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HOW DO I DO IT: Surgery for Pilocytic Astrocytoma

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PA - Introduction

- **Pilocytic astrocytoma** also known as **juvenile pilocytic astrocytoma** or **cystic cerebellar astrocytoma**
- Usually slow growing.
- Can reach very large sizes
- Associated single or multiple cysts

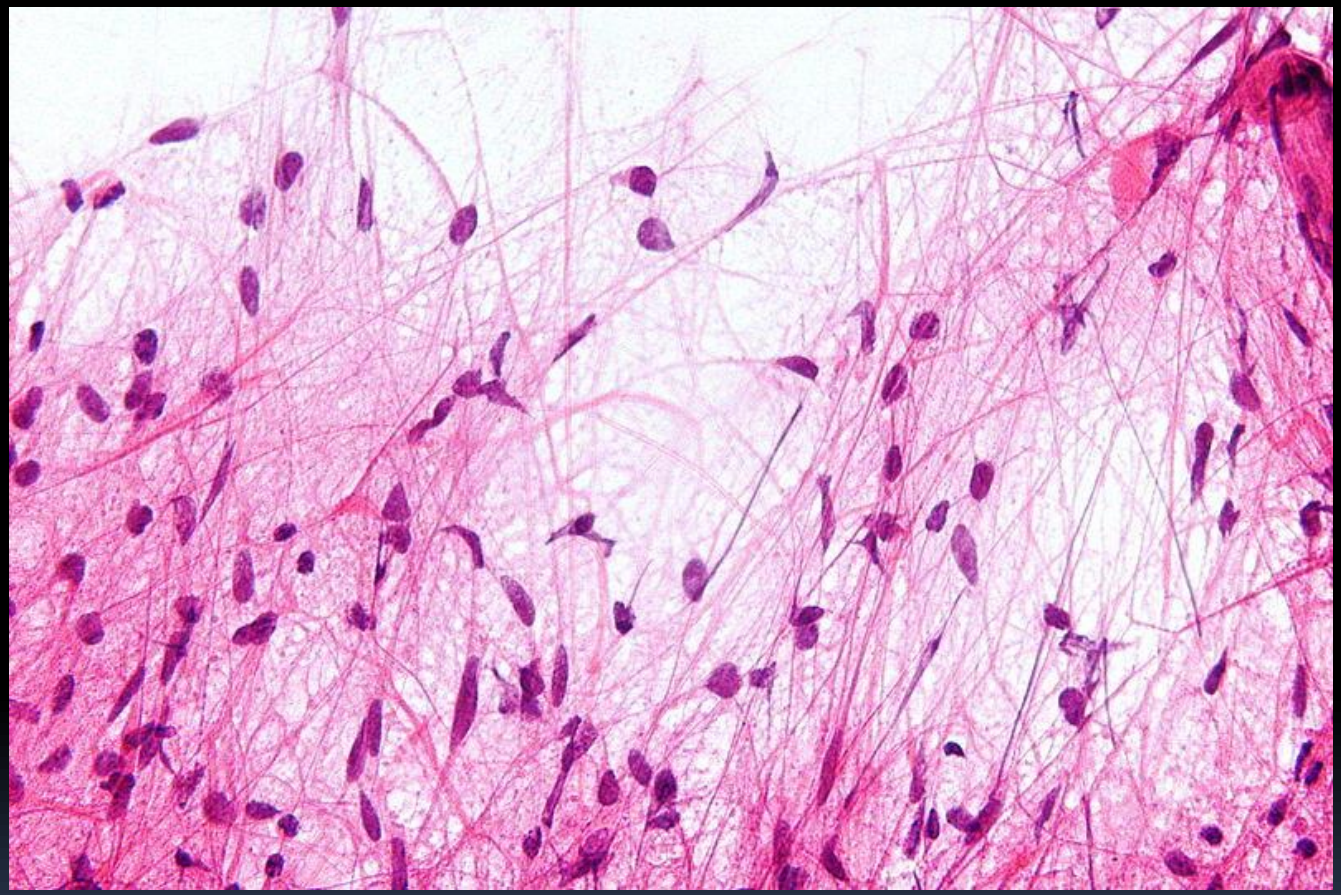
Epidemiology

- Brain tumours:
  - most common solid tumour in children.
  - > 50% are infratentorial.
- Commonest Tumours:
  - Cerebellar astrocytoma and brain stem gliomas
- Pilocytic astrocytoma:
  - ¬10% of all primary brain tumours.
  - 75% of Cerebellar astrocytomas are pilocytic
  - 25% of posterior fossa tumours in children.

Clinical Presentation

- Symptoms of raised ICP from mass effect and hydrocephalus often develop late and include
  - Headaches, nausea and vomiting
  - Irritability, drowsiness, blurred vision
  - Clumsiness and ataxia
- Pilocytic astrocytomas are slow growing lesions
  - grumbling non-specific symptoms often go on for weeks to months before a diagnosis becomes clear
- Radiologically a large cerebellar hemispheric or vermian mass that is predominantly cystic in a child younger than 10 years.

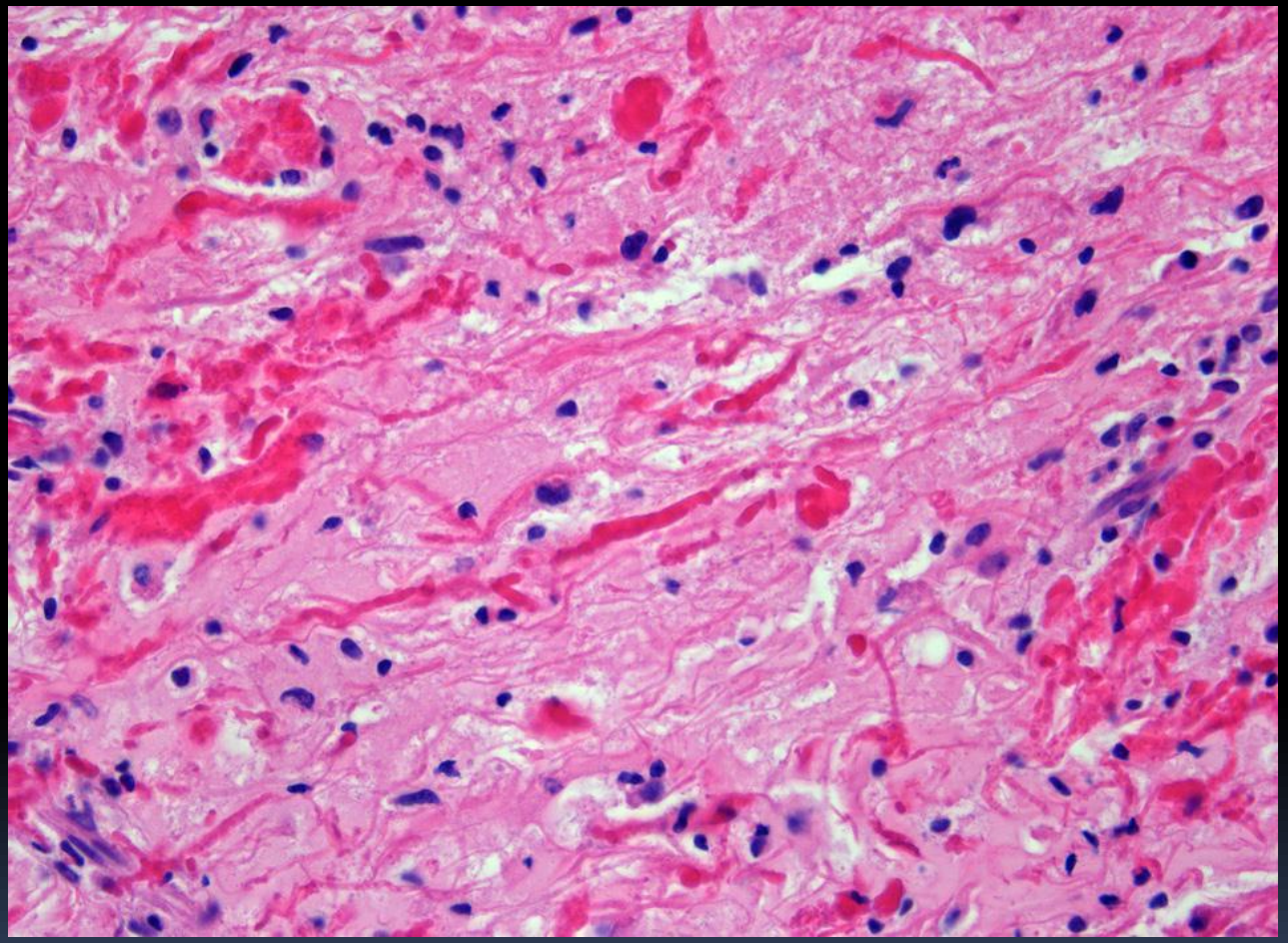
Histological appearance



H&E Stain:

characteristic bipolar cells with long pilocytic (hair-like) processes

Histological appearance



Rosenthal-fibres in pilocytic astrocytoma
H&E staining showing elongated eosinophilic fibre-like structures

Imaging

- **CT:**
  - LGG difficult to visualize on CT (isointense with parenchyma).
  - Cystic lesions with mural nodules are however easy to identify

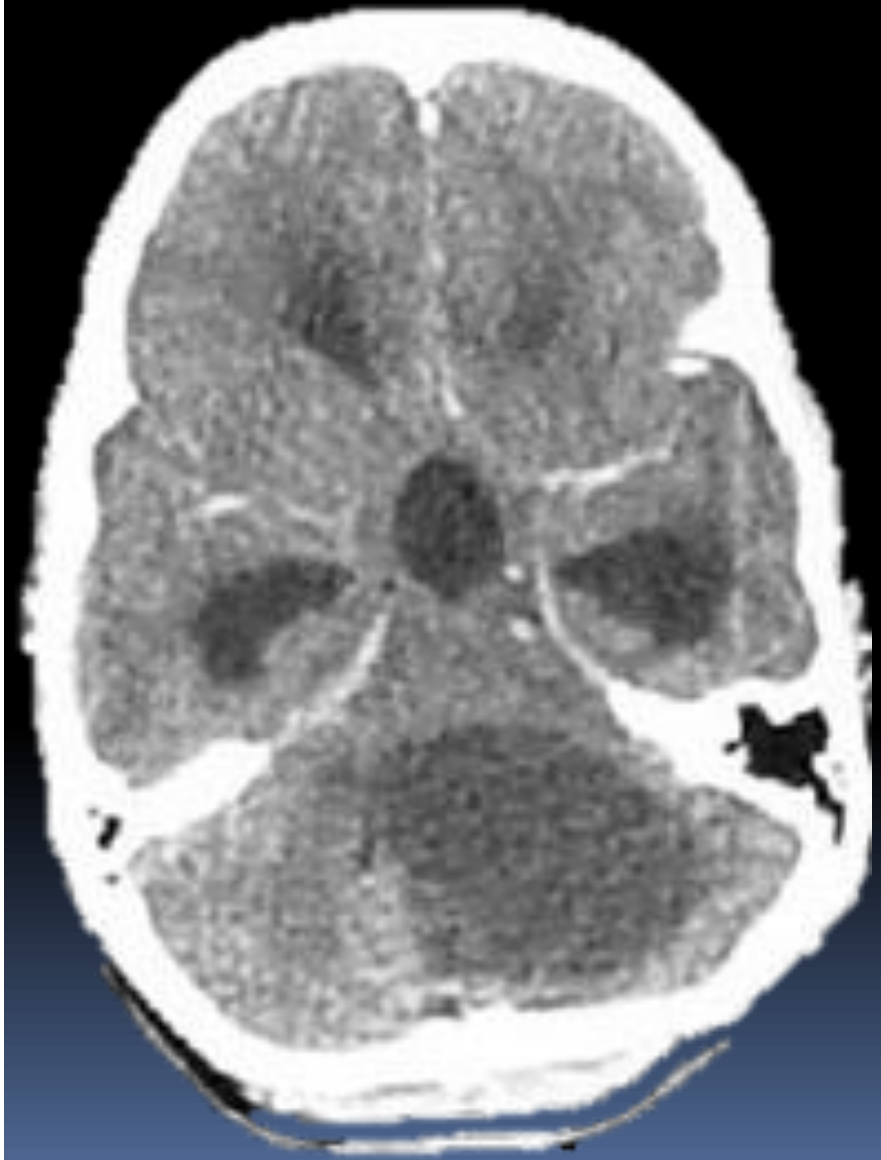
- **MRI:**
  - LGG appear as low intensity on T2W scans. The exception is the pilocytic astrocytoma (well circumscribed, intensely enhancing)

  - **Location:** Intra-axial mass (midline or hemispheric)
  - **Cystic component:** Prominent
    - T1W= hypointense; T2W= hyperintense; Enhancement +/-
  - **Mural nodule:** Hyperintense on T2W images, Enhances on GAD
  - **4th Ventricle:** Displaced or effaced
  - **Hydrocephalus:** Acute Tri-ventriculomegaly

Tumour Patterns

- Mainly large cystic with smaller mural nodule
- Mainly solid with small cyst(s)
- Solid mainly Vermian or midline lesions

Mainly Cystic with mural nodule



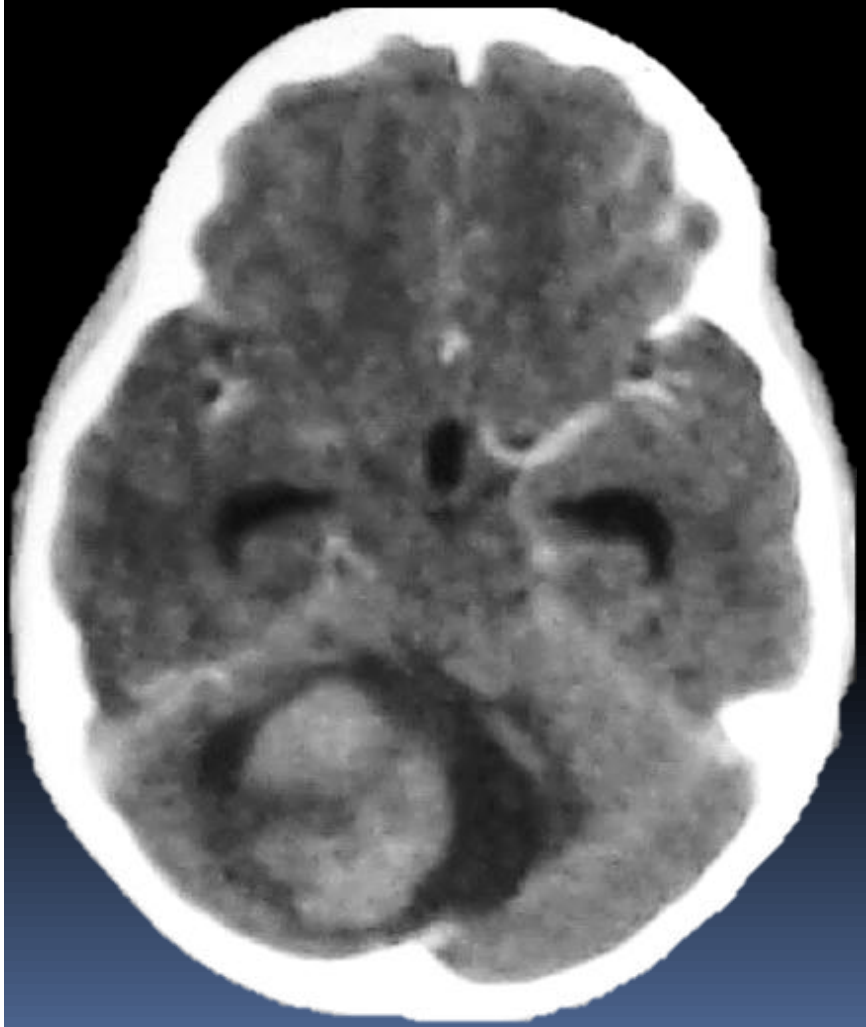
About half of pilocytic tumours are simple cysts with a single mural nodule.

