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Congenital craniopharyngioma: report of two cases

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Introduction:
Craniopharyngiomas are slow growing epithelial tumors located in the sellar or suprasellar region of the brain. Adamantinomatous subtype affects mainly children and accounts for 5-10% of all intracranial paediatric tumors. Diagnosed antenatal and neonatal craniopharyngiomas are very rare, about 40 such cases have been detected to date. They are characterized by large size, progressive hydrocephalus, and a poor prognosis.

Aim:
The aim of the study was to analyze the clinical symptoms and treatment efficacy in children with a diagnosis of congenital craniopharyngioma (adamantinomatous subtype).

Materials and Methods:
A retrospective analysis included two children with craniopharyngioma diagnosed in prenatal period (28 hbd) and in the second month of life.

Results:

Case 1: The first patient was diagnosed at 28 Hbd of pregnancy using an MRI scan. A 36-week gestation boy was delivered by cesarian section. The newborn weighed 3410g and scored 9 points on APGAR scale. Postnatal MRI of the brain showed solid-cystic tumor with the solid part measuring 49x40x58 mm and the cystic part: 29x24x31 mm in the suprasellar region. Four weeks later, due to an increasing hydrocephalus, the baby underwent radical resection. It was diagnosed with an adenohypophysis, diabetes insipidus, and blindness. Aged 7 now, the boy suffers from epilepsy, hypotonia and is disabled.

Case 2: A 39-week-gestation girl was from uneventful pregnancy and normal vaginal delivery. At birth, she weighed 3680 g and scored 9 points on APGAR scale. At 2 months of age, due to vomiting, respiratory distress and bradycardia up to 40/min, the girl was hospitalized. The MRI of the brain revealed the presence of a mass measuring 22x26x24 mm in the supra and intrasellar region. At the 5 months of age, the baby underwent radical resection. After the surgery, an adenohypophysis and temporary diabetes insipidus (1-year duration) was diagnosed. From 1st to 18th year of age, growth hormone therapy was used. Now, the 18-year-old girl measures 167,6 cm of height, weights 67,0 kg and is a capable student.

Conclusions:
Congenital craniopharyngiomas are rare tumors which are characterized by a wide spectrum of specific symptoms, complex treatment and high mortality, but some patients are experiencing a good quality of life.
Evaluation of immunohistochemical prognostic factors for craniopharyngiomas recurrence (Rosenthal fibers, Ki-67 labeling index, p63 protein expression).

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ABSTRACT
Craniopharyngioma is a benign tumor of the sellar region, classified by WHO (2016) as grade 1 tumor. It constitutes 5.6-14,1% of CNS tumors in children. The incidence of craniopharyngioma is 0.5-2 / million / year. Although it is a benign histopathological tumor, it tends to infiltrate growth and recurrence.

AIM
Evaluation of immunohistochemical prognostic factors for craniopharyngiomas recurrence (Rosenthal fibers, Ki-67 labeling index, p63 protein expression).

RESULTS
In 85 patients with adamantinomatous craniopharyngiomas histopathological examination was extended with immunohistochemistry, in tumor sections using the monoclonal sera, the Ki67 proliferation index and p63 protein expression, as well as the presence of Rosenthal fibers, was determined. In 11 patients, Ki67 and p63 were also determined in the recurrent tumor (recurrence/tumor progression).

There were no statistically significant differences between the distribution of Ki67 proliferation index values in preparations from patients in whom no tumor recurrence was observed in relation to those patients in whom the event occurred (median 3.0 and 2.5%, p = 0.67). The median values of the Ki67 proliferation index in the progression and recurrence groups differed significantly (1 and 4% respectively). These differences were not statistically significant (p = 0.067), a clear trend was observed for higher Ki67 values in recurrent tumors. Despite the lack of statistical significance (p = 0.61), there was also a trend towards higher Ki67 values in recurrent tumors, the median Ki67 in the primary tumor was 3.0 (values from 0 to 20%), in the recurrent tumor 5.0 (0-14%).
The p63 protein was overexpressed in 68.6% of primary and 63.6% recurrent tumors. There was no significant difference in the distribution of p63 protein in primary tumors with and without recurrence (median equal to +2, p = 0.33). There was no significant difference in p63 protein expression in the recurrent or progressive group (p = 0.645), median equal to +2. Medians of p63 protein expression in the primary and recurrent tumor had similar values (p = 0.558).

