Pediatric Posterior Fossa Tumors

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Acadamic Half Day Seminar

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Pediatric Posterior Fossa Tumors

- Represent 70% of all childhood tumors in patients <10 years old
- In patients <2 years old, most brain tumors are supratentorial

Pediatric Posterior Fossa Tumors

Age	% Infratentorial
0-6 mos	27%
6-12 mos	53%
12-24 mos	74%
2-16 yrs	42%

Pediatric Posterior Fossa Tumors

Tumor Type[1]	% of Total
Infratentorial	54%
Cerebellar astrocytomas	15%
Medulloblastomas	14%
Brainstem gliomas	12%
Ependymomas	9%
Supratentorial	46%

[1]Section of Pediatric Neurosurgery of the AANS, *Pediatric Neurosurgery*, 1st ed. Grune and Stratton, New York, 1982

Pediatric Posterior Fossa Tumors

- Medulloblastomas
  - 15-30% of pediatric brain tumors
  - 30-55% of pediatric posterior fossa tumors
  - Commonest primary brain tumor in children < 2 years old
  - 80% are diagnosed between 1-10 years of age
  - Male predominance 1.3-2.7:1

Pediatric Posterior Fossa Tumors

- Cerebellar Pilocytic Astrocytomas
  - 10% of pediatric brain tumors
  - 25% of pediatric posterior fossa tumors
  - Average age at presentation – 17 yrs old
  - M=F

Pediatric Posterior Fossa Tumors

- Ependymomas
  - 8% of pediatric brain tumors
  - 20% of pediatric posterior fossa tumors
  - Present between 3-6 years of age
  - 10% spinal, 90% intracranial (60% of these are infratentorial)

Pediatric Posterior Fossa Tumors

- Less Common Pediatric Posterior Fossa Tumors

- Hemangioblastoma
- Choroid Plexus Papilloma
- Ganglioglioma
- Dermoid
- Epidermoid
- Atypical teratoid/Rhabdoid
- Sarcoma
- Rhabdo
-

Acoustic Neuroma
Fibrosarcoma
Meningioma
Chordoma
Subependymoma
Metastases
- Neuroblastoma
- Embryonal
- Wilms Tumor

Pediatric Posterior Fossa Tumors

- Presentation

  Increased ICP due to Hydrocephalus
  - Headache
  - Vomiting
  - Worse in AM (secondary to recumbency and increase P_aCO_2)
  - In infants: irritability, lethargy, macrocephaly

  Ataxia
  - Gait or Truncal (medulloblastomas/ependymomas)
  - Limb (cerebellar astrocytomas)

  Nystagmus

  Papilledema

  Diplopia
  - secondary to CN IV or VI dysfunction

Pediatric Posterior Fossa Tumors

- Presentation

Medulloblastoma

- Symptom onset < 6 weeks in 50%
- < 12 weeks in 75%

Cerebellar Astrocytoma

- usually < 2 month history of H/A, vomiting, gait ataxia, limb clumsiness, and later onset increase in ICP

Ependymoma

- up to 3yrs of symptoms
- longer the symptoms prior to presentation, the more

Medulloblastoma

- Primitive Neuroectodermal Tumor (PNET)
- Commonest malignant brain tumor of childhood
- Arises from the cerebellar vermis
- 1/3 have leptomeningeal spread at diagnosis
- Work-up should involve total spine MRI to exclude drop mets
-

Medulloblastoma

- Genetics
  - Loss of heterozygosity of 17p in up to 50% of cases
  - p53 gene located here
  - Small subset of tumors have a loss of small area of 17p that doesn't include the p53

Medulloblastoma

- Syndromic associations:
  - Gorlin Syndrome
    - AKA Nevoid Basal cell Carcinoma Syndrome
    - Autosomal dominant
    - Chromosome 9q13 (inconsistent)
    - Characterized by multiple BCCs, odontogenic keratocysts of the jaws, palmar and plantar dyskeratoses, skeletal anomalies including rib malformations

Medulloblastoma

- Syndromic associations:
  - Turcot Syndrome
    - Multiple colonic polyps
    - APC involvement
    - Risk of developing medulloblastoma is
      - 92x that of general population

Medulloblastoma

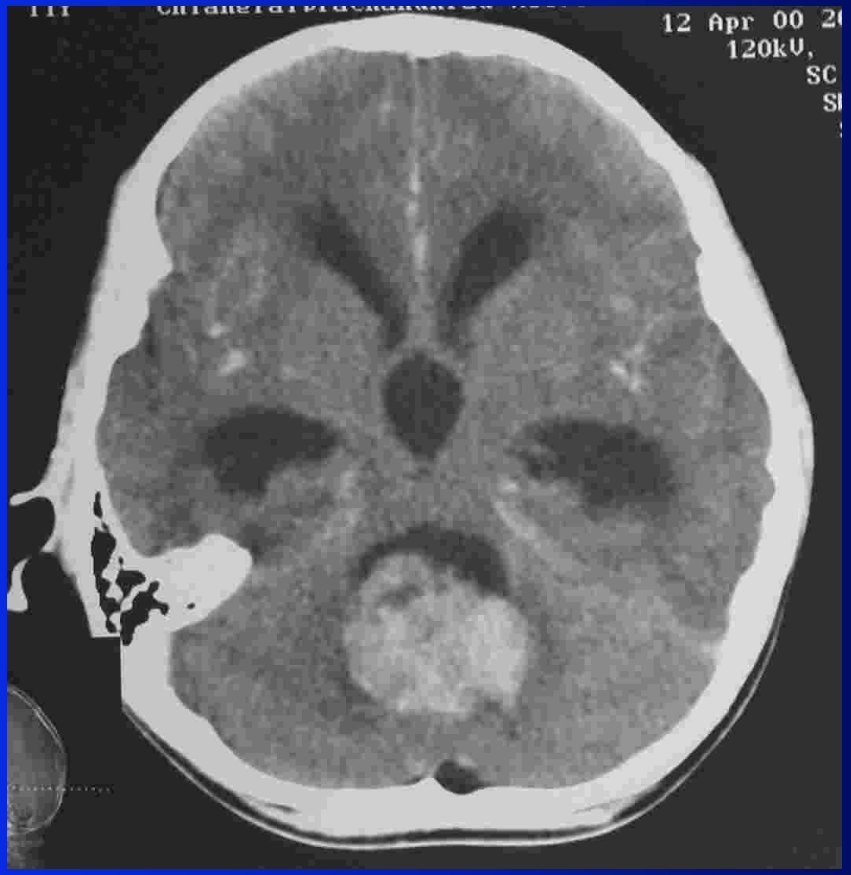
- Imaging Features:
  - Well defined midline cerebellar mass
  - Isolated cerebellar hemisphere involvement uncommon
  - Calcifications in 20%
  - Cystic or necrotic regions in 20-50%
  - Intratumoral hemorrhage is rare, but more common than in cerebellar astrocytoma or ependymomas

Medulloblastoma

- Imaging Features:
  - NECT
    - Hyperdense because of dense cellularity
  - ECT
    - Diffuse or patchy enhancement
  - T1
    - Hypo to isointense
  - T2
    - Can be hypo, hyper, or isointense. Heterogenous secondary to cysts, vessels, and calcifications
    - Hypointensity suggests medulloblastoma, unlikely astro
  - Enhanced MRI
    - Uniform or heterogenous enhancement

