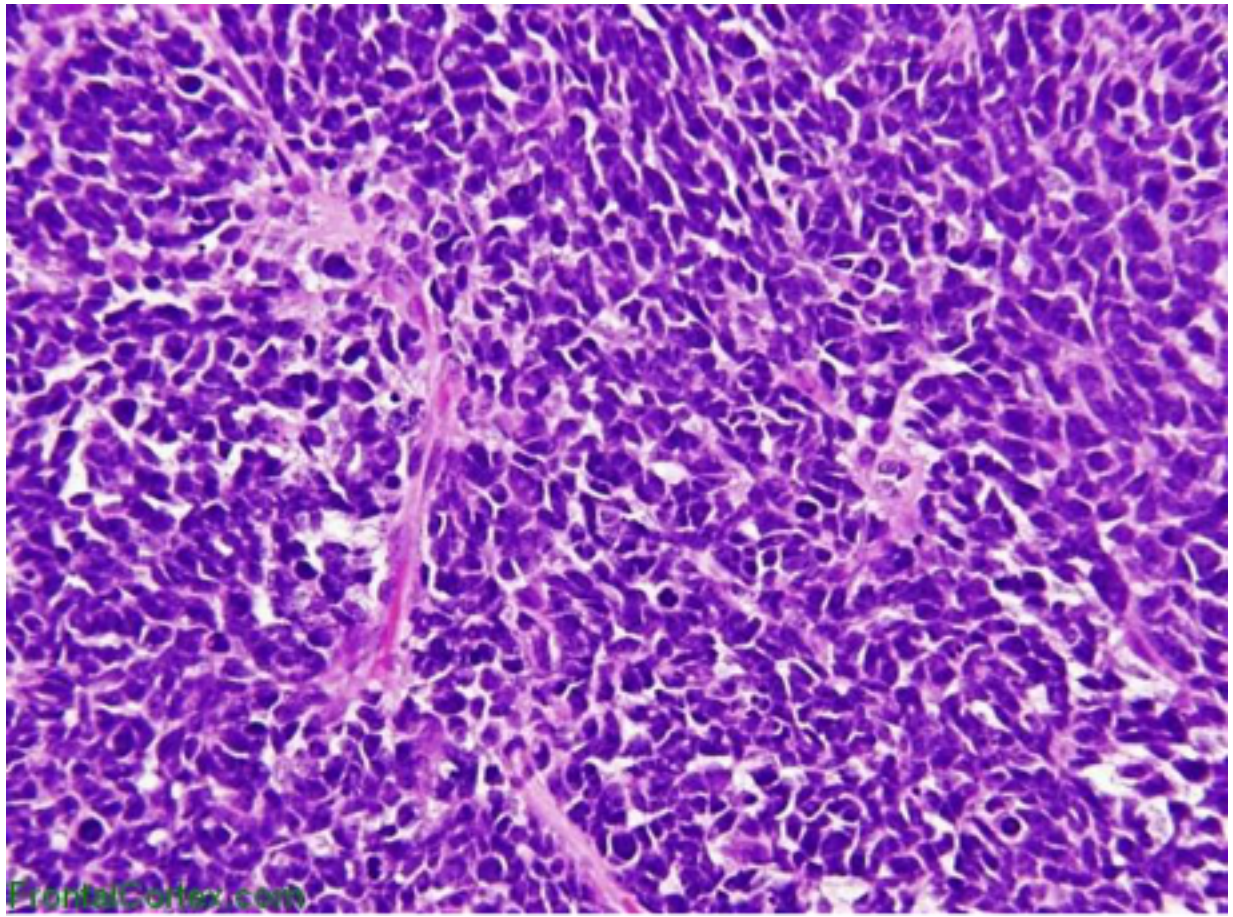
CSMMU, Lucknow

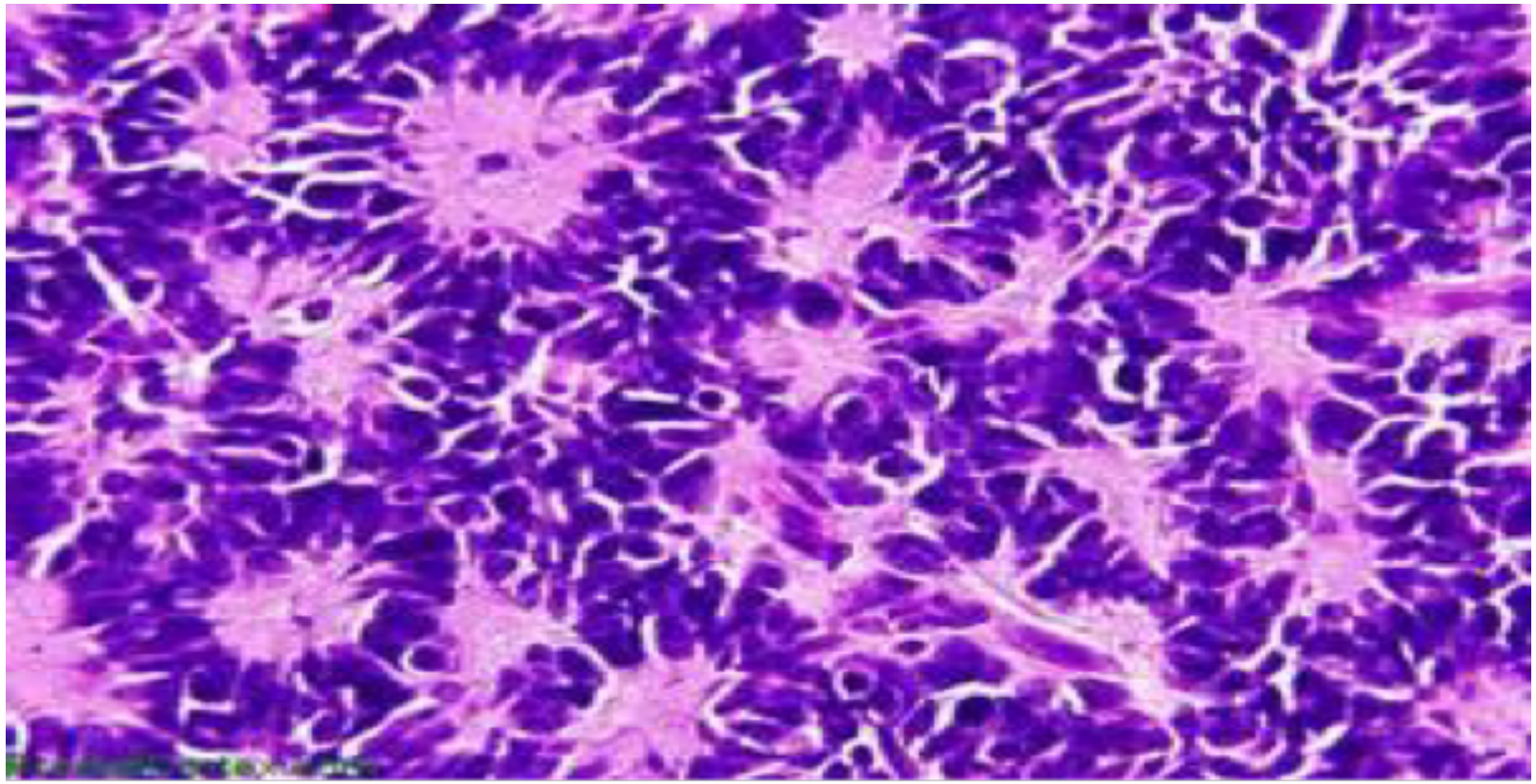
Histology of medulloblastoma

- Highly cellular
- Sheets of small 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

