
بسم الله الرحمن الرحيم

PEDIATRIC CHORDOMAS

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Chordomas

- Introduction
  - Rare, midline primary malignant tumors of bone
  - Slow growing but aggressive and locally invasive
  - Arise from remnant of primitive notochord
  - Predilection for axial skeleton
  - Most common sites: sacrum, clivus, spine
  - Rare sites, sella, paranasal sinuses, nasopharynx, intradural chordoma
  - High recurrence rate, rarely metastasize at advanced stage, poor prognosis

Adult Chordomas

- Epidemiology
  - Account for 1-4 % of all malignant bone tumors
  - Less than 0.1-0.4% of primary brain tumor
  - Peak age is 50-60 years of age
  - Male to female ratio is 2:1
  - More than 95% occur above 40 years age
  - Most common locations are
    - Sacrococcygeal, 50%
    - Clivus/skull base, 35%
    - Spinal column, 15%

Pediatric chordomas

- Epidemiology
  - Extremely rare in children
  - Less than 5% chordomas occur in children
  - Less than 300 cases reported in literature
  - Average age at diagnosis is 10 years
  - Youngest patient, neonate with clival chordoma
  - Male to female ratio is 2:1
  - Mostly sporadic, familial in children with TSC
  - Most common locations
    - Clivus/skull base/Sphenooccipital synchondross, 50%
    - Sacrococcygeal, 35%
    - Spinal column, 15%

Pediatric chordomas

- Historical background
  - 1856, Luschka, Clivus Blumenbashi
  - 1857, Virchow, Ecchondrosis physaliphora sphenooccipitalis
  - 1858, Muller, Suggested notochordal origin
  - 1864, Klebs, First case of Chordoma
  - 1890, Ribbert, Introduced the term Chordoma
  - 1909, Cushing, First successful resection of chordoma
  - 1923, Andre Thomas, First pediatric case

Pediatric chordomas

Clinical Presentation

Clival chordomas

- Headache
- Cranial nerve palsies
- Most common 6th nerve palsy, Diplopia
- Raised ICP
- Torticollis
- Nasopharyngeal mass, nasal obstruction, epistaxis
- Failure to thrive

