Brain tumours

General features

Tentatively classified according to embryogenesis

"Blastic" and "Cystic" refer to specific morphological features

Embryonal tumours reproduce specific maturative stages of neural cells

Grading as a correspondence of morphology with clinical course

Several types arise at specific sites (topographic correlations)

New entities frequently added (based on IHC and molecular studies)

Mesenchymal tumours increase

Primary non-Hodgkin Lymphomas increase (HIV)

PRIMARY CNS TUMOURS

10% of all primary tumours

10/100.000 subjects/yr.

Adulthood to elderly people

10% in pediatric age (3-5% before 5 ys.)

Prognostic criteria

Histopathology:

- Histotype
- Grading

Clinical data

- Age & site
- Imaging
- Performance Status (Karnowski index)

- **Slowly growing**
- **Local invasion**
- **Liquoral diffusion**
- **Rare extra-cranial metastases** **Exceptions: Medulloblastoma, Glioblastoma**

Symptoms:

Space occupying lesion (SOL)
- Endocranic hypertension
- Headache
- Vomiting
- Papillary oedema

Neural irritation

Seizures

Neurological deficit (sensory or motor)

Symptoms related to:

Tumour size

Tumour site

Midline	Medulloblastoma (cerebellar worm)
	Spongioblastoma (brain and cerebellum)
Lateral ventricles	Papilloma, ependymoma
Pineal and 3rd ventricle	Pinealoma
Ponto-cerebellar angle	Neurinoma (acoustic nerve)

Tumor type and age

Infancy and childhood

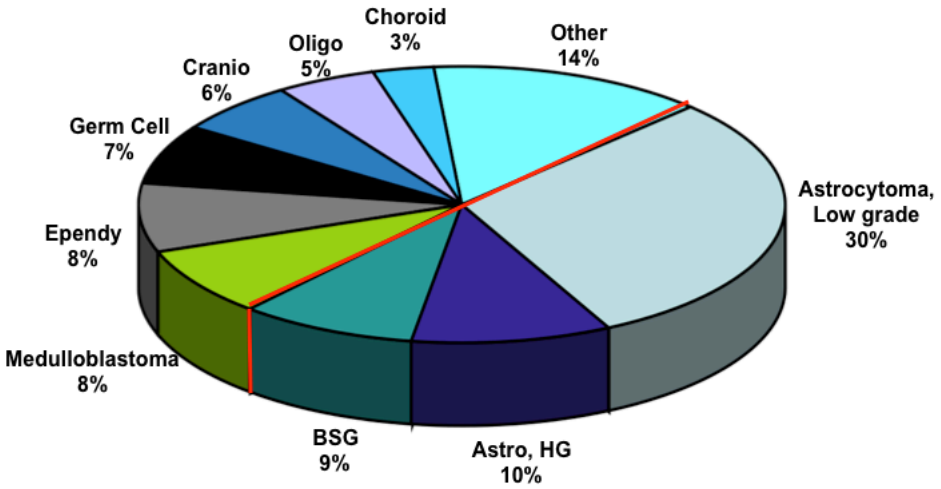
- Medulloblastoma
- Pinealoblastoma
- Spongioblastoma

Teenage and young adulthood

- Ependimoma
- Papilloma
- Astrocitoma

Adulthood and elderly

- Oligodendroglioma
- Glioblastoma
- Neurinoma



Primary brain tumours

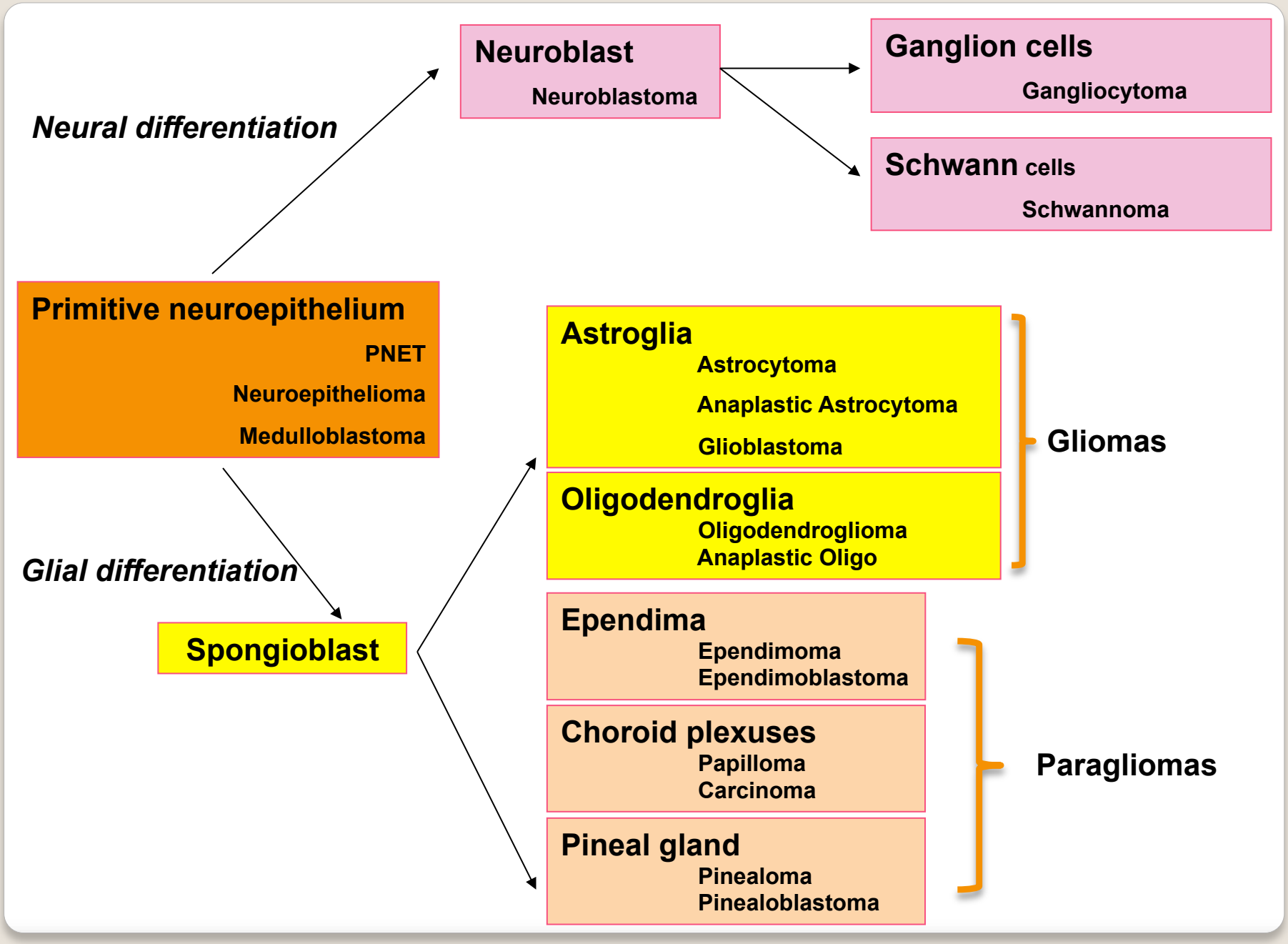
Meningeal: meningiomas

Neuroectodermal (derived from neuroepithelial cells)

- from undifferentiated cells, typical of the early developmental phases, before separation into neural vs. glial
- from mature and differentiated (committed) cells

Dysontogenetic

- Teratoma
  - Dermoid cyst
  - Epidermoid cyst
- Craniopharyngioma
- Angioma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Gliomas
Ependima
Ependimoma
Ependimoblastoma
Choroid plexuses
Papilloma
Carcinoma
Pineal gland
Pinealoma
Pinealoblastoma
Paragliomas

Nomenclature and taxonomy of SNC tumours

NEURAL AND GANGLIONEURAL TUMOURS

- **Gangliocytoma**
- **Ganglioglioma (+ infantile desmoplastic)**
- **Central Neurocytoma**
- **Dysembryoplastic neuroepithelial tumour**

Nomenclature and taxonomy of SNC tumours

GLIAL TUMOURS

Astrocytic

- Astrocytoma
  - Pylocytic
  - Pleomorphic xanthoastrocytoma
  - Sub-ependymal, giant cells
  - Infantile desmoplastic
- Anaplastic Astrocytoma
- Glioblastoma

Oligodendroglial

- Oligodendroglioma
- Anaplastic Oligodendroglioma

Mixed, olygo-astrocytoma

Ependymal

- Ependymoma
- Anaplastic Ependymoma

Choroid plexuses

- Papilloma
- Carcinoma

Nomenclature and taxonomy of SNC tumours

Embryonal tumours

- Neuroblastoma and ganglioneuroblastoma
- Medulloblastoma (+/- melanotic) Medulloepitelioma Medullomyoblastoma
- Ependimoblastoma
- Retinoblastoma
- Primitive neuroectodermal tumour (PNET)
- Melanotic neuroectodermal tumour

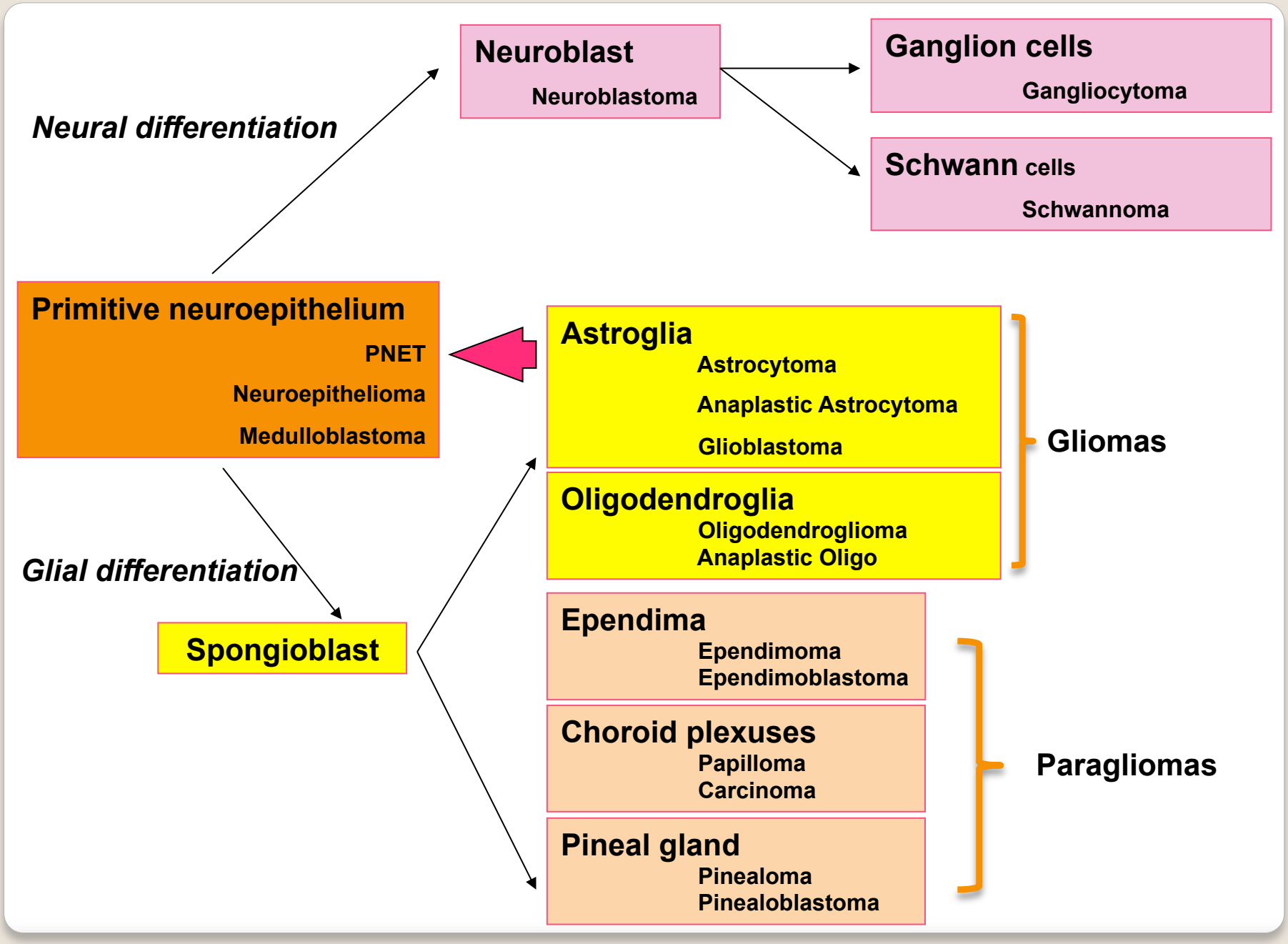
Pineal gland

- Cysts
- Pinealoma
- Pinealoblastoma

Germ cell tumours

Uncertain origin

- Haemangioblastoma
- Polar Spongioblastoma
- Rhabdoid tumour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PNET

