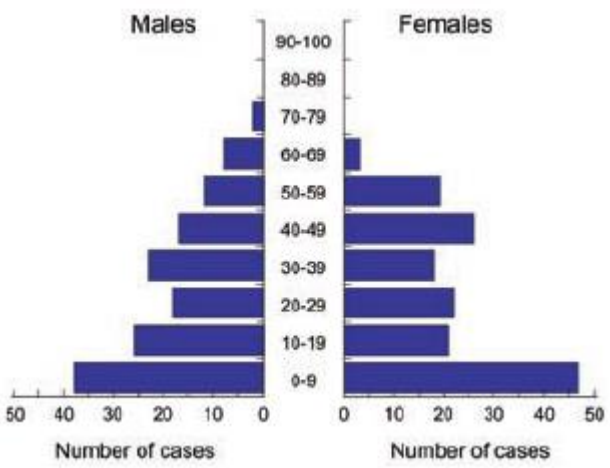
Ependymoma

Last updated: April 12, 2019

EPENDYMOMA - neoplasm of *ependymal cells* (lining of ventricles and central canal of spinal cord).

- 2-8% of adult brain tumors; twice more common (8-12%) in **children**, esp. < 2-3 yrs.
- 50% ependymomas occur in first 2 decades of life (peak 7-16 yrs, mean - 3.7 yrs).

Pediatric 4th ventricle tumor



GENETICS

- genetic lesions occurring in astrocytomas are not commonly found in ependymomas (i.e. different evolutionary pathways).
- 30% cases have loss of whole 22 chromosome.

RELA fusion-positive ependymoma - recently accepted variant recognized in the 2016 update to the WHO classification

- result of *chromothrypsis*.
- this variant is responsible for the majority of supratentorial ependymomas in childhood.
- worst prognosis of all molecular subtypes.

CLASSIFICATION

1. **Subependymoma** (WHO grade I) - features of both **ependymoma** and **astrocytoma** – tumor attached to ventricular wall
2. **Ependymoma** (WHO grade II); variants (not used today):

   True ependymoma is grade II

   a. clear cell type with perinuclear halo (resemble oligodendrogliomas) – worst prognostically
   b. papillary type with extensive epithelial component
   c. tanycytic type
   d. true rosette* formation
   e. melanotic type* (rare) containing lipofuscin and no melanin pigment.

   *only a-c types are recognized in WHO 2016
3. **Anaplastic ependymoma** (WHO grade III)

   N.B. distinction between grade II and III is unreliable and prognostically unclear; molecular stratification is the future (see table below)
4. **Myxopapillary ependymoma** (WHO grade I; young adult low-grade tumors in ***conus medullaris, cauda equina*** and ***filum terminale***) with papillary arrangement of cells and prominent perivascular-intercellular mucin / myxoid stromal cores

Table 3.01 Key characteristics of the nine molecular groups of ependymoma; based on data from a single study {1880}

Anatomical location	Group	Genetic characteristic	Dominant pathology	Age at presentation	Outcome
Supratentorial	ST-EPN-*RELA*	*RELA* fusion gene	Classic/anaplastic	Infancy to adulthood	Poor
	ST-EPN-*YAP1*	*YAP1* fusion gene	Classic/anaplastic	Infancy to childhood	Good
	ST-SE	Balanced genome	Subependymoma	Adulthood	Good
Posterior fossa	PF-EPN-A	Balanced genome	Classic/anaplastic	Infancy	Poor
	PF-EPN-B	Genome-wide polyploidy	Classic/anaplastic	Childhood to adulthood	Good
	PF-SE	Balanced genome	Subependymoma	Adulthood	Good
Spinal	SP-EPN	*NF2* mutation	Classic/anaplastic	Childhood to adulthood	Good
	SP-MPE	Genome-wide polyploidy	Myxopapillary	Adulthood	Good
	SP-SE	6q deletion	Subependymoma	Adulthood	Good

Molecular groups of ependymoma
Transcriptome and methylome profiling have established the relevance of anatomical site to ependymoma biology. In a recent study that will likely serve as the basis for the future molecular classification of the disease {1880}, nine groups of ependymoma were described; three for each of the three major CNS anatomical compartments (i.e. the supratentorial compartment, posterior fossa, and spinal compartment). The modal patient age at presentation, clinical outcome, and frequencies of histopathological variants and genetic alterations vary across these groups.

PATHOLOGY

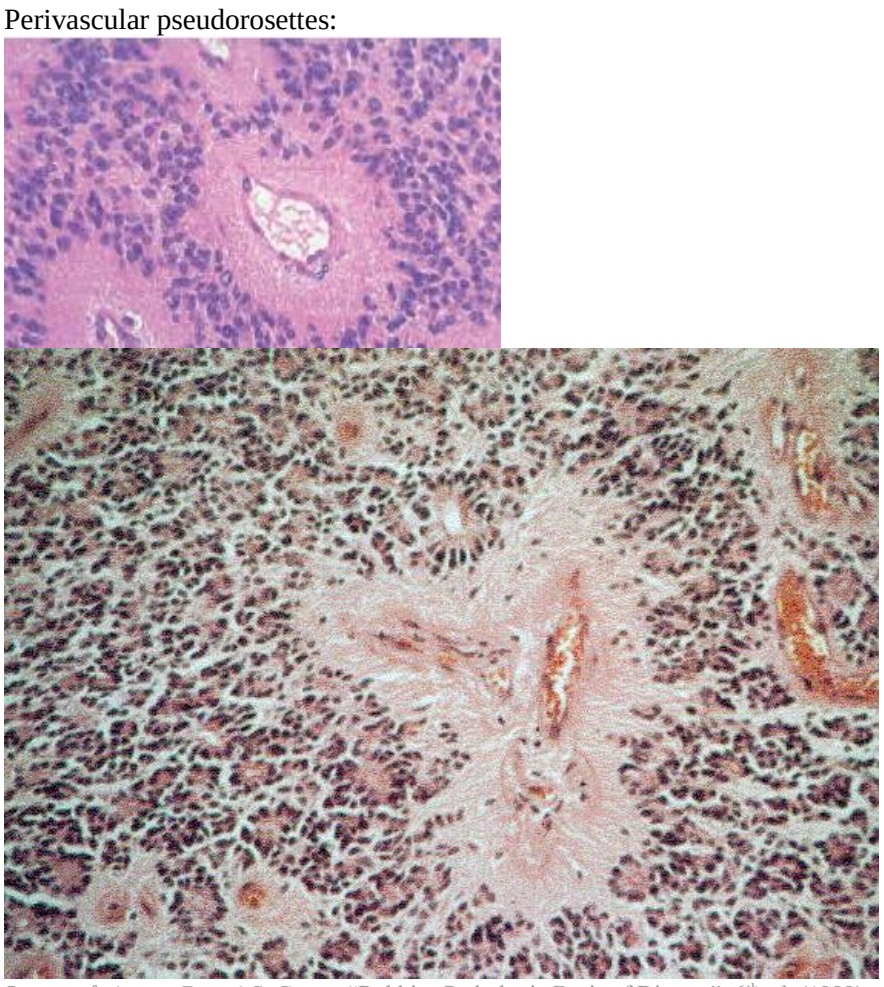
- do not proliferate rapidly – slowly growing.
- 100% IDH-1 negative.
- not invasive*, 90% do not metastasize (*morbidity by local space-occupying effects*); only ≈ 12% spread via CSF (esp. high-grade posterior fossa tumors) – **"drop metastases"**.