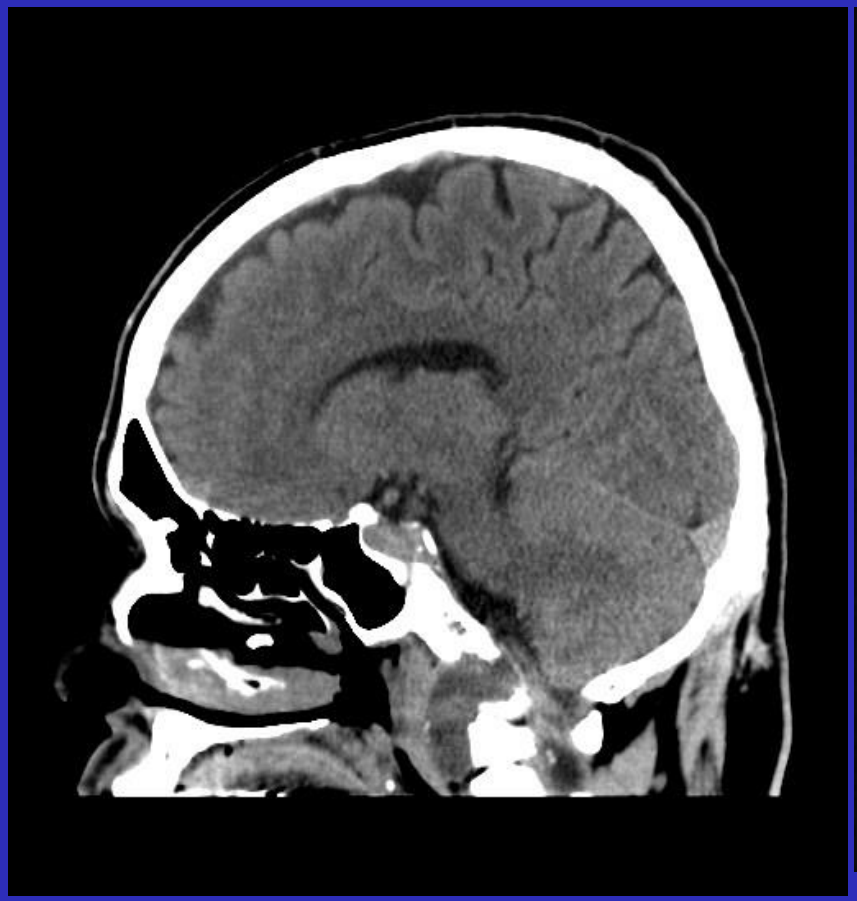
Sacrococcygeal chordomas

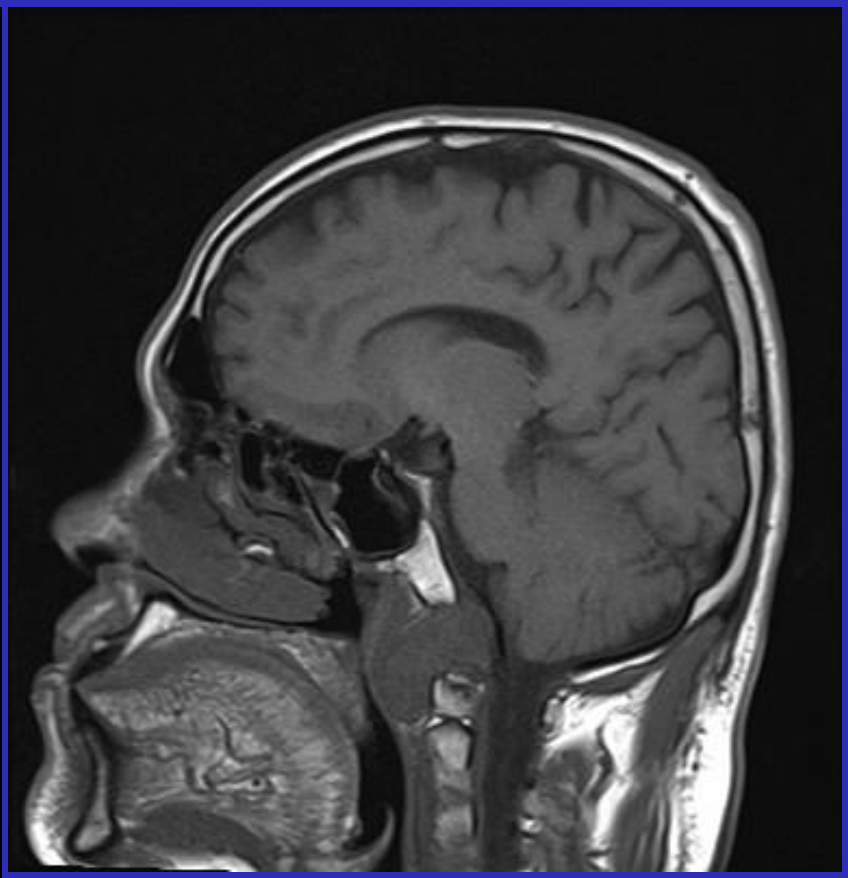
- Backache
- Radicular pain
- Mass on back
- Pelvic mass
- Deformity
- Cauda equina syndrome

Pediatric chordomas

- Diagnosis
  - CT
  - MRI
  - X-ray spine
  - Angiography

Pediatric chordomas





Pediatric chordomas D/D

Common

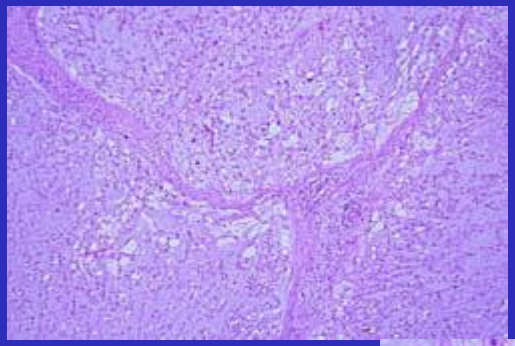
- Chondrosarcona
- Nasopharyngeal ca
- Clival Meningioma
- Aggressive pituitary adenoma
- Retroclival craniopharyngiomas
- Rhabdomyosarcoma