Thin transparent cyst walls are often clear of tumour. Removal of the mural nodule may be sufficient for treatment.

Thick walled cysts are likely to contain tumour within their walls and resection is necessary to avoid recurrence

CT scan
large cerebellar cystic lesion with a small enhancing nodule. Cyst wall may or may not enhance.

Mainly Solid within Cyst(s)

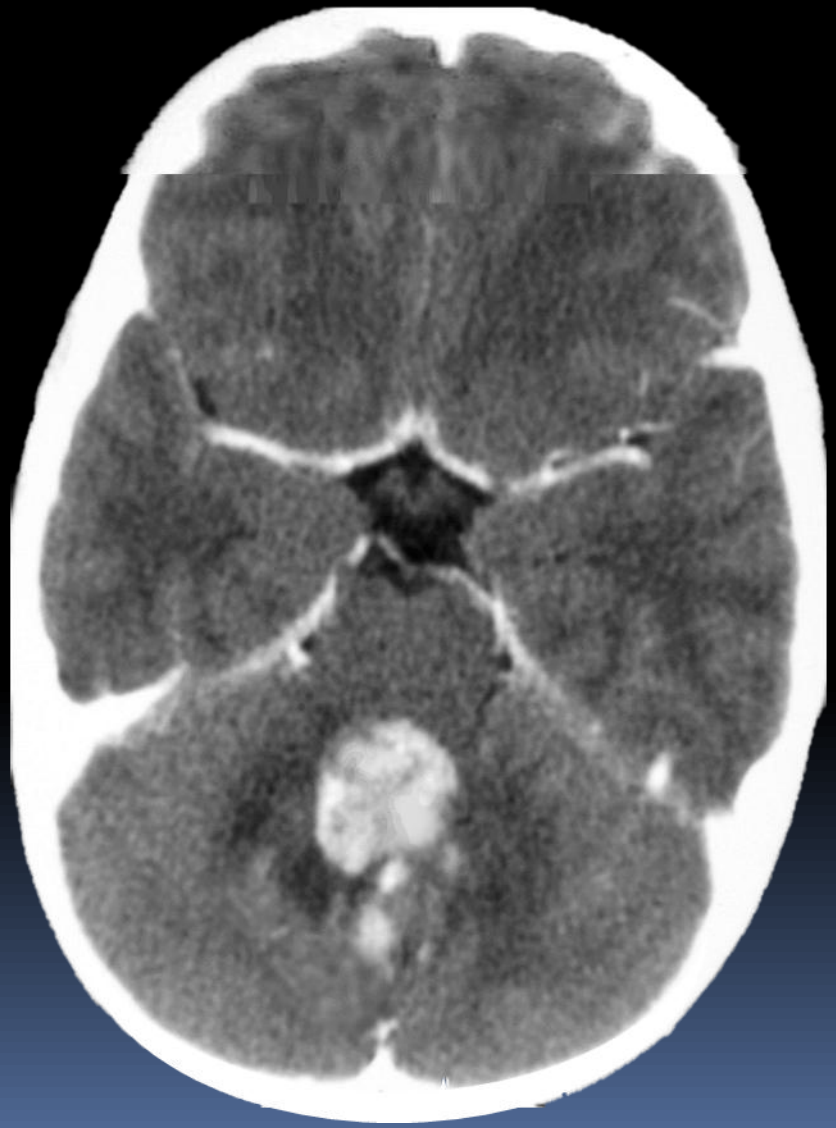


About 40% are solid tumours with necrotic areas within appearing like multilocular cysts.

The cyst lining enhances and tumour is often present in the cyst wall confirmed by histology. Resection of the entire wall is required.

CT showing a large solid enhancing lesion with micro-cyst (necrotic) within. There is a small cystic area around the lesion with enhancement of the non-necrotic portions of the tumour.

Midline solid



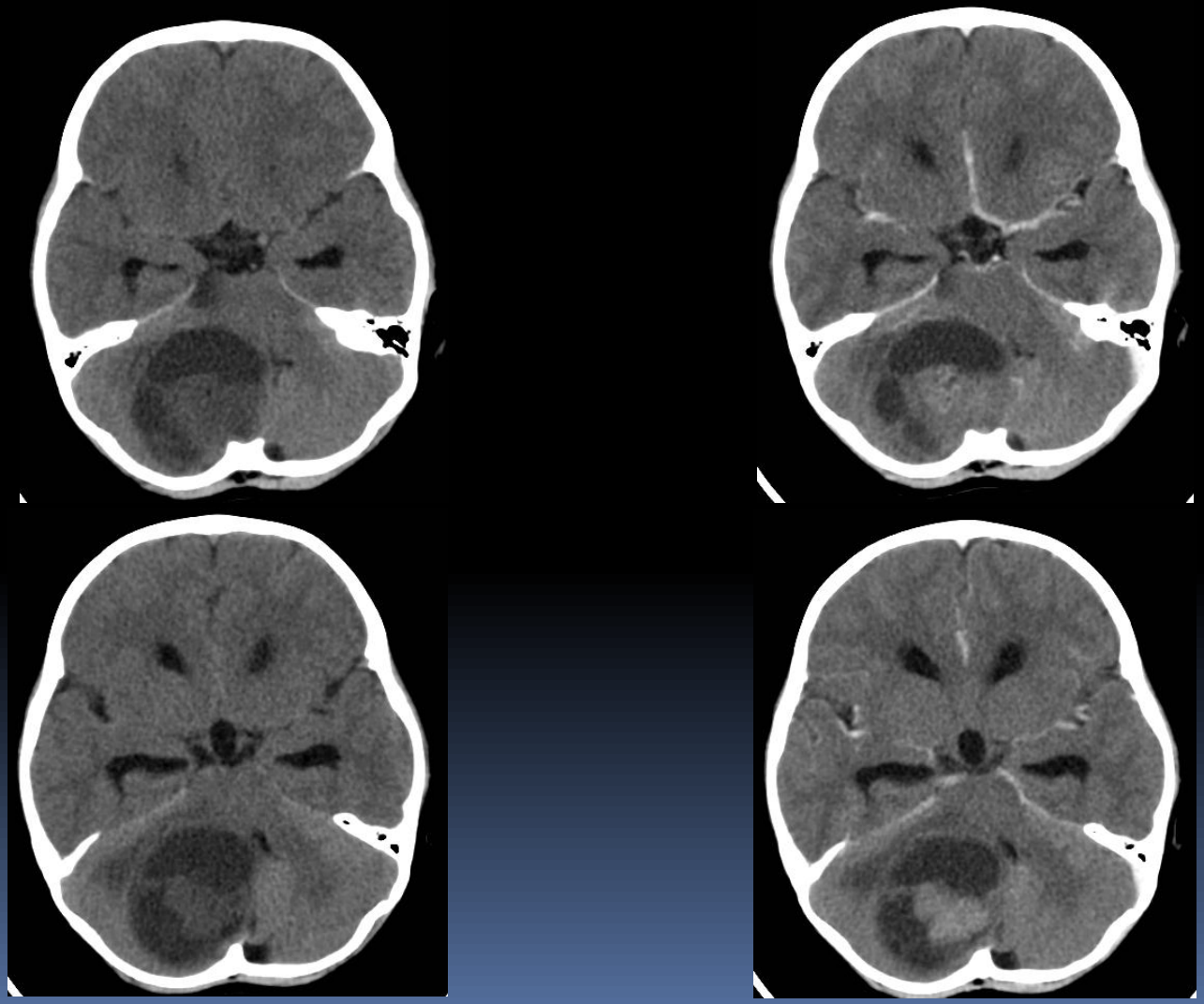
- About 10% are midline tumours .
- They enhance sometimes heterogeneously.
- MIdline tumours are often vermian and more likely to present with hydrocephalus.

JK - PA

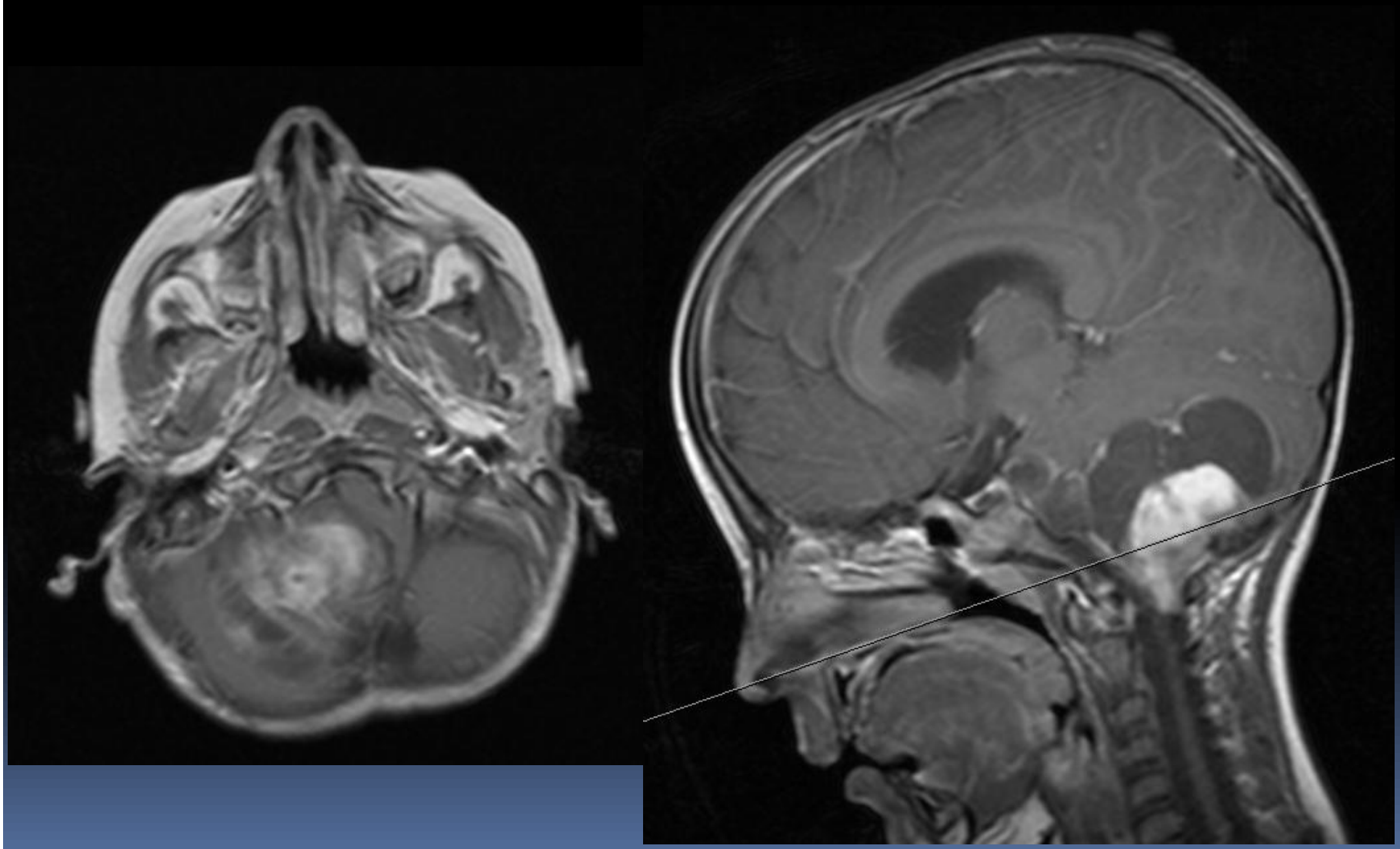
3 year old generally clumsy developed progressive headaches, vomiting, ataxia over a 3 week period

O/E
Papilloedema, nystagmus and ataxia with asymmetric dysmetria

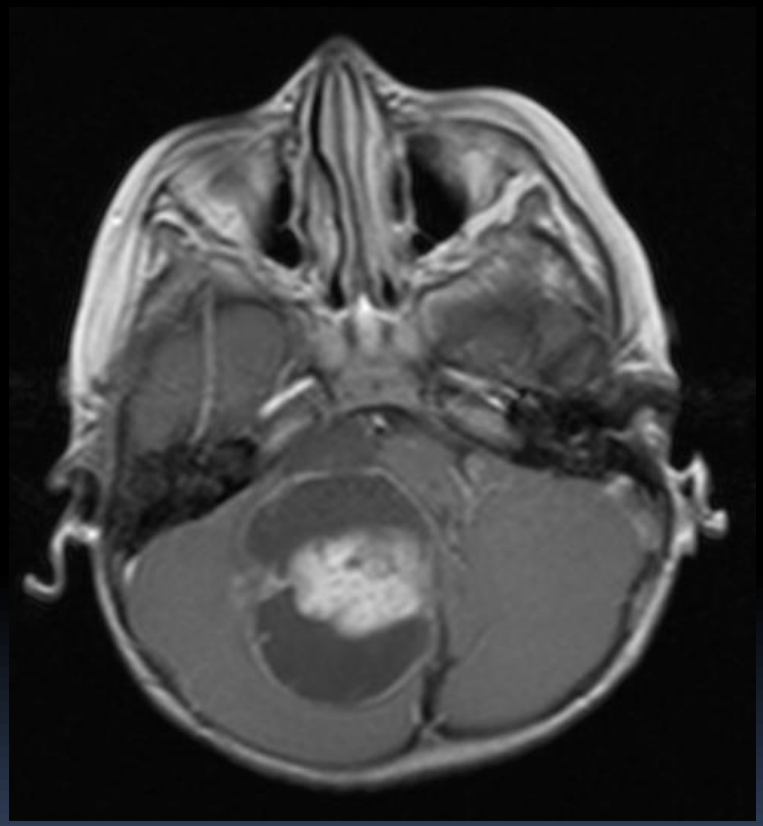
CT: Hemisheric Cystic lesion with mural nodule