  *displaces (rather than infiltrates) brain parenchyma with minimal peritumoral edema.
- moderate cellularity (uniform cells), punctuated by areas of acellular, fibrillary eosinophilic halo surrounding blood vessel (perivascular pseudorosettes).
- ependymal rosettes (diagnostic, but uncommon feature of ependymoma) - ependymal cells radially aligned about central lumen with long, delicate processes (cilia) extending into lumen (gland-like

round or elongated structures); cells contain **BLEPHAROPLASTS** (basal bodies of cilia near nucleus – identified with special stains).

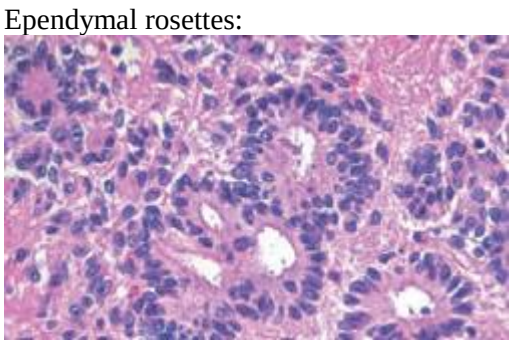
EPENDYMOMA

Perivascular pseudorosettes:

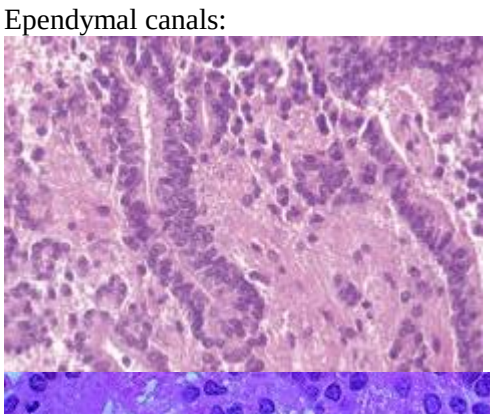


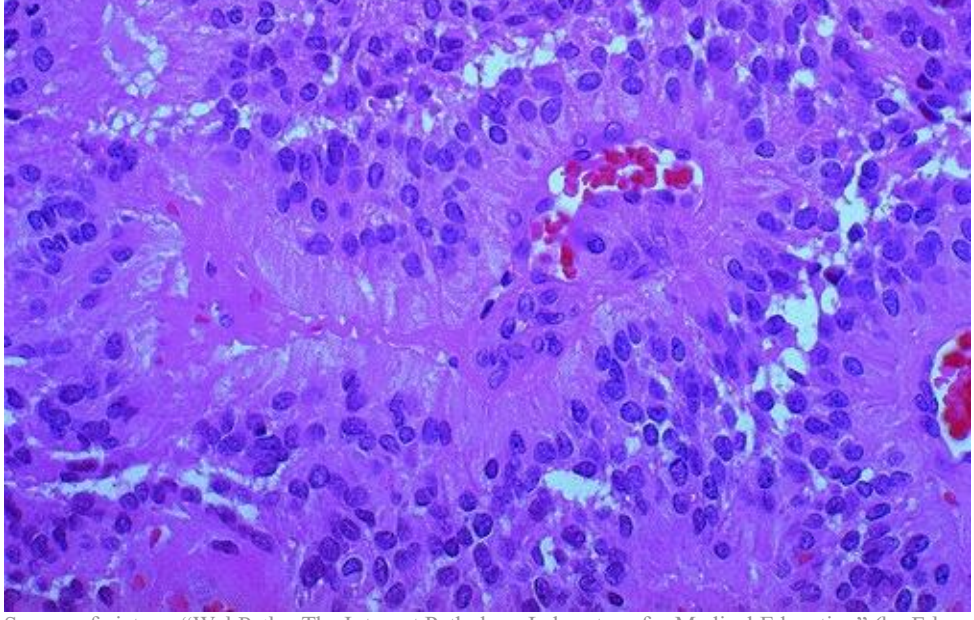
Source of picture: Ramzi S. Cotran "Robbins Pathologic Basis of Disease", 6th ed. (1999); W. B. Saunders Company; ISBN-13: 978-0721673356 >>

Ependymal rosettes:



Ependymal canals:





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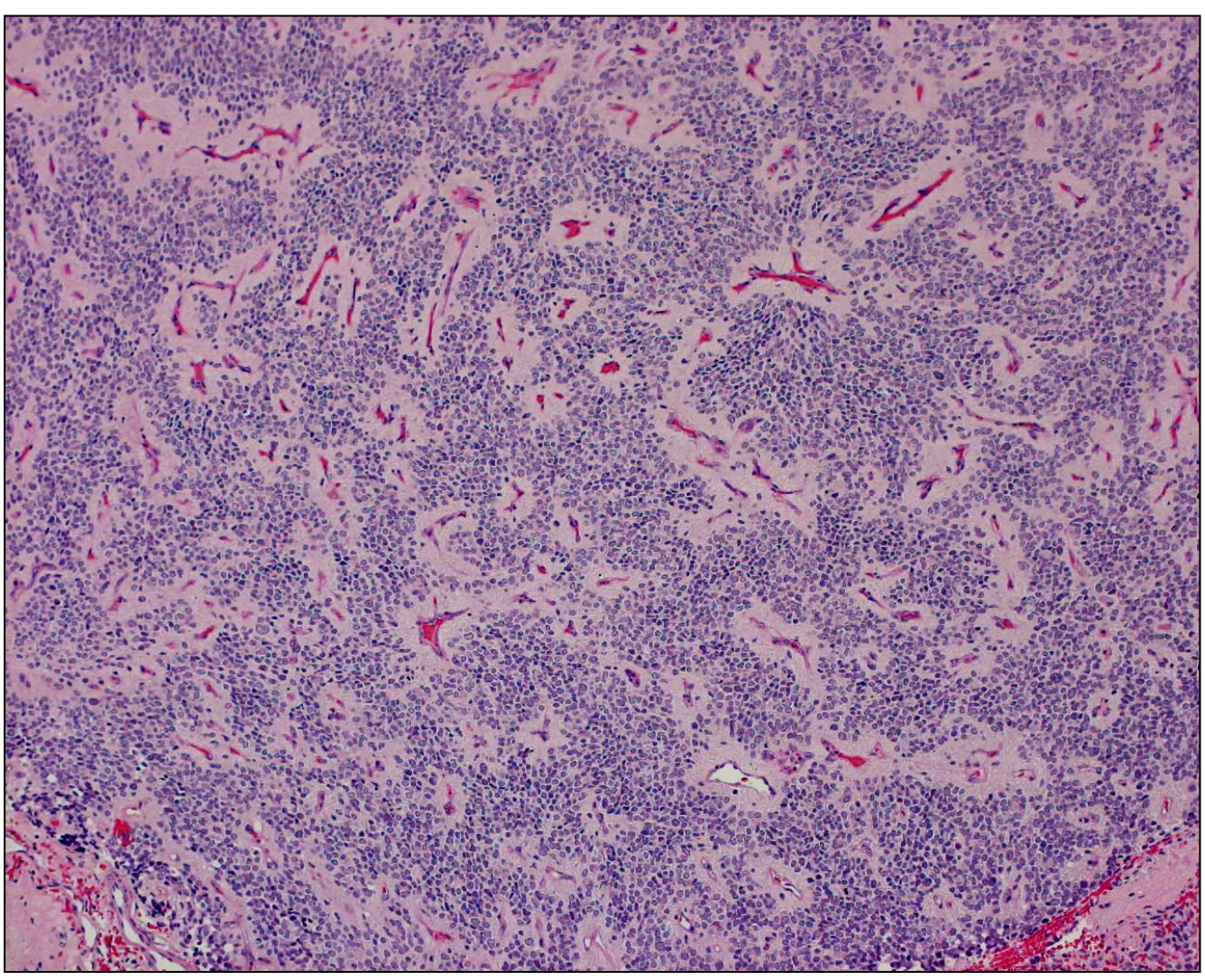


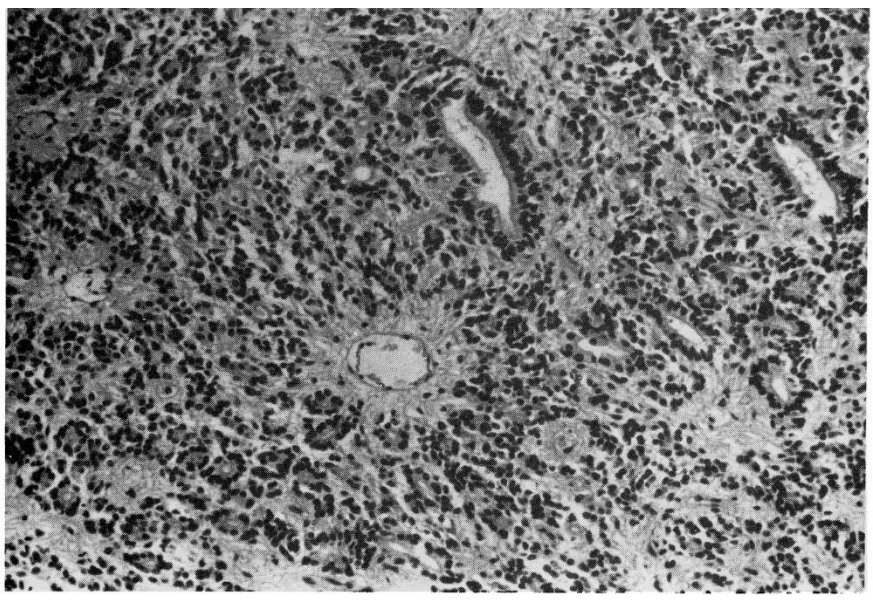
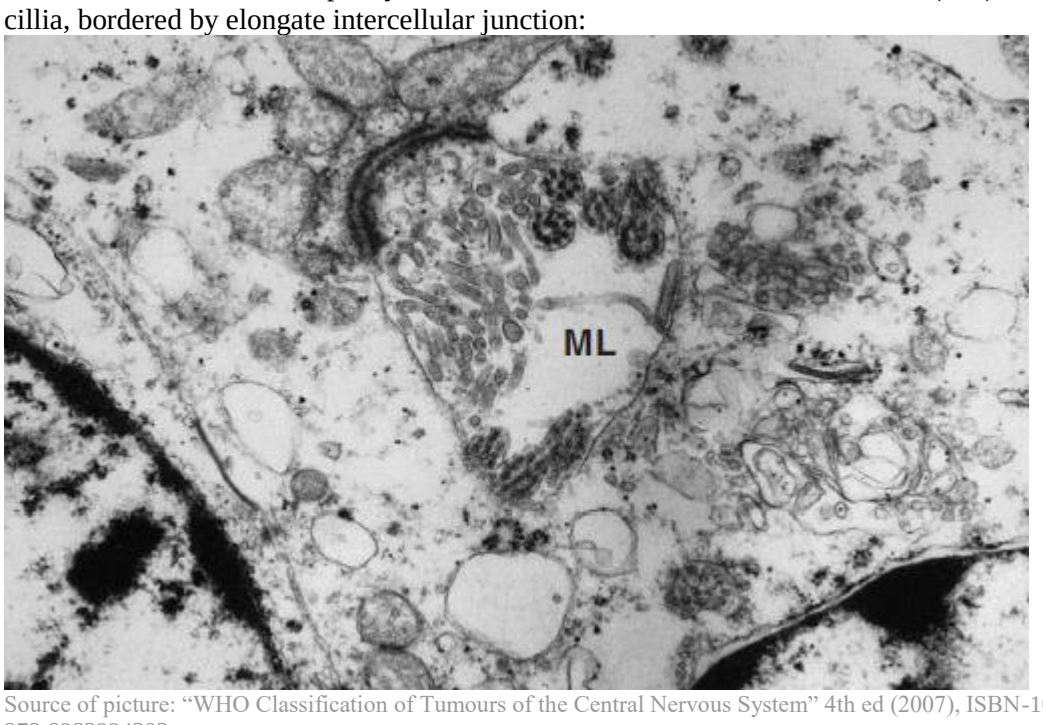
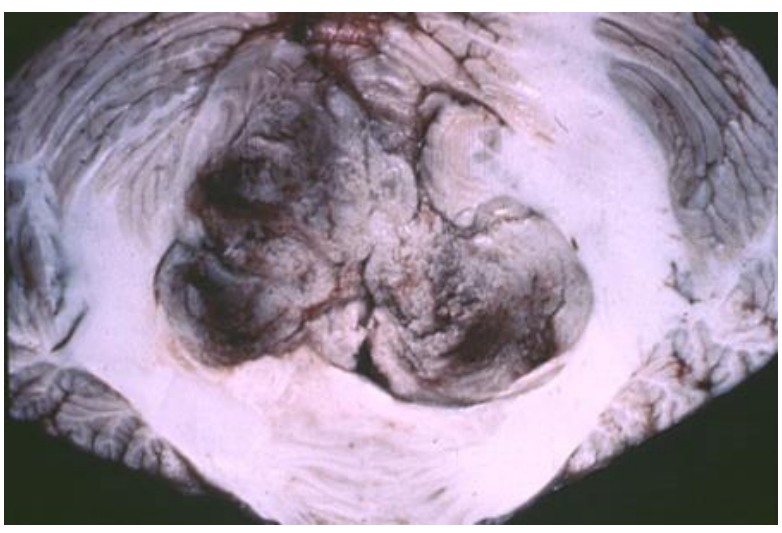