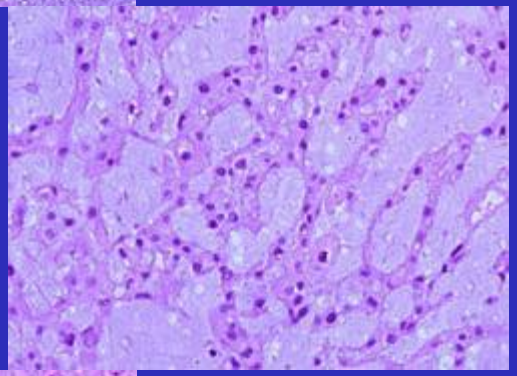
Rare

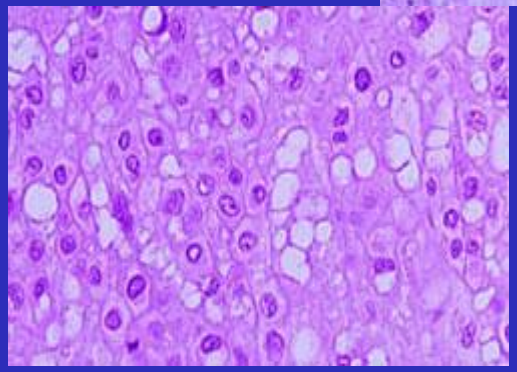
- Fibrous dysplasia
- Aneurymal bone cyst
- Dermoid/epidrmoid cyst
- Lymphoma
- Metastasis
- Plasmacytoma
- Infection, TB. Fungal
- Echordosis physilophora
  - Benign, non neoplastic remnant of notochord,
  - Attached to clivus, usually asymptomatic
  - 2% of autopsies,

Pediatric chordomas

- Histopathology
  - Lobulated architecture
  - Cells arranged in cords or sheets
  - Separated by fibrous septa
  - Abundant myxoid stroma
  - Two types of cells
  - Small ovoid cells
  - Large cells with multiple vacuoles in cytoplasm
  - Physalipherous cells
  - Bubble bearing cells
  - High MIB-1







Pediatric chordomas

- Histopathology types
  - Conventional Chordomas
  - Chondroid chordomas
  - Undifferentiated chordomas
- Immunohistochemical stains
  - Cytokeratin (CK 8, 18, 19)
  - Epithelial membrane antigen (EMA)
  - S-100 protein
  - Bachyury

Pediatric chordomas

Chordoma

- Cytokeratin, positive
- EMA, positive
- Brachyury, positive

Chondrosarcoma

- Cytokeratin, negative
- EMA, negative
- Brachyury, negative

Pediatric chordomas

- Molecular markers
  - **Brachyury growth factor**
  - Tyrosine kinase receptors overexpression
    - EGFR, PDGFR
  - Mutation in TSC1, TSC2 gene
  - Loss of INI1, Rhabdoid tumor predisposition syndrome

Pediatric chordomas

- Molecular marker
  - Brachyury growth factor
    - Transcription growth factor
    - Present in normal notochord cells
    - Gene for Brachyury is present on Ch.6q27
    - Overexpressed in all chordomas
    - Marker specific for chordomas
    - Helpful to differentiate chordomas from chondrosarcoma, metastatic carcinoma

Management

- Multidisciplinay
  - Surgical resection
  - Radiotherapy
  - Chemotherapy

Pediatric chordomas

- Management
  - Surgery
    - Tissue diagnosis
    - Maximum safe resection of tumor
    - To relieve mass effect from neighboring structures
    - Complete tumor resection is possible in 0-36.4% in major pediatric series

Pediatric chordomas

- Management
  - Surgical approaches
  - Choice of surgical approach depends upon location of tumor
    - Frontobasal
    - Retrosigmoid
    - Subtemporal/presigmoid
    - Transsphenoidal
    - Transoral
    - Transmaxillary
    - Transmandibular
    - Combined

Pediatric chordomas

- Management
  - Radiotherapy
    - Conventional
    - Radiosurgery(Gamma knife, Cyber knife, LINAC)
    - Proton beam