Primitive neuroectodermal tumours:

Age: 4 weeks – 2 years

Sex: M/F = 2/1

PNET C (central)

PNET P (peripheral)

PNET P includes:

- **Ewing sarcoma**
- **Toraco-pulmonary Askin tumour**
- **Neuroblastoma**
- **Neuroepitelioma periferico**

<u>Composed by undifferentiated or poorly differentiated neuroepithelial cells, able to follow distinct functional maturation:</u>

- **Neuronal**
- **Astroglial**
- **Ependymal**
- **Muscle**
- **Melanocytic**

Small round blue cell tumours of infancy

Central neuroblastoma = when showing evident neural differentiation

Ganglioneuroblastoma = when showing both neural and gangliar differentiation

PNET

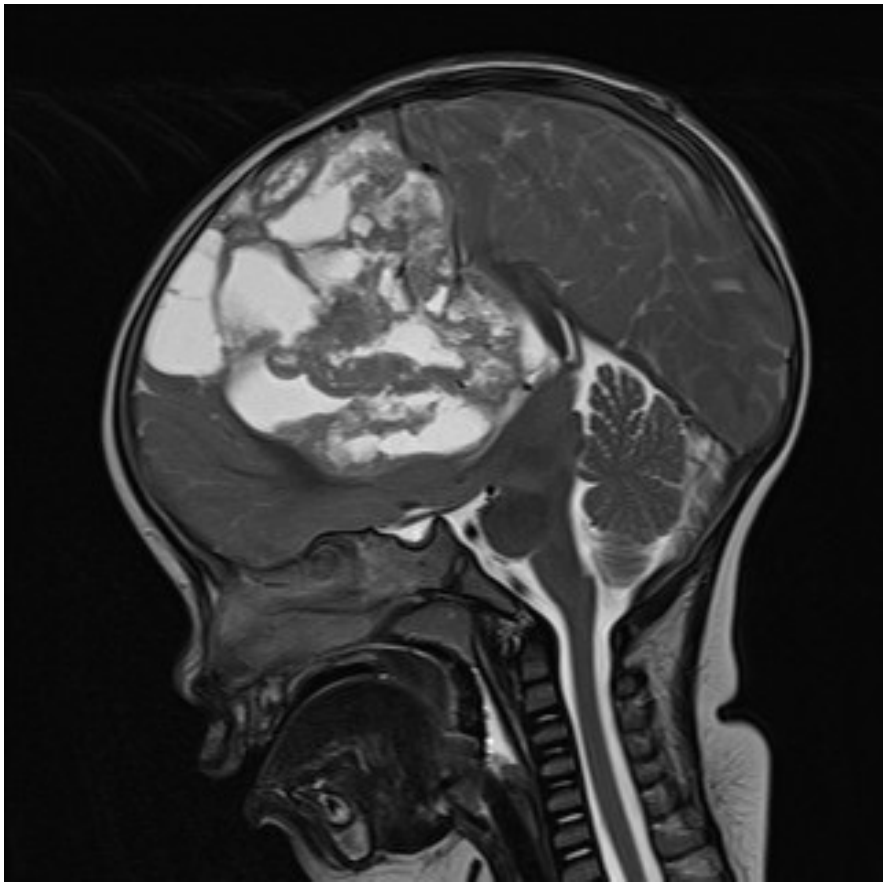
Symptoms:
- Seizures
- Endocranic hypertension
- Motor-sensitive (view) deficit
- Endocrine failure

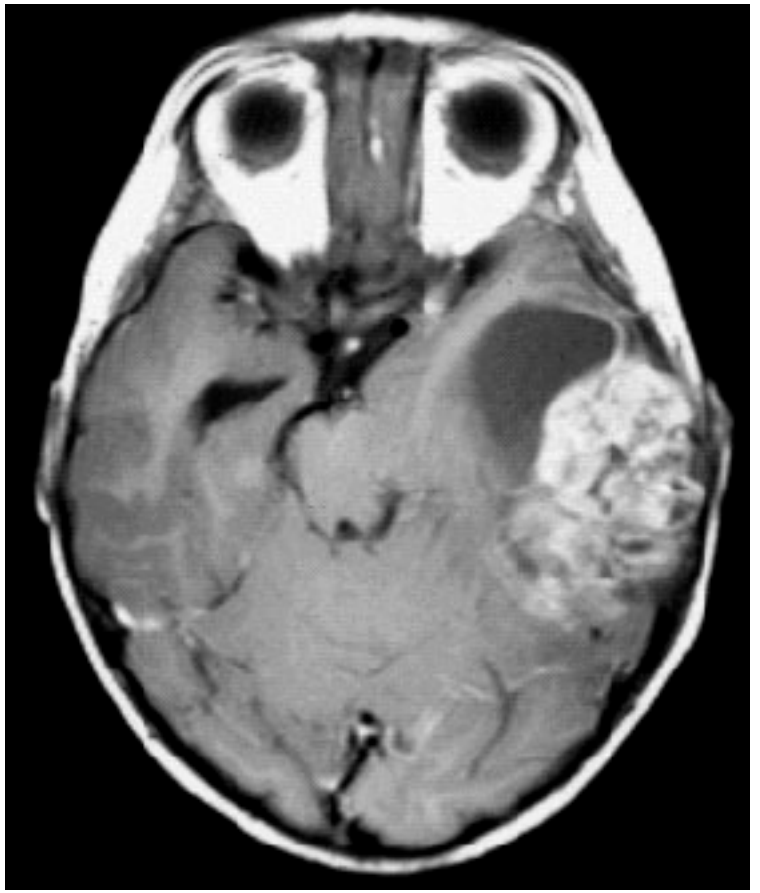
Gross:
- Cystic
- Haemorrhagic
- Friable

Micro:
- Similar to medulloblastoma

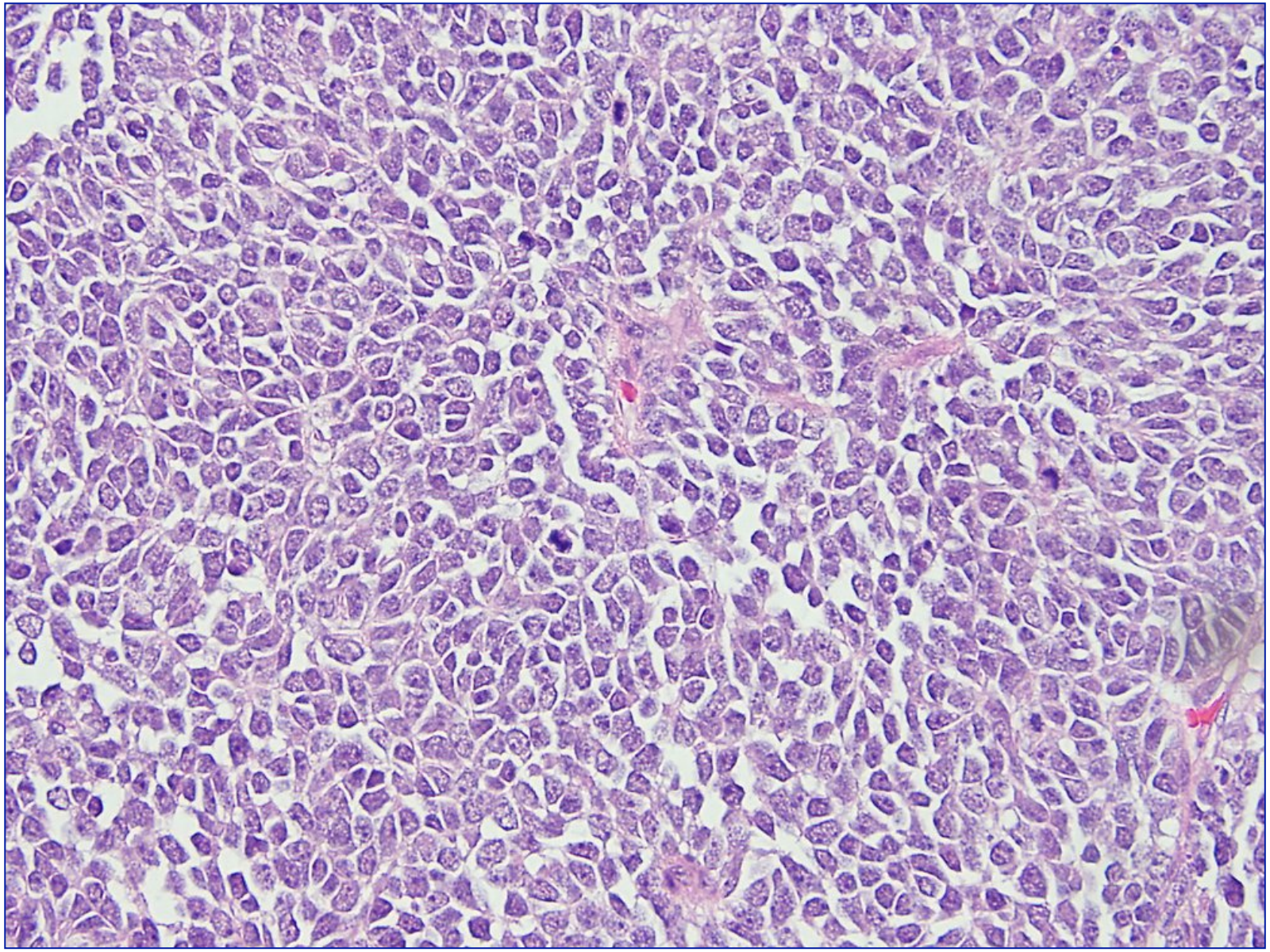
PNET C may arise in subject irradiated for CMS lymphomas/leukemias

