Treatment Strategies in Childhood Craniopharyngioma

Case for Aggressive resections

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NEUROSURGEONS FOR KIDS

Disclosure

- No author/collaborator of this presentation has a disclosure……..

  But I do have biases. I trained in Virginia, when John Jane Sr. was aggressive in his management of suprasellar masses, overlapping for a brief time with Ed Laws and observing both surgeons.

Object

Current treatment of craniopharyngioma includes:

1. Complete surgical removal
2. Incomplete surgical removal with
    A. No adjuvant treatment
    B. Radiation therapy
    C. Intracystic ablation
        a. Bleomycin
        b. P32
        c. Other(e.g. Interferon)

The authors propose that complete resection is the goal of surgical treatment in craniopharyngioma

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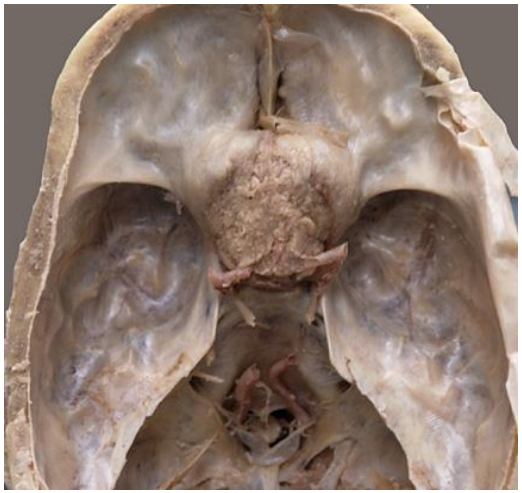
Incidence



Incidence of 0.1cases/100,000 person years[1]

6.6% of sellar tumors[1]

[1] Central Brain tumor Registry of the United States: Primary Brain Tumors in the United States, 1997-2001:Statistical Report. Hinsdale IL:Central Brain tumor Registry of the United States: 2004.

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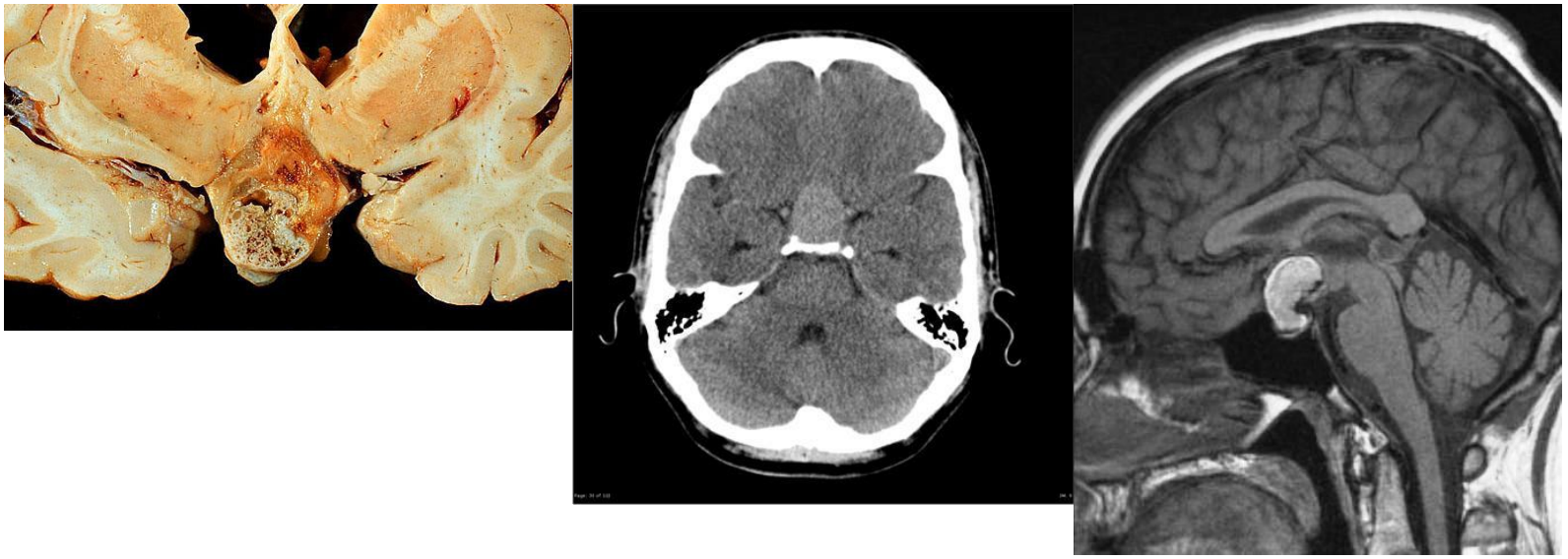
Anatomy