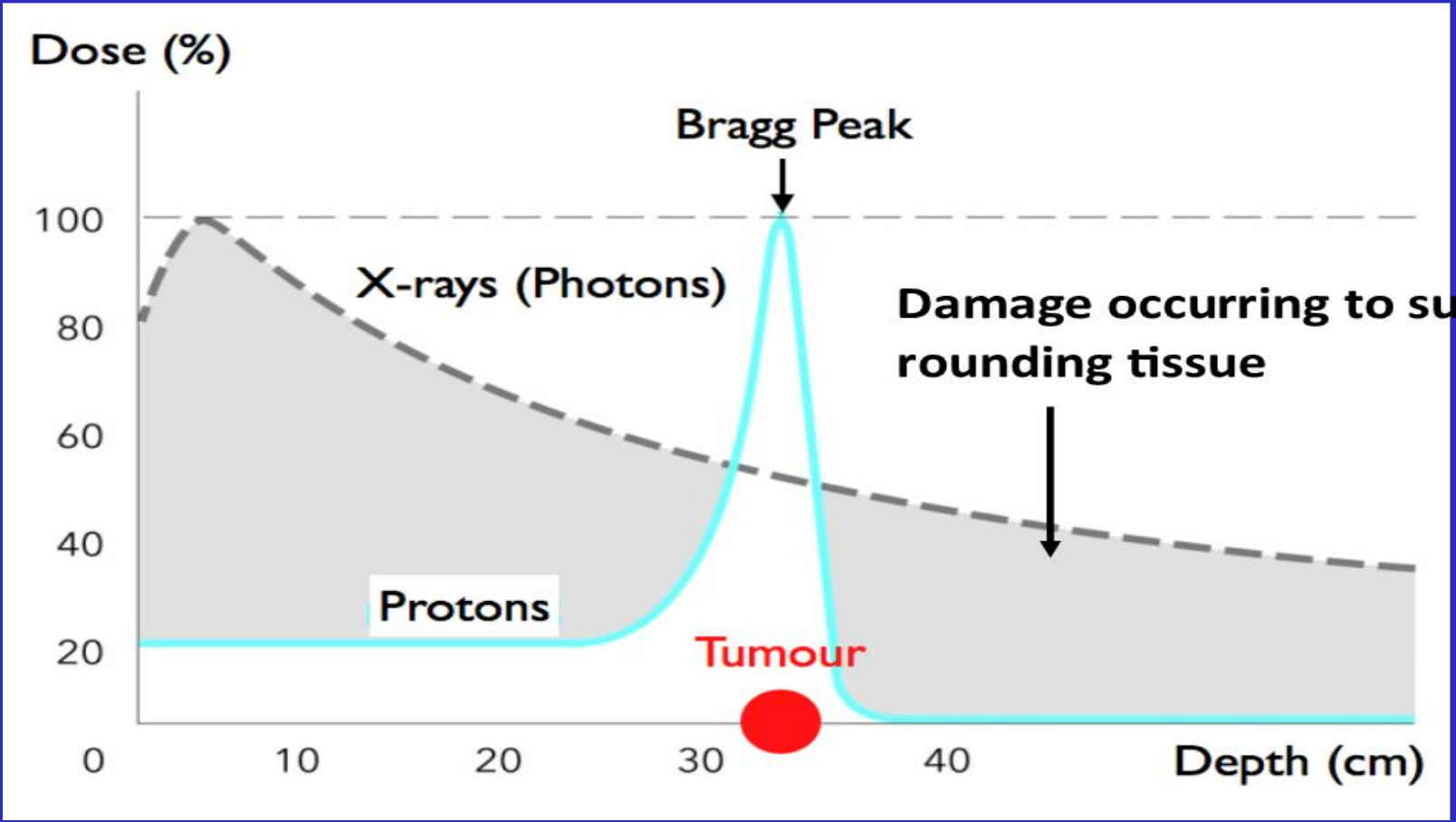
Pediatric chordomas

- Radiotherapy
- Conventional radiotherapy
  - 50-60 Gy
  - Poor local control
  - Recurrence rate 50-100%

Pediatric chordoma

- Proton beam radiotherapy
  - High radiation dose
  - 65-80 Gy
  - Bragg peak effect
  - Maximum dose to the target tumor volume
  - Less dose the neighboring structure
- Advantages
  - Safe
  - More effective
  - Less side effects
- Disadvantages
  - Costly
  - Limited availability