PNET

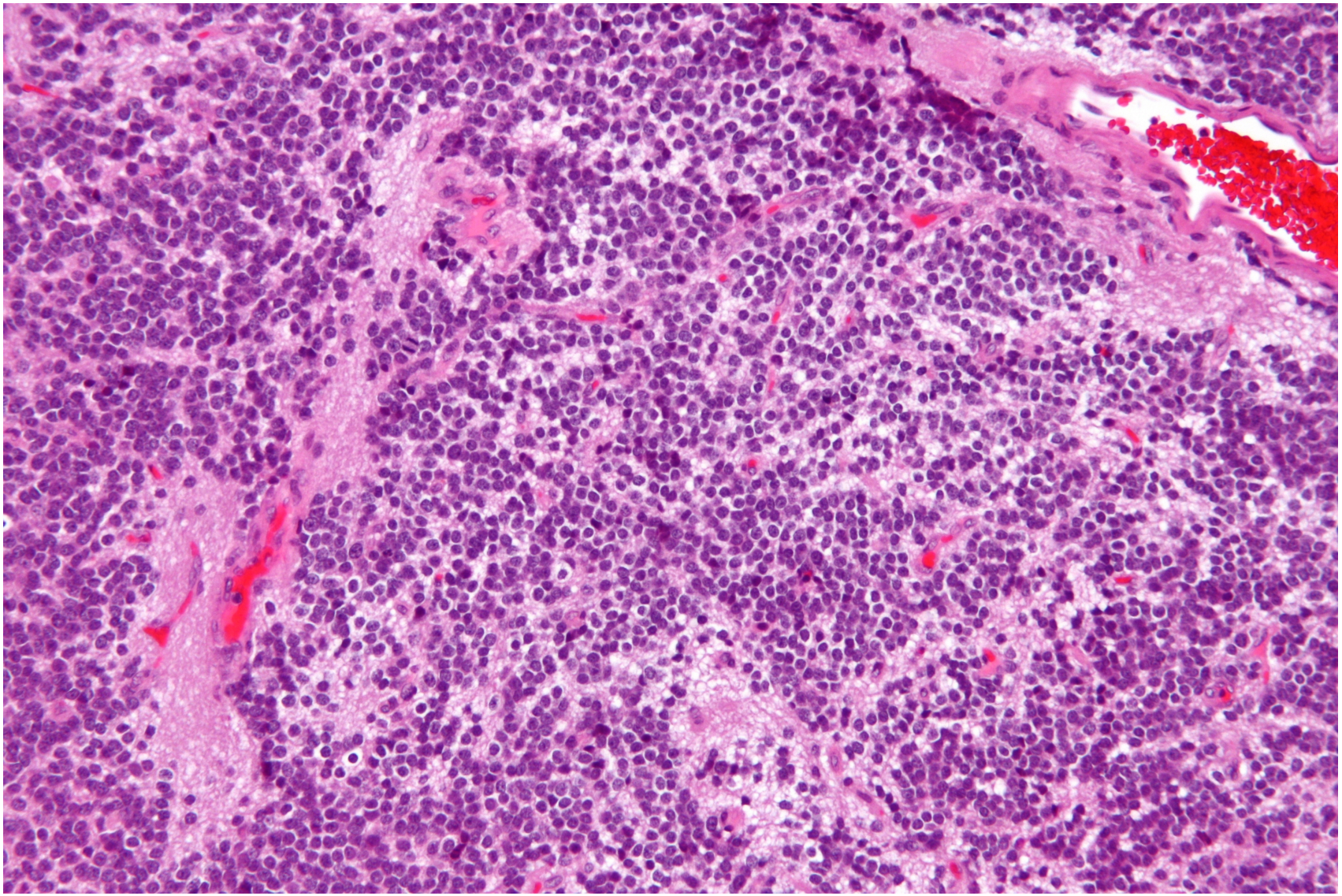


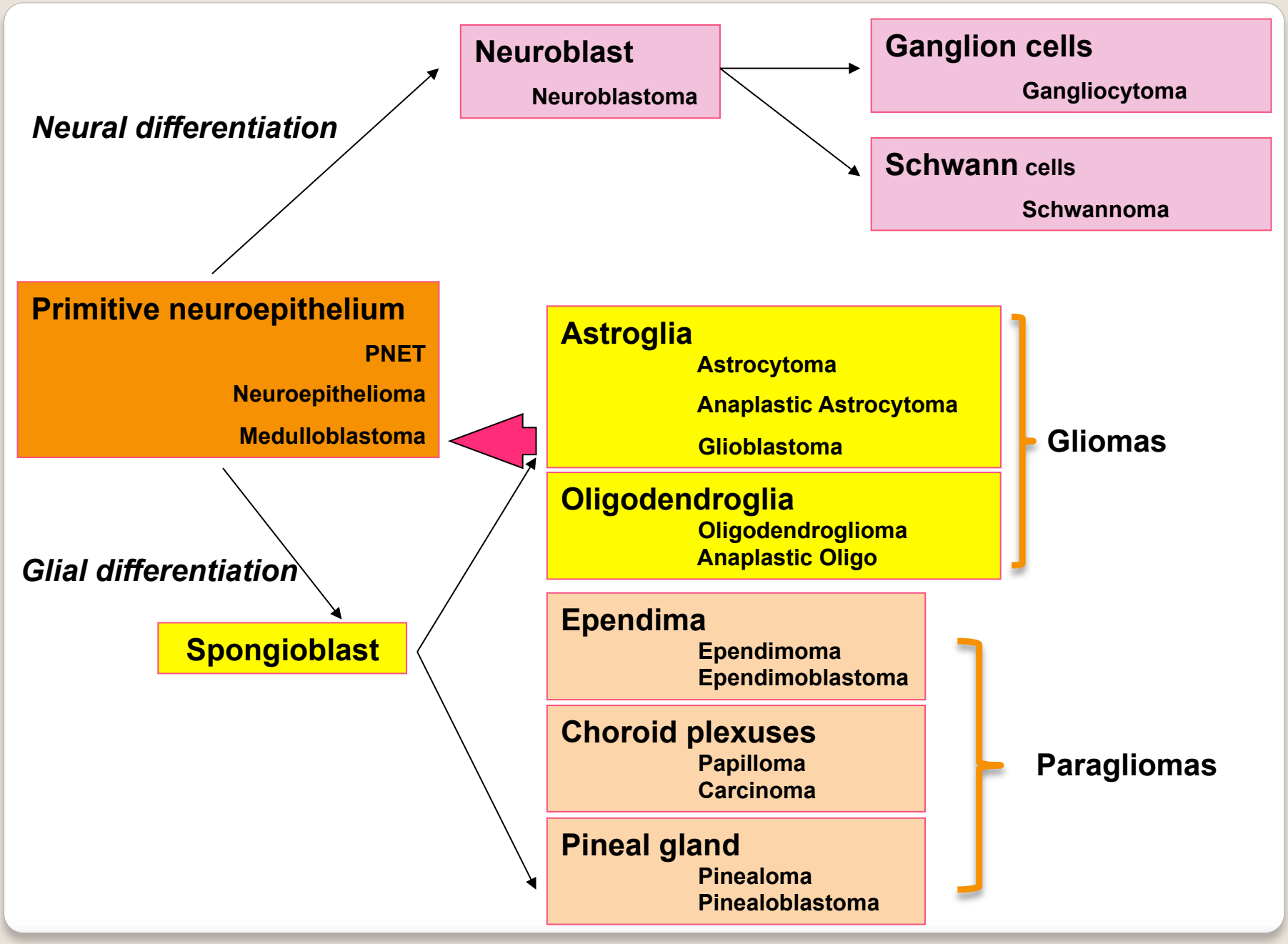


PNET



CENTRAL NEUROCYTOMA

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MEDULLOBLASTOMA

(= PNET C with cerebellar localization)

Incidence:	**0.5 /100.000 (< 15 ys.)**
Age:	**7 ys. (peak)** **70% <16 ys.** **Exceptional after IV decade**
Sex:	**65% M**
Site:	**75% vermis involving the IV ventricle**

Symptoms:

- **Seizures**
- **Endocranic hypertension**
- **Motor-sensitive (view) deficit**
- **Endocrine failure**

Imaging:	**Solid mass, hyperdense, contast-enhanced**
Diffusion:	**Invasive (liquoral) growth with metastatic potential**
	Leptomenyngeal or ventricular nodules at presentation (1/3)

MEDULLOBLASTOMA

Gross:

- Cystic
- Haemorrhagic
- Friable

Micro:

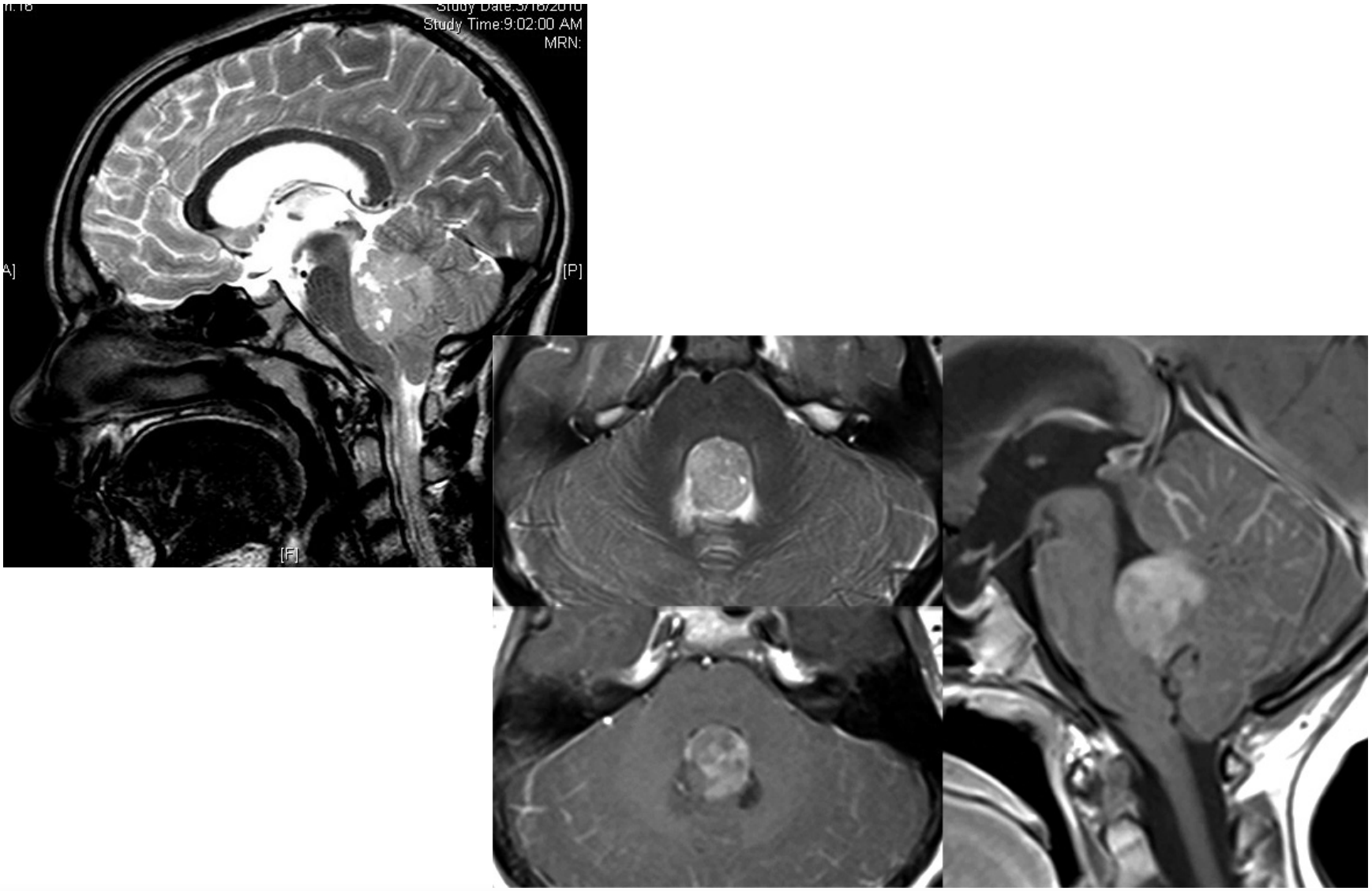
- Lymphocyte-like cells
- Hyperchromatic nuclei
- Homer-Wright (perivascular) pseudorosettes
- High mitotic rate
- Synaptophisin +

Small round blue cell tumours of infancy

ADVERSE PROGNOSTIC FACTORS:

- Age < 3 ys.
- Presentation with metastases
- Incomplete surgical removal
- Large cell pattern
- Ki67 LI >20%