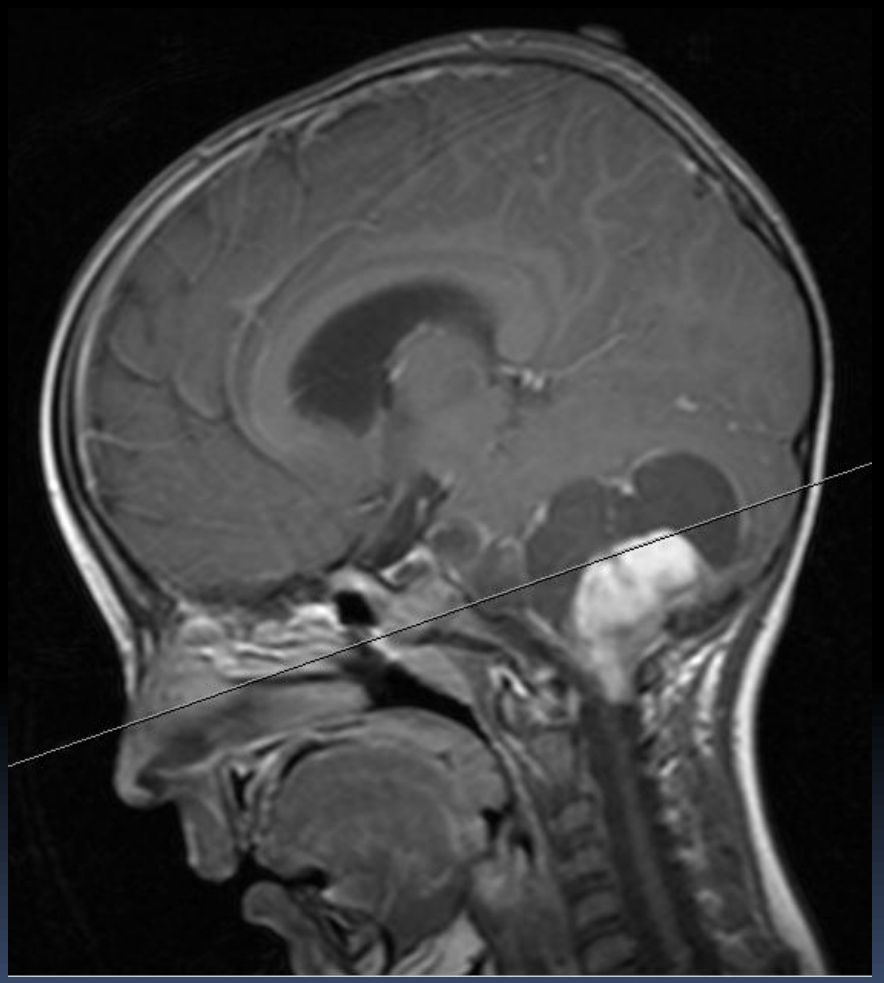


MRI: Hemispheric lesion, enhancing nodule, brainstem, 4th Ventricle distortion



MRI: Hemispheric lesion, enhancing nodule, brainstem, 4th Ventricle distortion

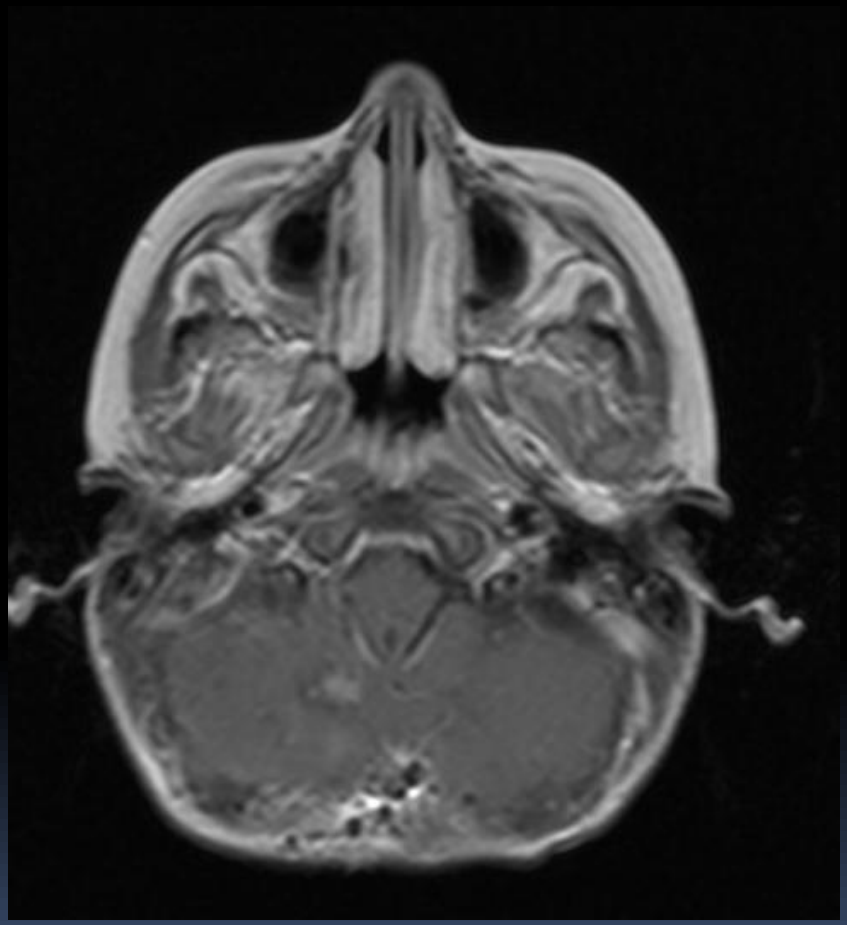


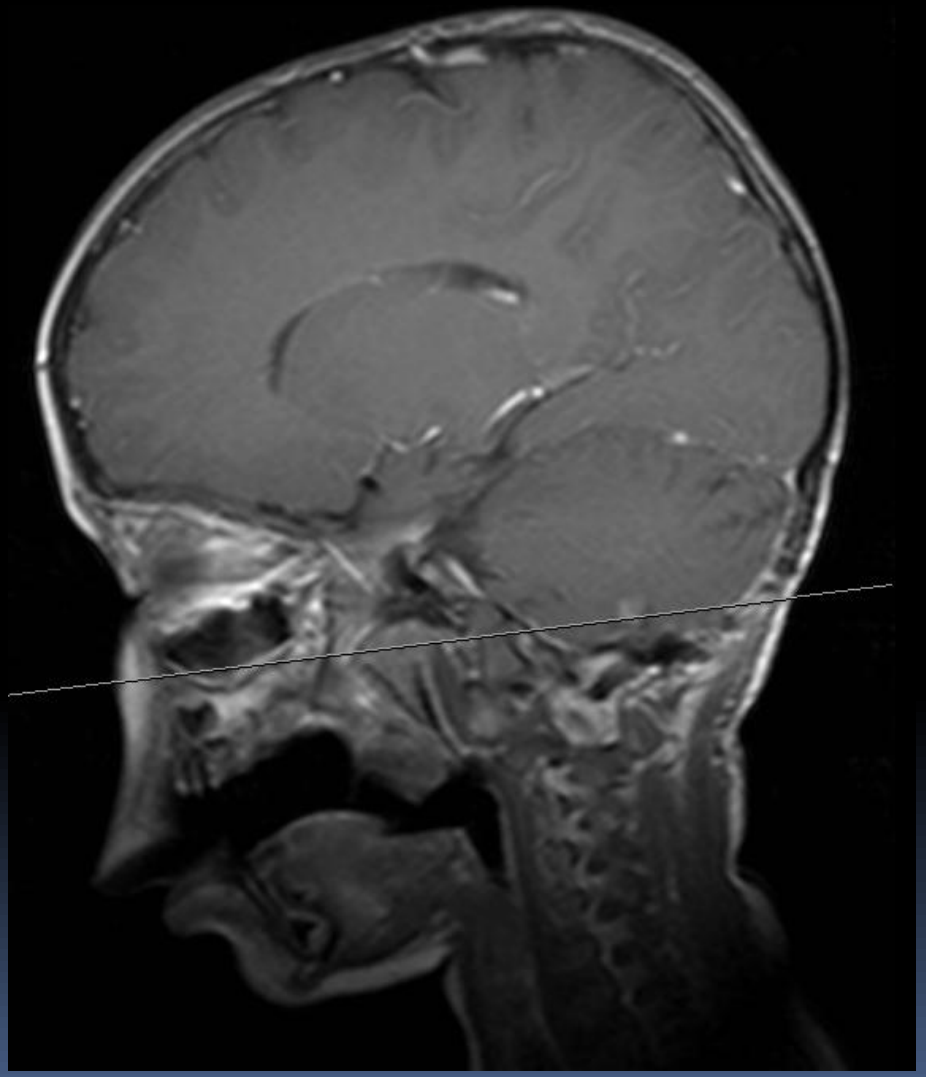


Excision of Lesion

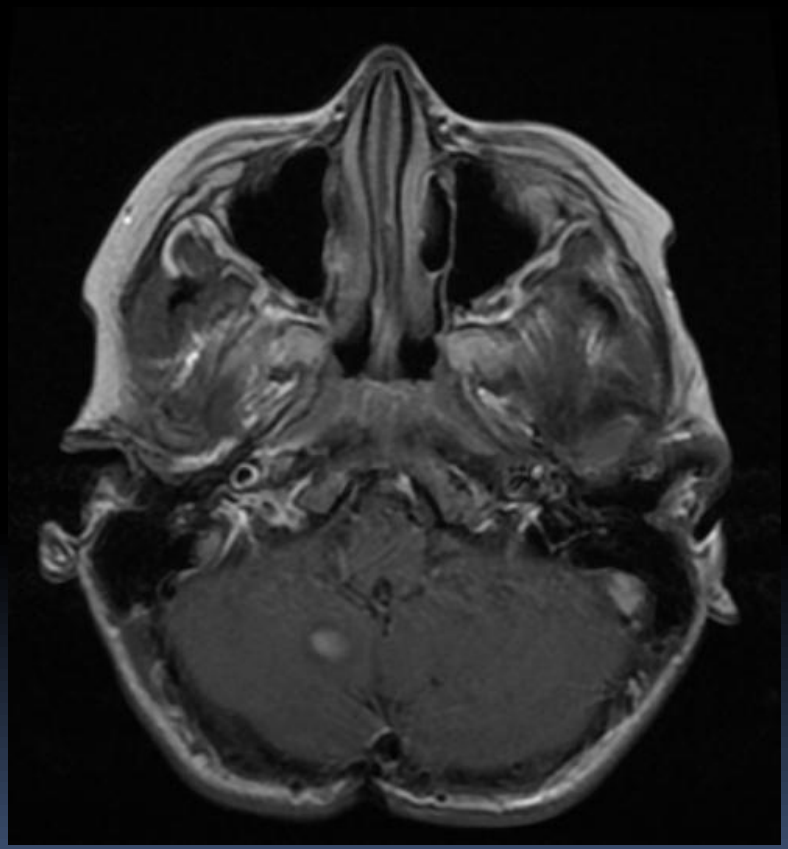
- Video

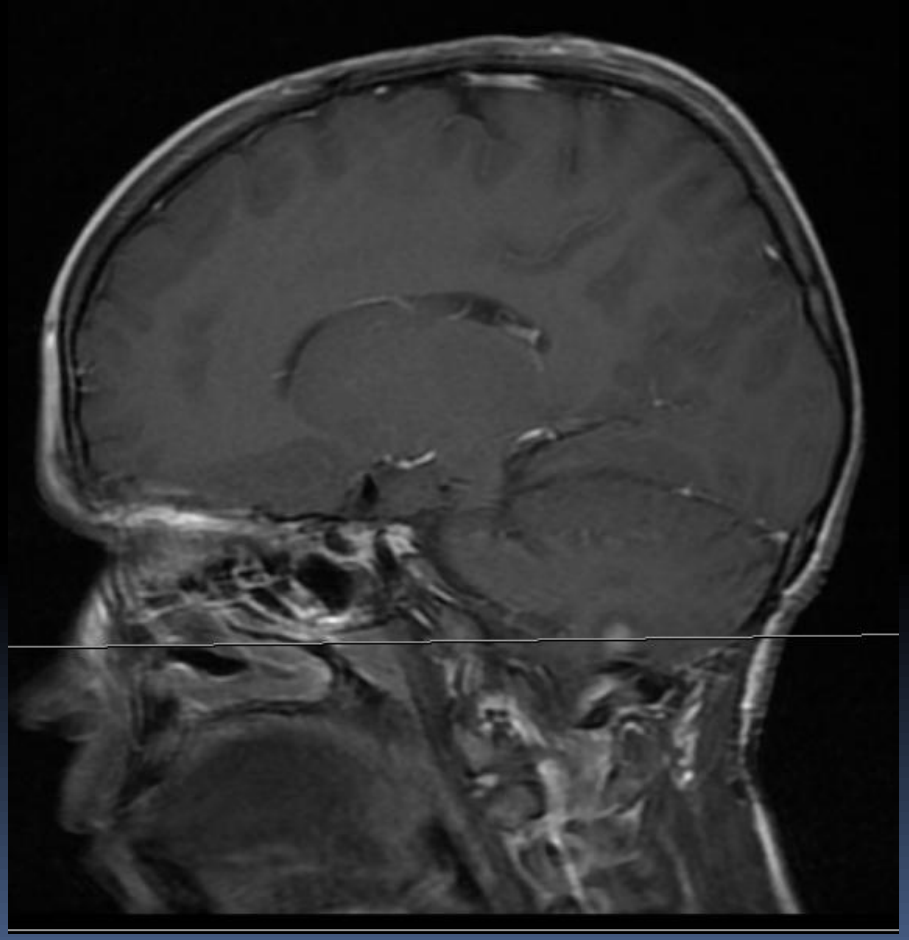
Post-op Residue





5 years post-resection: Increase in residue



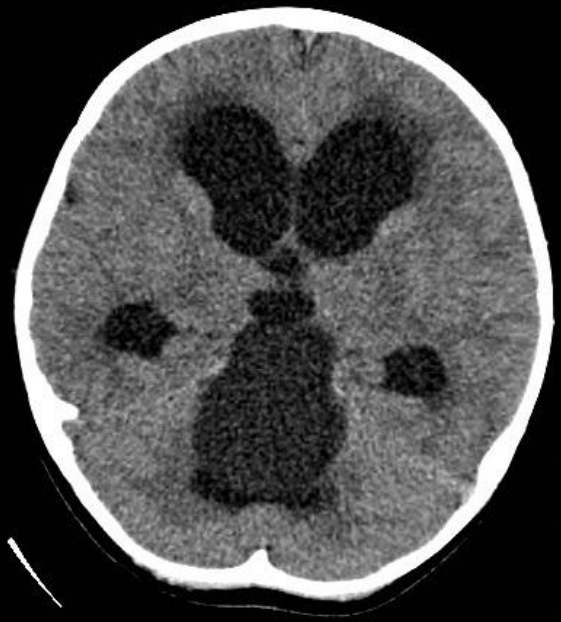
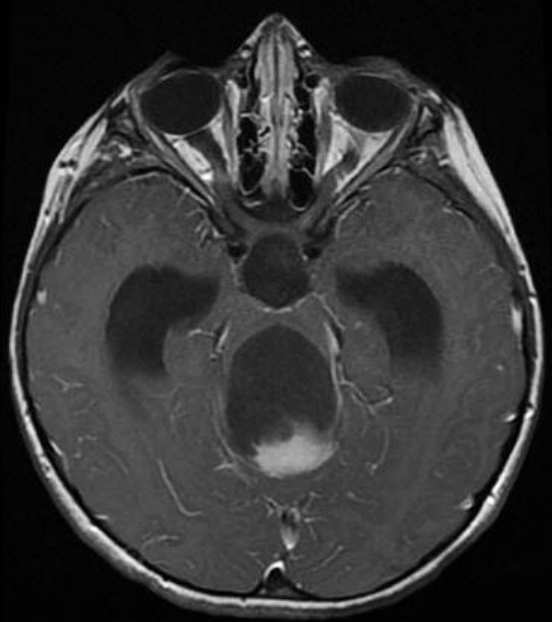
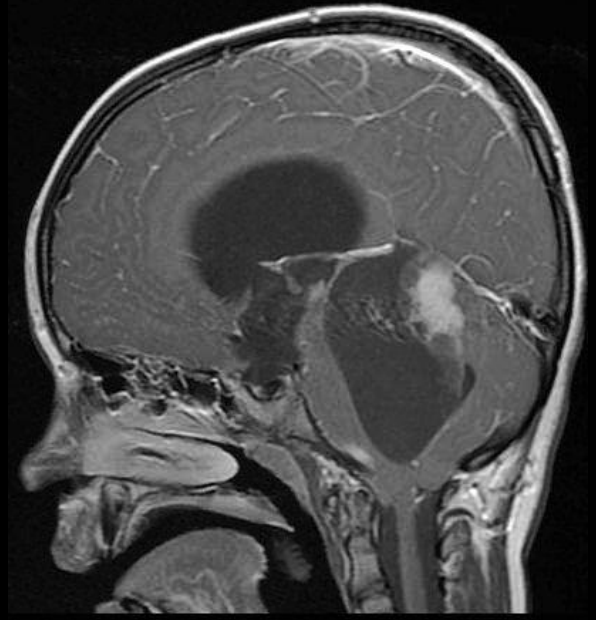
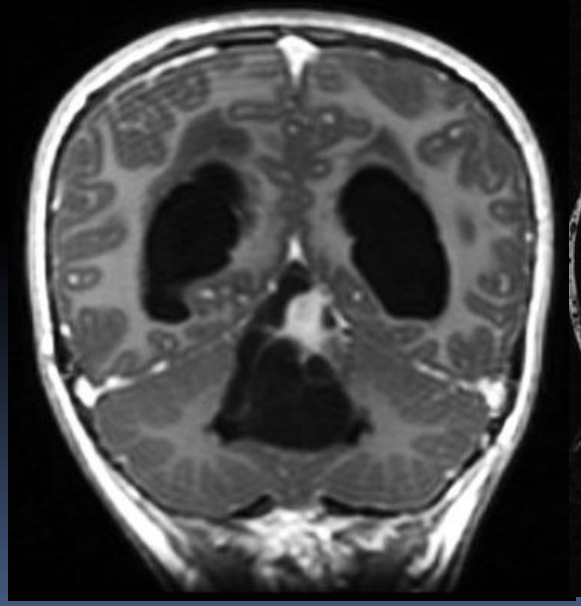
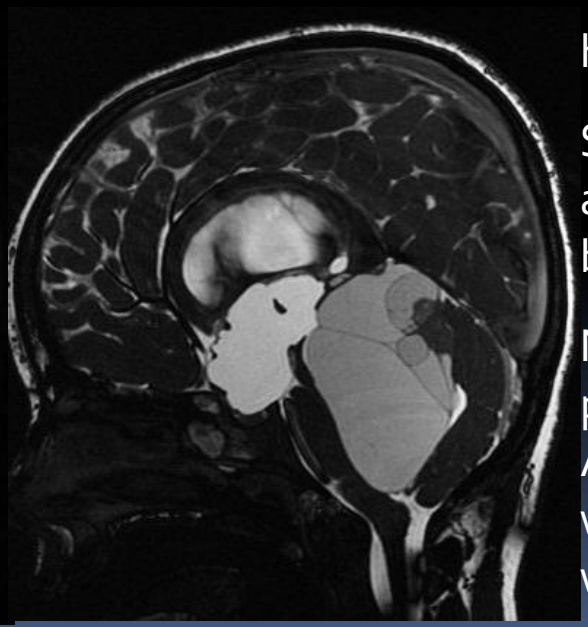


MS

- 7 yr F
- Headaches 7/7
- Unsteadiness of gait

O/E

- No Papilloedema
- Horizontal Nystagmus