Pediatric chordomas



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Proton Beam Therapy for Pediatric Chordomas: State of the Art

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Abstract

Chordomas are a rare form of primary bone tumors arising from clivus, vertebra, and sacrum. Although it usually occurs in adults, children can be affected too. Multidisciplinary treatment is required and is particularly challenging because the chordoma's proximity to critical structures creates a high risk for significant adverse events. Standard procedure consists of extensive surgery followed by high-dose radiation therapy in excess of 70 Gy. Proton beam therapy has become one of the standard procedures to achieve high, local intensity while maximally sparing normal tissue in adults and children. Results achieved so far are promising and are superior to what has been achieved with surgery alone or conventional radiation therapy. When compared with modern photon radiation techniques, such as intensity-modulated radiation therapy, proton beam therapy may be of particular interest for children to provide high conformality while reducing the irradiated volume and therefore potentially minimizing the risk for secondary cancer induction. The role of chemotherapy remains to be defined.

Keywords: children; chordoma; proton beam therapy; irradiation

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Outcome of Pediatric Chordomas

Table 1 Outcome of paediatric chordomas observed in the major paediatric series of the literature.

Author	Number of cases	Treatment			Mean follow-up in months (min-max)	Progression free survival (%)	Overall survival (%)
		Surgery	Radiotherapy	Chemotherapy			
Benk et al.[19]	18	Partial resection (18)	Proton (18)	-	72 (19–120)	63 (5 years)	68 (5 years)
Borba et al.[16]	79 (review)	Not precise	Not precise	Not precise	39 (1–300)	-	56.8
Hoch et al.[20]	73	Total/Partial resection (73)	Proton (73)	-	90 (12–252)	-	81
Ridenour et al.[18]	20	Partial (14)	Conventional (10)	(2)	129 (1–501)	-	63
			Proton (2)				
			None (2)				
		Total (4)	Conventional (2)				
			None (2)				
		Biopsy (2)	Conventional (2)				
Necker - Lariboisière (not published)	34	Partial (24)	Conventional (2)	(3)	78 (0.3-239)	54.3 (15 years)	63
			Proton (3)				
			Conventional + Proton (12)				
			Radiosurgery (1)				
			Tomotherapy (1)				
			None (4)				
			Unknown (1)				
		Total (6)	Conventional (2) Proton (3) Conventional + Proton (1)	(1)			
		Unknown (4)					

Pediatric chordomas

Author	Pts	Radiation	TD in CGE	% LC at 5 years	% OS at 5 years	Med F/U in months
Hug et al	10	P	73.7 (70-78.6)	60	60	30
Hoch et al.	73	P	NA	NA	81	86.5
Habrand et al.	26	P + Ph	69.1	77	100	26.5
Rombi et al.	19	P	74.0 (73.8-75.6)	81	89	46
Combs et al.	7	I	60-66.6	1 progression	-	49

Legend: Pts: patients; P: protons; Ph: photons; I: ions; CGE: Cobalt Gray equivalent; LC: local control; OS: overall survival; med: median; F/U: follow-up; TD: Total dose; NA: not available.

Table 5. Series of skull base pediatric chordoma treated with particles

The role irradiation in the treatment of chordoma of the base of skull and spine, Current cancer treatment

Pediatric chordomas

- Prognosis
  - Age
  - Location
  - Histopathology
  - Extent of resection
  - Use of high dose proton beam radiation