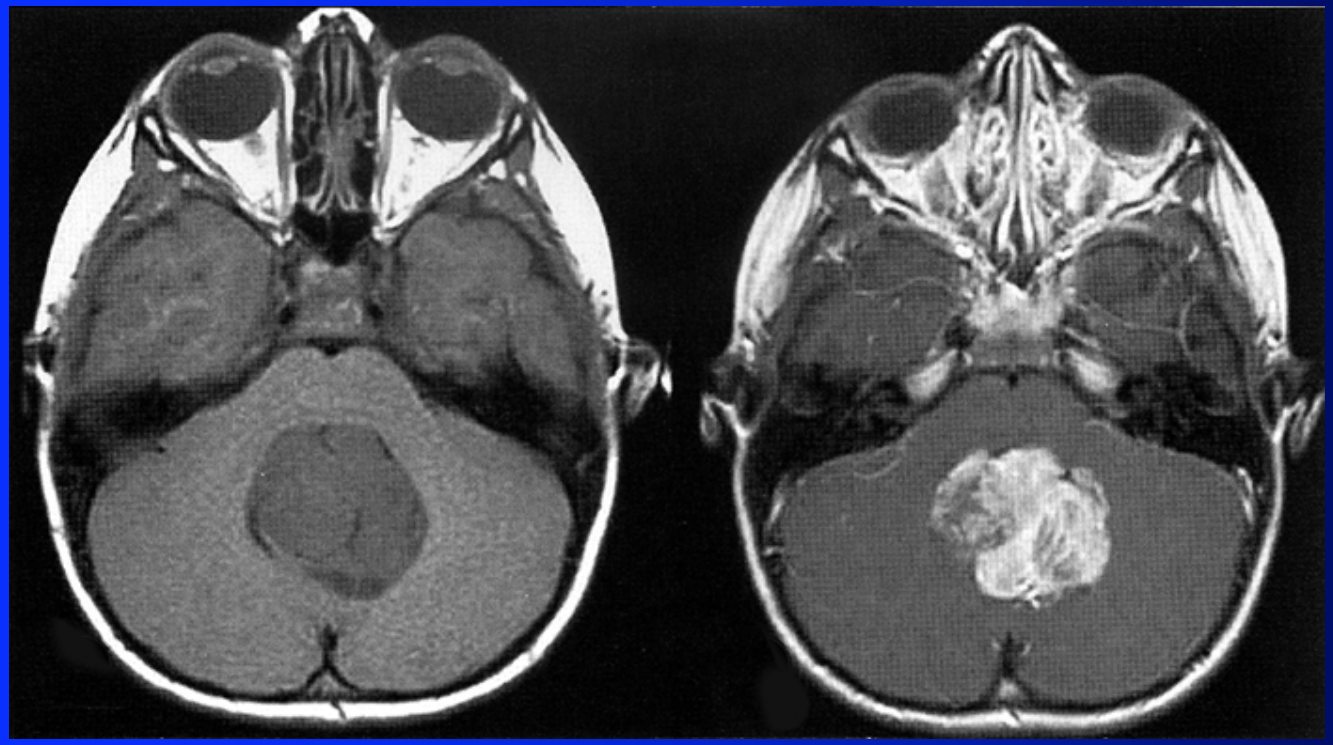
Medulloblastoma

- Imaging



Medulloblastoma

- Imaging

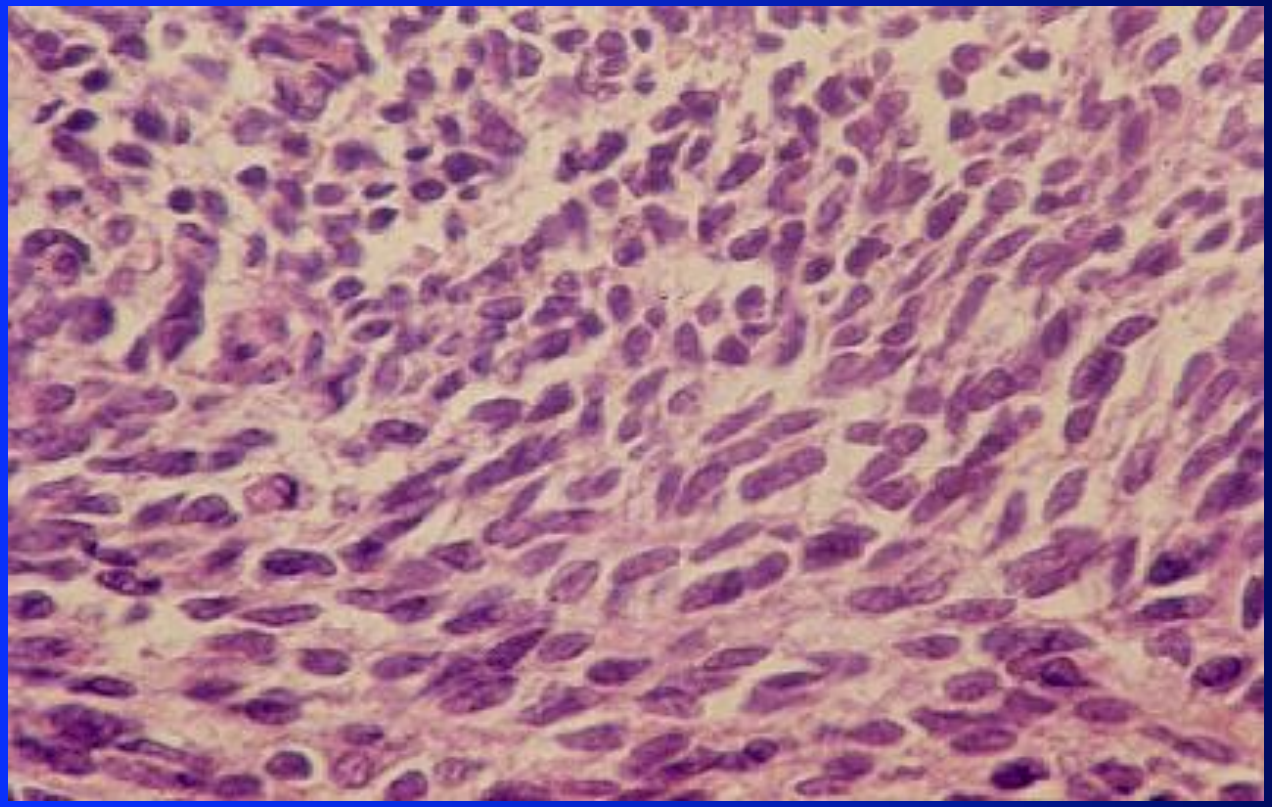


Medulloblastoma

- Histopathology
  - First described by Bailey and Cushing in 1929
    - Described as a highly cellular tumor in roof of 4th ventricle
    - Thought to arise from the embryonal medulloblast
  - In early 1970s, the concept of PNETs intriduced to account for a group of undifferentiated neoplasms
    - Cell of origin still controversial
    - Most accept medulloblastoma as a PNET arising from cerebellum