- Ataxia

Very large midline tumour with acute hydrocephalus.

Significant mass effect with aqueductal obstruction, tectal and brainstem distortion

Note multi-locular and high proteinaceous content within cyst. At surgery a thick tumour-laden cyst wall with necrotic tumour within cyst was found.

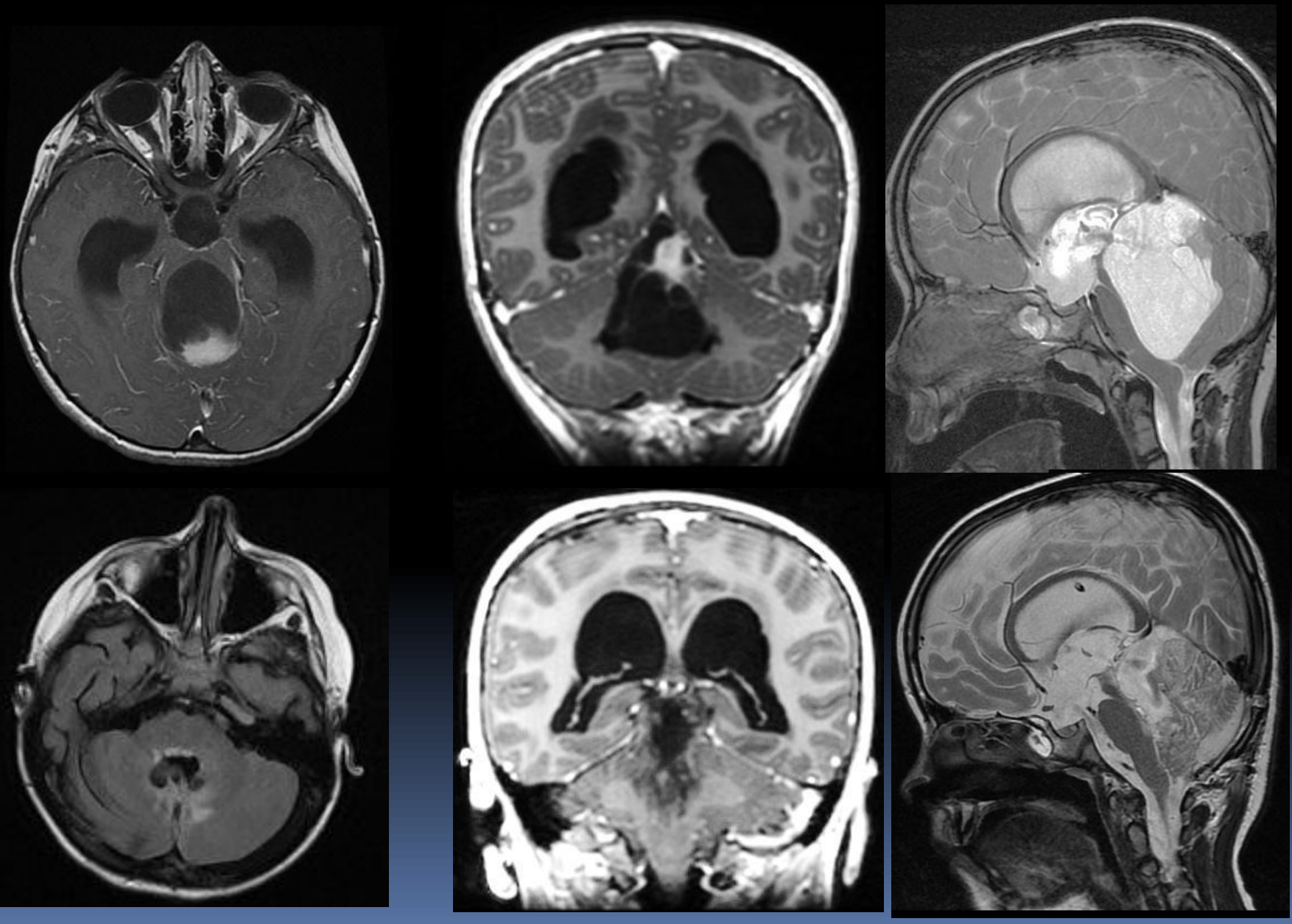
MS

- Prone, Concorde position
- Image-guided posterior fossa midline craniotomy

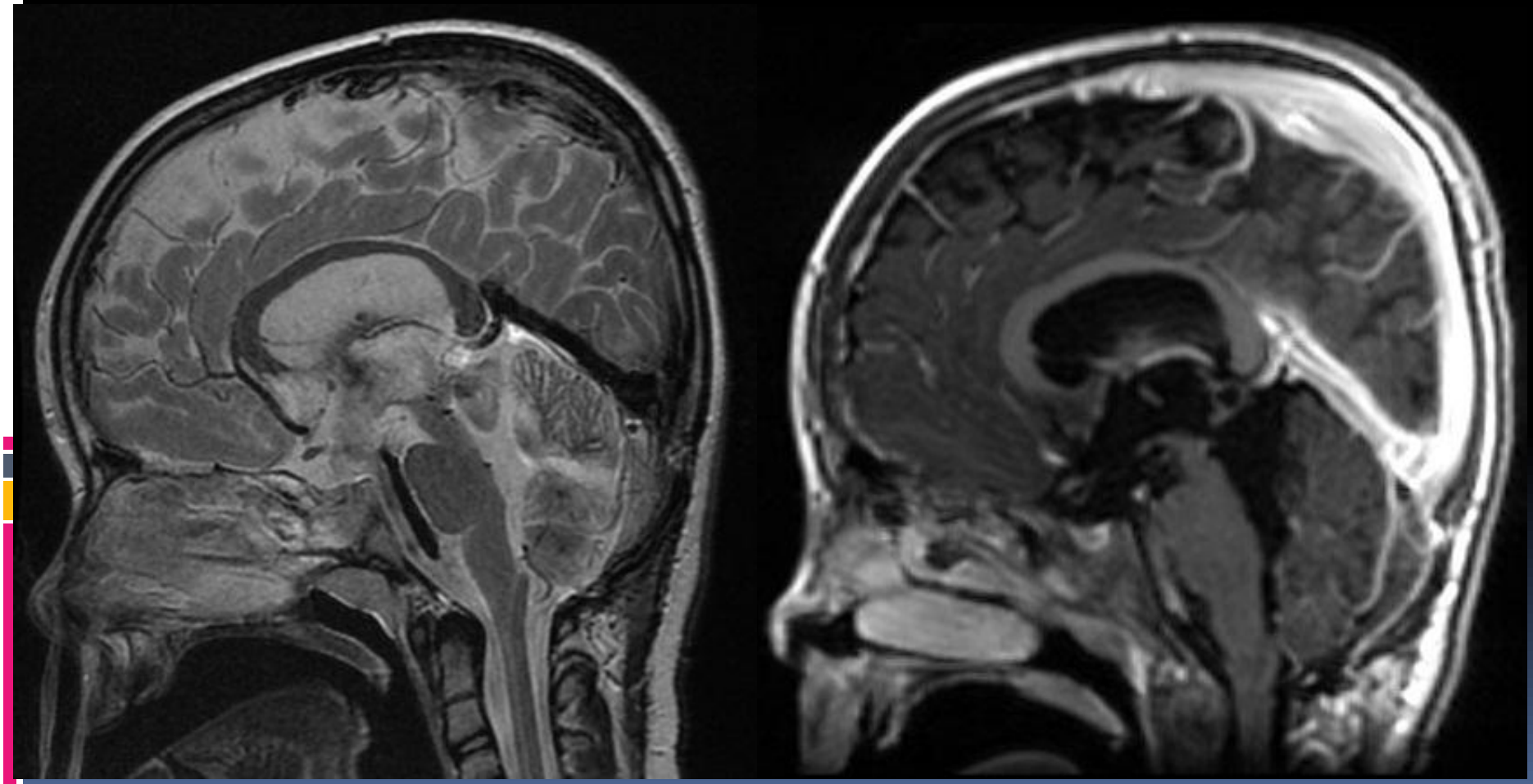
- GTR including thick walled multi-loculated cyst

- Post-op:
  - Gradual improvement
  - EVD required and removed in 5 days
  - mobilized gradually
  - ataxia improved over 2 weeks

Pre and Post-op op



Patient well,
no deficits at 3/12 review



BS

History:

9 year old with a 2 year history of headaches.