Pediatric chordomas

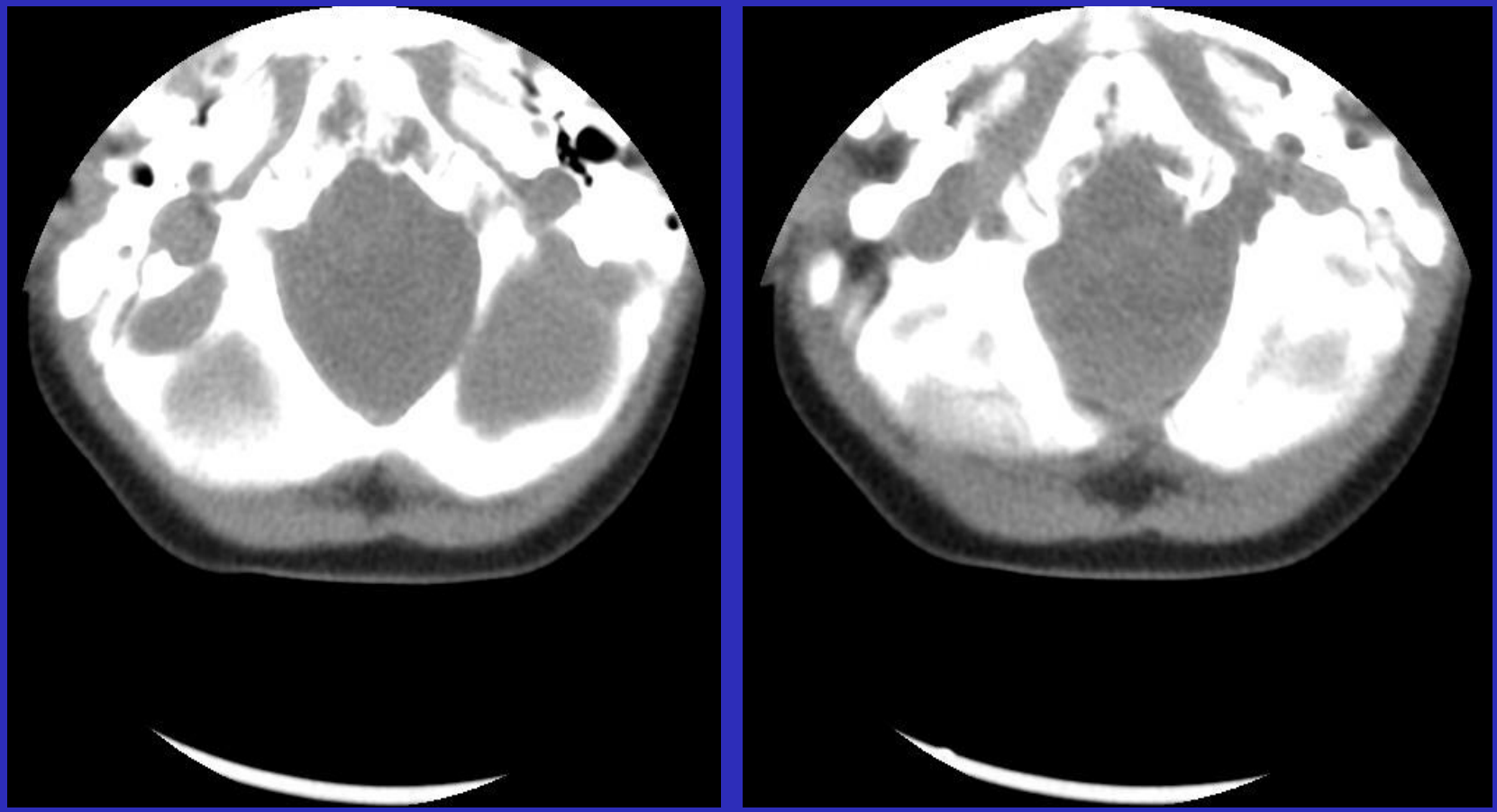
- 5 years overall survival
  - Children 81%
  - Adults 55%

Proton beam therapy for pediatric chordomas: State of the art
International Journal of particle therapy , Sep 2014