Anatomy complicated by proximity to:

1. Pituitary gland
2. Optic chiasm/tracts/nerves
3. Hypothalamus
4. Cavernous sinus/ICAs(if large)

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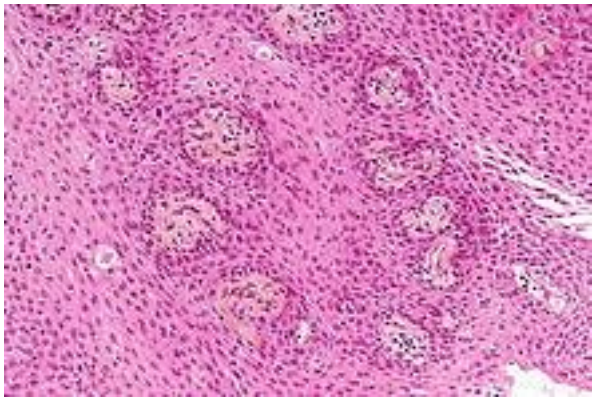
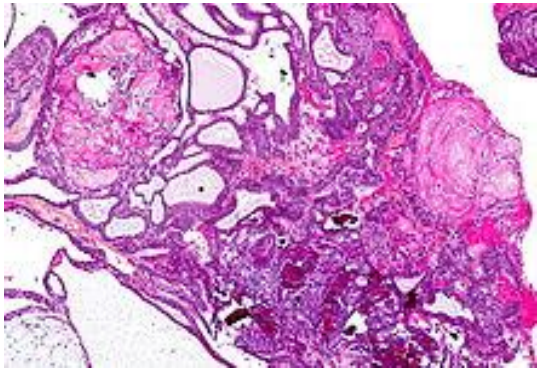
Pathology



Craniopharyngiomas are disembryogenetic tumors whose pathology takes 1 of 2 distinct forms



Papillary

Adamantinomatous

Adamantinomatous pathology may slightly increase the risk of recurrence per:

1. Adamson TE, Wiestler OD, Kleihues P, Yasargil MG: Correlation of clinical and pathological features in surgically treated craniopharyngiomas. J Neurosurg 73:12-17, 1990

2. Szeifert GT, Sipos L, Horvath M, et al: Pathological characteristics of surgically removed craniopharyngiomas: analysis of 131 cases. Acta Neurochir(Wien) 124:139-143, 1993.

3. Tena-Suck ML, Salinas-Lara C, Arce-Arellano RI et al: Clinico-pathological and immunohistochemical characteristics associated with recurrence/regrowth of craniopharyngiomas. Clin Neurol Neurosurg 108:661-669, 2006

Treatment Controversy

- Craniopharyngiomas are benign tumors with a non-benign course/anatomy

- The goal of any treatment with any disease is to maximize quality/quantity of life with minimal morbidity and mortality

Evolution of Surgical Technique

- '50s-'60s – Donald Matson(BCH) applied the right subfrontal approach(followed later by R. Michael Scott, Harold Hoffman, etc)
- '70-'80s – John Jane Sr and Gazi Yasargil promoted an expanded pterional approach
- '80s-'90s – Ed Laws advocated the extended trans-sphenoidal/endoscopic skull base approach
- Lesser used approaches include trans-callosal and infra-temporal

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What are the risks and benefits of aggressive resection of craniopharyngiomas?

RISKS

Injury to surrounding brain tissue, including cognitive and hypothalamic dysfunction

Worsening endocrine status

Vision loss

Vascular injury

CSF leak

BENEFITS

Improved long term survival

Reduced recurrence rate

Obviate need for adjuvant therapy(intracystic or XRT)

Reduce risk of requiring second surgery, with its concomitant much higher risk of complications(see list on left)

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RISKS

Injury to surrounding brain tissue, including cognitive and hypothalamic dysfunction

Hypothalamic dysfunction may be measured, in part, by incidence of morbid obesity

17% of children with craniopharyngioma are morbidly obese on presentation[1]

65% of children are morbidly obese surgical management of craniopharyngioma[2]

HOWEVER, 90% of children are morbidly obese after surgery plus radiation therapy[2]

The incidence of morbid obesity or any other hypothalamic dysfunction has never been shown to be higher in patients with gross total resection of their craniopharyngioma(although gross total resection may not be possible in those patients in whom there is significant hypothalamic invasion/adhesion).