In the immunohistochemical study, Rosenthal fibers were found in 23/100 primary tumors (23%), 7/23 tumors with relapse and 16/77 without recurrence. There was a statistically significant correlation between the presence of Rosenthal fibers and tumor recurrence (p = 0.001).

CONCLUSION
The prognostic factor for the recurrence of craniopharyngioma was the presence of Rosenthal fibers, there was no statistically significant relationship of tumor recurrence with the Ki76 value and p63 protein expression.
Rathke's cleft cysts, xanthogranulomas and craniopharyngiomas: clinical and histopathological features in a single center cohort

Y. Wang, A. Koch, S. Hammersen, D. Moskopp

Objective: The treatment of epithelial lesions of the sellar region, especially of craniopharyngiomas, can be challenging as outcome may be poor due to severe endocrinological or neurological dysfunction. The histopathological differentiation may be difficult due to the limiting amount of cells. We investigated the clinical outcome in our cohort, as well as the molecular pathological features.

Method: 317 patients with sella pathology underwent surgery between 2007-2017. To determine the clinical outcome, ophthalmological and endocrine evaluations were performed before and after surgery, as well as complications and recurrence rate. Median follow-up was 32 months. BRAF and CTNNB1 mutation status were not only investigated in craniopharyngiomas, but retrospectively also in surgical samples initially classified as Rathke's cleft cyst and xanthogranuloma.

Results: 35 patients with epithelial tumor of the sellar region underwent surgery. Histopathological investigation revealed the presence of 12 craniopharyngiomas (9 adamantinomatous, 3 papillary), 16 Rathke cysts and 7 xanthogranulomas. In 1 case the lesion was initially classified as xanthogranuloma, after additional identification of BRAF mutation re-evaluated as craniopharyngioma. Prior to surgery chiasmal syndrome was present in 8 patients with craniopharyngioma, 2 patients suffered from panhypopituitarism and 2 patients showed mild pituitary deficiency. After surgery CSF leakage occurred in 1 case and visual acuity improved in 6 cases (50%). 4 patients (33%) suffered from severe endocrine disorders. 2 patients showed tumor recurrence and underwent repeat surgery after 6 and 8 months. In long-term follow-up 3 patients died due to septic shock with severe and acute panhypopituitarism.

Conclusion: This study provides a detailed description of the clinical and histopathological features in a well-defined cohort of patients with rare epithelial lesions around the sellar region. The identification of mutation status allows the detection of craniopharyngiomas in samples with limited lesional cells and should be routinely performed.
Periostin Concentrations in Childhood-onset Craniopharyngioma Patients

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Purpose: The expression of the extracellular matrix protein periostin has been found to be increased in adamantinomatous craniopharyngioma-associated fibroblasts. It has been further identified as a novel marker for Non-Alcoholic Fatty Liver Disease (NAFLD). Half of childhood-onset craniopharyngioma (CP) patients with hypothalamic involvement develop a NAFLD. We hypothesized that periostin concentration is elevated in CP patients with pathological hepatic parameters.

Methods: We analyzed 35 patients with childhood-onset CP, 3 patients with isolated growth hormone deficiency (GHD), 5 patients with low insulin-like growth factor (IGF)-1 (IGF-1D) and 7 healthy controls. Periostin concentration was determined in serum (34 CP, 3 GHD, 5 IGF-1D and 7 healthy controls), urine (27 CP, 3 GHD, 5 IGF-1D and 7 healthy controls) and saliva (18 CP, 3 GHD, 3 IGF-1D and 7 healthy controls).

Results: Periostin serum, urine and saliva concentrations in CP patients were similar to concentrations of the other groups. Hypothalamic involvement/hypothalamic lesion as well as hepatic enzymes were not associated with elevated periostin concentrations. However, due to low patients numbers with pathological hepatic parameters (8 of 35 CP showed increased hepatic enzymes) no conclusions can be drawn from measured periostin concentrations in serum. Interestingly, the subgroup of patients with low IGF-1 levels showed elevated concentrations of serum periostin when compared with other groups.