Various visits to the GP

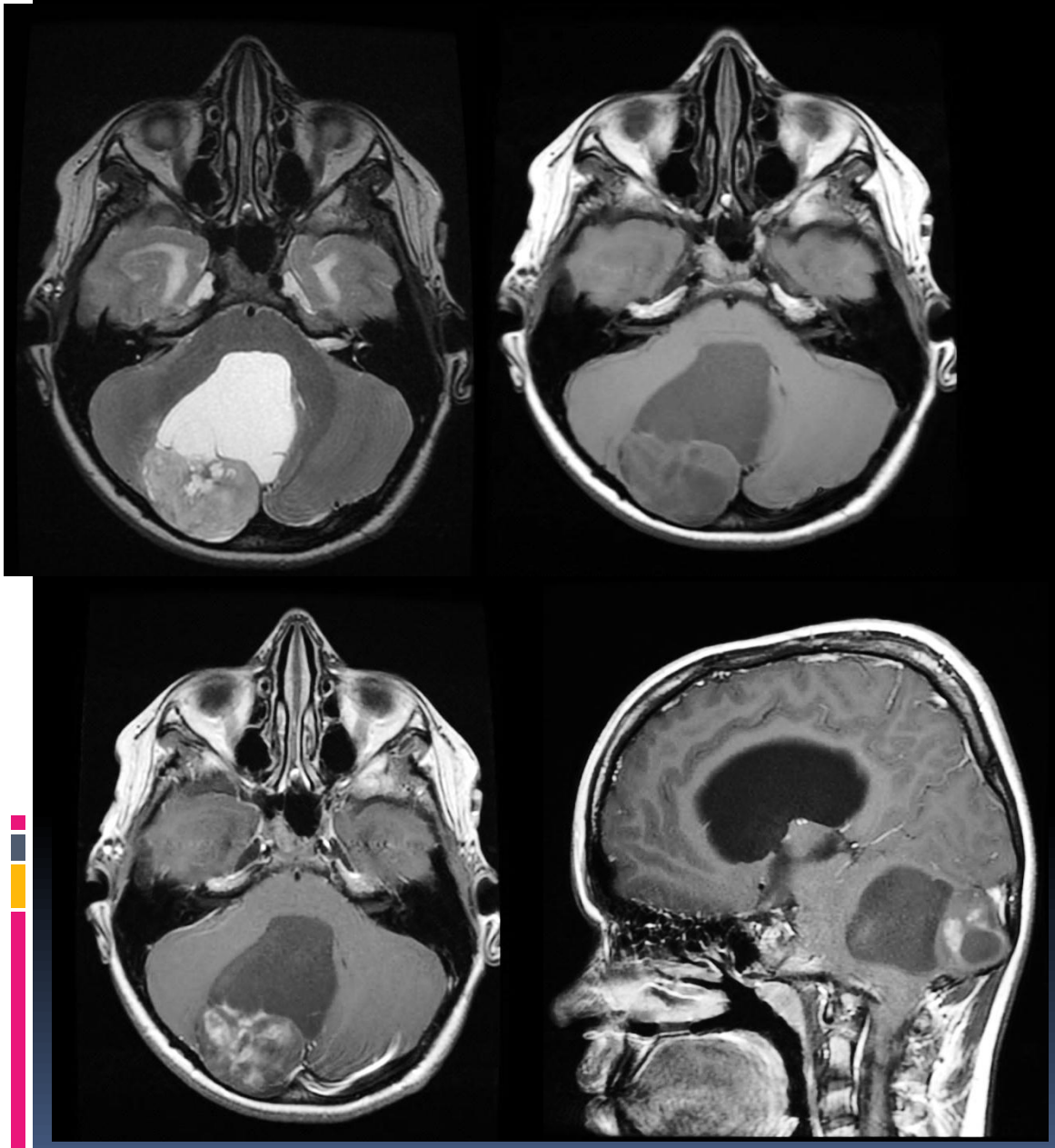
Started on migraine therapy

Acute presentation with headaches, vomiting

Examination

- Papilloedema, nystagmus
- Right sided cerebellar findings

Pre-op

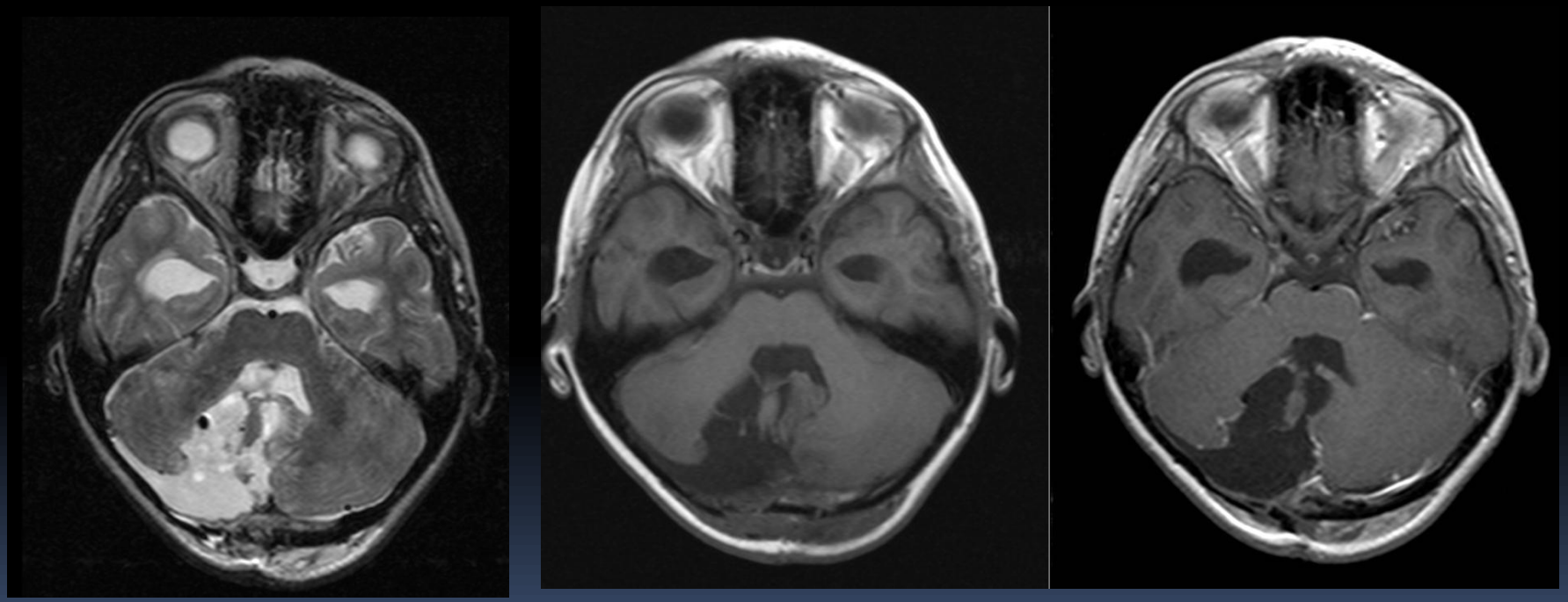


Large proteineceous solid/cystic mass right cerebellum, involving vermis.

Several ring-enhancing areas within nodule and cystic/necrotic areas.

Likely a little haemosiderin/blood products within and along the edge of the solid component.

Post-op BS



Treatment Strategy

- Operations are performed to treat hydrocephalus, diagnose and remove the tumor.
- Cerebellar Pilocytic astrocytoma is a "surgical disease"
  - – Its gross total resection is associated with a 5 year 94% survival
- ***There is no role for subtotal resection and postoperative irradiation unless the tumour cannot be excised safely (A.L. Albright)***

Timing of Surgery

Pilocytic astrocytomas are generally large tumours and may cause significant mass effect, brainstem distortion and hydrocephalus.

The goals of surgery are to relieve raised ICP, protect from secondary deficits, obtain histological diagnosis and achieve curative resection

- **Acutely unwell with lethargy and or neurological deficits:**
  - In exceptional circumstances, with a rapidly deteriorating GCS you may need to **operate on the same day**.
  - With severe obstructive hydrocephalus as the main problem, start steroids, insert EVD, get as much of the pre-op imaging as possible and **operate next day**.
  - If persistent lethargy despite improvement in GCS following EVD for hydrocephalus, proceed to surgery without delay (within 24 hours as the urgency dictates).
- **Subacute presentation:**
  - Initiate steroid therapy, obtain all pre-operative imaging, including spine, DTI and spectroscopy and consider MDT discussion with parents towards inclusion into (any existing) trials.

Risks

- Risks should ideally be based on (available) audit of surgeon's and or departmental performance and current best literature outcomes most pertinent to the particular case
- Risk to life <1%
- Neurological Deficits
  - Immediate gait ataxia &
  - cranial nerve paresis ~25%
  - Permanent deficits ~10%
  - posterior fossa syndrome ~3 to 20%
- CSF related:
  - Ventriculitis/meningitis ~5% (23%)
  - CSF leakage /Pseudomeningocoele ~7% (1%-33%)
- Wound Healing: ~5%

Pre-Operative Care

- **Steroids**
  - Reduces symptoms
  - Post-operative oedema
- Anti-convulsants
  - **no**
- Anti-sepsis:
  - Clean the scalp with antibacterial shampoo if possible
    - Night before and morning of surgery
  - **No Pre-op antibiotics**
- **Treat hydrocephalus**
  - if delay in performing resection, by ETV or EVD
- **Sedation:**
  - **Avoid.** Prefer a GA for imaging studies
  - Critical to monitor: Pulse Oxymetry and continuous HR monitor
  - Risk of hypercarbia and raised ICP without monitoring

Surgical Approach: Intubation & Monitoring

- GA + ETT preferably fibreoptic
  - Neck in neutral position
  - Short-acting boost for Pin application
- Neurophysiology monitoring (SSEP, BAERs,MEPs)
  - Brainstem surgery
  - Cervico-Medullary surgery
- Monitoring:
  - **Invasive Arterial monitoring:** HR,BP,O_2 sats
  - **Central Line Venous monitoring:** JVP
- Image guidance
  - Surgiscope w Leica ceiling mounted microscope focal length IR guidance
  - Stealth Optical / Electromagnetic (Medtronic)
- Microscopic surgery, endoscopic assisted

Anaesthesia

- **Induction:**
  - Thiopental and maintained with a mixture of intravenous ramifentanyl / fentanyl plus nitrous oxide or with an inhalation agent such as isoflurane.

- After final head positioning (flexing the neck 30 deg) re-check ETT position by chest auscultation
  - ETT may advance into the right main bronchus following flexion.

Surgical Exposure: Position

- **Midline Tumour: Prone, Concorde position**
  - Child placed closest to surgeon
  - Neck flexed and tilted (away) 30 degrees
- **Lateral Tumour: Park Bench Position**

- **Head Fixation: Pins vs. no pins**
  - **Infants and children under 2 years** – EM IGS, no pins, Mayfield head rest

  - **Older children**
    - Carbon fibre Mayfield head fixation and EM IGS
    - Standard (Aluminium) Mayfield head fixation with Optical IGS

Surgical Exposure: Hydrocephalus

- **EVD:**
  - Posterior parietal burr hole and EVD insertion as required.
  - Prepare patient and drape for this
- **Pre- resection ETV :**
  - Supine position for ETV
  - Reposition prone
- **No intervention for HCP**
  - Cyst drainage often permits decompression prior to resection
  - **if significant dural tension =>** image guided cyst aspiration via a Dandy Cannula, prior to dural opening

Surgical Exposure: Incision

- **Midline and paramidline tumors**
  - Midline incision is made from the inion to the C1-2 interspace.

- **Lateral hemispheric tumours**
  - Vertical incision is made between the midline and mastoid, centred over the maximal volume of the tumour.

Surgical Exposure: Exposure

- Midline Post. Occip. Protub. to C2 scalp incision

- Intermuscular midline dissection
- T-Shaped Muscle flap exposure
- **Craniotomy (**vs. Craniectomy)
- Y or Crescentic shaped dural opening
- If midline occipital sinus present, prior to division:
  - diathermy
  - occlude temporarily with hemostats
- Cisterna magna arachnoid opened in a straight line
- Identify Vallecula
- Choose Approach depending on tumour location
  - **Vermian** or **Telovelar** approach for midline tumours
  - **Inter-Folia** or **folia splitting** for lateral tumours

Tumour Resection: Cystic vs. Solid

- **Cystic often with a solid mural nodule** (commonest)
  - Cyst can be aspirated but more often than not has multiple septations
  - Septations usually filled with thick proteinaceous "gluey" material.

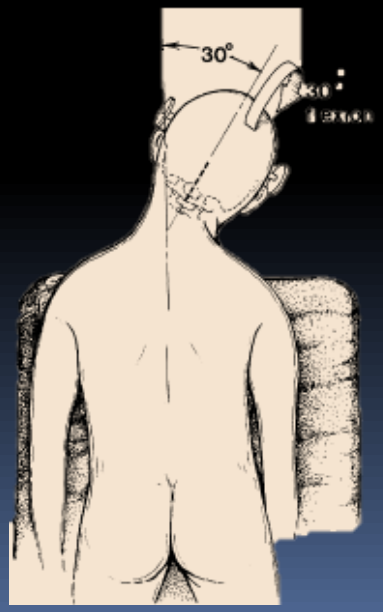
- **Cyst Walls**
  - often will need to be dissected out from cerebellum
  - **Thick walls (>1-2 mm thickness)** because of tumour infiltration or haemorrhagic clot must be dissected out.
  - **Thin transparent cyst walls** need not be removed
    - but if lying around aqueduct or foramina of Luschka and Magendie) should be fenestrated, disrupted or removed
- **Nodule dissection**
  - using microdissectors or irrigating bipolar cautery.
  - Rubbery lesions may need debulking with scissors.