1 Fournier A, Pauli A, Cecile JP et al: Craniopharyngioma having the appearance of isolated obesity. J Sci Med Lille 1968, 86(3):171-175.

2 Muller HL, Emser A, Faldum A et al: Longitudinal study on growth and body mass index before and after diagnosis of childhood craniopharyngioma. J Clin Endocrinol Metab 2004, 89:3298-3305.

RISKS

Worsening Cognitive Status

Early studies reported “No changes were found in the overall IQ verbal and performances scores before and after operation.”[1]

More recent studies raise the concern that transcranial surgery has a higher incidence of cognitive decline(loss of IQ points) for gross total resection than sub-total resection + XRT with <5 year follow-up(and did not meet statistical significance)[2]

Trans-sphenoidal approaches have been shown to have a lower incidence of cognitive decline than trans-cranial approaches(equal to, if not better than, sub-total resection)[3]

1 Galatzer A, Nofar E, Beit-Halachmi N et al: Intellectual and psychosocial functions of children, adolescents, and young adults before and after operation for craniopharyngioma, Child: Care, Health, and Development, 1981, 7:307-316.

2 Merchant TE, Kiehna EN, Sanford RA, et al: Craniopharyngioma: the St. Jude Children’s Research Hospital Experience 1984-2001, Int J Radiat Oncol Biol Phys, 2002, Jul 1;53(3):533-42.

3 Elliot RE, John JA jr, Wisoff JH: Surgical Management of craniopharyngiomas in children: Meta-analysis and comparison of trans-cranial and trans-sphenoidal approaches, Neurosurgery, 2011 69;630-643.

RISKS

Worsening Cognitive Status

Therefore, perhaps the danger is not in the extent of resection but in the:

1. Location
2. Adhesion
3. Approach

RISKS

Vision Loss

Outcome	Biopsy	STR	GTR	p Value†
postop visual dysfxn				
yes	12 (14)	3 (4)	11 (6)	0.03
no	74 (86)	69 (96)	180 (94)	

2012 meta-analysis from UC-SF documents the highest incidence of visual dysfunction in patients who underwent biopsy only

Clark AJ, Cage TA, Aranda D: Treatment-Related morbidity and the management of pediatric craniopharyngioma-A systematic review, 2012, JNS-Ped(10); 293-301.

RISKS

Vascular Injury and CSF Leak

Almost all reports of vascular injury are case reports

Dr. Sutton from CHoP did report a 15.7% incidence of “fusiform dilatation of the carotid artery following radical surgical excision of craniophayrngioma.” [1]

CSF leak is rare except for the extended trans-sphenoidal approach, in which the post-operative CSF leak rate is documented to be 3.8%[2]

[1]Sutton LN: Vascular complication of Surgery for Craniopharyngioma and Hypothalamic Glioma, Pediatr Neurosurg 1994; 21: 124-128.

[2] Leng LZ, Greenfield JP, Souweidane MM et al: Endoscopic, endonasal resection of craniopharyngiomas: analysis of outcome including extent of resection, cerebrospinal fluid leak, return to pre-operative productivity, and body mass index, Neurosurgery 2012 70(1):110-123.

BENEFITS

Improved Long Term Survival

In these pathologically benign tumors, the mortality is sufficiently low that no study ahs ever shown improved long term survival with any treatment modality

BENEFITS

Reduced Recurrence Rate

Recurrence rates for GTR in craniopharyngioma has been documented to be between 19-27%.[1,2]

91-100% with sub-total resection[1,2]

20-37.5% with STR + XRT[1,2]

[1]Caldarelli M, Massimi L, Tamburriini G: Long-term results of the surgical treatment of craniopharyngioma: the experience at the Policlinico Gemelli, Catholic University, Rome, Child's Nervous System 2005 21:747-757.

[2] Tomita T, Bowman RM: Craniopharyngiomas in children: surgical experience at Children's Memorial Hospital, Child's Nervous System 2005 21:729-746.

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BENEFITS

Obviate Need for Adjuvant Therapy & Reduced Risk of Requiring Additional Surgery

These really go hand in hand. Most centers do not treat unless there is a recurrence in patients with GTR.