MEDULLOBLASTOMA



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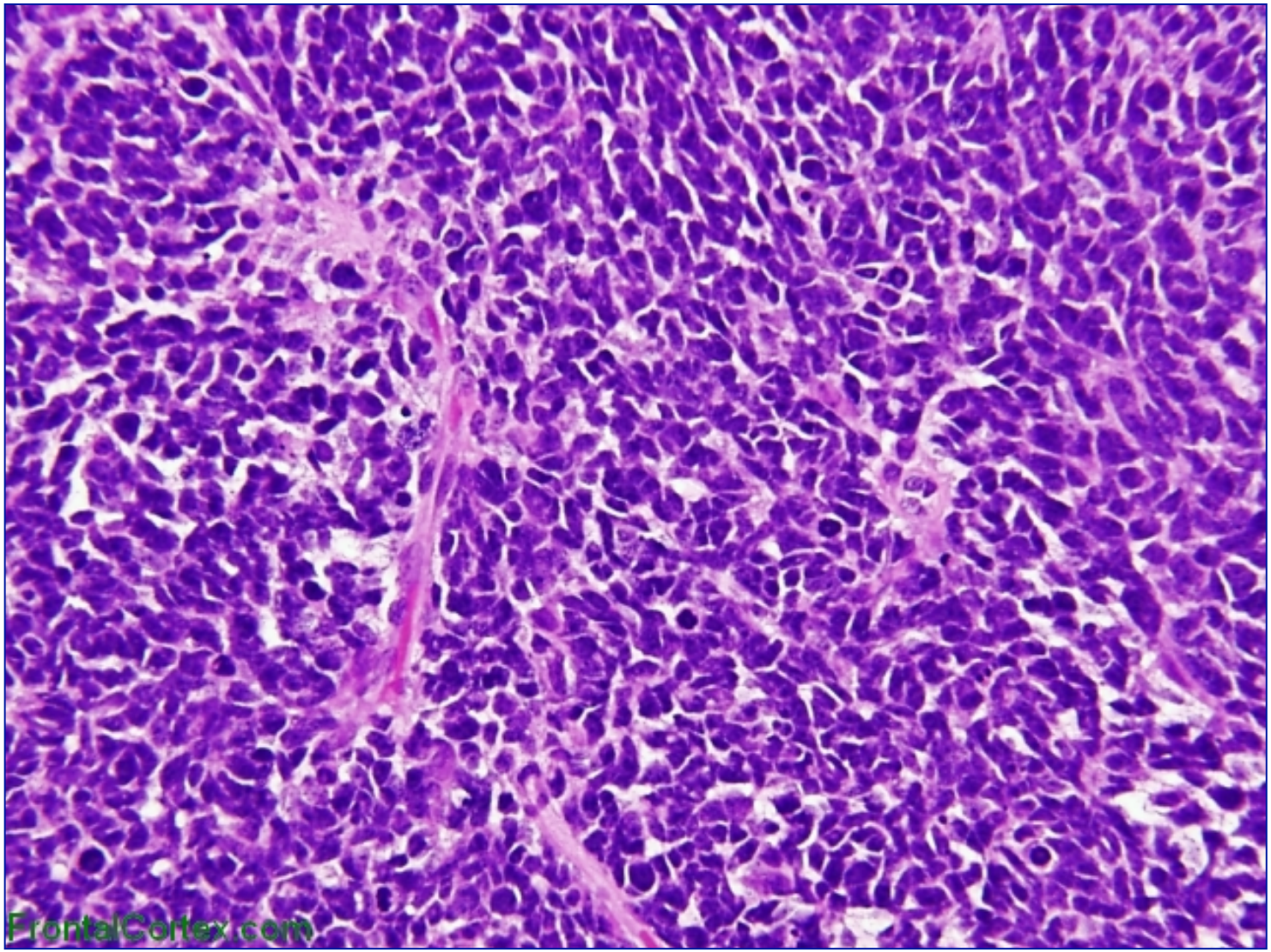
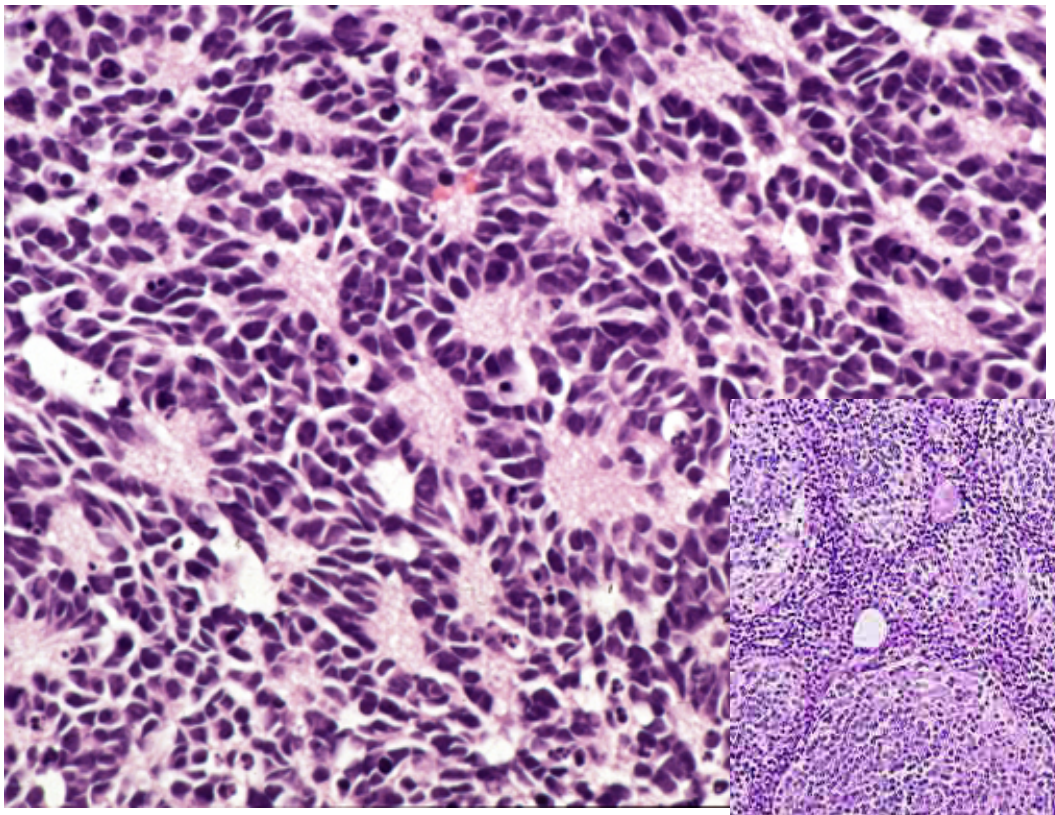
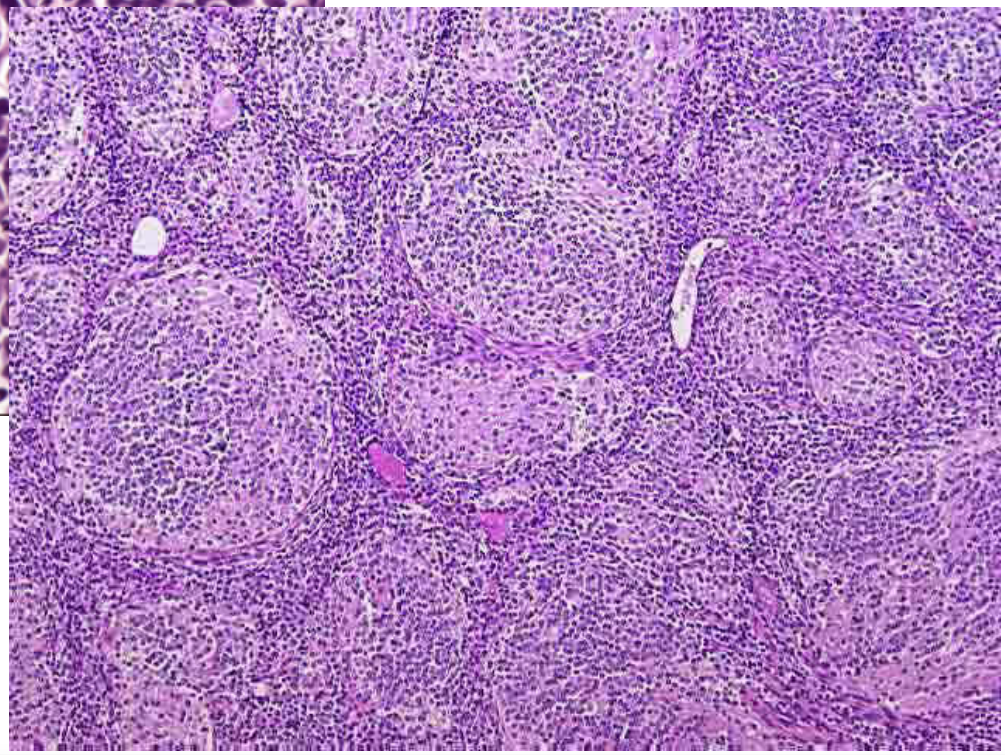


MEDULLOBLASTOMA



Homer-Wright rosettes



Desmoplastic

Medulloblastoma desmoplastico

Età Adulta **Sede** Emisferi cerebellari

Aspetto istologico **Nodulare** per la proliferazione di fibre reticoliniche che circondano aggregati di cellule neoplastiche piuttosto rarefatte **Aspetto a isole pallide**

ISTOGENESI

Medulloblasti
mai identificati in neuroembriologia

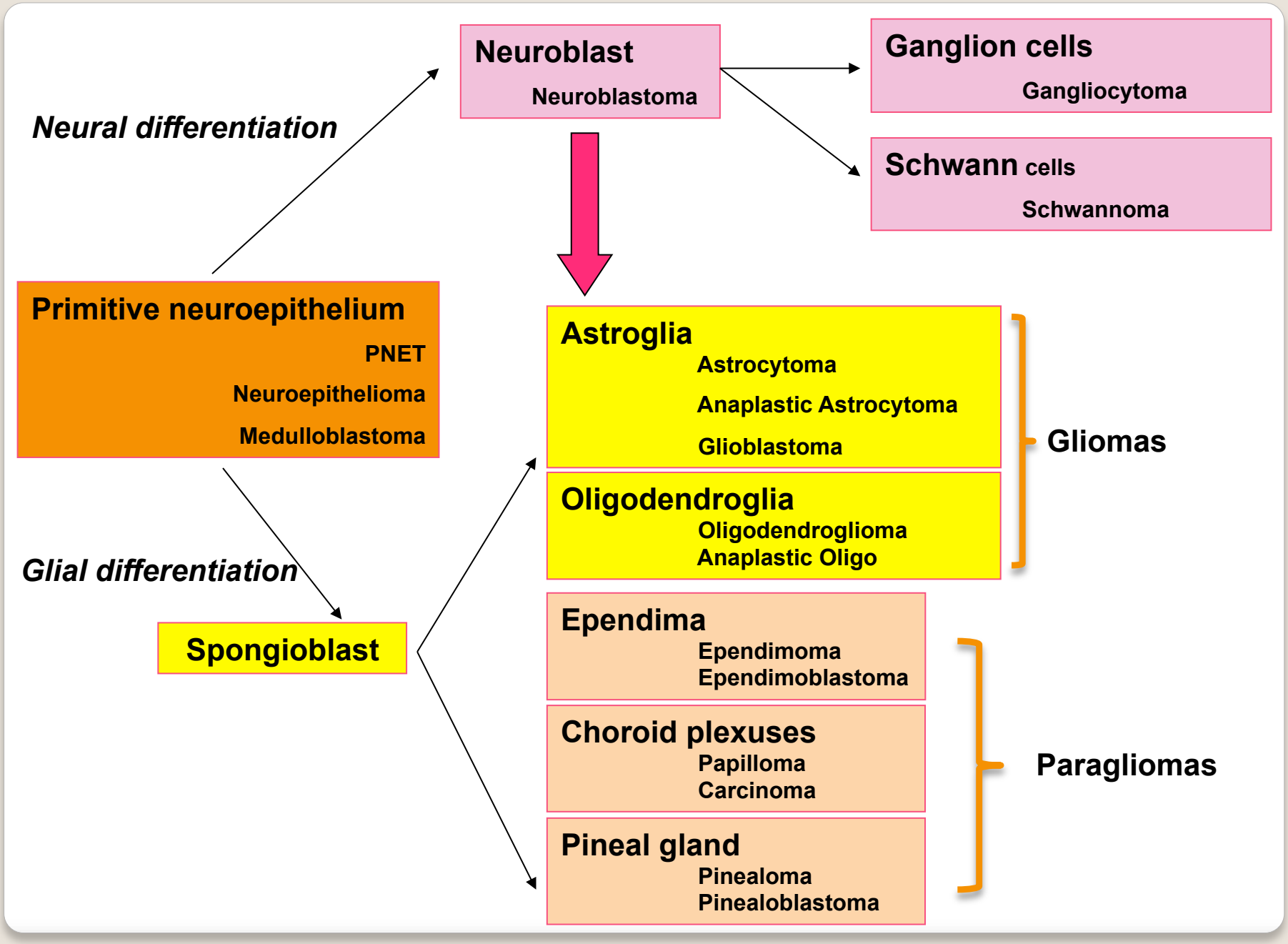
Bailey e Cushing : Derivazione dai Medulloblasti
Cellule embrionali proliferanti capaci di differenziarsi come neuroblasti e come spongioblasti

I Ipotesi

Origine dallo strato granulare esterno del cervelletto che si forma durante l'embriogenesi per migrazione di cellule indifferenziate dal tetto del IV ventricolo verso la superficie della corteccia cerebellare fetale dove successivamente formano i neuroni dello strato granulare