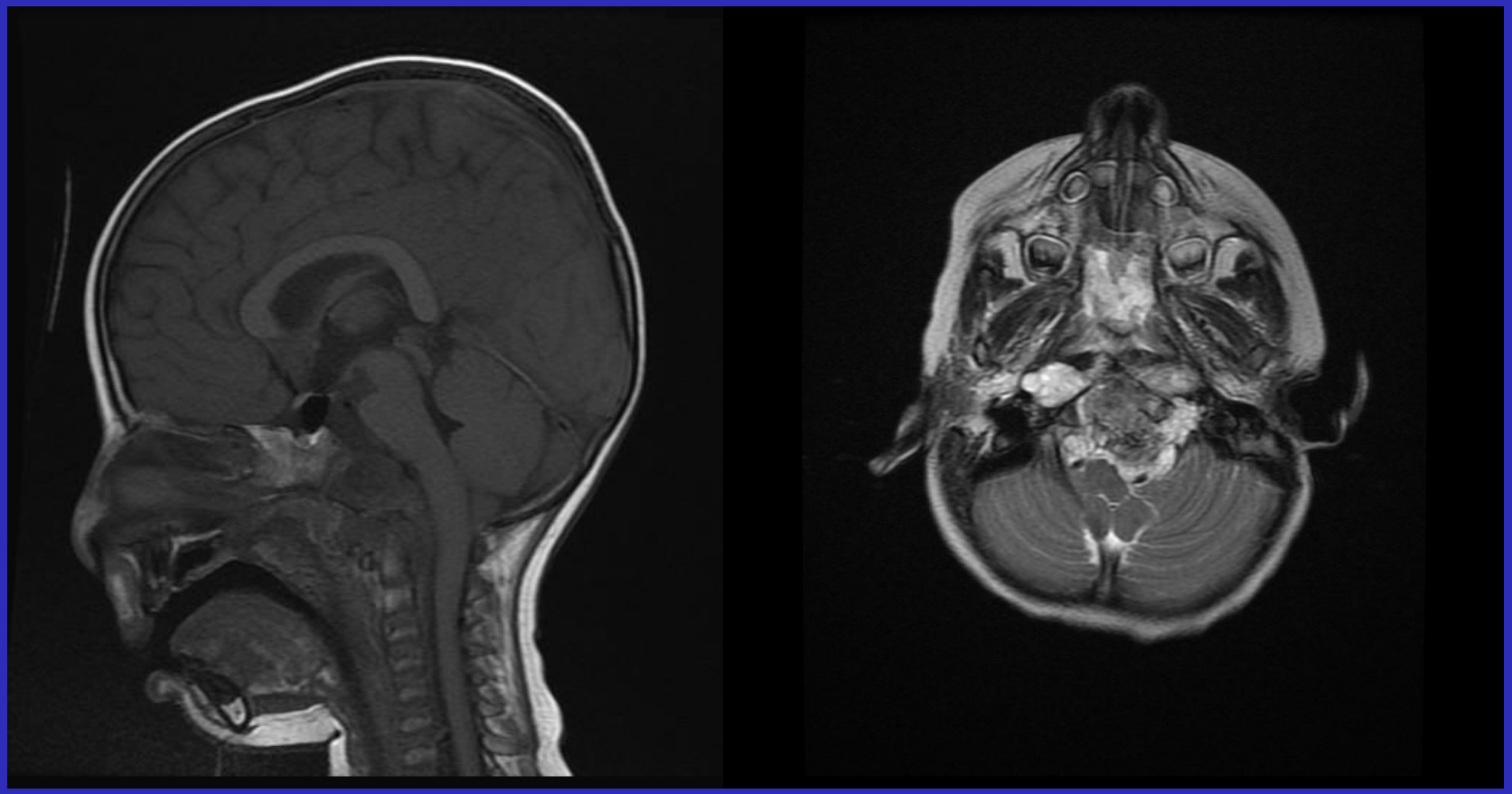
Case

- 3 years old boy
- On and off headache
- MRI showed Clival tumor
- Transoral approach, Debulking of tumor, May,2012
- Proton Beam Therapy, December 2012, in USA
- 6660 cGy, 37 fractions/180cGy/fraction
- 3 years follow up, no recurrence
- No neurological deficit