Conclusions: Periostin does not seem to be a suitable marker for NAFLD in childhood-onset CP. However, the association between low IGF-1 levels and periostin should be part of further investigations.
Long-term psychosocial outcomes of paediatric craniopharyngioma survivors: A systematic review

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Background: Paediatric craniopharyngioma is a benign epithelial brain tumour originating in the Rathke's pouch. Due to the tumour's proximity to vital structures and aggressive treatment, survivors are often left with chronic conditions including impaired pituitary function and visual problems. This morbidity may lead to an increase in psychological problems and poor social outcomes.

Aim: To conduct a systematic review to determine the long-term psychological and social consequences of craniopharyngioma at least 5 years after diagnosis.

Method: Medline, PsychINFO, EMBASE, and Web of Science were searched for relevant studies published after 2004 that included self-report measures of psychological and social outcomes in craniopharyngioma survivors more than 5 years post-diagnosis.

Results: Of the 548 papers identified in the initial search, 8 met the inclusion criteria. All were cross-sectional studies. Five studies reported good/fair overall quality of life but all highlighted significantly low scores for mental health. Questionnaires that assessed psychological outcomes consistently highlighted symptoms of depression and anxiety in survivors, compared to age-matched controls. Most survivors completed or attended a mainstream school, but three studies reported that patients had experienced problems in school. Four studies reported that a high proportion of patients were still living with their parents, highlighting an issue of independence with young adult survivors.

Conclusion: The diversity of measures used in these studies and outcomes reported limited the analysis of patterns of adverse psychosocial outcomes. However, the results of this review suggest that there is an unmet clinical need for psychosocial support for craniopharyngioma survivors. Well-designed, context-specific studies using large homogenous groups with in-depth statistical analysis are needed to benefit future interventional research.
Hypothalamic Hyperphagia Post Craniopharyngioma Resection

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We describe a case of severe hypothalamic hyperphagia post craniopharyngioma resection. The proband presented at 4.78 years with 6 months history of headache, 2 months history of poor appetite and marked weight loss (3.8kg), and a 2 week history of vomiting and irritability. Examination identified left ptosis, left optic disc pallor and bilateral reduced visual acuity. Her weight, height and body mass index (BMI) at presentation were 13.5 kg (-2.31 SDS), 100 cm (-1.67 SDS) and 13.5 kg/m² (-1.70 SDS).

Investigations showed normal full blood count, liver and renal function and negative coeliac screen. MRI head showed a large, heterogeneous, partly solid and partly cystic suprasellar mass measuring 4x4.4cm (axial) and 5.4cm (craniocaudal). Posteriorly, the mass splayed both cerebral peduncles and compressed the third ventricle with dilatation of lateral ventricles. Marked calcification was seen within the suprasellar and hypothalamic region on CT head.

Endocrine investigations showed normal thyroid function (fT4 14.3pmol/L, TSH 1.5mU/L), normal prolactin (545mU/L), undetectable IGF1 (<3.3nmol/L) and normal response to standard Synacthen test (peak cortisol 1050nmol/L). Serum alpha-fetoprotein and β-HCG (human chorionic gonadotropin) were normal.

She underwent endoscopic fenestration of a large tense cyst and biopsy of tumour mass, followed by near complete tumour resection through right sub-frontal craniotomy. Histological appearances were of adamantinomatous craniopharyngioma (WHO grade 1). Following resection, she developed central diabetes insipidus, secondary adrenal and thyroid insufficiency and was commenced on appropriate hormone replacement. Growth hormone treatment was added after 3 months.

Within 3 weeks after surgery, she was severely hyperphagic and gained 5 kg weight (Weight SDS +0.36; ΔWeight SDS 3.01). Psychological input and medical treatment (dexamphetamine 5 mg oral twice daily) was commenced with some improvement. On return to school, she sneaked food from other pupils.

Unfortunately, craniopharyngioma recurred within 6 months as 2 cysts (22 x 22 mm suprasellar; 24 x 22 mm retroclival moulding the left side of pons and midbrain) with recurrence of hydrocephalus. She underwent a second debulking surgical procedure through the previous skull opening prior to conventional photon radiotherapy (54Gy in 30 fractions). At this stage (age 6.14 years), she had attained peak BMI (+2.92 SDS). She showed an excellent response to GH replacement. Hyperphagia was managed by parents and teachers at school with behavioural modification with eventual stabilisation of BMI. At last follow up (age 9.05 years), her height, weight and body mass index (BMI) was +0.46 SDS, +1.83 SDS and +2.13 SDS respectively.
Low concordance between surgical and radiological assessment of degree of resection and treatment-related hypothalamic damage: results of KRANIOPHARYNGEOM 2007

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Background Assessment of presurgical hypothalamic involvement (psHI) and treatment-related hypothalamic damage (trHD) is relevant for the decision on risk-adapted treatment and rehabilitation strategies in craniopharyngioma.