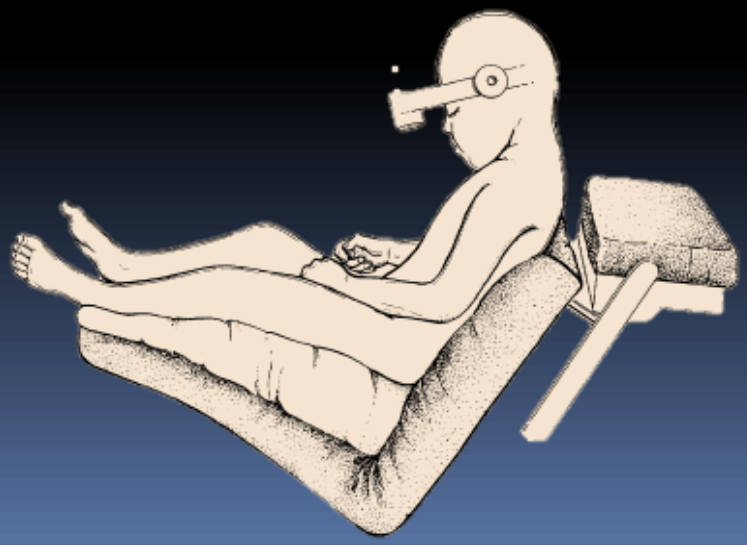
Tumour Resection: Cystic vs. Solid

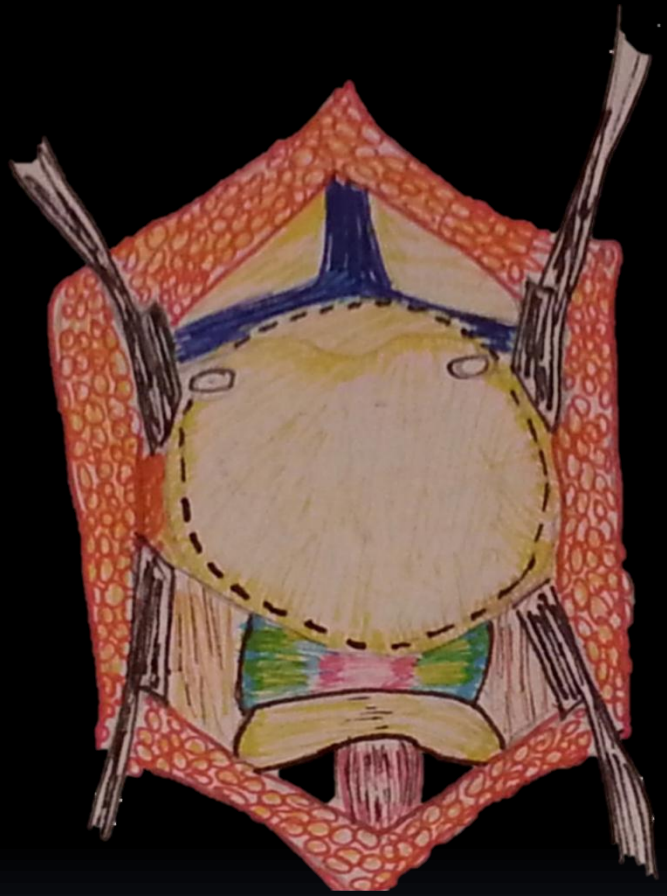
- **Solid Tumour often with multiple small cysts**
  - Pial dissection with microscissors.
  - Cerebellar folia splitting over dome of tumour.
  - CUSA to debulk centre of tumour
  - Careful identification of collapsing tumour edges and meticulous separation from surrounding cerebellum

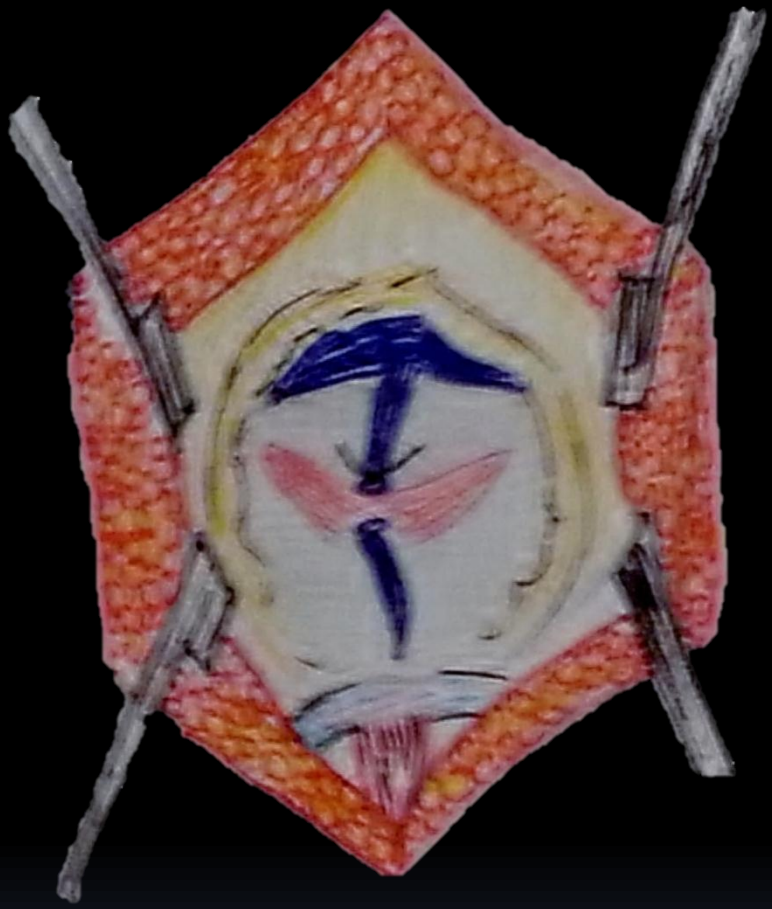
Standard Positions

- Prone, neck flexed in "concorde" position with head tilted away 30 degrees
- Lateral, "Park bench" with neck flexed and head turned 30 degrees to floor
- Sitting up

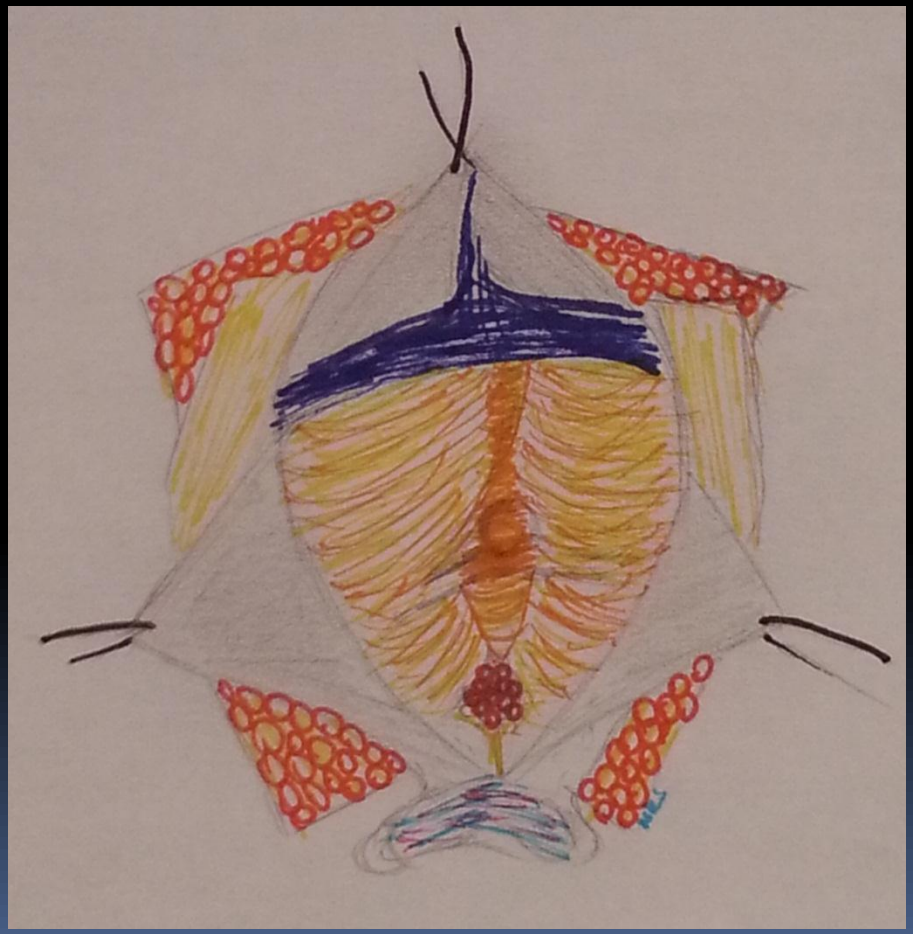








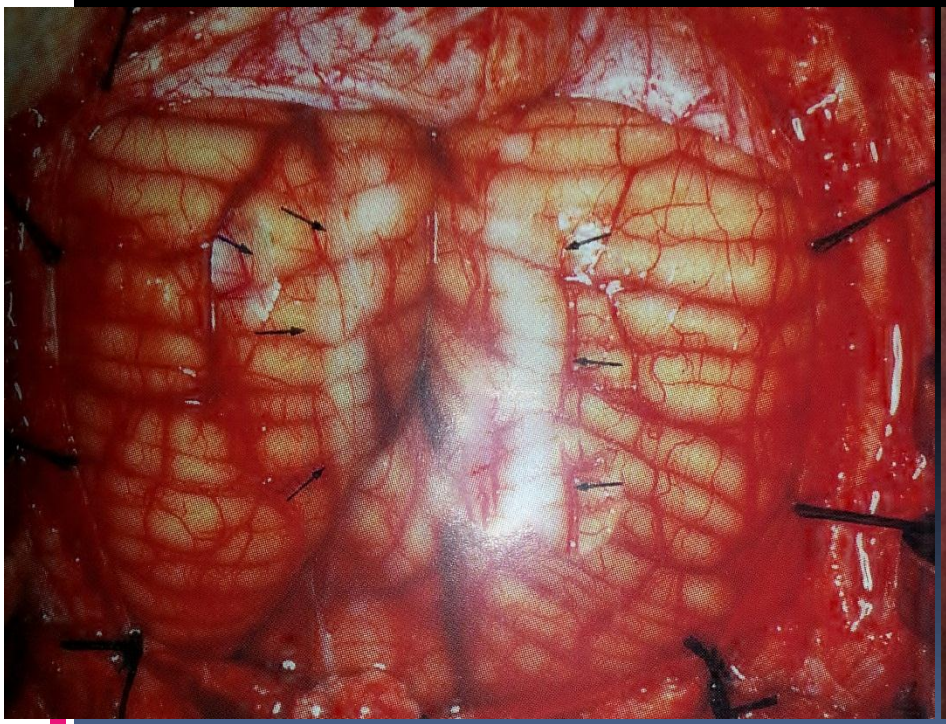
- Bone exposure to edge of transverse sinus
- May need to excise central part separately (drill out so you can tie it back again)
- Y shaped dural incision
- Ligate veins/sinus

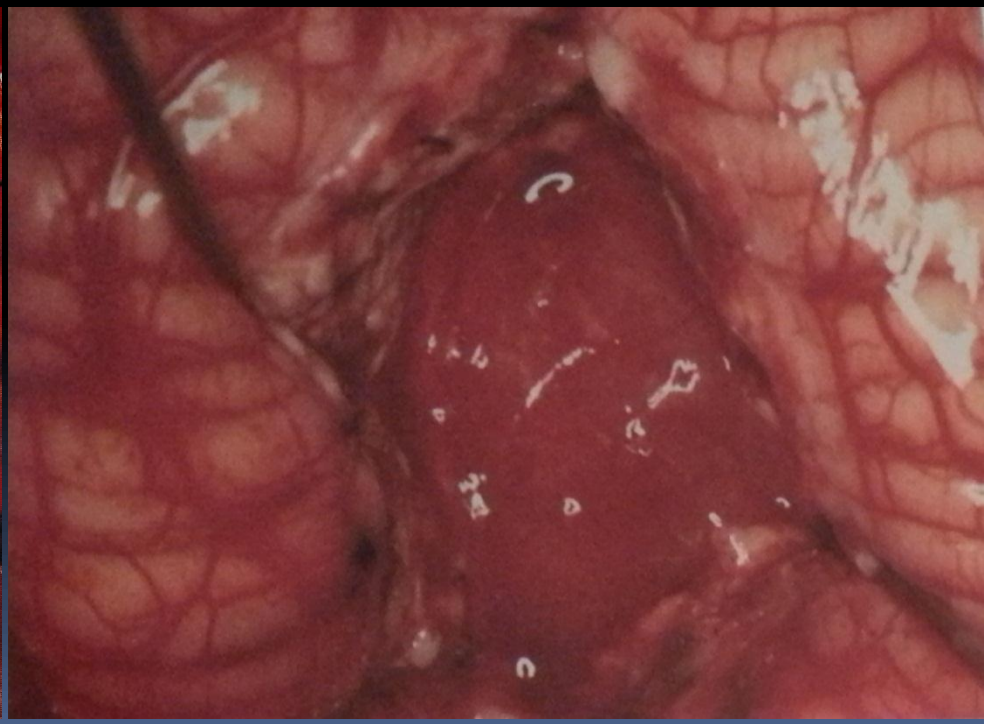


- Dural edges everted with 4-0 vicryl sutures
- Arachnoid over cisterna magna incised linearly
- Vallecula between tonsils exposed
- Tumour noted protruding out

Vermian Approach

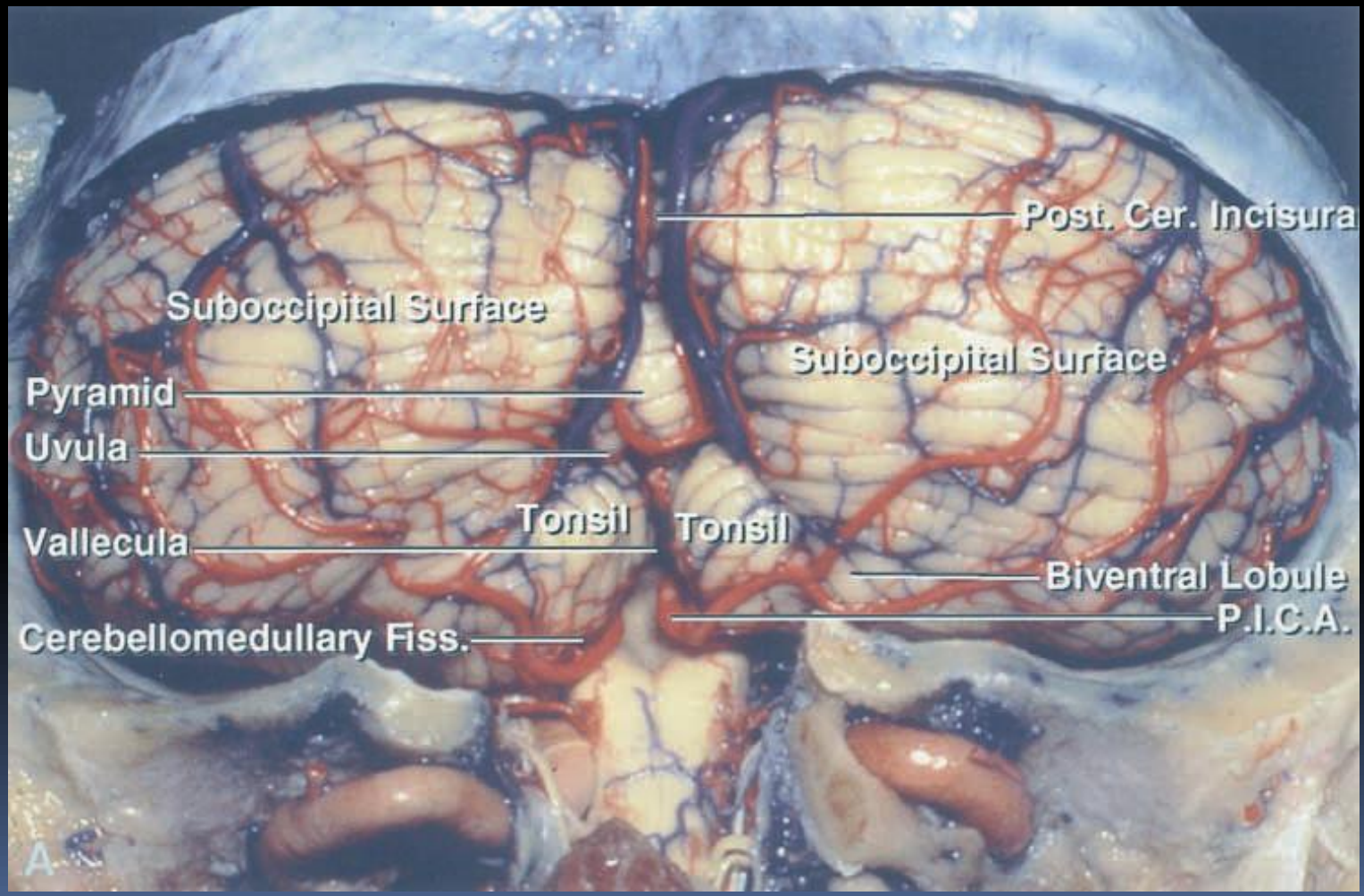
- Incise the cortical aspect of bulging vermis
- Arrows mark the resection zone
- Exposure of the tumour without much retraction