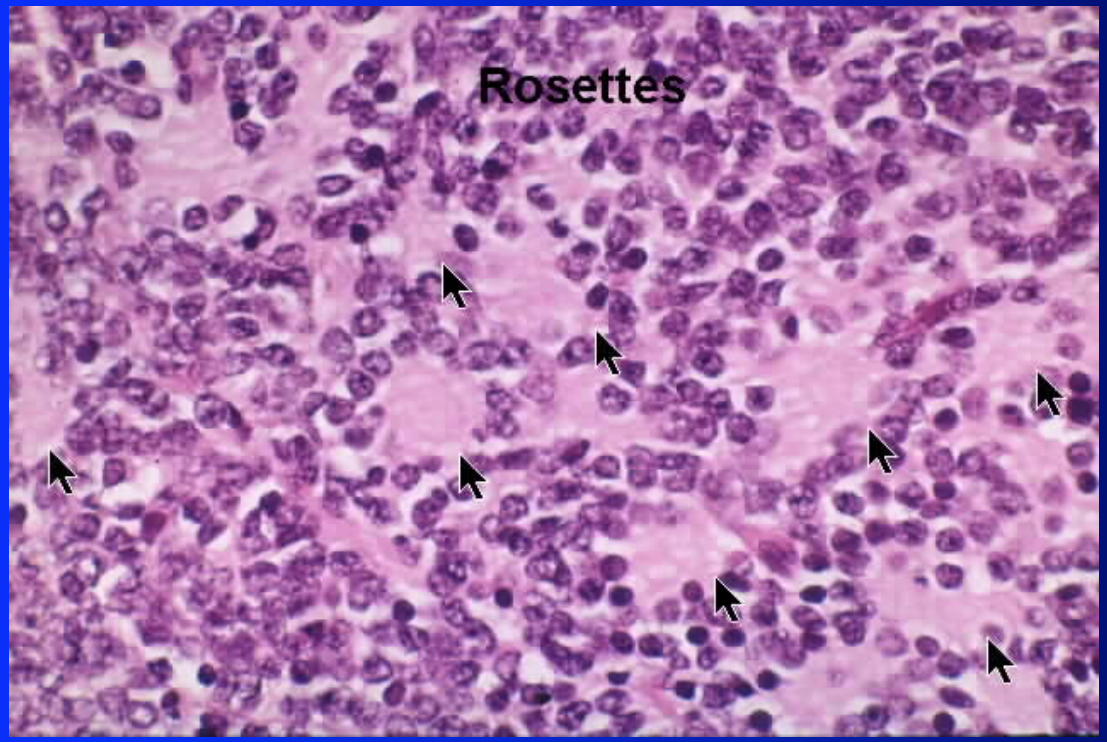
Medulloblastoma

- Histopathology



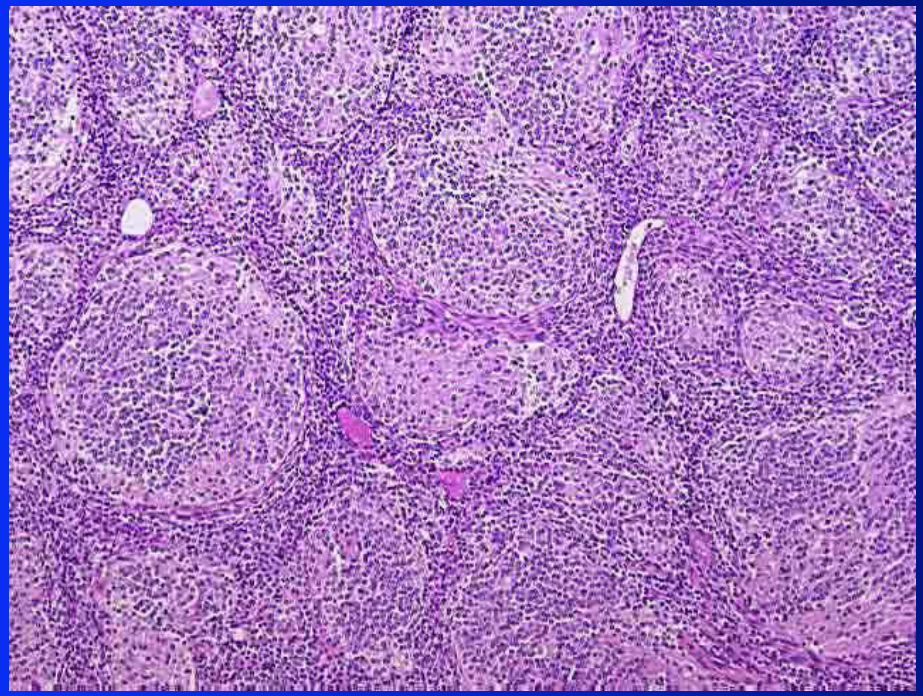
Medulloblastoma

- Histopathology



Medulloblastoma

- Histopathology



Desmoplastic variant

Medulloblastoma

- Histopathology
  - Subtypes:
    - Classic
    - Desmoplastic
    - Large Cell
    - Nodular

Medulloblastoma

- Adjuvant Therapy
  - Post-operative Craniospinal radiation (CSRX)improves survival
    - Incidence of spinal mets is 13% compared with 75% without post-op CSRX
    - Incidence of supratentorial mets also increases without CSRX
    - Typical plan includes 5000 cGy to posterior foss with 4000-4500 cGy to remainder of intracranial compartment and 3000-3500 cGy to the spinal axis
    - Cognitive impairment, growth retardation, and leukoencephalopathy increased significantly if RxTX < 3 years of age

Medulloblastoma

- Adjuvant Therapy
  - Chemotherapy
    - Benefit of Chemotx following successful GTR and standard CSRX remains uncertain
    - Pediatric Oncology Group study shows improved survival with surgery, radiation, and chemotherapy compared with surgery and radiation alone.
    - Other studies show particular benefit with metastatic disease or locally unresectable tumors
    - May be useful in delaying CSRX in children < 3years old
    - Study shows that post-op chemo with delayed radiation is equivalent to standard post-op radiation