Patients and methods 129 surgical reports of childhood-onset craniopharyngioma patients recruited 2007–2014 in KRANIOPHARYNGEOM 2007 were analyzed. Data on psHI were available based on surgeon’s (63%), reference neuroradiologist’s (95%), and local radiologist’s (23%) assessment. The surgical degree of resection (DoR) was assessed by neurosurgeon (95%), reference neuroradiologist (73%), and local radiologist (61%). TrHD was assessed by neurosurgeon (33%), by reference neuroradiologist (95%), and by local radiologist (2%). Neurosurgical center size was categorized based on patient load.

Results Surgical assessments on psHI (n = 78), DoR (n = 89) and trHD (n = 42) as documented in surgical reports could be compared with the assessment of respective parameters by reference neuroradiologist. Differences with regard to DoR (p = 0.0001) and trHD (p < 0.0001) were detectable between surgeon’s and reference neuroradiologist’s assessment, whereas psHI was assessed similarly. Concordance for DoR and trHD was observed in 48 and 62%, respectively. Surgeons estimated a higher rate of complete resections and a lower rate of trHD. Neuroradiological reference assessment of trHD had higher predictive value for hypothalamic sequelae than surgical assessment. Observed differences were not related to neurosurgical center size.

Conclusions Observed differences between surgical and neuroradiological estimation of risk factors in craniopharyngioma support the necessity of neuroradiological reference review to assure standards of quality. This could be established by central internet-based neuroradiological review in KRANIOPHARYNGEOM 2007. Standardization of surgical reports including specific assessment of tumor/damage location is recommended.
Quality of Life and Growth after Childhood Craniopharyngioma: Results of the Multinational Trial KRANIOPHARYNGEOM 2007

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Context: Quality of life (QoL) after childhood-onset craniopharyngioma (CP) is frequently impaired due to tumor and/or treatment-related factors such as endocrine deficits and hypothalamic involvement/lesions.

Patients and methods: In a multinational trial, we prospectively analyzed parental and self-assessment of CP patient QoL at 3 months, one and 3 years after CP diagnosis related to growth hormone (GH) substitution. 47 of 194 CP recruited between 2007 and 2015 in KRANIOPHARYNGEOM 2007 were analyzed for QoL one and 3 years after CP diagnosis. QoL was assessed by Pediatric Quality of Life (PEDQOL) questionnaire and PEDQOL scores of parental and self-assessed QoL during 3 years follow-up after CP diagnosis were analyzed.

Results: Parents estimated QoL of their children worse than patients did themselves. GH substitution had no relevant effect on short-term weight and height development. CP patients GH-treated at 3 years follow-up presented at baseline (one year after diagnosis, before GH substitution) with reduced self-assessed QoL when compared with GH non-treated CP. QoL stabilized during 1–3 years of follow-up in GH-treated patients, whereas non GH-treated patients experienced decreases in autonomy (p=0.03), cognition (p=0.01), and physical function (p=0.04).

Conclusions: Parents assess QoL in CP survivors worse than their children. GH substitution should be considered as a therapeutic option to ameliorate imminent impairments of QoL after CP.
Intracystic α-interferon in multiply-recurrent adamantinomatous craniopharyngioma

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INTRODUCTION

Majority of childhood craniopharyngioma has adamantinomatous histology with cyst formation. Treatment of choice is surgical resection with a role for adjuvant radiotherapy. Other treatment options include instillation of sclerosing agents for recurrent cystic tumours.

OBJECTIVES

To present our case report of multiply-recurrent adamantinomatous craniopharyngioma and the use of intracystic interferon as a treatment modality for cystic recurrences.

METHODOLOGY

Clinical data was retrieved from case records and corroborated with radiological and pathological information.