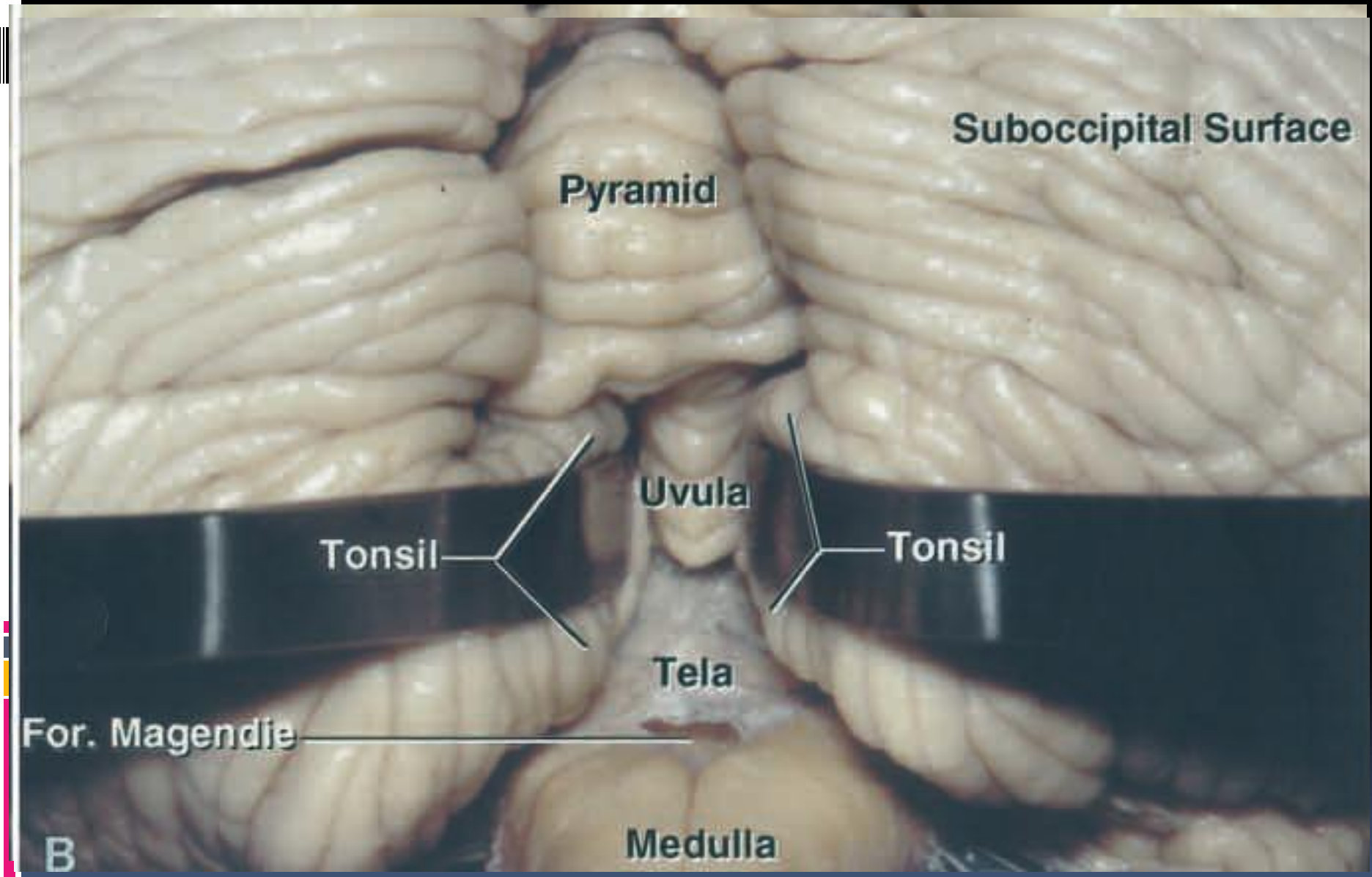


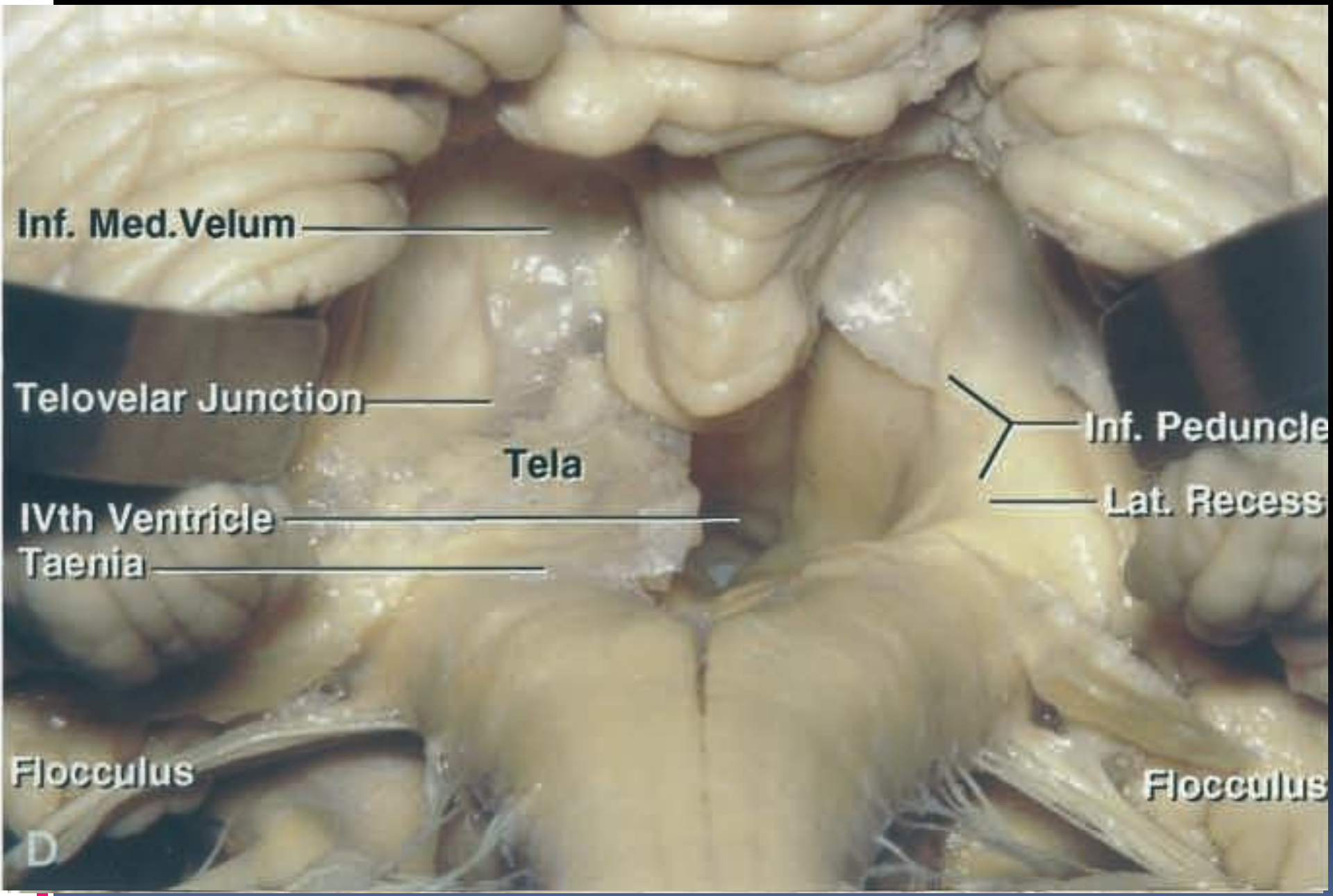


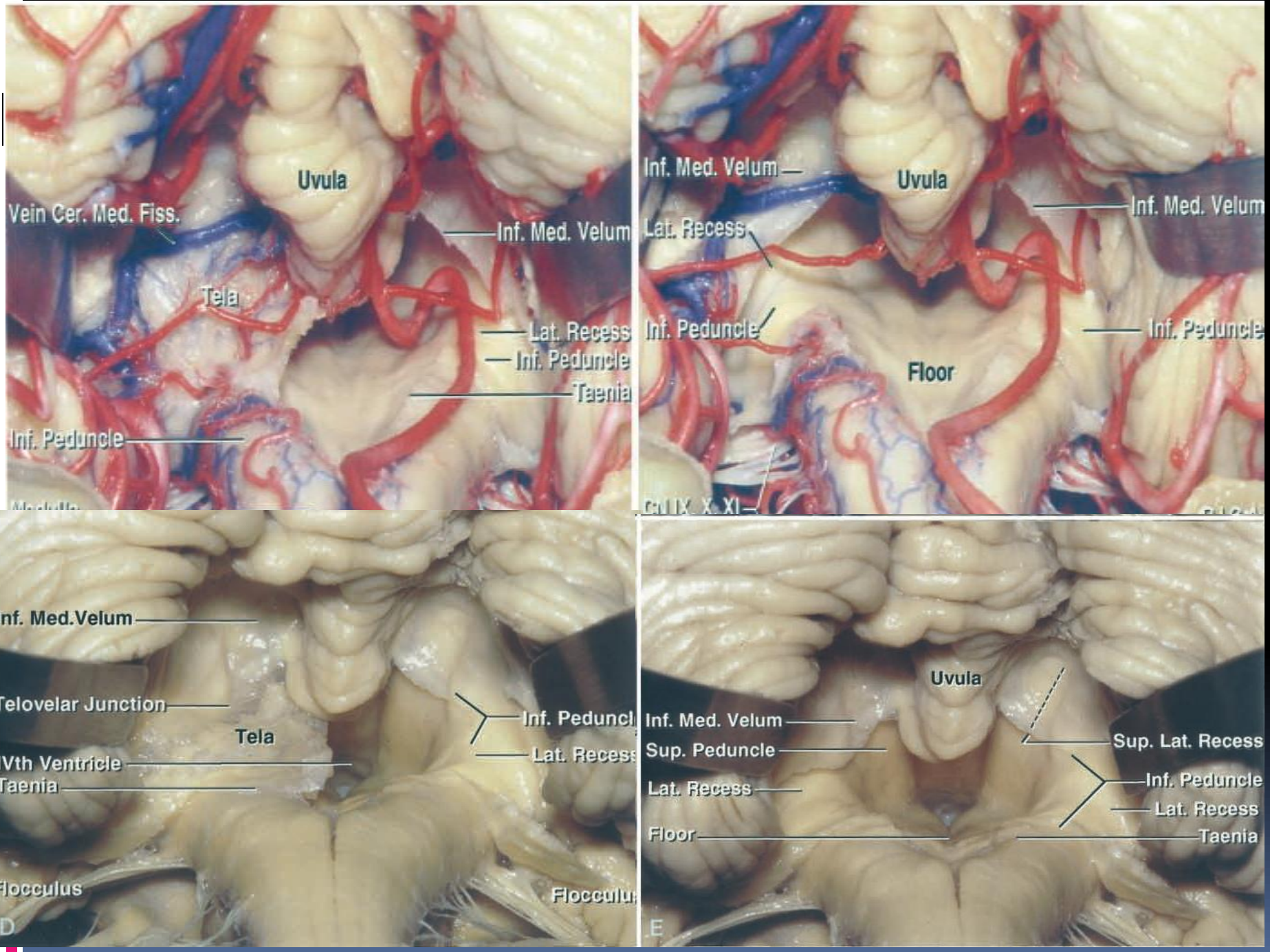
Telovelar Approach

Antonio C. M. Mussi & Albert L. Rhoton, Jr. Telovelar Approach To The Fourth Ventricle: Microsurgical Anatomy, J Neurosurg 92:812–823, 2000




Suboccipital Surface
Pyramid
Uvula
Tonsil
Tonsil
Tela
For. Magendie
Medulla
B


Inf. Med.Velum
Telovelar Junction
Tela
IVth Ventricle
Taenia
Flocculus
D
Inf. Peduncle
Lat. Recess
Flocculus