II Ipotesi

Derivazione da cellule della matrice subependimale in corrispondenza del IV ventricolo capaci di differenziarsi in senso neuronale e gliale e dare quindi origine al medulloblastoma ed ai PNET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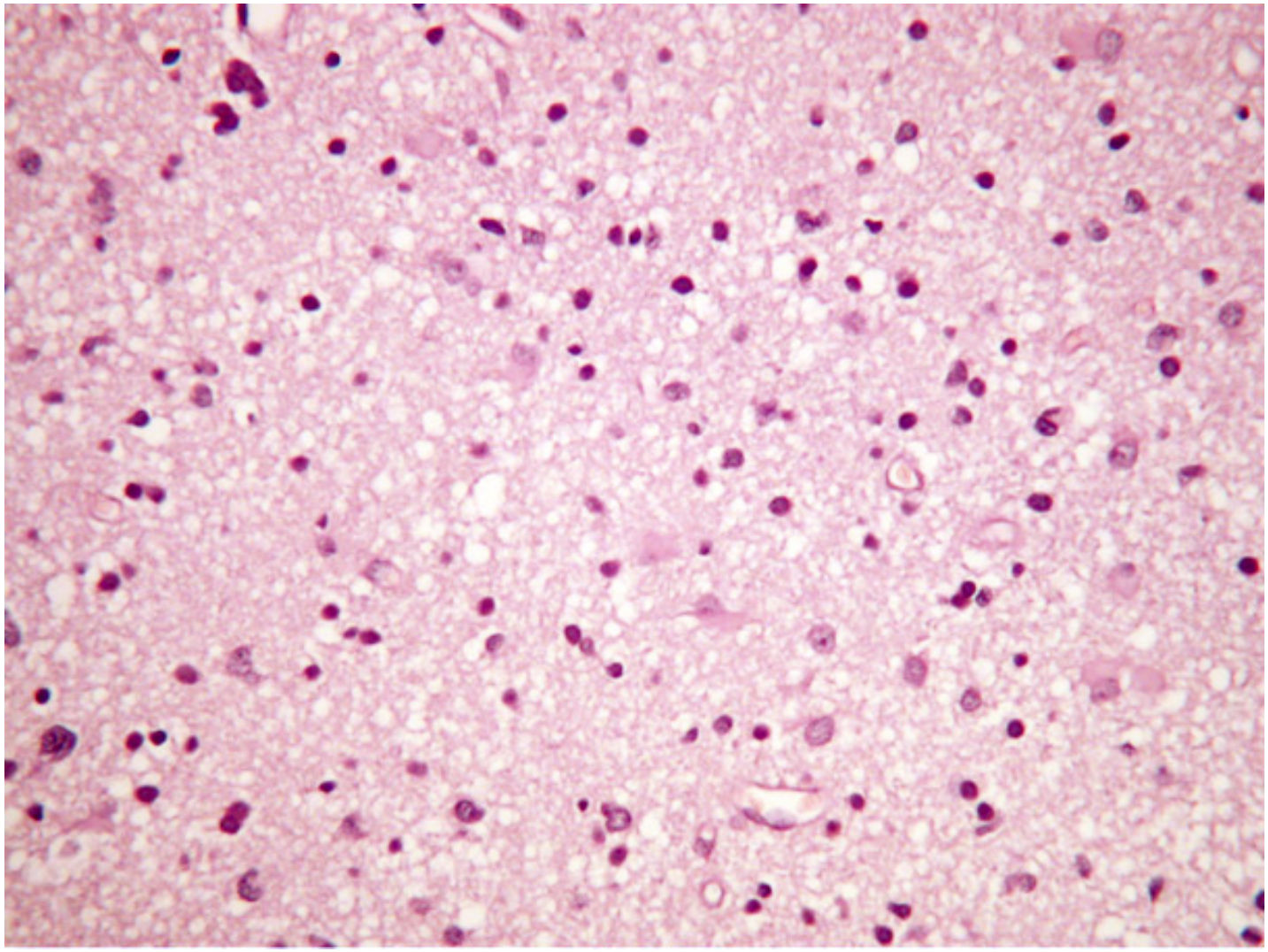
ASTROCYTOMA

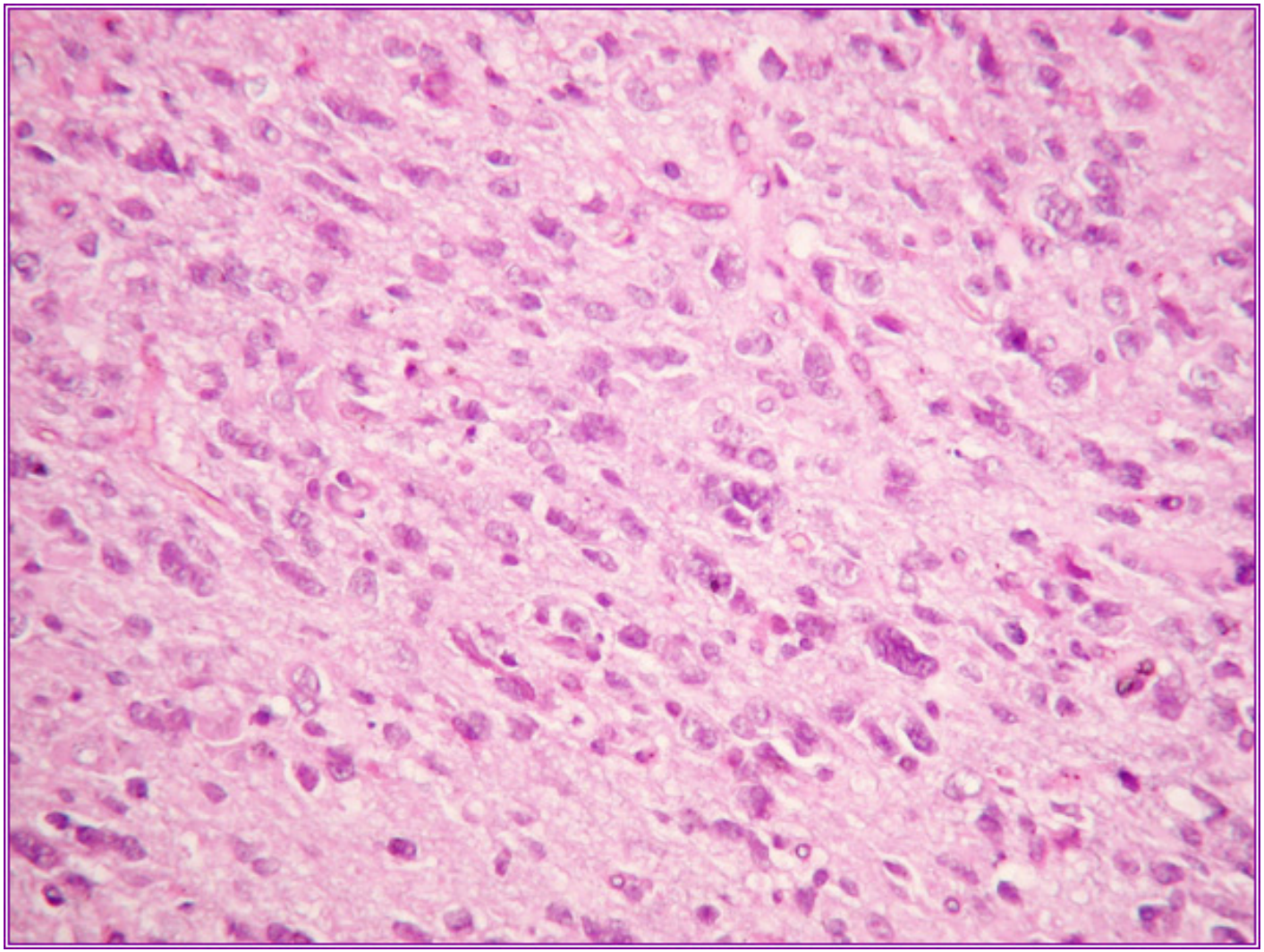
Incidence:	**1.4/100,000 (10-15 % CNS tumours)**
Age:	**40 ys. (peak)**
Sex:	**60% M**
Site:	**Hemispheric, temporal lobe (supra-tentorial)**
Gross:	**Hard to friable, cystic areas**

Micro:	**Pilocytic: bipolar cells, fasicles of fibrils, GFAP+**	**Grade 1**
	Protoplasmatic: well defined cell borders **Fibrillary: round cells embedded in a rich fibrillary network** **Ghemistocytic: globoid cells with eosinophilic cytoplasm** **Microcystic**	**Grade 2**
	Anaplastic: increased cellularity, Ki67, intra-tumoural vessels **Invasive growth**	**Grade 3**

ASTROCYTOMA - fibrillary



ASTROCYTOMA - anaplastic



Astrocytoma progression

More frequent before 45 ys.
Latency: 4-5 ys.
Sequential, additional genetic damage
Previous glial tumours (astro, oligo, ependymal)

A → AA

- **TP53 mutations**
- **PDGFR hyperexpression**

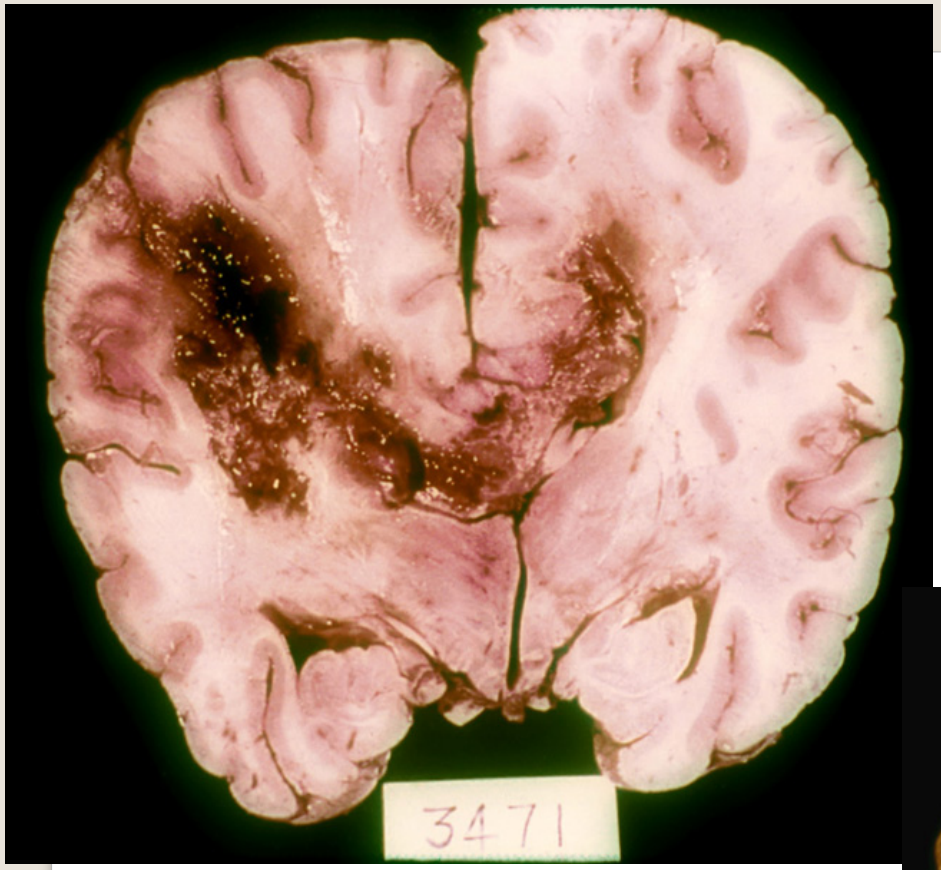
AA → G

- **LOH 10q**
- **PDGFRA amplification**

GLIOBLASTOMA = Grade 4

Incidence:	**2-3/100,000 (20% CNS tumours)**
Age:	**Adults, elderly people (peak: 55)**
Sex:	**70% M**
Site:	**Frontal & temporal lobes (supra-tentorial)**
Gross:	**Hard to friable, haemorrhage, necrosis**
	Hemispheric asimmetry
	Ventricular dilation / dislocation / compression
	Prominent invasive growth
	Metastases (intra-cerebral, lymph nodes, lungs)