Figure 29–29. Ependymoma. Note tumor cells align themselves around tubular spaces resembling the ependymal cavity and also around blood vessels. (H and E stain.)

Ultrastructural features of ependymal differentiation: intercellular microlumen (ML) containing microvilli and cillia, bordered by elongate intercellular junction:



Source of picture: "WHO Classification of Tumours of the Central Nervous System" 4th ed (2007), ISBN-10: 9283224302, ISBN-13: 978-9283224303 >>



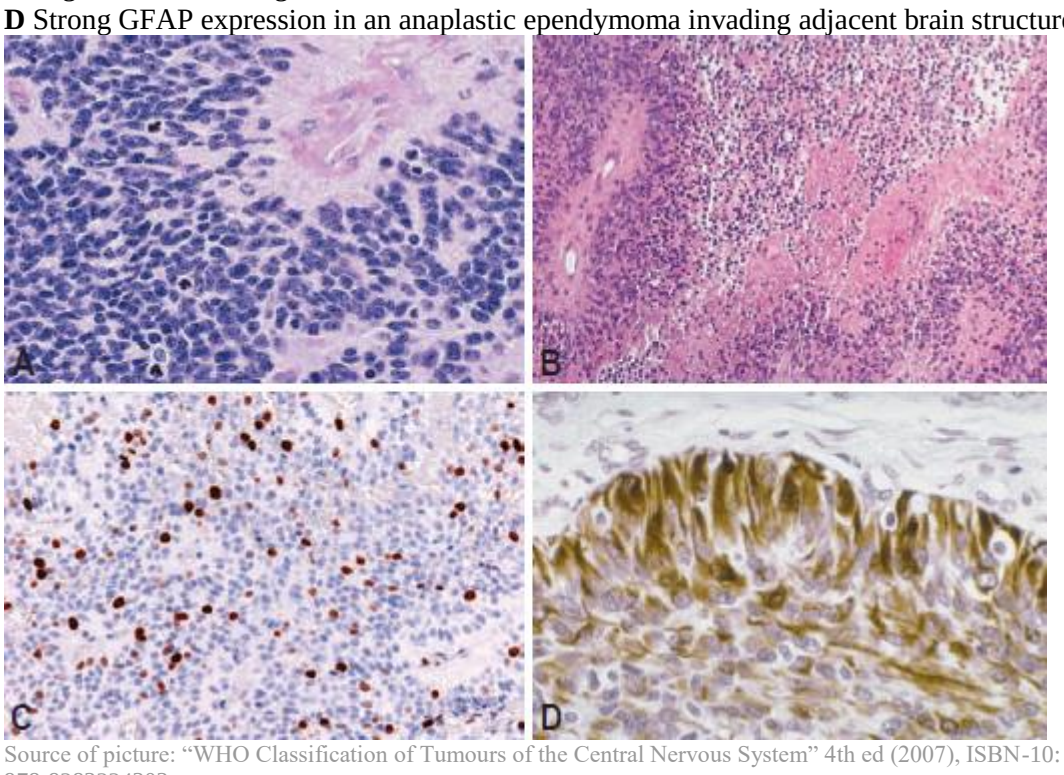
TANYCYTIC EPENDYMOMA

– does not form rosettes.

Tanycytes [Greek. *tanus* – elongated] are special ependymal cells found in the third ventricle and on the floor of the fourth ventricle and have processes extending deep into the hypothalamus. It is possible that their function is to transfer chemical signals from CSF to CNS.

ANAPLASTIC EPENDYMOMA

A Poorly differentiated tumor cells with brisk mitotic activity.
B Large foci of necrosis.
C High MIB-1 labelling index.
D Strong GFAP expression in an anaplastic ependymoma invading adjacent brain structures.