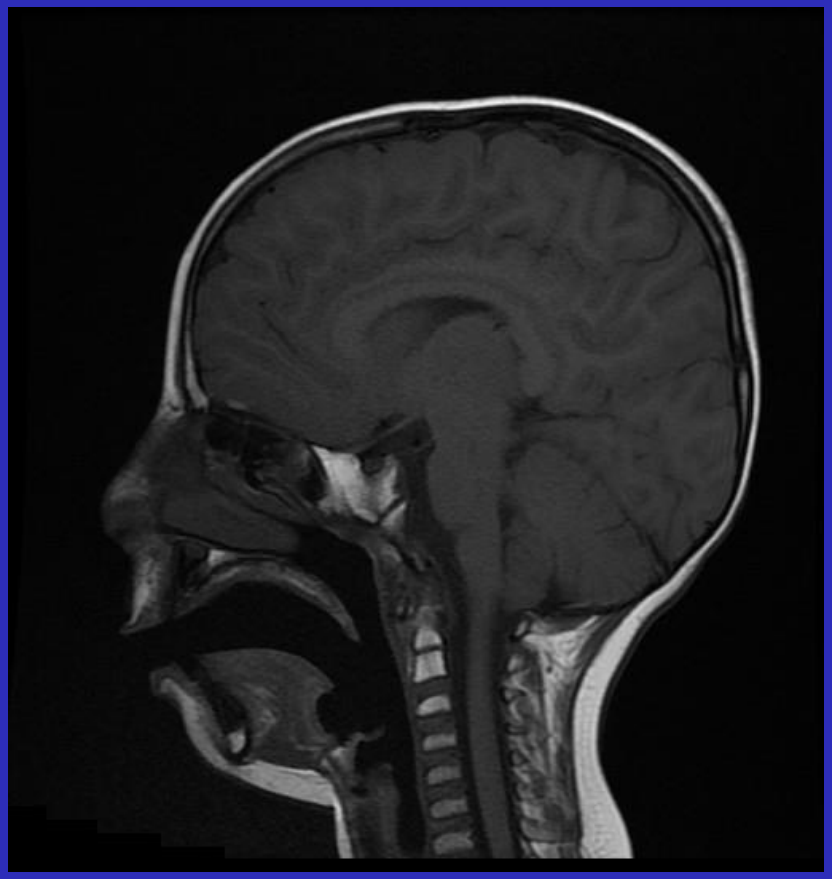
case

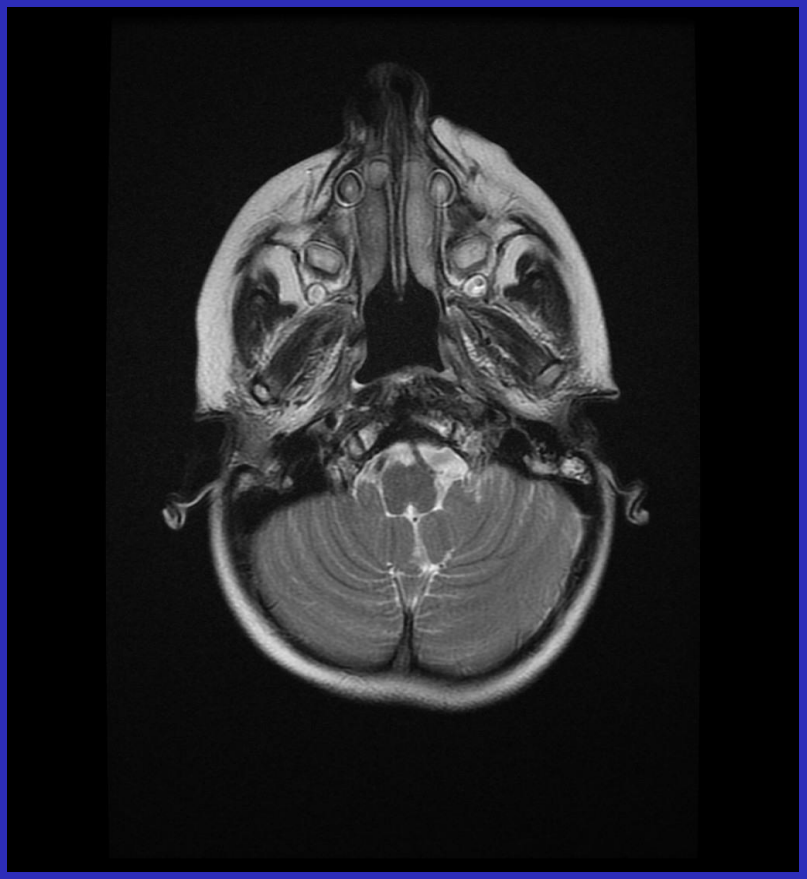


case



Proton beam therapy, Three years follow up





Pediatric chordomas

- Conclusion
  - Chordomas is extremely rare disease in children
  - Maximum safe surgical resection followed by
  - High dose radiation treatment with proton beam is the treatment of choice
  - Pediatric chordomas have better prognosis than adult chordomas except
  - For children less than 5 years of age, chordoma has aggressive behavior and poor prognosis

THANK YOU