Micro:	**Pleomorphic cells, giant cells with bizarre nuclei**
	Rich and abnormal vessel network, perivascular palisading
	Plump endothelial cells, thrombosis
	Extensive necrosis
	High mitotic rate (>>> Ki67)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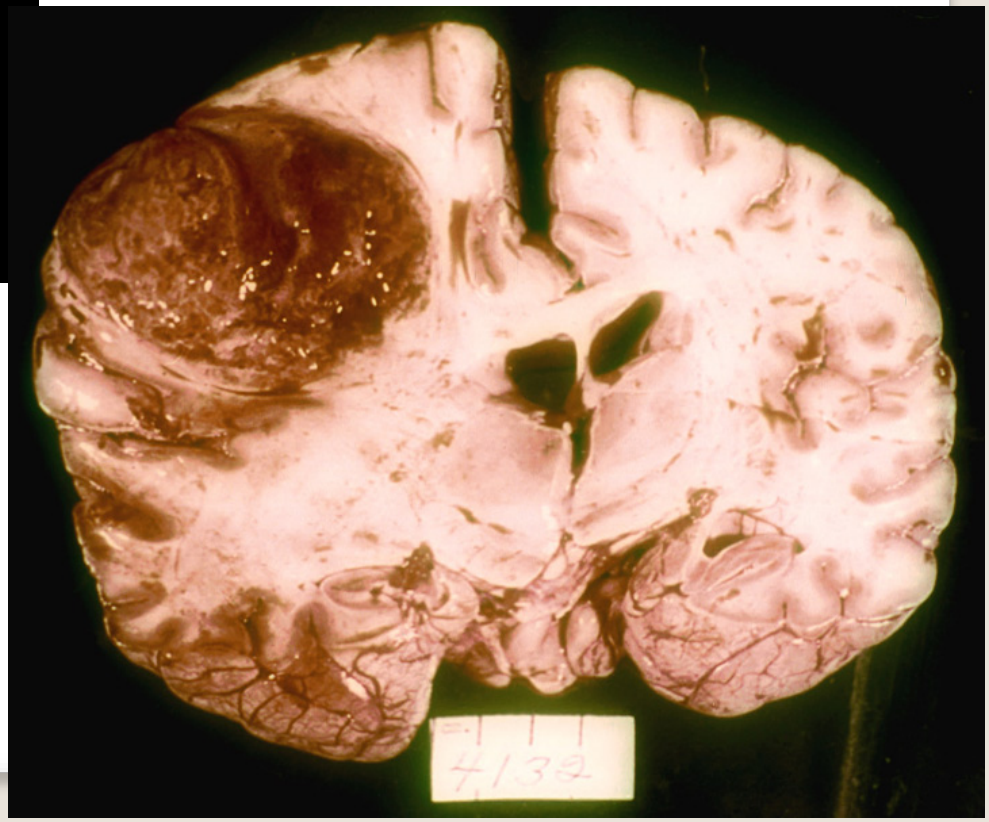
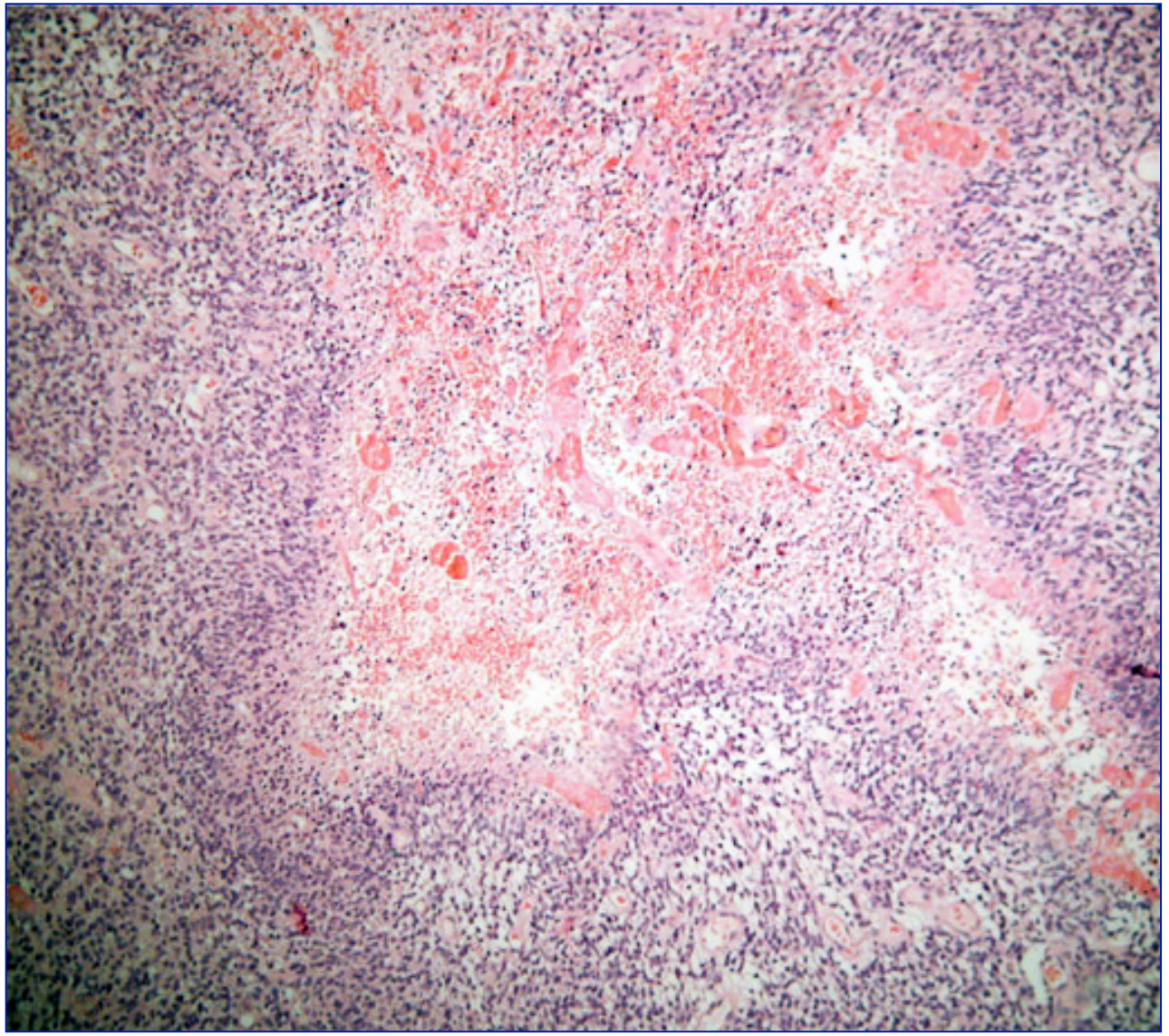


GLIOBLASTOMA



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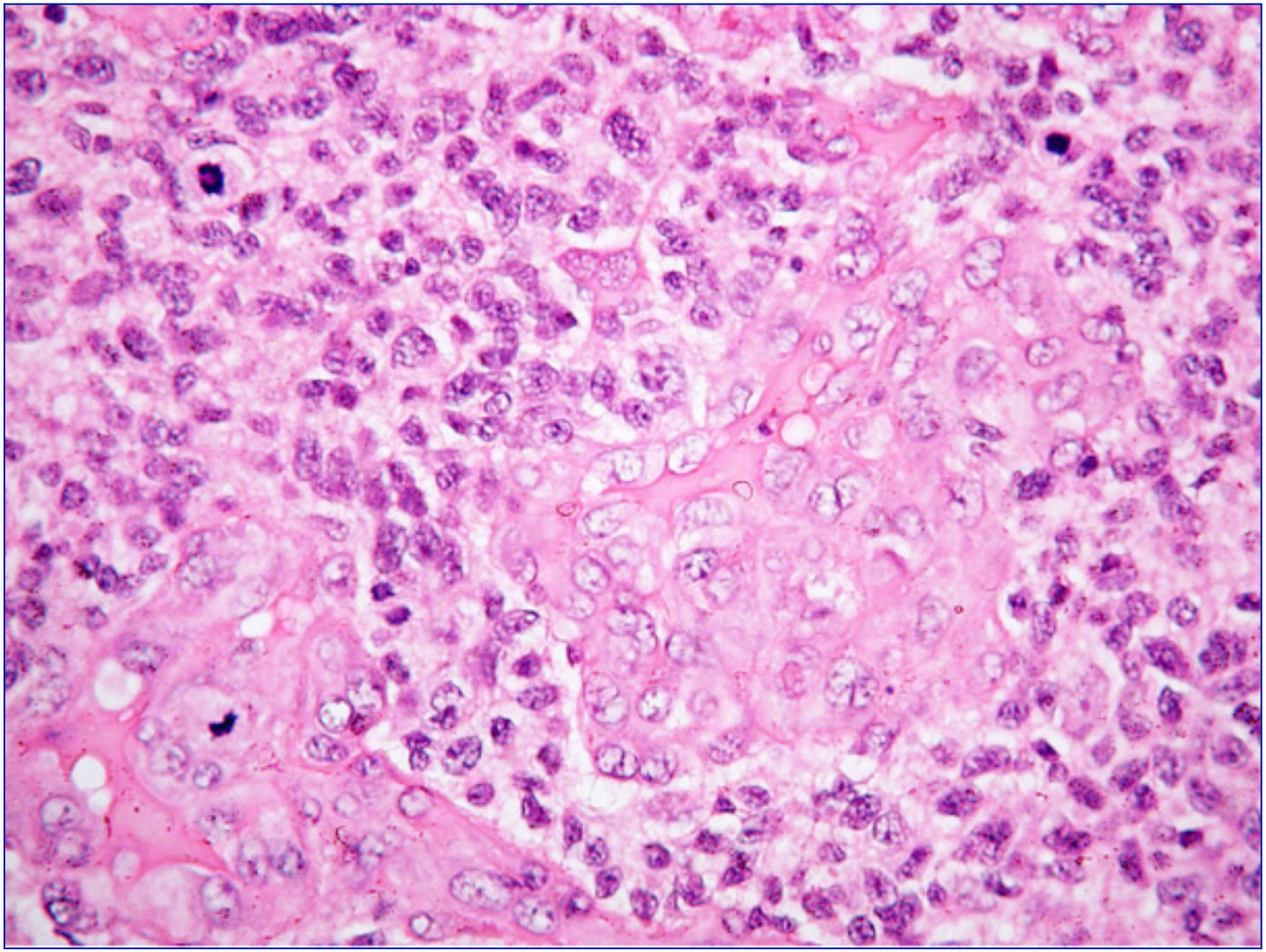
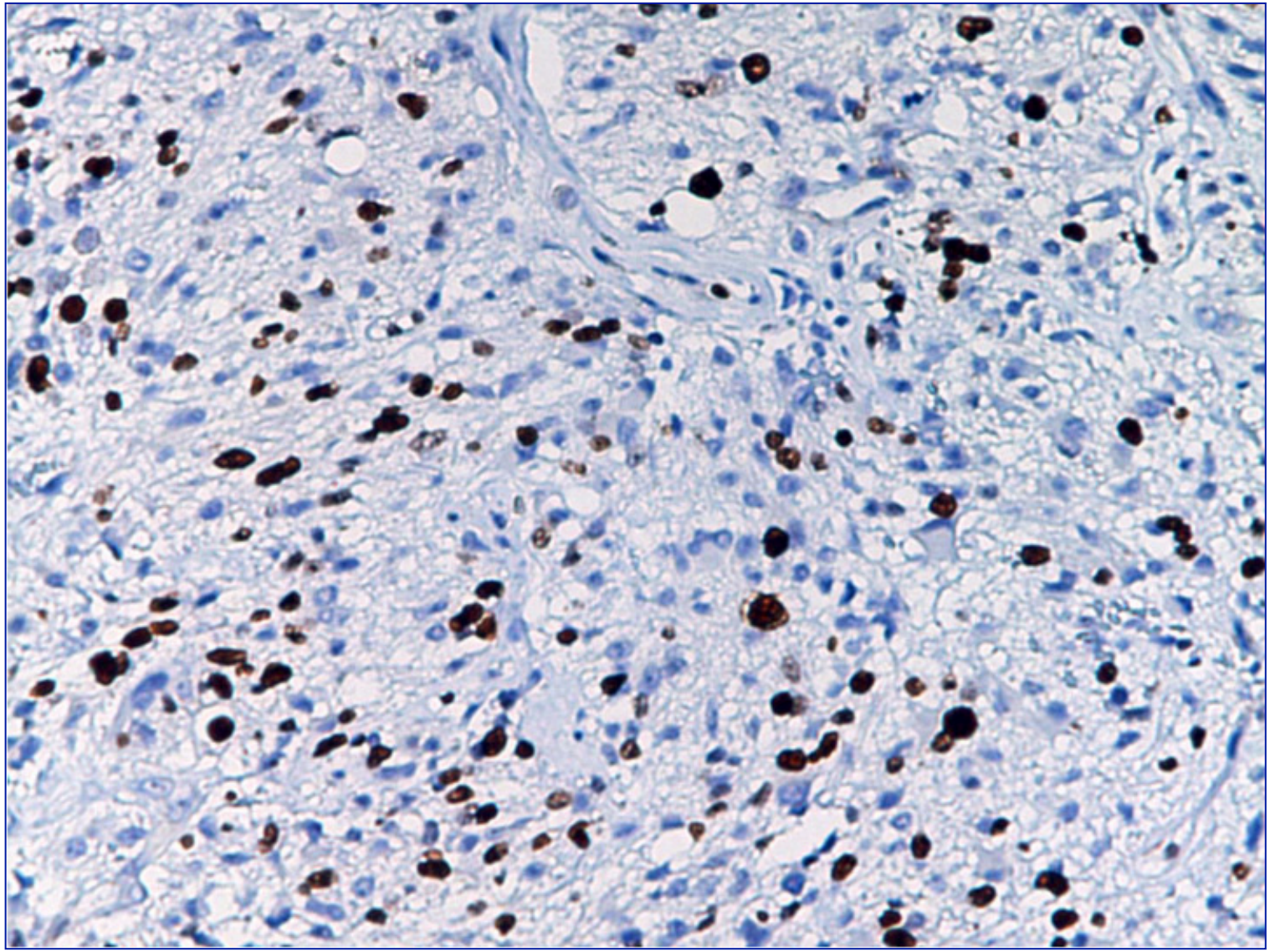
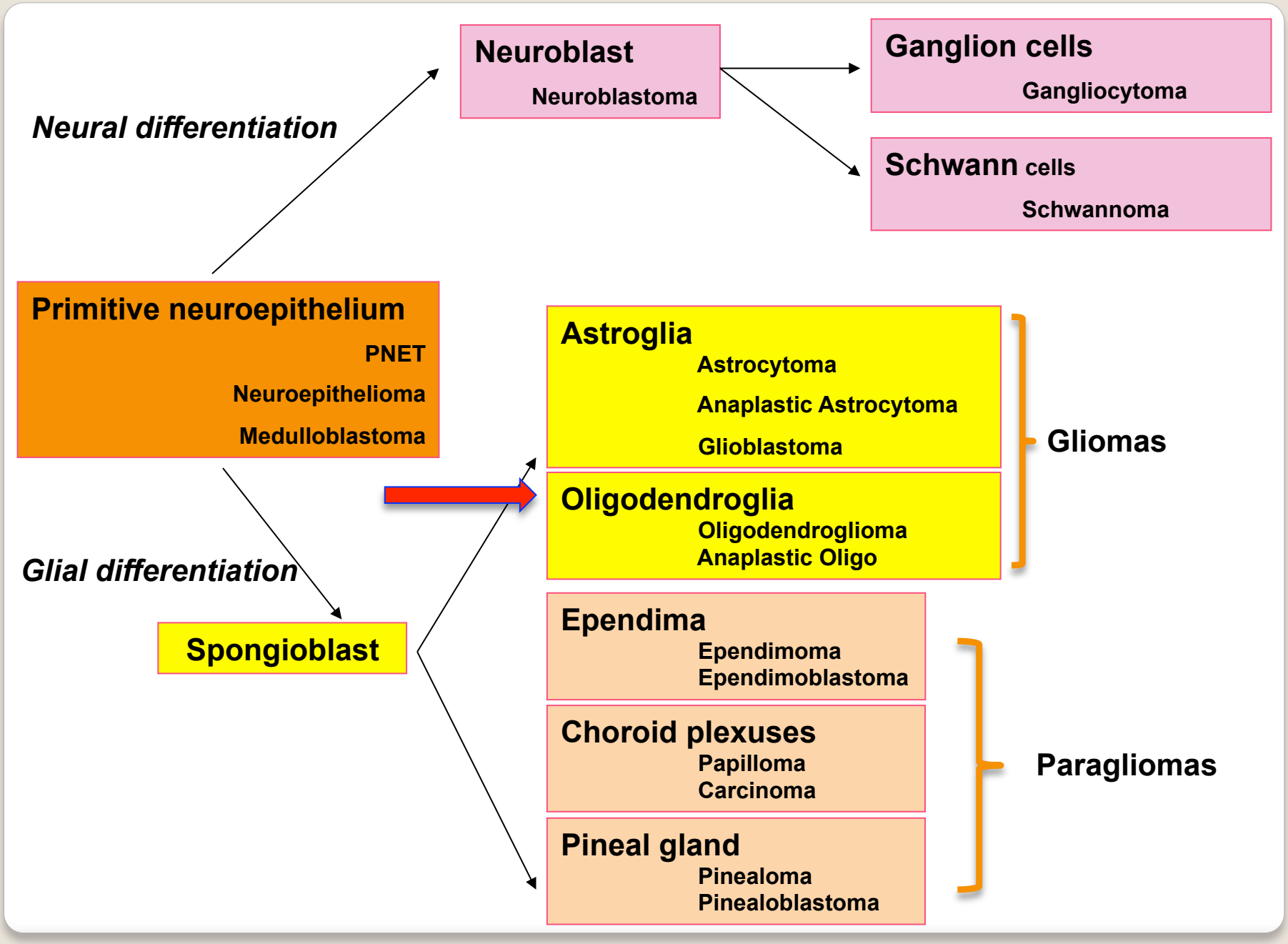