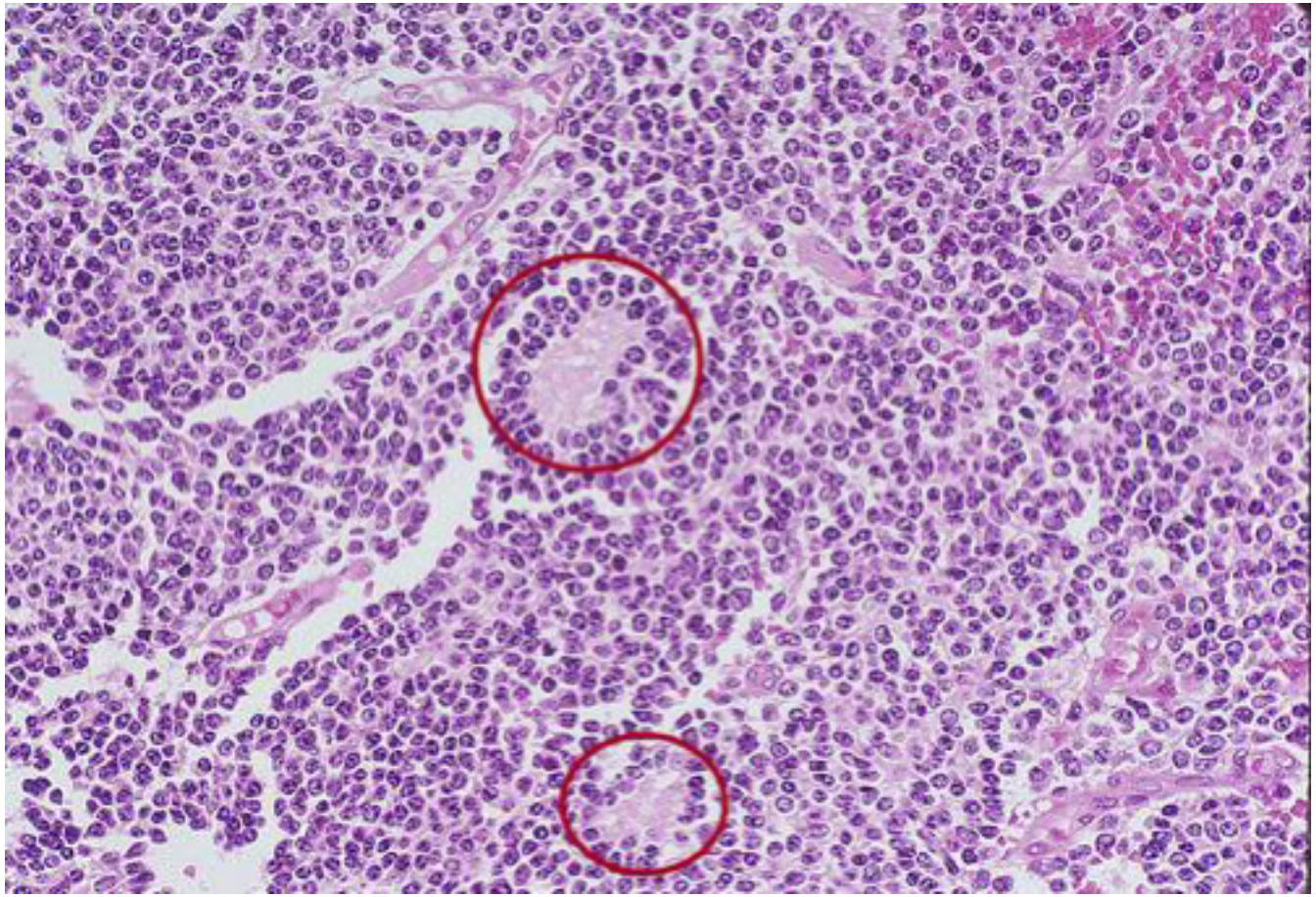
medulloblastoma



Homer Wright Rosettes



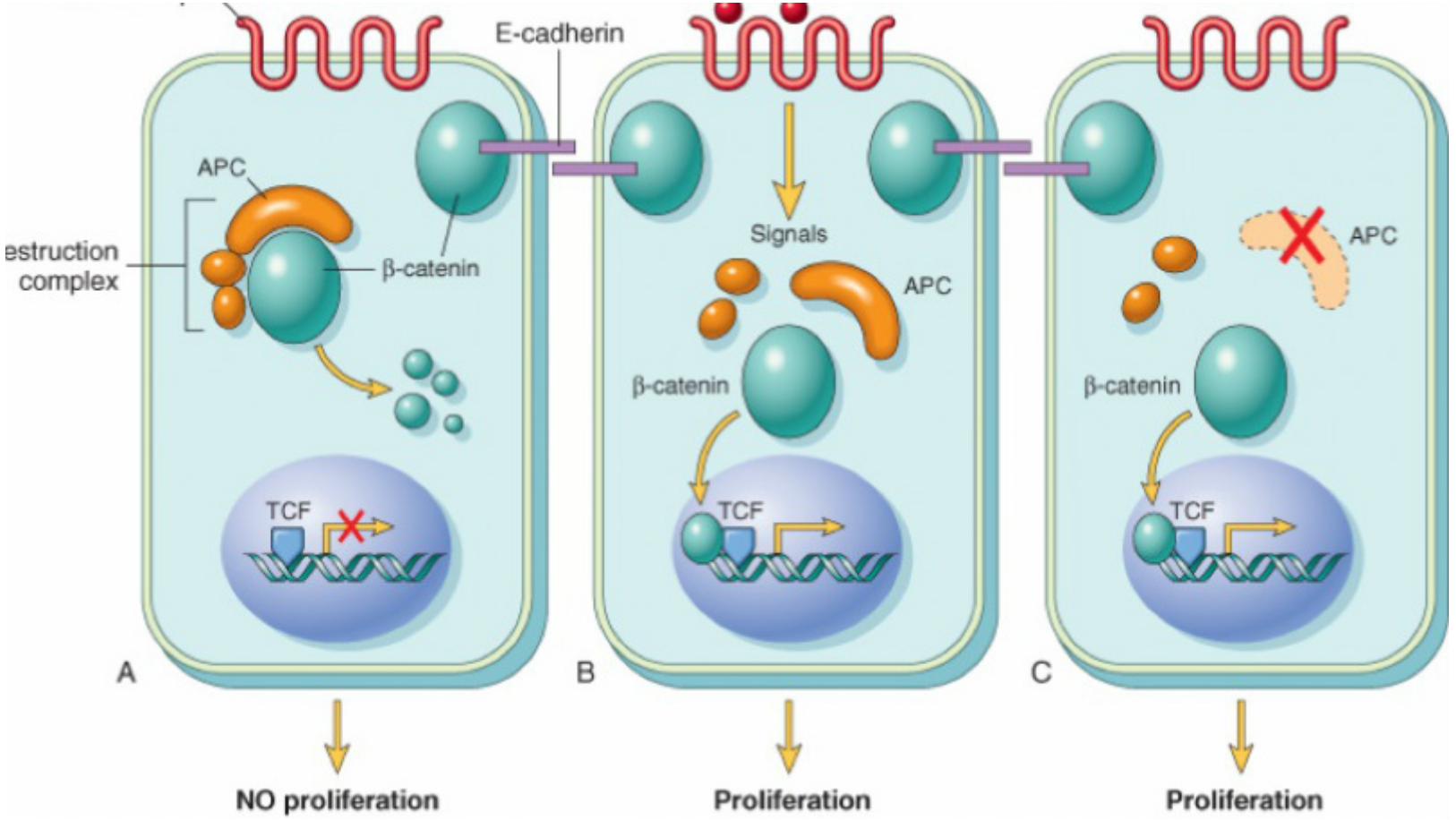
Homer wright rosettes



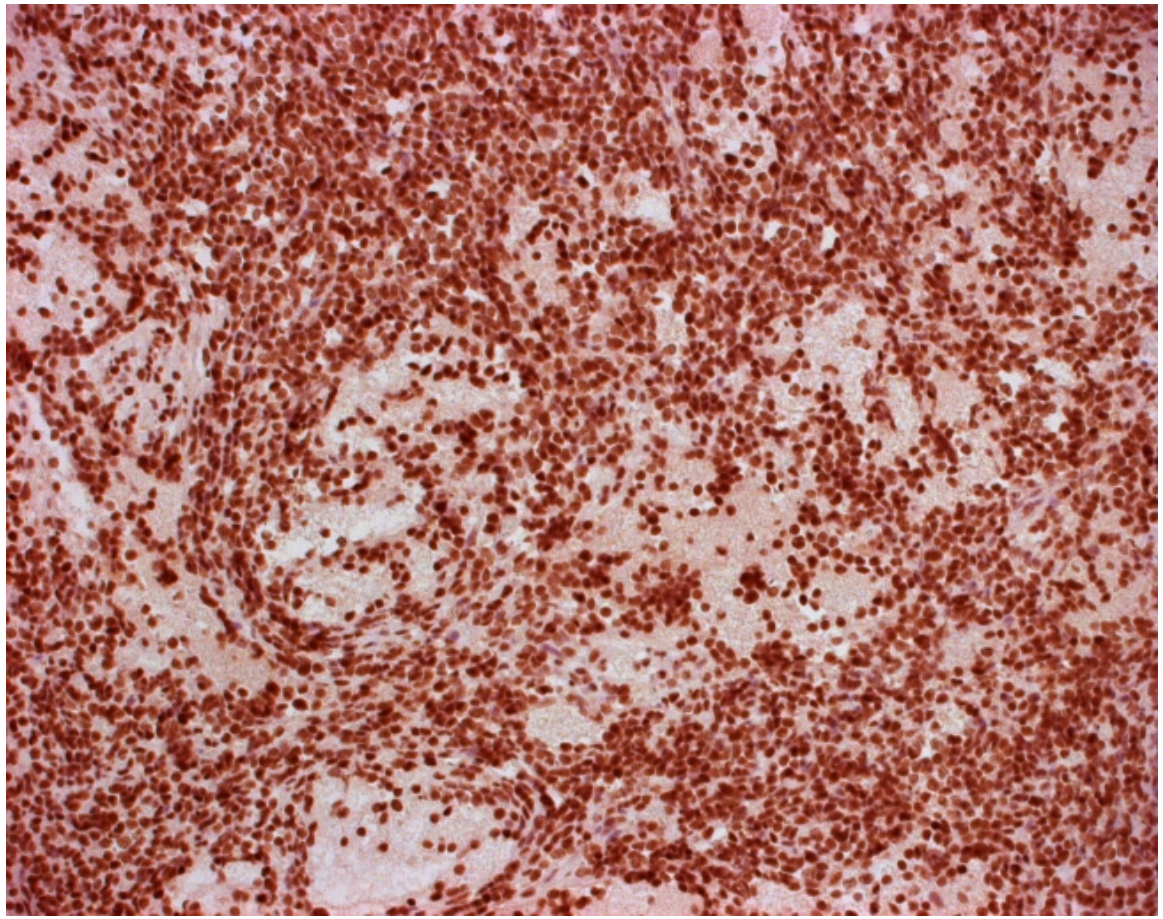
genetics

- 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



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



- 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.

Treatment of medulloblastma

- 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

- THANK YOU