RESULTS

Our patient was first diagnosed at 5 years old with a large suprasellar tumour for which near total resection was achieved in two consecutive surgeries, followed by stereotactic radiotherapy upon primary site recurrence. Metastatic lesions at the right frontal lobe, left thalamus/third ventricular space and anterior interhemispheric region were detected 18 months from first diagnosis, and were completely resected.

Subsequently, she required repeat resections for recurrent lesions at the anterior interhemispheric and suprasellar regions, and received stereotactic radiosurgery for a pineal lesion.

A new left cerebellopontine angle cystic lesion detected at 6 years post-diagnosis required repeat intermittent aspirations through the Omaya reservoir. Intracystic α-interferon was delivered over 3 months with good response seen on MRI. However, recurrence was noted 9 months after cessation of intracystic interferon, and required surgical resection.

Histology of various tumour resections show adamantinomatous craniopharyngioma. CTNNB1 mutation was detected on genomic testing.

Eight years post-diagnosis, recurrent lesions at the skull base, pineal and suprasellar regions have again surfaced. Clinically, she has hypothalamic obesity, panhypopituitarism and minimal vision with light perception.

CONCLUSION

Childhood craniopharyngioma with its endocrine and visual deficits is a chronic disease in which optimal treatment of multiple recurrences can be very challenging. Intracystic interferon can be used for cystic recurrences.
ENDOSCOPIC ENDONASAL TRANSSPHENOIDAL APPROACH FOR PEDIATRIC CRANIOPHARYNGIOMAS: A CASE SERIES

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Aims: Most series of pediatric craniopharyngiomas includes only a small number of patients treated using an endoscopic endonasal transsphenoidal approach (EETA). It has been performed especially in cases of purely sellar and infradiafragmatic lesions. The aim of this paper is to analyze our series of pediatric patients with craniopharyngiomas removed by EETA.

Methods: The authors retrospectively evaluated 12 craniopharyngioma pediatric patients who underwent an EETA between 2012 and 2017 at IOP/GRAACC/UNIFESP. Data regarding tumor location, imaging studies, surgical resection and endocrinological disturbances were collected.

Results: From the 12 patients included in this series (8 boys and 4 girls), 9 underwent transsphenoidal surgery as the primary procedure and 3 as a secondary surgery after previous craniotomy. The average age at treatment was 6.7 years (range 3–15y). 7 tumors were sellar/suprasellar, 3 extended into third ventricle, and 2 were purely intra-sellar. Complete tumor resection was achieved in 7 patients, subtotal removal in 4 and partial in 1 (5%). There were no cases of CSF leaks. After an average follow up of 2.3 years (range 2-4y), 8 patients (66%) progressed to panhypopituitarism.

Conclusion: EETA is a safe, feasible and an effective surgical approach to remove craniopharyngiomas in children. There was no age limit. Poorly pneumatized sphenoid sinus were not considered contraindications to EETA. Tumor location with extension from the sellar to the suprasellar compartment or to the third ventricle were not contraindications either. Panhypopituitarism occurs at same rates as those obtained after transcranial surgery.
Childhood Cystic Craniopharyngioma: 15 years of intra-tumoral chemotherapy with interferon-alpha at IOP/GRAACC/UNIFESP.

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INTRODUCTION: Although histologically benign, craniopharyngiomas are clinically aggressive tumors, difficult to manage and associated with poor quality of life for the patients. Gross total resection was advocated for many years, despite post operatory clinical conditions. Since 2002, patients with cystic craniopharyngiomas have been treated with intralesional interferon-alpha (IFN-alpha) at IOP/GRAACC/UNIFESP. The goal of this treatment is to control or reduce the volume of tumor, decreasing or delaying the morbidity from conventional treatment.

OBJECTIVE: To analyze the several treatment strategies and outcomes of craniopharyngioma patients in 15 years of experience in a single institution.

METHODS: The authors retrospectively evaluated 110 craniopharyngeoma patients treated between 2002 and 2017, at IOP/GRAACC/UNIFESP. Data regarding initial clinical presentation, body mass index (BMI), endocrinological complications, treatment modalities and outcomes were collected.