GLIOBLASTOMA – Ki67

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Pineal gland
Pinealoma
Pinealoblastoma
Paragliomas

OLIGODENDROGLIOMA = Grade 2

ANAPLASTIC OLIGO = Grade 3

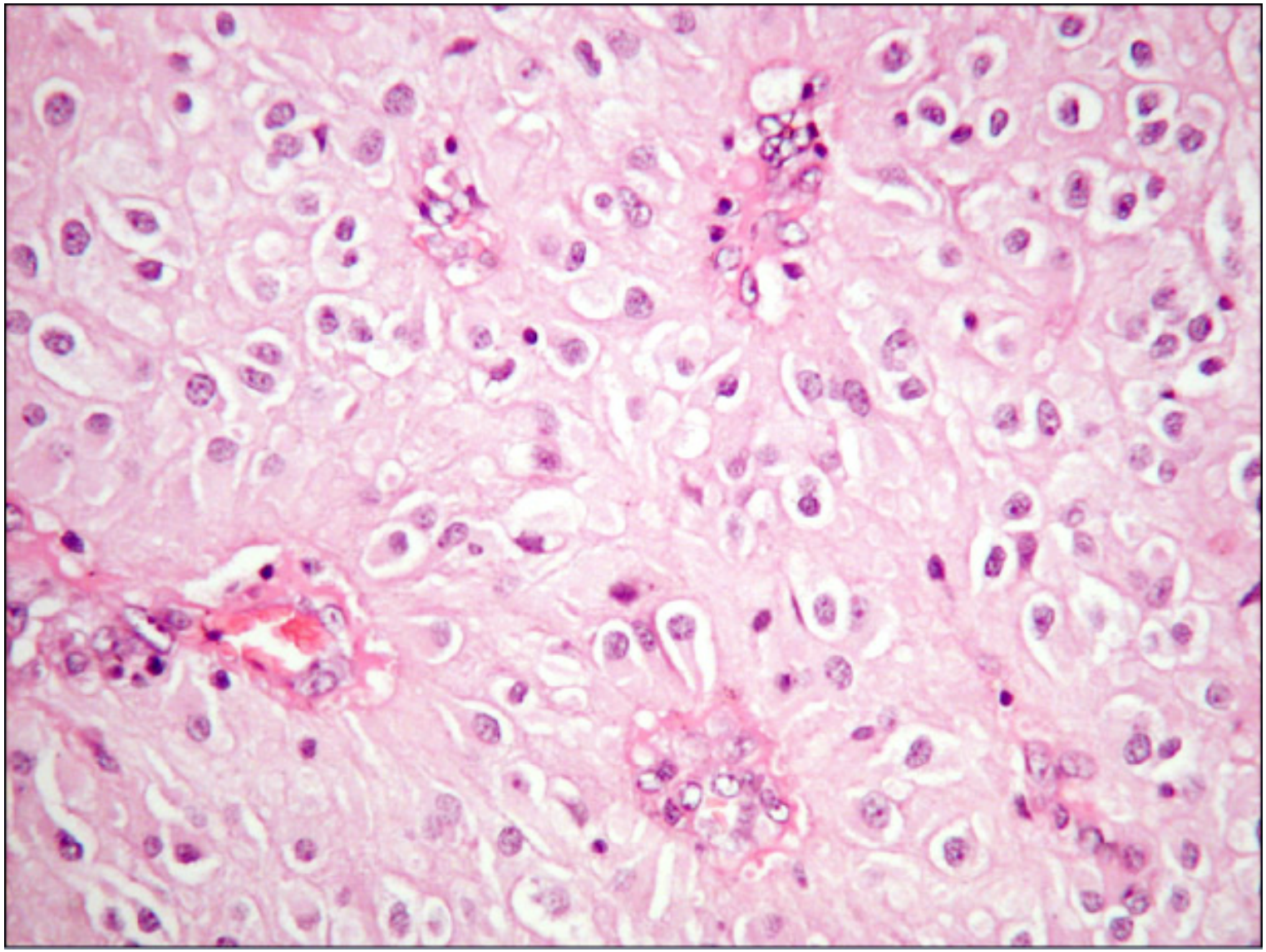
Incidence:	**2-3/100,000 (20% CNS tumours)**
Age:	**Adults, elderly people (peak: 355)**
Sex:	**60% M**
Site:	**Frontal & parietal lobes (supra-tentorial)**
Gross:	**Soft, jelly, cystic**
	Calcifications

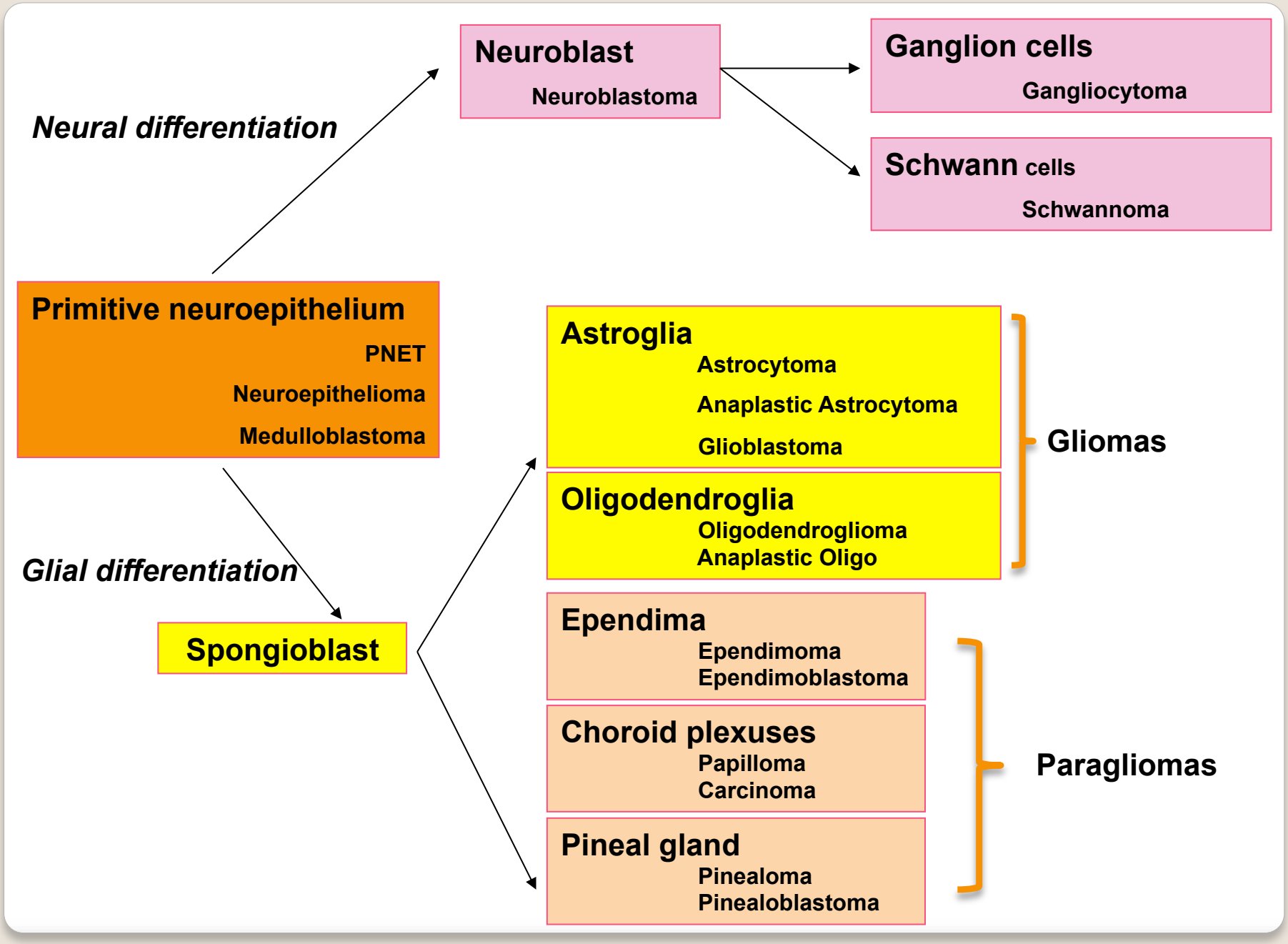
Micro:

- **Beehive architecture**
- **Rounded cells with evident borders**
- **Central nuclei with perinuclear halo**
- **Perivascular microcalcifications**
- **Invasive growth**
- **High mitotic rate (>>> Ki67)**
- **Necrosis**

} **ANAPLASTIC**

OLIGODENDROGLIOMA

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Paragliomas

EPENDIMOMA

Age: Juvenile

Site: IV ventricle (dilated & stuff), hydrocefalus

Cervical spine (myxo-papillary = lumbar)