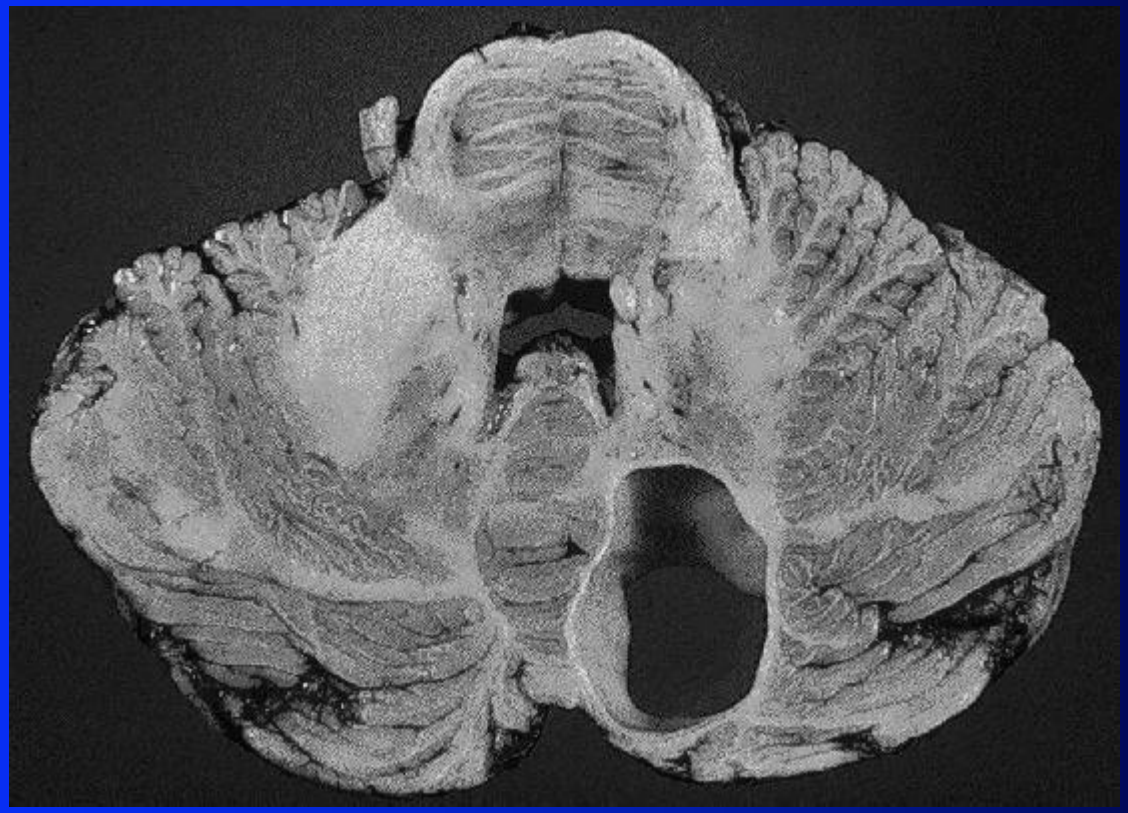
Medulloblastoma

- Follow-up and Recurrence
  - Mendel et al. suggests f/u MRI Brain every 3 months for 2 years, then every 6 months for 2 years, then each year for 5 years
  - Majority recur in the posterior fossa in close proximity to the surgical site
  - Mean time to recurrence is 13-15 months
  - Local posterior fossa recurrences should be treated surgically
  - Focal recurrence may be treated with radiation and diffuse metastatic disease with chemotherapy
  - Average life expectancy for children with recurrent medulloblastoma varies, 8-27 months

Cerebellar Astrocytoma

- Arise from the cerebellar hemisphere
- Occasional isolated vermian lesions
- Typically pilocytic, & well demarcated
- WHO Grade I
- Diffuse subtypes may have infiltrating characteristics
- <10% invade brainstem

Cerebellar Astrocytoma



Cerebellar Astrocytoma

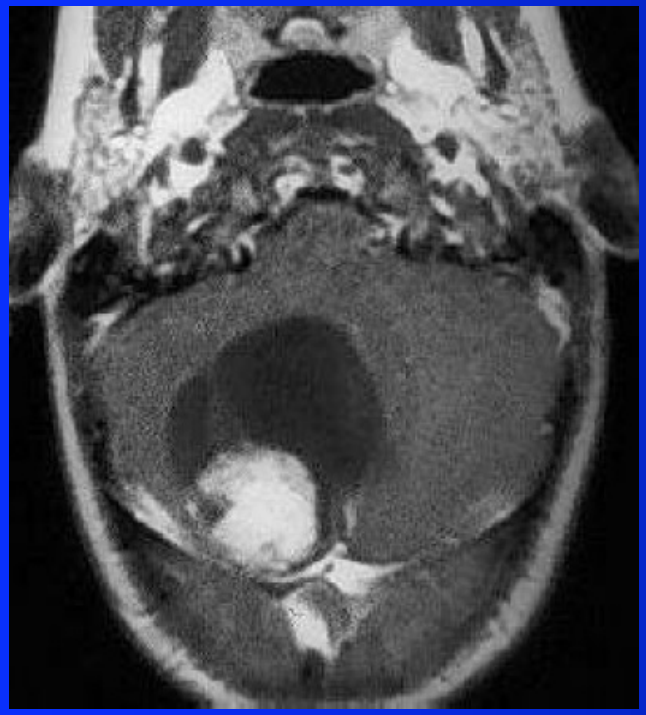
- Imaging Features:
  - Predominantly solid (48%)
  - Cystic/Solid combination (41%)
  - Predominantly cystic (11%)
  - Cyst walls may or may not be neoplastic
    - Thick (>1-2mm) and enhancing cyst walls are more likely to be neoplastic
  - Peritumoral edema absent or mild, less mass effect & more often calcified than medulloblastoma or ependymoma of comparable size

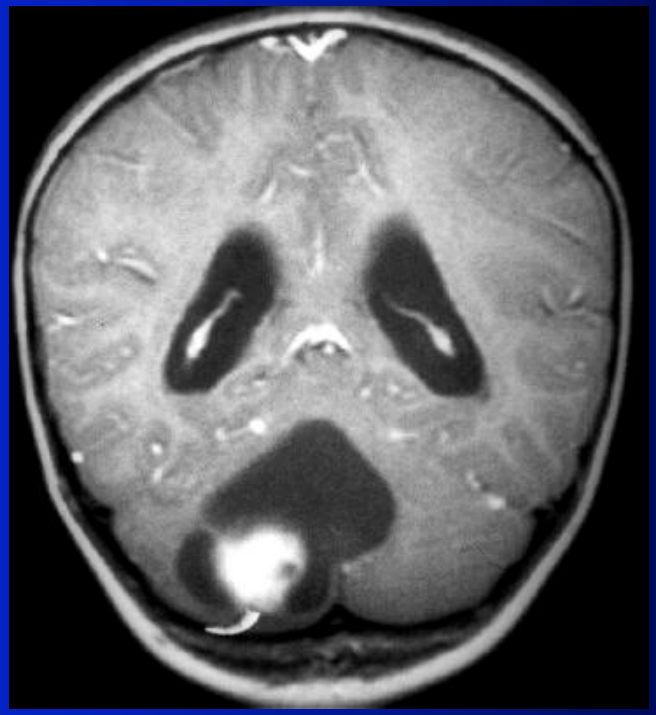
Cerebellar Astrocytoma

- Imaging Features:
  - NECT
    - Isodense or hypodense
  - ECT
    - Heterogenously enhancing
  - T1
    - Hyperintense Nodule, Hypointense Cyst
  - T2
    - Always hyperintense
  - Enhanced MRI
    - Heterogenous enhancement of nodule

Cerebellar Astrocytoma

- Imaging



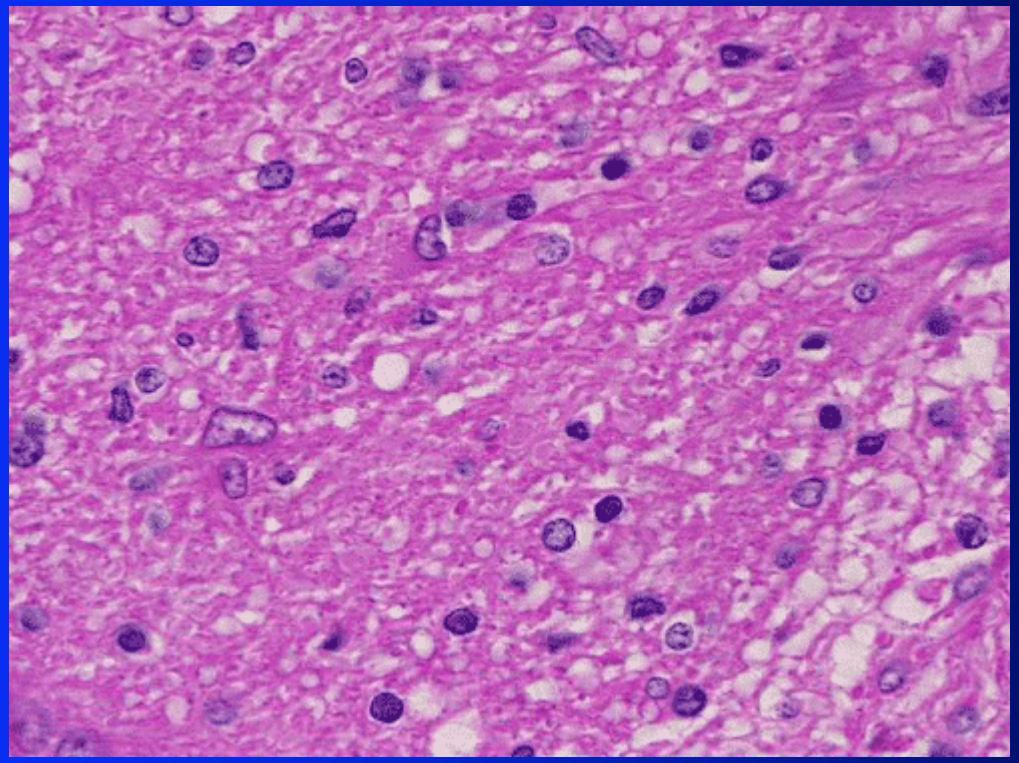


Cerebellar Astrocytoma

- Histopathology
  - Subtypes:
    - Pilocytic (commonest, 70-80%)
      - WHO Grade I
      - Low cell density, Rosenthal fibers, granular bodies
      - Histologically, can show necrosis, vascular proliferation, local invasion, but does not carry a worse prognosis
    - Low-grade,diffuse (5%)
    - Anaplastic
      - WHO Grade III, IV (20%)