RESULTS: From 110 patients treated with craniopharyngioma at our institution, 95 patients were eligible for evaluation and 15 excluded for loss of follow-up. Fifty-five were boys and 40 girls. The mean age at treatment was 10.5 years (range 3.25-25.08). Fifty-six percent of children presented with signs and symptoms of intracranial hypertension, 24% with visual impairment and 38.5% with endocrinological disturbances. At the time of diagnosis, the mean BMI was 20.48 kg/m^2 (range 12.7-32.8). Predominantly cystic tumors (cystic portion ≥ 60% of total lesion volume) occurred in 38 children and were treated with intralesional interferon-alpha; of these patients, 13 progressed to surgical intervention and adjuvant radiotherapy. Among the remaining 52 patients, 9 were treated with microsurgery only, 29 with microsurgery + radiotherapy, 12 with endoscopic transesphenoidal surgery + radiotherapy and 7 patients, in whom the tumors that recurred after surgical treatment followed or not by radiotherapy, with intracystic interferon-alpha as alternative therapy. In total, 45 (47%) patients were treated with intralesional IFN-alpha chemotherapy, 38 treatment-naïve patients 7 had already received other therapies. Side effects of interferon alpha were well tolerated. No treatment was discontinued. The mean BMI of patients treated exclusively with interferon-alpha was 22.88 kg/m^2 (ideal weight), with IFN-alpha + microsurgery was 31.23 kg/m^2 (grade 1 obesity) and microsurgery + radiotherapy was 29.65 kg/m^2 (overweight). After treatment, 61 cases (65%) progressed to panhypopituitarism. The mean follow up was 7.13 years (range 1-14), and 11 deaths occurred. Currently 41 patients are out of treatment.

CONCLUSION: The management of children with craniopharyngiomas is very challenging and several efforts have been made to improve the prognosis so unfavorable for these patients. The significant morbidity associated with important recurrence rates require that these patients be treated as having chronic disease. The reference centers should be able to offer several therapeutical options and the treatment is individualized to each patient. Intracystic therapy with interferon-alpha offers best body mass index control. However, panhypopituitarism is the most common and important complication irrespective of treatment modalities. The intracystic therapy with interferon-alpha has been show to be effective in the control of predominantly cystic tumors, in prepubertal patients, in patients without hormonal deficits or in cases of tumor recurrence after surgery or radiotherapy.
Results of combined (surgery +/- radiation) treatment of 135 children with craniopharyngioma (CP)

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Patients and methods. We analyzed 135 CP patients primary operated in Burdenko Neurosurgery Institute (188 surgical procedures) and 75 radiated CP patients in 2005-2012 (standard fractionated RT 54 Gy in 30 pts, hyperfractionated on Cyberknife in 30 pts (3-5 fr, sum dose 18-27.5 Gy), and radiosurgery (γ-knife in 9 pts and linear accelerator in 6 pts, dose 10-20 Gy, M 16 Gy). Neurologic, endocrine, visual functions, QoL and neuroimaging data before and after treatment were assessed.

Patients were divided in 2 groups according to CP location: 48.5% endosellar (ESCP), and 51.5% suprasellar (SSCP).

Surgical treatment included tumor excision (total in 34.9%, subtotal in 25.7%, and partial in 24.8% cases), transnasal cyst evacuation in 10.1% pts, Omaya implantation in 4.5%.

Results.

PFS: 5-year PFS after total resection was 79%, it was significantly (p<0.01) higher then after nonradical resection 20% (after subtotal resection 4%, after partial resection 37%, transnasal cyst aspiration 27%, and Omaya implantation 0%). There was no significant difference in PFS between subtotal and partial tumor resection. 5-year PFS after subtotal or partial tumor resection followed by radiotherapy/radiosurgery was 86% - similar as after radical tumor excision.

There was no significant difference between incidence of endosellar and suprasellar tumor remnants growth, but in cases of endosellar CP relapse occurred significantly earlier (7.2 months after tumor resection), than in suprasellar (15 months after tumor resection), p=0.003 (M-U test).

50 patients were irradiated after surgery (M 2.3 months), and 25 pts after tumor relapse.

5-year PFS after adjuvant irradiation was 100%, bus after salvage RT/RS (at relapse, median in 24.9 months after surgery) it was 79%, though the difference was not significant (log-rank test, p=0.5).