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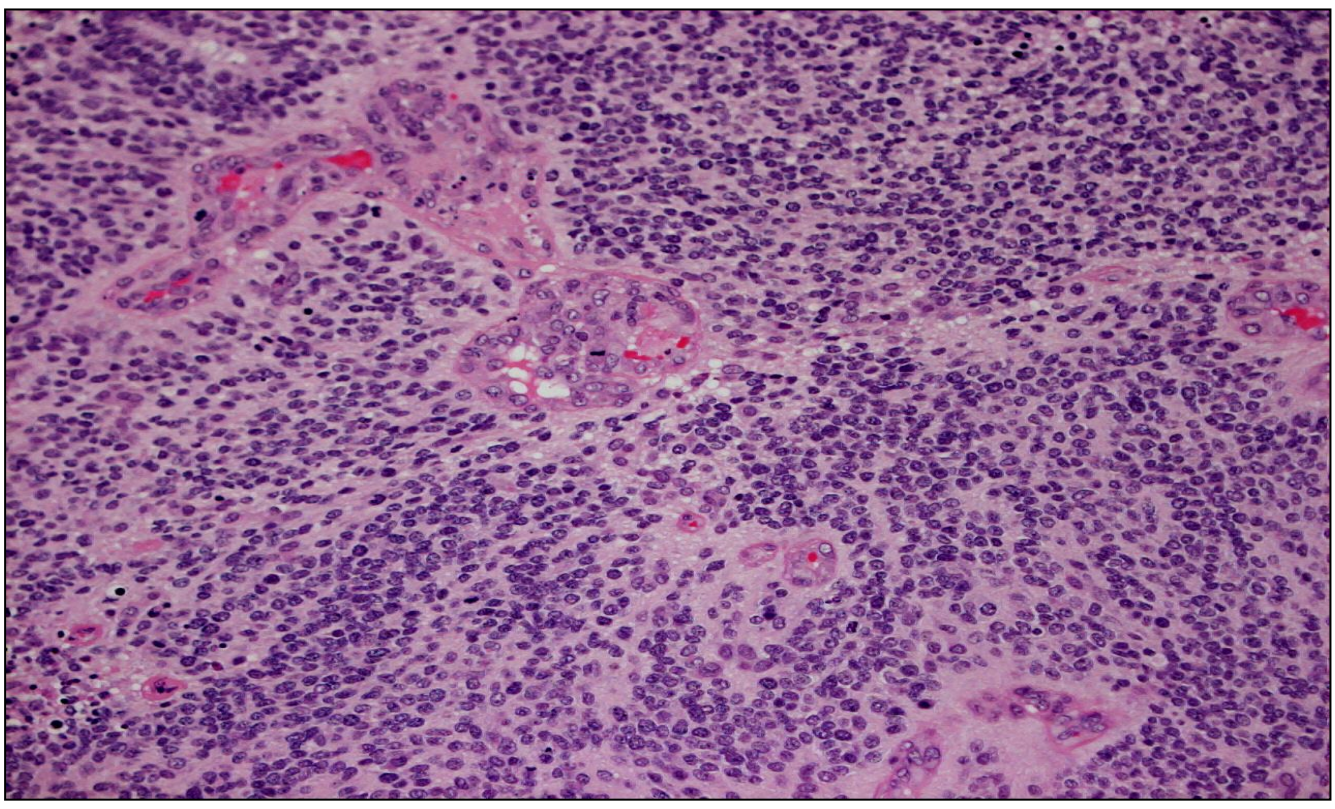
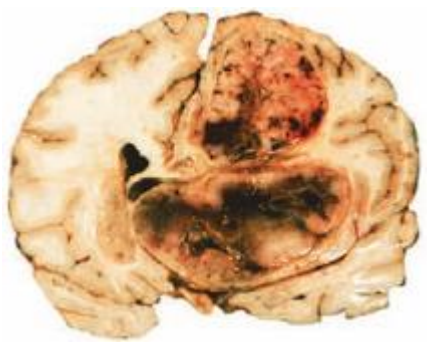


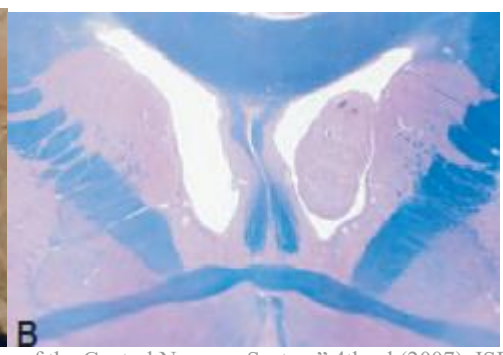
MYXOPAPILLARY EPENDYMOMA

- spinal ependymoma in *conus medullaris.* see p. Onc50 >>

ANAPLASTIC EPENDYMOMA



SUBEPENDYMOMA



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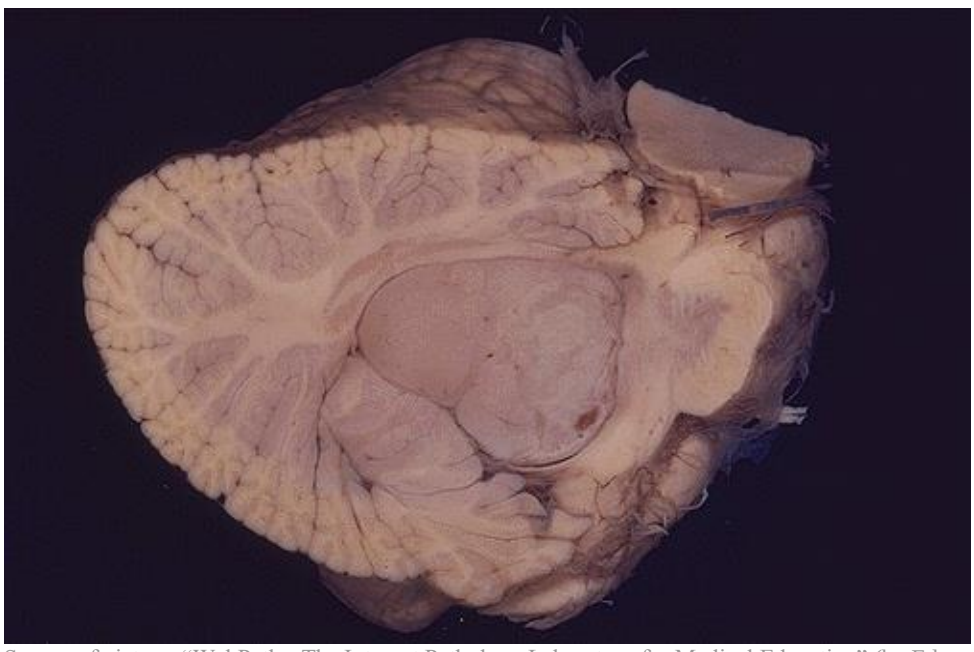
LOCATION

1) INTRACRANIAL (90%)
   - 2/3 are located in posterior fossa (> 90% in 4th ventricle with tendency to spread along outlets to cerebellopontine angle and into cervical spinal canal)!
   - 1/3 are supratentorial (esp. in adults).
   - usually *intraventricular*, although *extraventricular* rests* of ependymal cells may give rise to hemispheric tumors (esp. near atrium of lateral ventricle).

   *where primitive fetal ventricular walls have fused

2) INTRASPINAL (often benign histology); most patients are > 12 yrs. see p. Onc50 >>
   - ependymomas are most frequent (56-70%) intramedullary tumors.
   - benign *myxopapillary type* occurs in filum terminale

3) unusual ECTOPIC SITES - mediastinum, ovary, broad ligament.