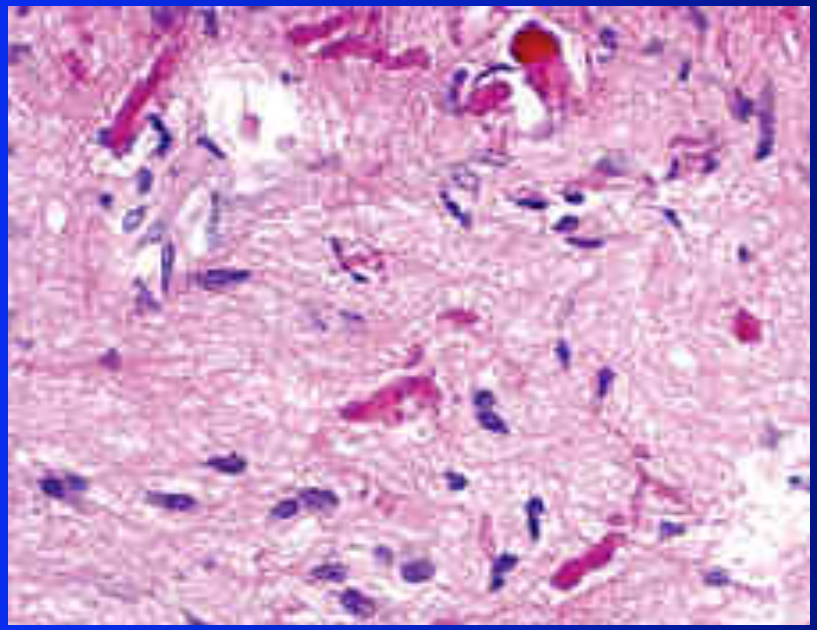
Cerebellar Astrocytoma

- Histopathology



Cerebellar Astrocytoma

- Histopathology



Cerebellar Astrocytoma

- Adjuvant Therapy
  - Not necessary after GTR
  - In certain patients with unresectable, or significant residual tumor, radiation may be useful
  - Radiation, however, may increase likelihood that recurrence will be of a higher grade
  - Radiosurgery alone not yet compared with surgical resection

Cerebellar Astrocytoma

- Adjuvant Therapy
  - Generally chemosensitive (CCNU, cyclophosphamide), but excellent results with GTR precludes need for chemo
  - May be useful as adjunctive therapy in pts where radiation should be avoided
  - Leptomeningeal dissemination, which occurs rarely with low-grade astrocytomas of cerebellum, treated with whole neuraxis radiation and chemo

Cerebellar Astrocytoma

- Recurrence
  - Incidence of recurrence following GTR up to 12%
  - May undergo malignant degeneration up to many years later
  - Children's Cancer Study Group recommends surveillance MRI brain imaging at 6 months, and 1, 2, 5, 7, and 10 years post-operatively
    - If resection is subtotal, follow-up MRI brain should be obtained at 6 months ten anually for 5 years
  - Recurrences should be treated surgically with the goal of GTR
  - If GTR not possible, resection with radiation or chemo is appropriate

Ependymoma

- 2/3 found infratentorially in children
- 2 common sites of origin within the fourth ventricle
  - Inferior fourth ventricle near obex (commonest)
    - 1/3 of these extend inferiorly through the foramen magnum
  - Lateral fourth ventricle
    - Often with extension through the foarmen of Luschka into the CPA
- Origin from roof of 4^{th} ventricle is rare
- Extension through the foramen is characteristic

Ependymoma

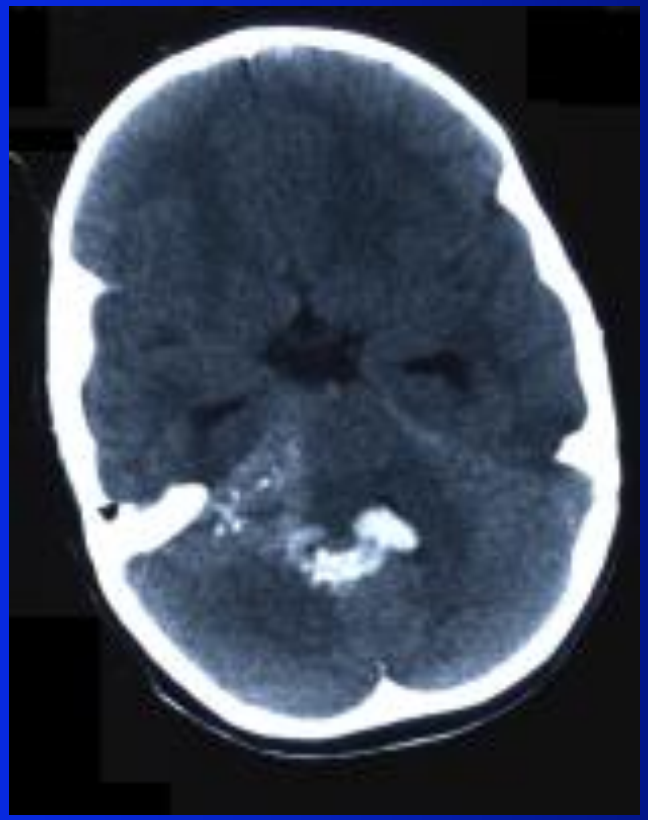
- Imaging Features:
  - Tend to displace rather than invade nearby neural structures
  - Multifocal calcifications in 50%
  - Signal characteristics are non-specific on MRI
  - Tumor extension through the foramen (Luschka or Magendie) is central to the radiographic diagnosis

Ependymoma

- Imaging Features:
  - NECT
    - Isodense
  - ECT
    - Heterogenously enhancing
  - T1
    - nonspecific
  - T2
    - nonspecific
  - Enhanced MRI
    - Heterogenous enhancement