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Most Recent Meta-analysis

Table 1

Variable	Value
sex (n = 531)	
male	243 (46)
female	288 (54)
age in yrs (n = 527)	
median	4
range	0–19
preop endo dysfxn (n = 145)	
yes	89 (61)
no	56 (39)
preop visual dysfxn (n = 161)	
yes	96 (60)
no	65 (40)
operation (n = 531)	
biopsy	165 (31)
STR	148 (28)
GTR	218 (41)
RT (n = 531)	
yes	156 (29)
fRT	110 (70)
SRS	47 (30)
no	375 (71)
intracystic chemo (n = 531)	
yes	76 (14)
no	455 (86)

Table 2

Outcome	Biopsy	STR	GTR	p Value†
postop endo dysfxn				
yes	18 (21)	39 (55)	112 (59)	<0.001
no	68 (79)	32 (45)	79 (41)	
postop DI				
yes	5 (6)	7 (10)	48 (25)	<0.001
no	81 (94)	64 (90)	143 (75)	
postop obesity				
yes	2 (2)	1 (1)	11 (6)	0.18
no	84 (98)	70 (99)	180 (94)	
postop panhypopit				
yes	2 (2)	10 (14)	30 (16)	0.006
no	84 (98)	61 (81)	161 (84)	
postop visual dysfxn				
yes	12 (14)	3 (4)	11 (6)	0.03
no	74 (86)	69 (96)	180 (94)	
postop neuro dysfxn				
yes	1 (1)	5 (7)	20 (11)	0.02
no	85 (99)	66 (93)	171 (89)	

Table 3

Outcome	GTR	STR + RT	p Value
postop endo dysfxn			
yes	108 (59)	11 (46)	0.22
no	75 (41)	13 (54)	
postop DI			
yes	46 (25)	1 (4)	0.02
no	137 (75)	23 (96)	
postop obesity			
yes	10 (6)	1 (4)	1.0
no	173 (94)	23 (96)	
postop panhypopit			
yes	27 (15)	7 (29)	0.08
no	156 (85)	17 (71)	
postop visual dysfxn			
yes	9 (5)	1 (4)	1.0
no	174 (95)	23 (96)	
postop neuro dysfxn			
yes	20 (11)	0 (0)	0.14
no	163 (89)	24 (100)	

Clark AJ, Cage TA, Aranda D: Treatment-Related morbidity and the management of pediatric craniopharyngioma-A systematic review, 2012, JNS-Ped(10); 293-301.

Meta-analysis Conclusion

"Although subject to the limitations of a literature review, this report suggests that GTR is associated with increased rates of endocrinopathies compared to STR + RT, and this should be considered when planning goals of surgery."

Clark AJ, Cage TA, Aranda D: Treatment-Related morbidity and the management of pediatric craniopharyngioma-A systematic review, 2012, JNS-Ped(10); 293-301.

Confounding Factors

Author bias – The studies with the strongest bias against aggressive surgery were always those whose first author was a radiation oncologist(e.g. Dr. Merchant at St. Jude's).

Literature reviews – No centers had large enough patient volumes to meet statistical significance for most criteria, meaning one ended up comparing dis-similar patient populations

Orlando Experience

In the last 15 years, we have treated 21 unique patients with craniopharyngioma(19 children and 2 adults).

Serious neurological complications occurred in 2(carotid injury in an adult and chiasmatic injury in a teenager) of the first 4.

No neurological post-operative complications have occurred since(although endocrinopathy is present in 20 post-operatively-19 pre-operatively).

Repeat surgery is much more difficult, particularly after XRT.

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Recommended Treatment Paradigm

FIRST DO NO HARM

Gross total resection is the goal for initial surgery in all patients with craniopharyngioma.

Choose the approach that best suits the anatomy.

Use all the tools in your armamentarium.

However, don't be a hero. If the hypothalamus is involved, back away. If the lesion is attached to neurovascular structures, back away.

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Conclusions

- Initial treatment of craniopharyngioma requires aggressive surgical management by an experienced team in an effort to remove as much as is safely possible.

Future Questions

- What does gross total resection mean?
- Does XRT reduce recurrence even in those without evident disease?
- Do craniopharyngiomas need to be treated differently based on presence/volume of cyst?
- How to avoid hydrocephalus/recurrence in this patient population?

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Thank you!