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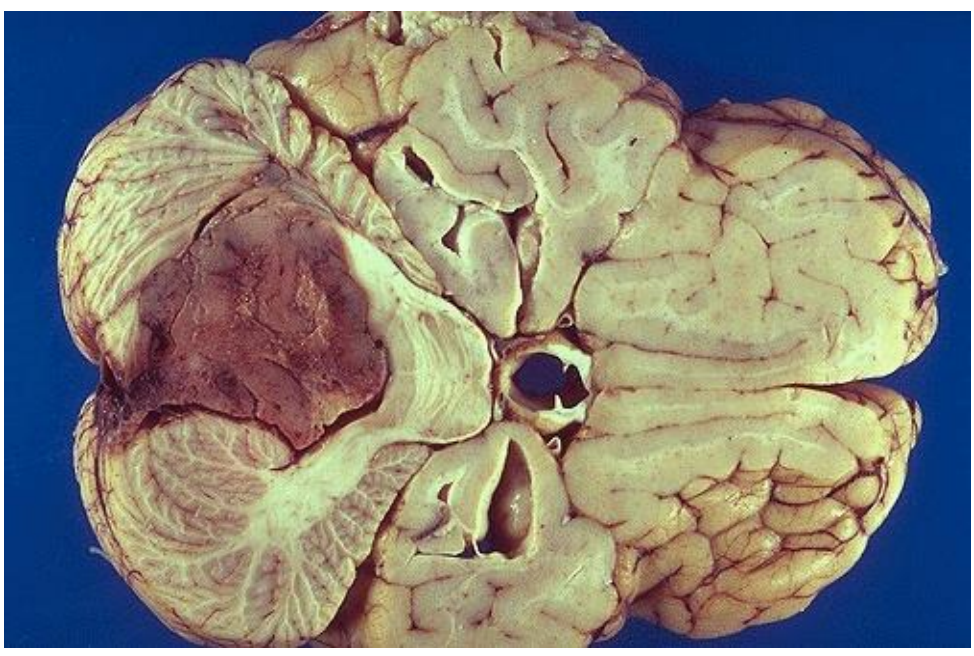

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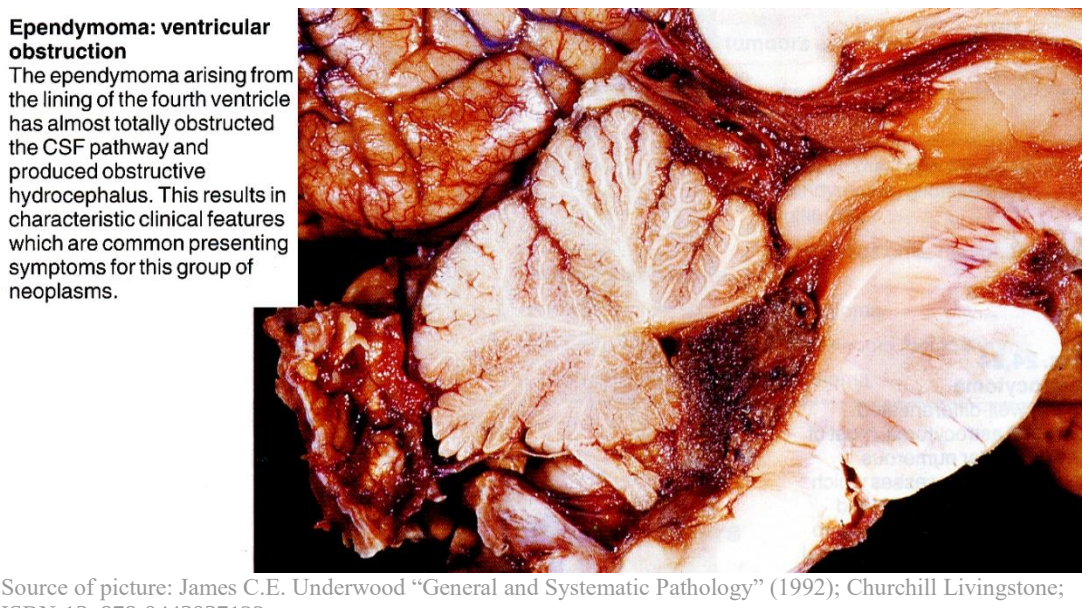
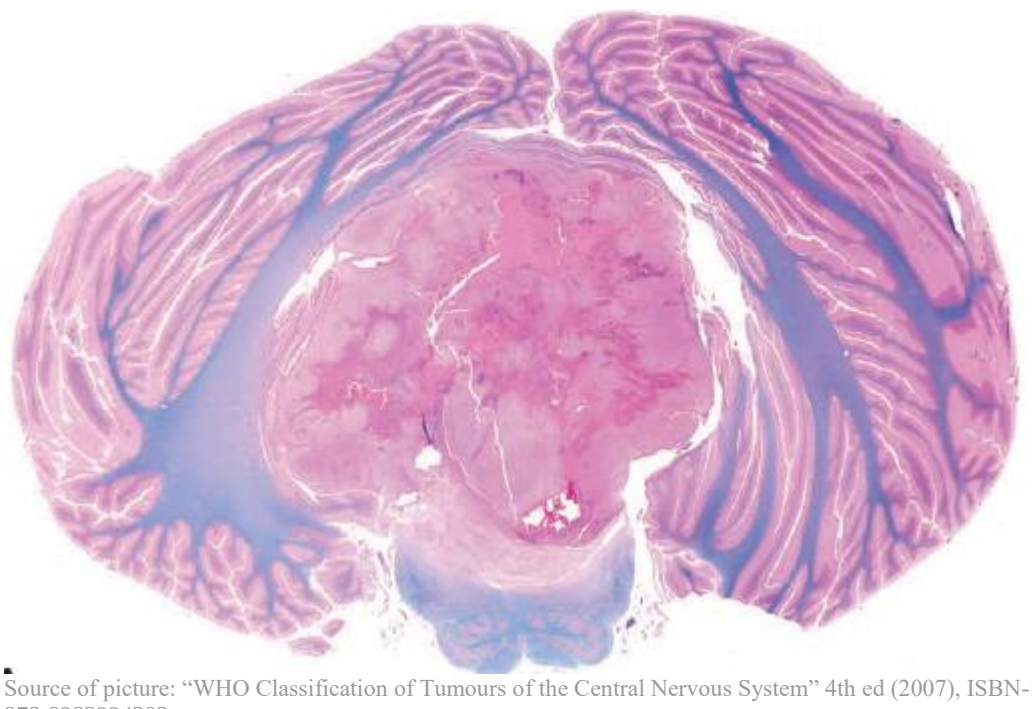


Source of picture: James C.E. Underwood "General and Systematic Pathology" (1992); Churchill Livingstone; ISBN-13: 978-0443037122 >>



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CLINICAL FEATURES

- insidious and progressive:

Nausea & vomiting is most common (80%) presenting symptom!

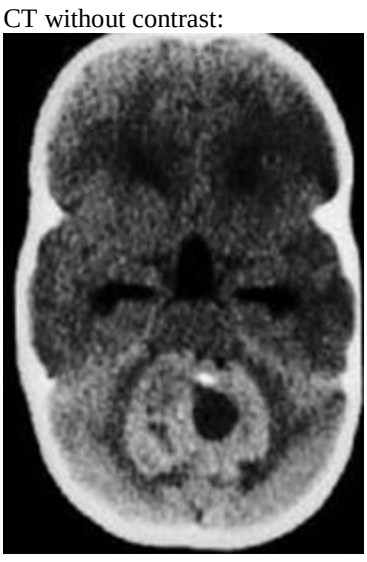
SUPRATENTORIAL tumors - mass effect, focal neurological signs, occasional ventricular obstruction.
POSTERIOR FOSSA tumors - obstructive hydrocephalus ± brain stem compression.