Uvula
Vein Cer. Med. Fiss.
Inf. Med. Velum
Tela
Lat. Recess
Inf. Peduncle
Taenia
Inf. Peduncle
Inf. Med. Velum
Uvula
Lat. Recess
Inf. Med. Velum
Inf. Peduncle
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Telovelar Junction
Tela
IVth Ventricle
Taenia
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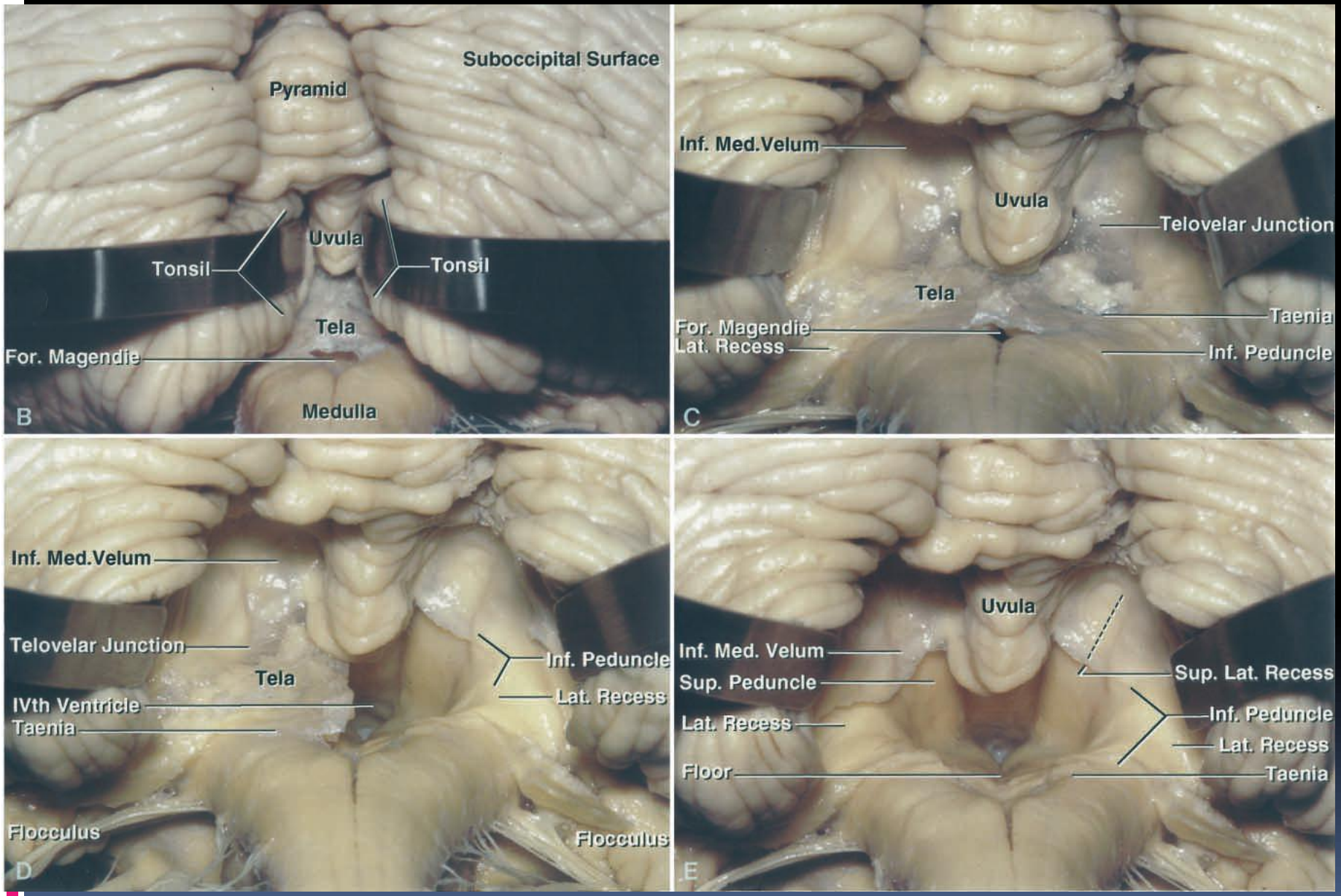
Taenia
E


Suboccipital Surface
Pyramid
Uvula
Tonsil
Tonsil
Tela
For. Magendie
Medulla
B
Inf. Med.Velum
Uvula
Telovelar Junction
Tela
Taenia
For. Magendie
Lat. Recess
Inf. Peduncle
C
Inf. Med.Velum
Telovelar Junction
Tela
Inf. Peduncle
Lat. Recess
IVth Ventricle
Taenia
Flocculus
Flocculus
D
Uvula
Inf. Med. Velum
Sup. Lat. Recess
Sup. Peduncle
Inf. Peduncle
Lat. Recess
Lat. Recess
Floor
Taenia
E

Closure: Craniotomy vs Craniectomy

- My choice is to perform craniotomy
- Better anatomical appearance.
- Allows for bone reformation and protection
- Removal of large tumours creates enough space to minimize risk for PF compression
- Reduces frequency of CSF leak / pseudomeningocoele as additional barrier

Dura: Closure vs open

- Always close Dura to avoid adhesions
  - Use Duragen & Tisseel to allow augmentation
  - Non-water tight dural approximation
  - Sandwich technique of dural closure
    - duragen on each side of the dura with tisseel seal

Post-op care & Imaging

- **Corticosteroids:**
  - Taper post-op over 5 days.
  - Correction of significant long-term brainstem distortion (due to very large cysts) can cause post-op brainstem and cerebellar dysfunction
- **EVD:**
  - Keep at 10 cms csf and gradually raise by 5 cms to 30 cms.
    - Evidence of reduced or no drainage prior to removal of evd
    - Consideration for shunting if no progress over 7 days.
- **MRI scan:**
  - should be obtained within the first 48 hours postoperatively.

Treatment Strategy for Residual or Recurrent diease

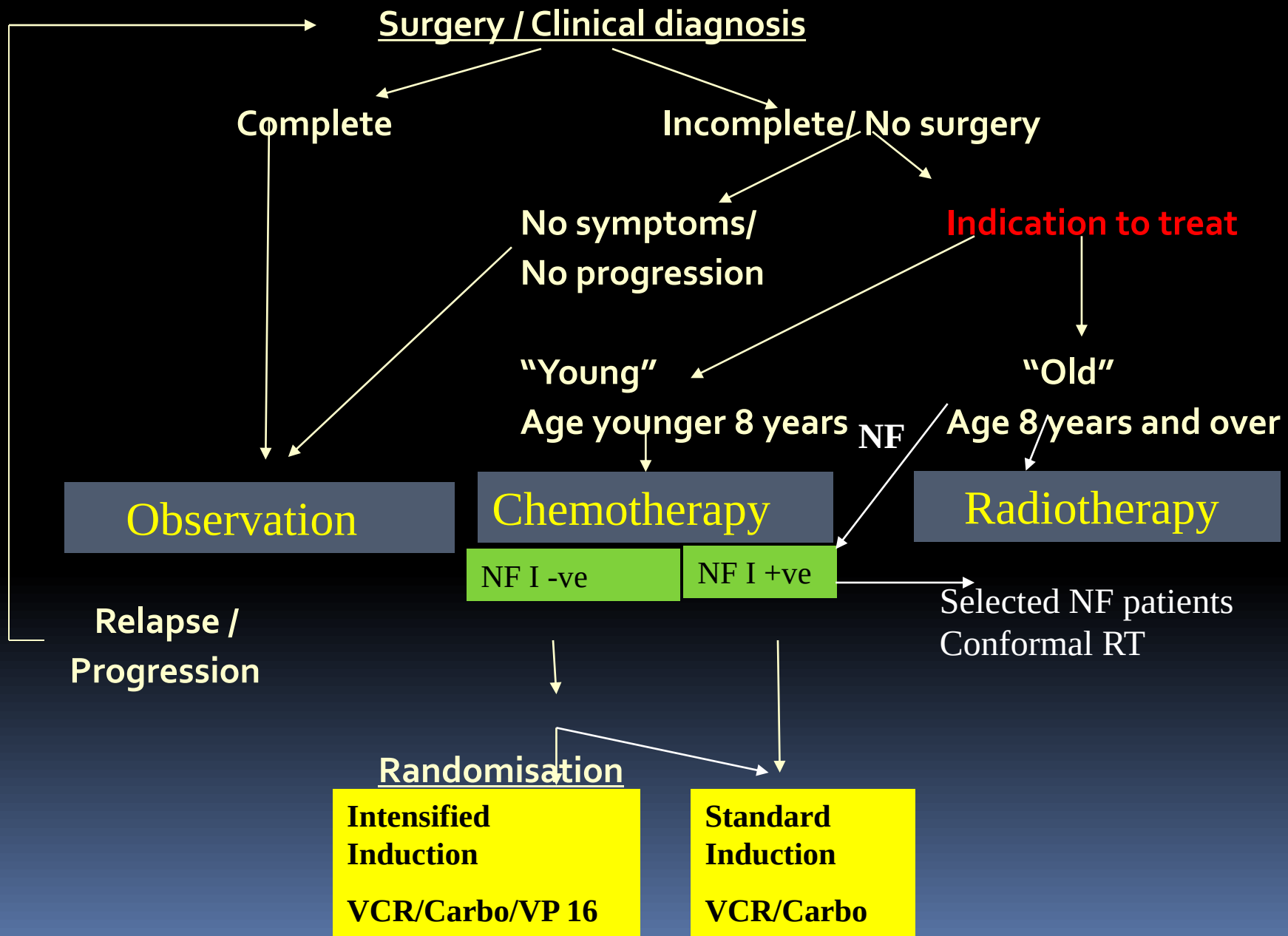
Immediate Post-op MRI shows safely excisable residue:

- Appropriate to consider further resection of residue.
- ***Consider Intra-operative MRI for 2nd surgery***
  - Pilocytic Astrocytomas and Ependymomas probably reflect best the benefits of intra-operative MR imaging
- Completeness of resection has best chance of cure and PFS.

STR: Progression or Recurrence

- **Patient fit for surgery => Second look surgery**
  - Avoid radiotherapy and chemotherapy
- **Patient unfit for surgery**
  - Monitor & repeat imaging
  - Re-attempt a complete surgical removal when appropriate.
  - If left unattended can undergo neoplastic transformation.
- **Further resection is not considered safe**
  - **Adjuvant Therapy:** careful use of chemotherapy and/or radiation therapy is useful in case of recurrence where further surgery is unsafe.
  - chemotherapy "buys time" to radiotherapy in **young children** & **NF1 +**
  - Consider conformal radiation therapy or stereotactic radiosurgery
    - Less acute and long-term radiation toxicity.

Overview of SIOP LGG 2003 treatment strategy



Mortality

- GTR:
  - 10-year survival rate is 90%.
- STR:
  - 10-year survival rate is as high as 45%.

Morbidity

- is determined by the location and accessibility of the tumour and complications following resection.

Factors associated with Survival

- ***Histology***:
  - Pilocytic astrocytoma had greater PFS and OS to non-pilocytic tumours.
- ***Extent of resection***:
  - GTR => 8-year PFS > 90% and OS of 99%.
  - **STR** => **8-year PFS only 50%,** although OS exceeded 90%.
- ***Age***:
  - Age <5 years => higher rates of tumour progression
  - no significant age effect for OS in multivariate analysis.
- ***Tumour location***:
  - Cerebellar and cerebral tumours showed higher PFS at 8 years vs. midline and chiasmatic tumours (84% ± 1.9% vs. 51% ± 5.9%).

Wisoff JH, Sanford RA, Heier LA, et al.: Primary neurosurgery for pediatric low-grade gliomas: a prospective multi-institutional study from the Children's Oncology Group. Neurosurgery 68 (6): 1548-54; discussion 1554-5, 2011

Postoperative Care

- **Early postoperative care**
  - Increased ataxia
  - Increased lower cranial nerve dysfunction
  - Apnea, or respiratory abnormalities
  - Feeding difficulties: consider early NG tube feeding or PEG

Quality of Survival

- Medical
- Education
- Employment
- Social assessment
- Health status

- Quality of Life
- Assessed at diagnosis, 1 year, 3 years, 5 years, 10 years from diagnosis and at age 20 years.

Follow-up

- Only surgery => Neurosurgeon
- Chemotherapy => Oncology
- Radiotherapy=> Endocrine (Late effects clinic)

Complications

- Lower Cr Nv paresis
- Facial nerve palsy
- Deafness
- Long tract deficits
- Hemiplegia
- Hemiparesis
- Sensory abnormalities

- Other postoperative complications
- Infection
- Prolonged coma
- Shunt obstruction or malfunction
- Chest infection
- Deep venous thrombosis
- Pulmonary embolism
- Cerebrospinal fluid leak
- Cerebellar mutism syndrome

Management & Outcomes

Comparative Outcome and Prognosis

- The 5-year survival rates exceed 60% for all patients and 80% for certain good-risk individuals with posterior fossa tumours.

- **Pilocytic cerebellar astrocytoma**
  - the 5-year survival rate exceeds 94%, 10 year 90%

- **Ependymomas**
  - 5-year survival rate is 60%.
  - In ependymoblastoma, the 5-year survival rate is only 6%.

- **Choroid plexus papilloma**
  - has excellent prognosis, as high as 100% survival rate.
  - Choroid plexus carcinoma has poor prognosis.

Reported Outcomes

- Cerebral tumours complete removal in 90%
- (Hirsch 1989).
- Cerebellar tumours complete removal in 2/3
- (Due-Tonnessen 2002, Smoots 1998).

- Subsequent PFS rates are 0-80% .

- Survival rates after complete resection >90%
- (Pencalet 1999, Campbell 1996, Pollack 1995, West 1995, Hirsch 1989, Wallner 1988, Gjerris 1978).

Outcomes for non-GTR

- However ……Not all tumours can be resected
- Prolonged stable disease is possible after subtotal resection
- Post op tumour volume predictor of progression
  - (Smoots 1998, Berger 1994).
- Early progression occurs in 15-50 %
  - (Campbell 1996, Smoots 1998, Pencalet 1999, Garvey 1996, Hoffman 1993, Sutton 1995)

Observe? or Treat?

- Delayed non-surgical treatment may permit irreversible neurologic impairment and ? lower probability of tumor control.
  - (Tarbell et al. 1996)

- During observation, clinical or radiographic progression, consider non-surgical treatment
  - (Grill et al. 2000, Janss et al. 1995, Packer et al. 1997, Souweidane et al. 1996, Tarbell et al. 1996).

Decision to Observe

- Surveillance interval and duration of follow up
- Clinical surveillance for symptomatic progression
- Imaging surveillance for evidence of progression
- Multidisciplinary involvement:
  - oncology-neurosurgery
  - oncology-ophthalmic
  - oncology-neurology
  - oncology-endocrine
  - oncology-developmental rehabilitation
  - oncology-genetic

Selection of treatment

- Multi-disciplinary assessment
- Intention:
  - curative or symptomatic or prevent progression
- Surgery
  - resection / control ICP
- Chemotherapy & Radiotherapy:
  - risks versus benefit
- Trial vs. conventional

Thank You