Gross: Papillary growth frequent

Micro: Cubic/columnar cells with perivascular rosettes

PAPILLOMA of the choroid plexuses

Age: Juvenile

Site: IV ventricle (dilated & stuff), hydrocefalus

Cervical spine

Gross: Typical papillary growth with vascular core

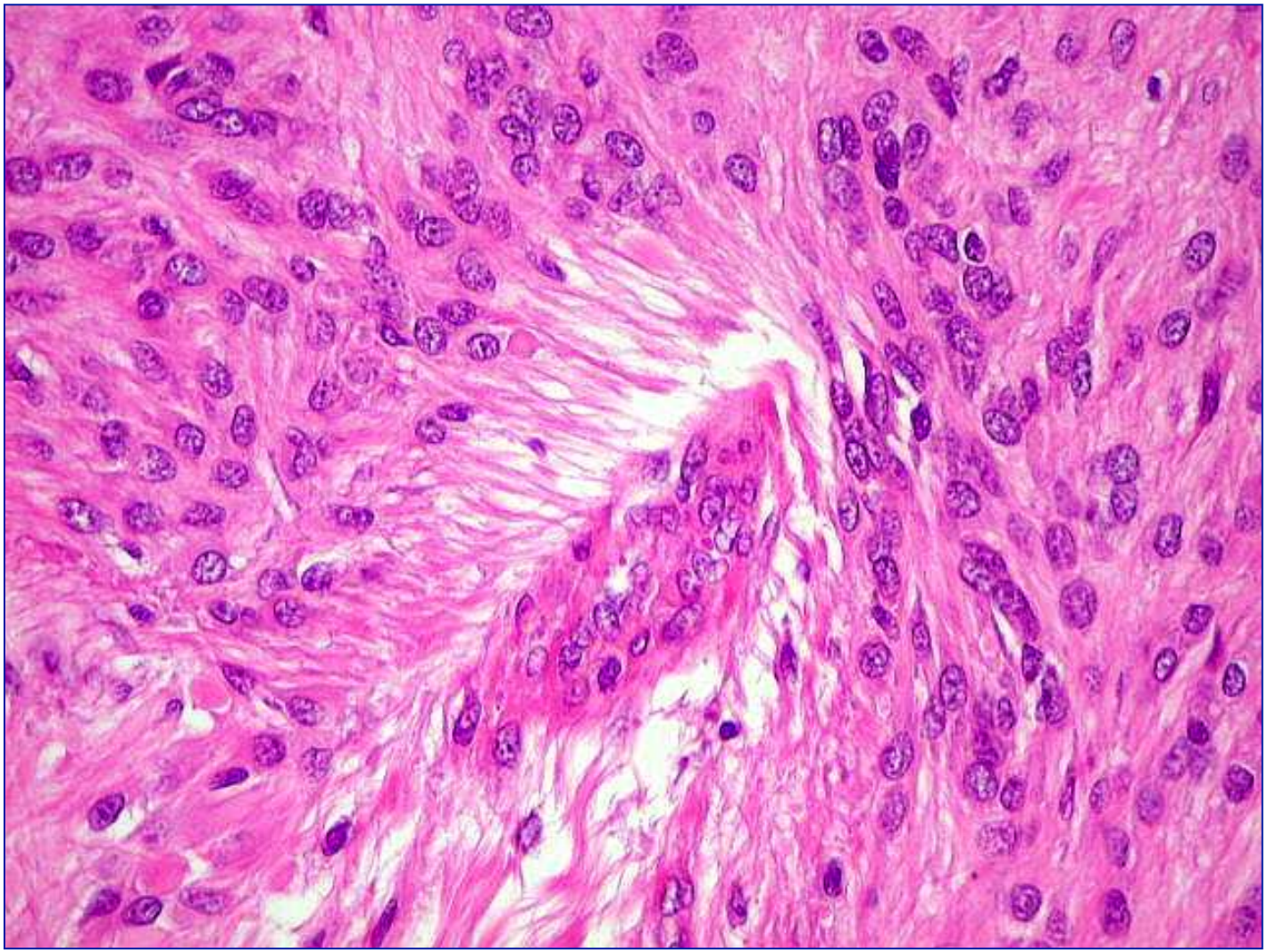
Micro: Monolayered cubic/columnar cells

PINEALOMA

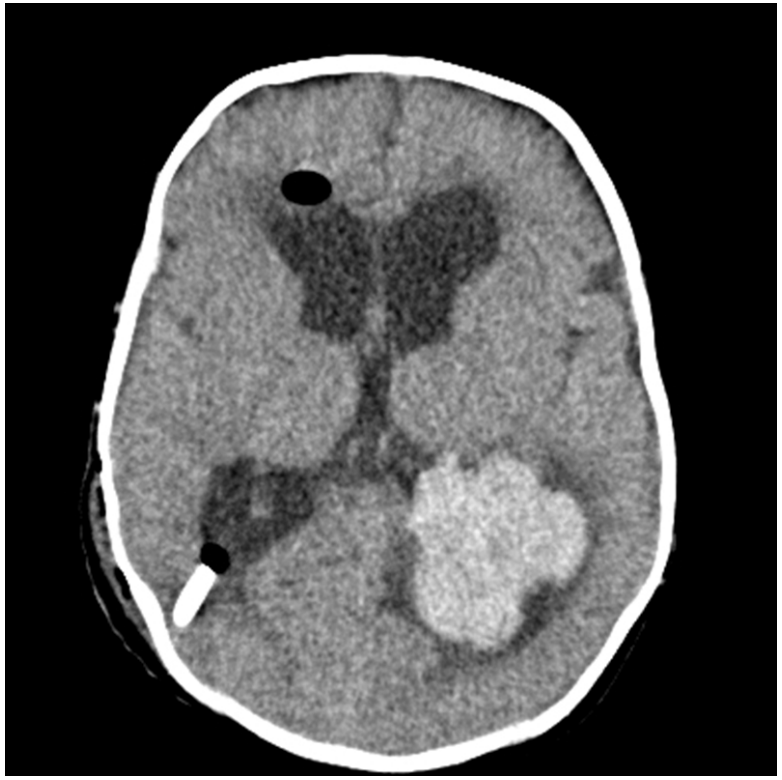
Age: juvenile **Sex: M>F**

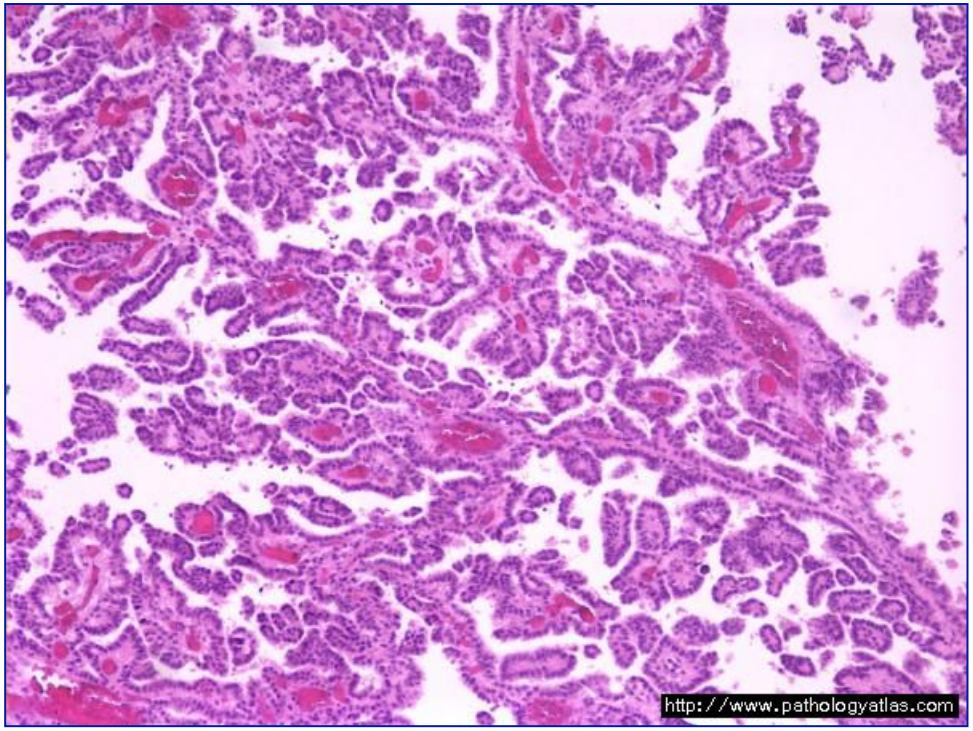
Micro solid growth pattern

EPENDIMOMA



CHOROID PLEXUS PAPILLOMA





SECONDARY TUMOURS

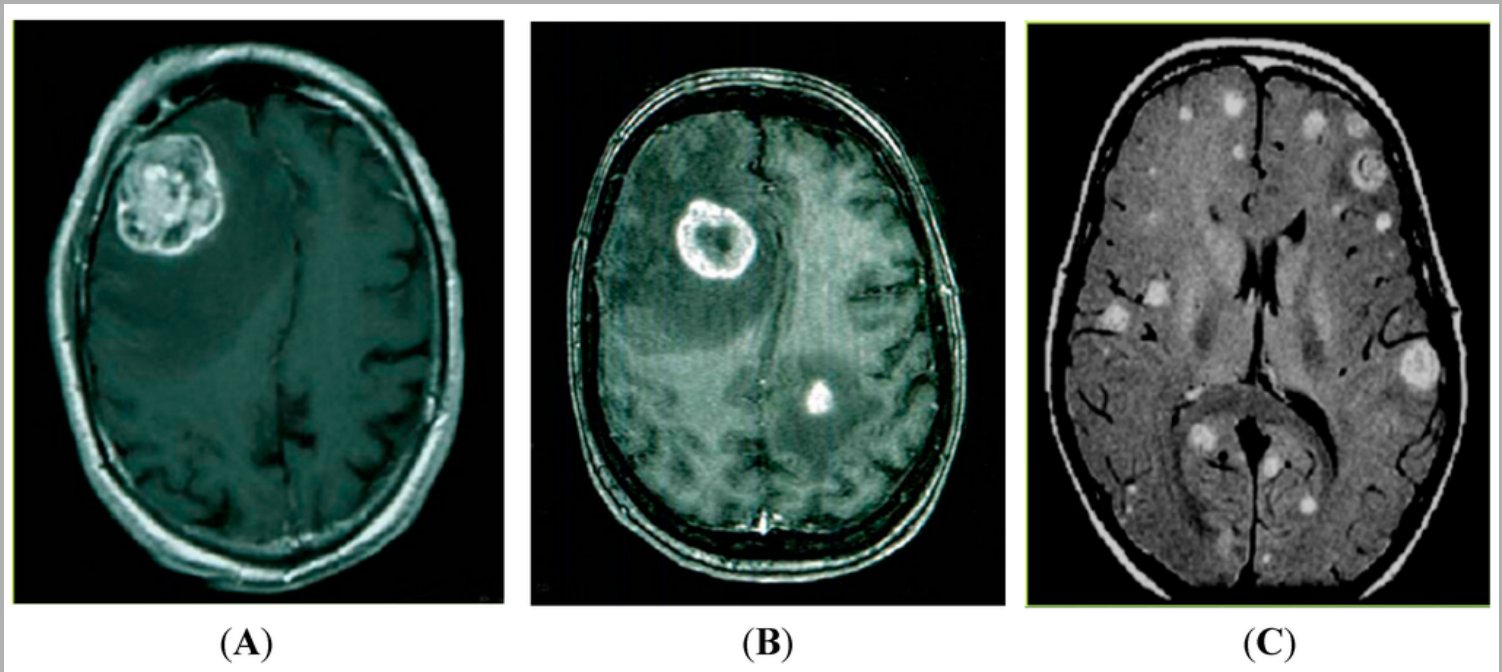
INCIDENCE: 4-11%
- Intra-cranial (3.4-8.3)
- Intra-spinal (0.7)

Age:	45-64 (31.1/100.000)
	>65 (42.7/100.000)
Sex M/F:	1.36/1 Intra-cranial
	1.16/1 Intra-spinal
Site:	24% Intra-cranial
	5% Intra-spinal

SECONDARY TUMOURS - SOURCES

- Lung (multiple): 50% Brain - 15% Spine
- Breast: 15% Brain - 22% Spine
- Prostate: 10 % Spine
- Melanoma (multiple): 10,5 % Brain
- Kidney
- Coriocarcinoma
- G.I. tract

SECONDARY TUMOURS



(A) (B) (C)

SECONDARY TUMOURS - PROGNOSIS

- Age
- Karnofsky index
- Number & site
- Aggressivness of primary tumour
- Chemosensistivity
- Overall survival: 3-6 months with RxT