DIAGNOSIS

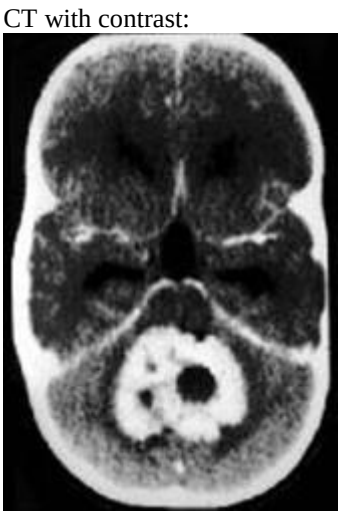
MRI (diagnostic tool of choice) - discrete, heterogeneous mass with variable enhancement, adjacent to ventricular system.

- ***hydrocephalus*** in almost all patients.
- ***calcification***, ***necrosis***, ***cystic change*** are frequent.
- *hemorrhage* is rare.
- spinal MRI is necessary!!!!!!

CT without contrast:

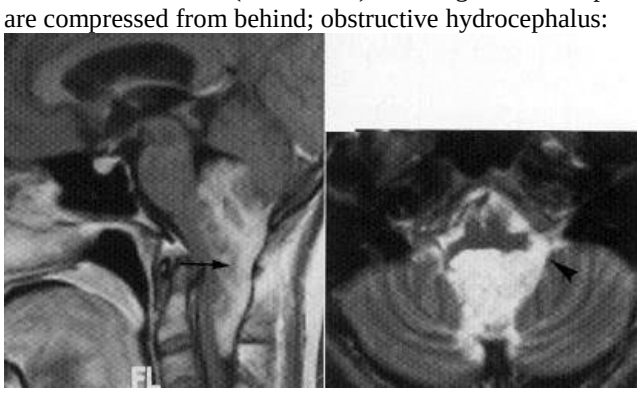


CT with contrast:

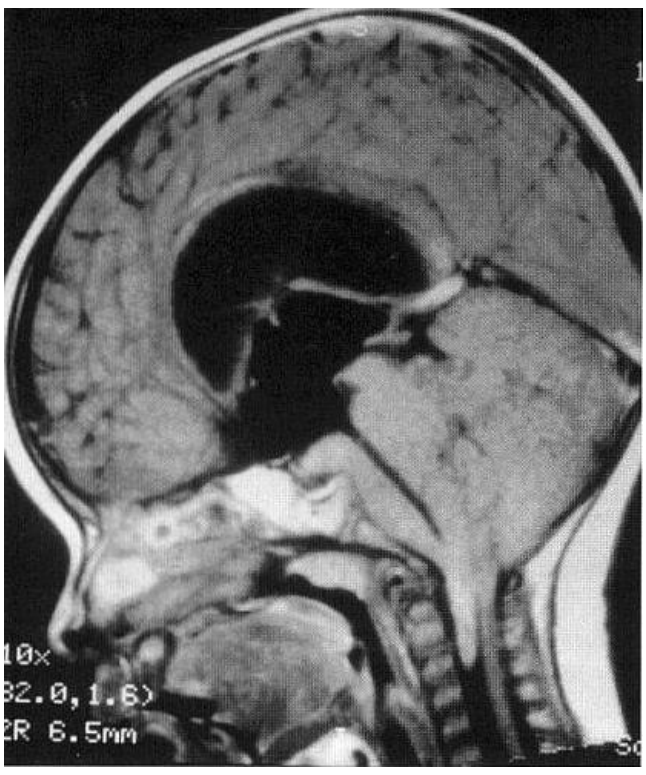


MRI (ependymoma of 4th ventricle, compressing cerebellum and brain stem):

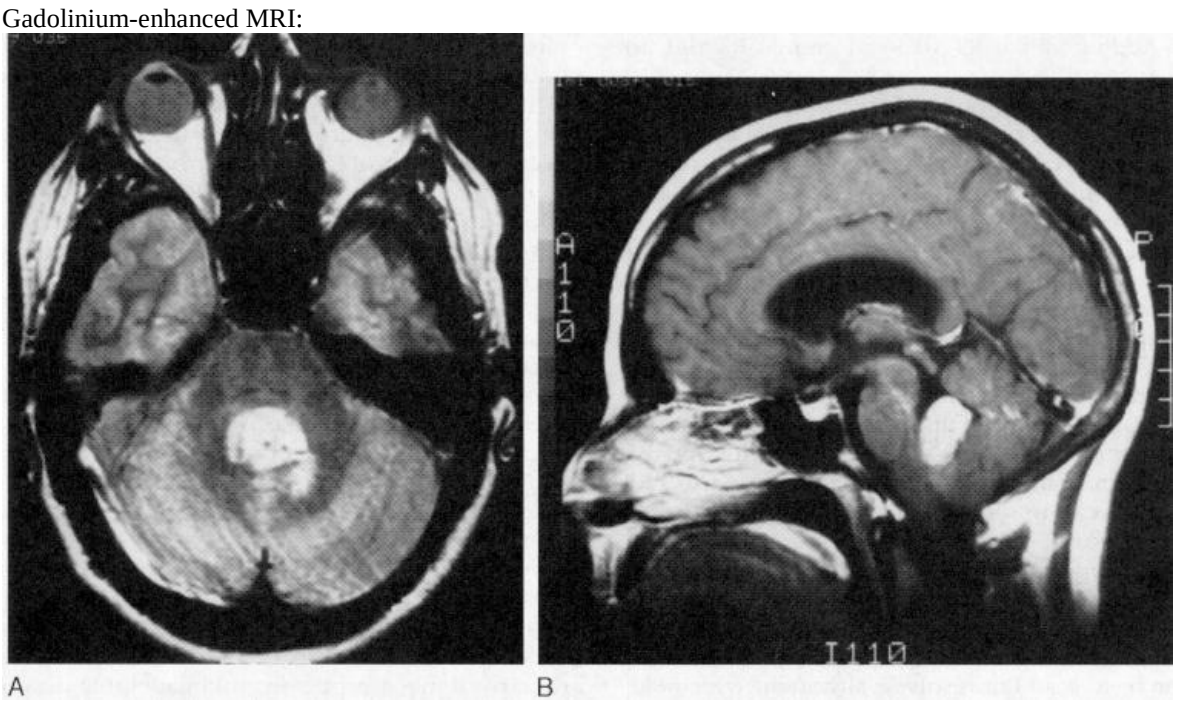
Contrast T1- and T2-MRI - heterogeneously enhancing mass (*arrow*) fills lower half of 4th ventricle and extends through foramina of Luschka (*arrowhead*) and Magendie to lie posterior to medulla oblongata and upper cervical spinal cord, which are compressed from behind; obstructive hydrocephalus:

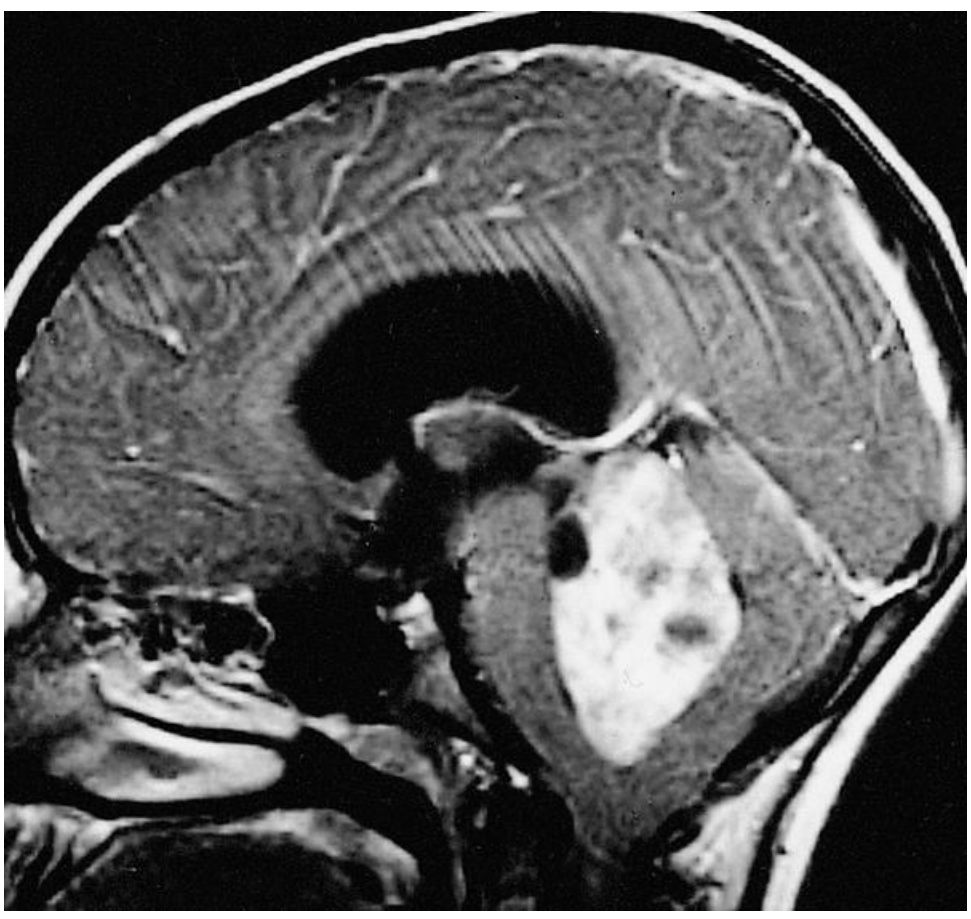


T1-MRI without contrast - large neoplasm encasing basilar artery and extending along premedullary cistern into upper cervical subarachnoid space:

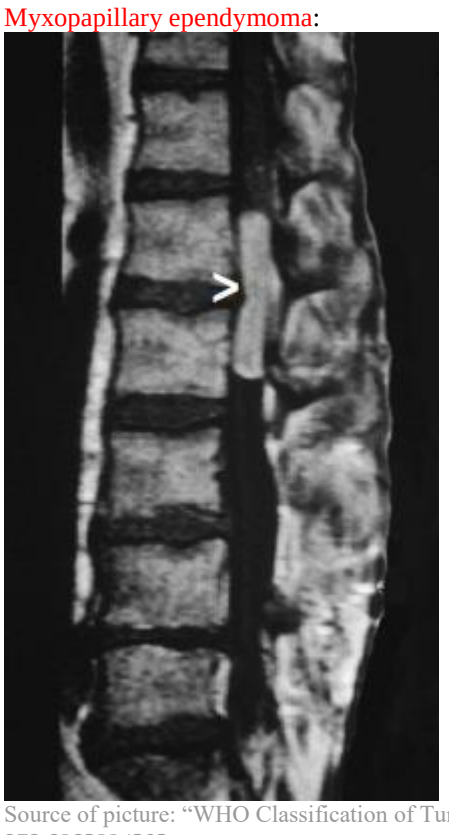


Gadolinium-enhanced MRI:





Myxopapillary ependymoma:



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CSF cytology (deferred for 2 weeks postoperatively*) - for microscopic leptomeningeal dissemination.

*to avoid herniation, to avoid identifying tumor cells that may have been disseminated as result of surgery.

TREATMENT

Ventriculostomy is not required preoperatively (patients are usually stable).

N.B. it should be avoided (risk of upward herniation or hemorrhage within tumor)

Surgery - most effective therapy

- unexpected residual lesion → ***second-look surgery*** (vs. residual medulloblastoma – treat with chemoradio).
- permanent ventriculoperitoneal shunt is rarely required.

- **postoperative MRI** for *residual disease* (within 72 hours of surgery - to avoid confusion with postsurgical inflammation).

Standard postoperative local (1-2 cm margin, 50-55 Gy) **radiotherapy** substantially improves survival (modern trend – even for kids < 3 yo; adults with GTR may be observed postop).

- aggressive *anaplastic features* or *residual tumor* → whole-brain radiation.
- documented *leptomeningeal dissemination* → craniospinal axis radiation.

N.B. most relapses are local! - *inability to eradicate primary tumor* remains single most important factor leading to treatment failure!

Chemotherapy - at present, no definitive conclusions.

- recommended for children < 3 yrs with residual tumor until they are old enough to receive radiation.
- CISPLATIN most effective (30% response rate).
- ETOPOSIDE in recurrence - response rates as high as 83%.

PROGNOSIS

Progression-free 5-yr survival (overall - 55%):
Gross total resection (up to 85% patients) – 70-80%.
Incomplete resection – 30-35%.

Extent of tumor resection is most important prognostic factor!

- age is second most important prognostic factor - *younger patient*, worse prognosis! (5-yr survival: infants - 25%, children 1-4 years - 46%, children ≥ 5 yrs - > 70%).
- prognosis is worse than medulloblastoma (later - exquisite sensitivity to adjuvant therapy).
- histology and tumor location* are not significant prognostic indicators!

*exception: spinal tumors have better prognosis

BIBLIOGRAPHY for ch. "Neuro-Oncology" → follow this LINK >>