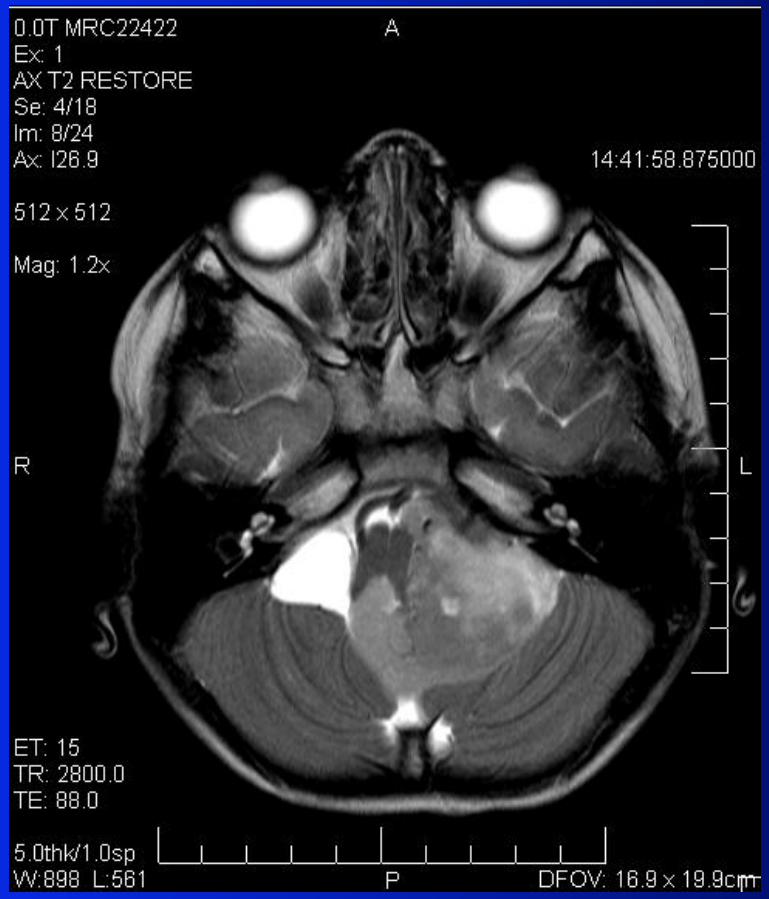
Ependymoma

- Imaging



Ependymoma

- Imaging



Ependymoma

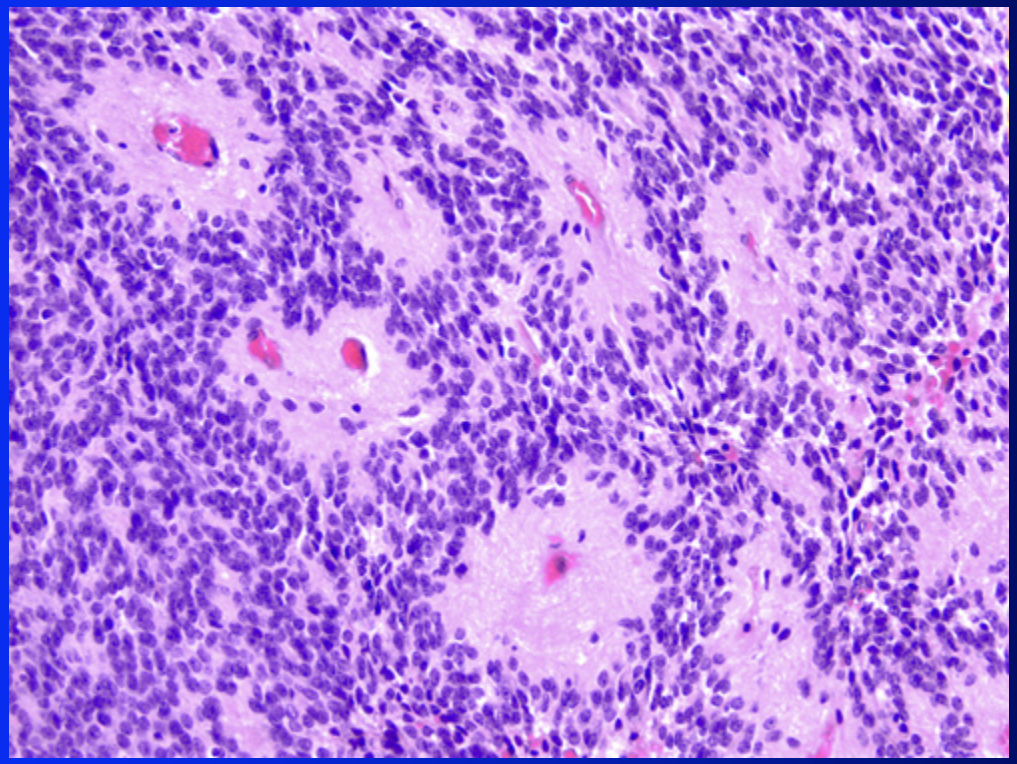
- Histopathology
  - 4 Subtypes:
    - Cellular
      - Perivascular psuedorosettes > true rosettes
    - Papillary
    - Clear-cell
    - Anaplastic
      - Variable degrees of cellularity, atypia, and necrosis may be present in all subtypes, but the highest quotient of malignant features present in anaplastic

Ependymoma

- Histopathology
  - Historically, histological interpretation varies by institution and individual
  - However, histologic class does not seem to affect survival
  - Worse outcome has been demonstrated with anaplastic variant, but without statistical significance

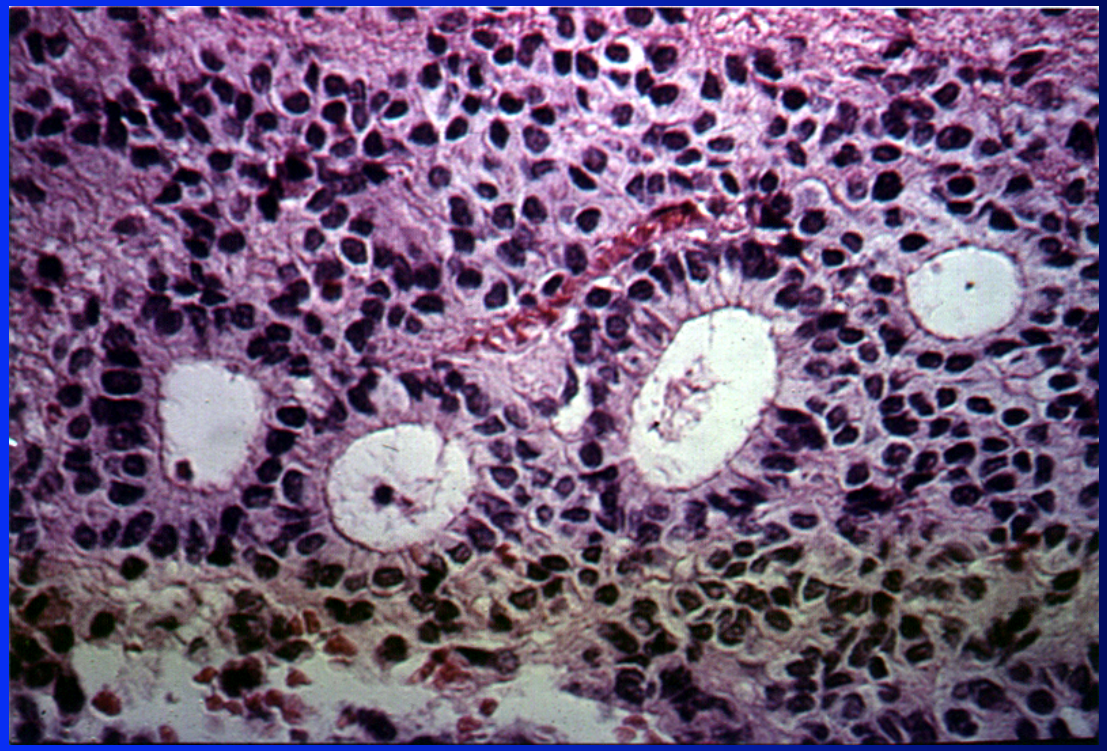
Ependymoma

- Histopathology



Ependymoma

- Histopathology



Ependymoma

- Adjuvant Therapy
  - GTR is most important predictor of patient outcome
  - No randomized trials on post-op radiation
  - Since majority of pts have subtotal resection with post-op radiation, this may suggest that radiation is of benefit without regard to degree of resection
  - Some advocate no radiation after GTR, with close f/u, and delayed radiation for recurrence

Ependymoma

- Adjuvant Therapy
  - Most believe that local radiation is sufficient
  - CSRX for patients with evidence of dissemination or anaplastic histology
  - No benefit in a large study with CCNU
  - Chemo limited to:
    - Tumor recurrences
    - To delay radiation in young children (cyclophosphamide and vincristine, Peidatric Oncology Group Study)

Ependymoma

- Recurrence
  - Typically recur at or adjacent to the site of tumor resection
  - Younger age and short duration of presenting symptoms are risk factors for recurrence
  - Median time to recurrence is 22 months
  - Recurrences should be treated surgically with the goal of GTR

Prognosis

- Medulloblastoma
  - 5 year survival > 70%
  - 5 year progression free survival > 50%
  - Shorter survival in presence of drop mets, < 3 years old, subtotal resection
- Cerebellar Astrocytoma
  - 5 year survival > 90%
  - 10 year survival with GTR 80-90%
  - Anaplastic astros have 7% 10 year survival
  - Younger age, pilocytic, lack of brainstem involvement are predictors of good outcome
- Ependymoma
  - 5 year survival 60%
  - 10 year survival 45%
  - More difficulty achieving GTR reflected in survival rates

Brainstem Gliomas

- Comprise 10-20% of pediatric CNS tumors
- 3rd commonest pediatric brain tumor after cerebellar astrocytoma and medulloblastoma
- 77% < 20 years old
- Previously thought of as having a uniformly poor prognosis
- Advances in neuroimaging, in particular, have made it possible to separate this broad category of tumors into prognostically different subgroups

Brainstem Gliomas

- Classification:
  - Diffuse
  - Focal Intrinsic
  - Dorsally and laterally exophytic
  - Cervicomedullary
  - Tectal

Brainstem Gliomas

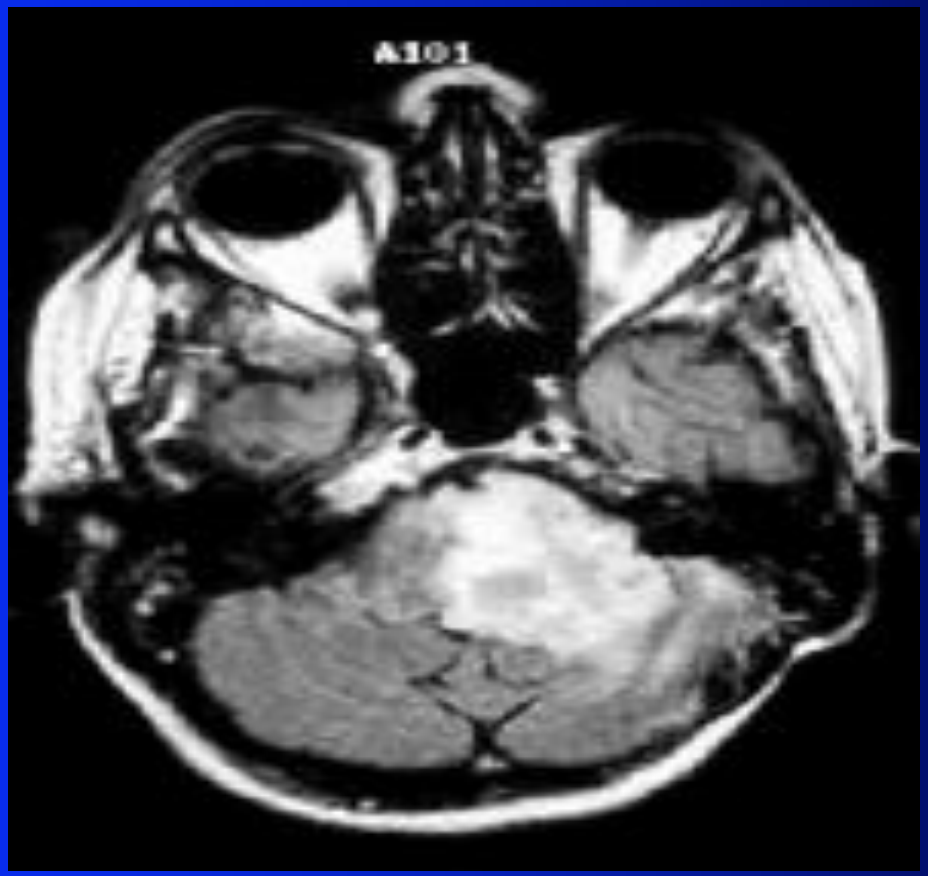
- Diffuse Tumors
  - Aggressive, highly invasive lesions
  - Present with rapidly progressive ataxia, weakness, and multiple, often bilateral, cranial nerve deficits
  - Biopsy rarely warranted, since imaging findings are characteristics and would place patients at risk without any benefit
  - Best treated with radiotherapy alone, which is largely palliative

Brainstem Gliomas
Diffuse Tumors

- Imaging Features:
  - NECT
    - CT shows enlarged pons
  - ECT
    - Variable, sometimes focal (but still irregular), enhancement
  - T1
    - Diffusely enlarged pons with no clear borders
  - T2
    - Diffuse high intensity signal that extends throughout the entire transverse diameter of the pons
  - Enhanced MRI
    - Variable, sometimes focal (but still irregular) enhancement

Brainstem Gliomas

Diffuse Tumors



Brainstem Gliomas

- Focal Intrinsic Tumors
  - Arise in midbrain, pons, or medulla; commonly medulla
  - Most (66%) are low grade astrocytomas
  - Characterized by a long natural history
  - Focality of these lesions mirrored by presentation
    - Isolated cranial nerve deficits with mild cerebellar or long-tract signs
    - Midbrain: extra-ocular movement dysfunction
    - Pontine: facial pariesis
    - Medulla: swallowing dysfunction
  - Surgery is an appropriate option, but still not proven against focused radiotherapy or chemotherapy considering the significant risks of neurological impairment

Brainstem Gliomas

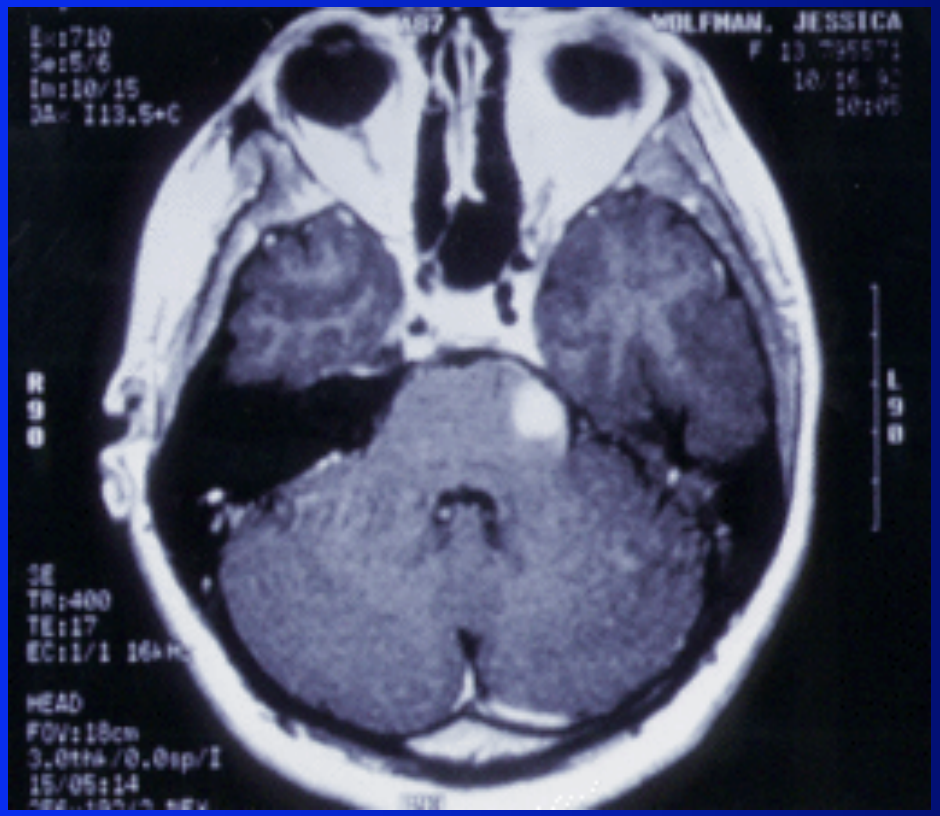
Focal Tumors

- Imaging Features:
  - NECT
    - Hypodense
  - ECT
    - Uniformly enhancing, nonenhancing, or cystic with mural nodule
  - T1
    - Hypointense
    - Grow by displacing tissue, creating cuff of normal brainstem tissue on T1 and T2
  - T2
    - Pattern overlaps completely with that on T1
  - Enhanced MRI
    - Uniformly enhancing, nonenhancing, or cystic with mural nodule

Brainstem Gliomas

Focal Tumors

- Imaging



Brainstem Gliomas

- Dorsally and Laterally Exophytic Tumors
  - Present with symptoms similar to other 4th ventricular tumors
    - Obstructive hydrocephalus: H/A, nausea, vomiting, ataxia
    - Months of gradually progressive symptoms
    - Have been diagnosed in kids presenting with intractable vomiting
  - Because they fungate dorsally, cranial nerve signs, if present, are often mild
  - Rarely present as a CPA mass
  - Many of these are pilocytic astrocytomas
  - Best treated with surgery and followed by serial imaging
  - Only 20-30% of post-resection patients require second surgery, despite a commonly subtotal resection

Brainstem Gliomas

Dorsally and Laterally Exophytic Tumors

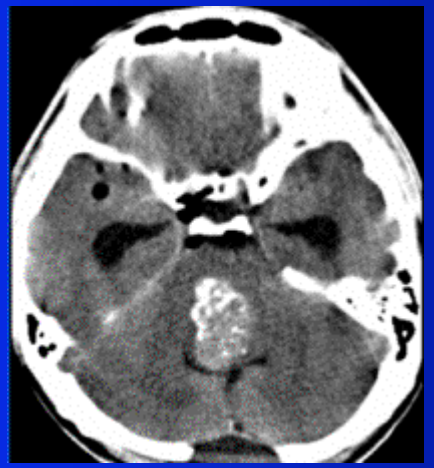
- Imaging Features:
  - NECT
    - Hypodense
  - ECT
    - Uniformly enhancing
  - T1
    - Hypointense
  - Enhanced MRI
    - Uniformly enhancing

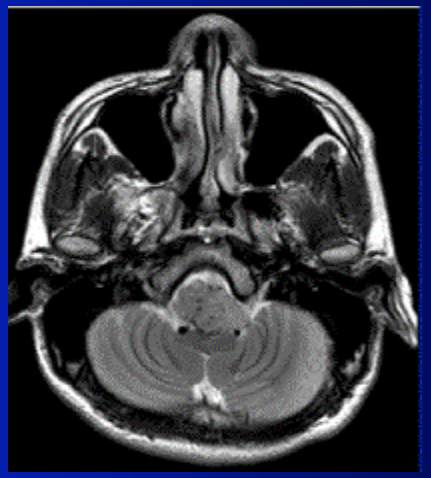
Osteochondroma

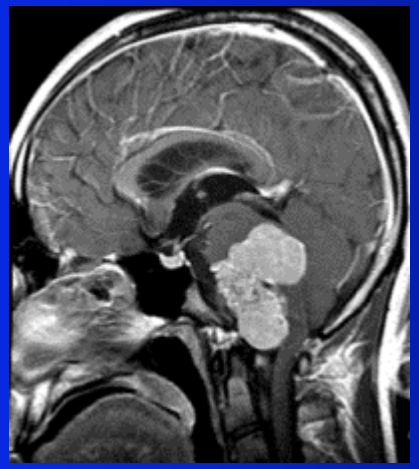
~~Brainstem Gliomas~~

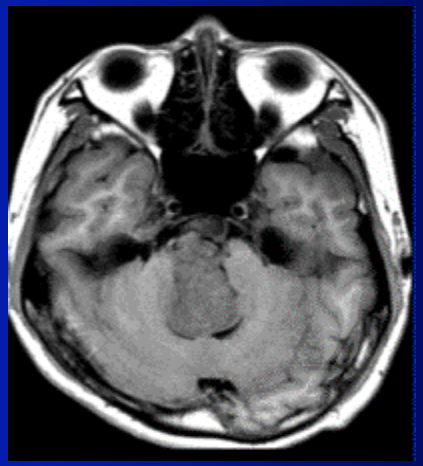
~~Dorsally and Laterally Exophytic Tumors~~

- Imaging









Brainstem Gliomas

- Cervicomedullary Tumors
  - Most (72%) are low grade astrocytomas
  - Usually represent cervical cord astrocytomas that extend rostrally into the medulla, rather than the converse
  - Majority present with symptoms referable to the spinal cord
    - Long history of neck pain, paresthesias, gradually progressive weakness
    - gradually progressive symptoms
  - Epicentre of growth on MRI is in the cervical cord, with the rostral pole of the tumor appearing to push the medulla upward
  - Dome of the tumor often extends into the cisterna magna in the region of the obex

Brainstem Gliomas

Cervicomedullary Tumors

- Imaging Features:
  - NECT
    - Hypodense
  - ECT
    - Uniformly enhancing, or cystic with an enhancing rim or mural nodule
  - T1
    - Hypointense
  - Enhanced MRI
    - Uniformly enhancing, or cystic with an enhancing rim or mural nodule

Brainstem Gliomas

- Tectal Tumors
  - Group of particularly benign astrocytomas
  - Characteristically produce symptoms of obstructive hydrocephalus
    - H/A, nausea, vomiting
  - Pre-MRI era: these patients were assumed to have “idiopathic late-onset aqueductal stenosis”
  - Initial ones that were biopsied were found almost uniformly to be low-grade
  - Indolent lesions with little or no evidence of clinical or radiographic progression
  - Best treated with CSF diversion, including 3rd ventriculostomy
  - Little or no role for surgical resection
  - Biopsy for lesions that progress

Brainstem Gliomas

Tectal Tumors

- Imaging Features:
  - NECT
    - Hypodense
  - ECT
    - Usually non-enhancing, may show focal enhancement that slowly fades over time
  - T1
    - Isointense
  - T2
    - Hyperintense lesion, centred on the tectum
    - If bulk of signal extends into tegmentum or caudal diencephalon, likely less indolent lesion
  - Enhanced MRI
    - Usually non-enhancing, may show focal enhancement that slowly fades over time

Brainstem Gliomas

Tectal Tumors