Transient cyst enlargement after RT: Enlargement of cysts within 2.7-9 months (mean 3.5 months) after RT/RS was identified in 10 patients (11.4%). It was transient enlargement with spontaneous regression in 9 of them, one patient required surgery due to visual deterioration.

A stable irreversible cyst growth was detected in 8 cases (10.1%) significantly (p<0.01) later - in 16.6-48.9 months (mean 26.3 monts) after irradiation.

Vision function improved after surgery in 22%, worsened in 14%, and was stable in 64% cases. Visual function deterioration more frequently occurred in patients with severe vision impairment before surgery (X2, p=0.01). After RT/RS visual functions were stable in 78%, improved in 16%, worsened in 6% patients. Vision function didn't deteriorate after irradiation in any child with severe vision impairment.

Endocrine function depended from tumor location. Patients with ESCP had more prominent pituitary deficiency, than patients with SSCP (Table 1).

Table 1. The incidence (%) of panhypopituitarism and DI before and after surgery in children with different location of CP

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<tr>
<th></th>
<th>ESCP</th>
<th>SSSP</th>
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<tr>
<td></td>
<td>Before surgery</td>
<td>After surgery</td>
</tr>
<tr>
<td>Panhypopit</td>
<td>20%</td>
<td>90%</td>
</tr>
<tr>
<td>DI</td>
<td>23%</td>
<td>75%</td>
</tr>
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Tumor resection caused endocrine status deterioration: 80% after surgery had panhipopituitarism and DI (Table 2).

**Table 2.** Endocrine deterioration after surgical treatment in CP patients depended on degree of tumor resection (deterioration = + at least one new hormonal deficiency after surgery) (%)

<table>
<thead>
<tr>
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<th>Total</th>
<th>Subtotal</th>
<th>Partial</th>
<th>Transnasal cyst evacuation</th>
<th>Omaya</th>
</tr>
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<tbody>
<tr>
<td>Anterior pituitary</td>
<td>84%</td>
<td>41%</td>
<td>65%</td>
<td>29%</td>
<td>0%</td>
</tr>
<tr>
<td>DI</td>
<td>93%</td>
<td>75%</td>
<td>73%</td>
<td>75%</td>
<td>0%</td>
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Anterior pituitary deterioration significantly more often occurred after total tumor resection (p<0.01), than after other surgical procedures. DI occurred after total resection more often too, though it was not significant (Fisher exact p=0.07). The incidence of new hormone deficit after subtotal, partial resection or after transnasal cyst evacuation didn’t differ. There was no endocrine deterioration after Omaya implantation.

15/75 patients before radiation had partially preserved anterior pituitary function. Surprisingly, but only in 1/15 cases RT/RS induced new hormone deficit – adrenal insufficiency 3.5 years after radiation.

**Quality of life (QoL) and BMI:** QoL score didn’t correlate with sex, height SDS, DI, anterior pituitary hormone deficiency, or visual function. There was significant correlation between QoL score and age at surgery (R=0.4, p<0.01), and QoL score and BMI SDS (R=0.3, p=0.001). BMI SDS slightly increased after ESCP excision (from -0.1 to 0.3, difference is NS). In patients with SSCP BMI SDS significantly increased after total resection (from 0.06 to 1.6, p<0.001), and subtotal resection (from 0.5 to 1.5, p=0.005), and not significantly increased after partial resection or Omaya implantation (from 0.5 to 1.0, p=0.3). In SSCP group QoL score was significantly higher after partial resection/Omaya followed by RT, than after total resection (p=0.01)

**Mortality:** One patient died 1.5 months after tumor resection due to sepsis. 10 patients died in 1.3-9.1 yrs after surgery: four cases adrenal insufficiency during acute illness, two cases hepatic cirrhosis (one esophageal variceal hemorrhage, one hepatopulmonary syndrome), one patient severe uncontrolled hypernatremia and hyperglycemia, one patient uncontrolled tumor progression, and in two cases the reason of death was unknown.

**Conclusion:** Optimal treatment for patients with ESCP with panhypopituitarism and DI before surgery is total tumor excision (via transnasal or transcranial approach). In cases of cyst ESCP and partially preserved pituitary function optimal choice is transnasal cyst evacuation followed by adjuvant RT/RS. Endosellar CP remnants should be radiated within short period after surgery due to high risk of relapse.

The optimal management of SSCP with risk of hypothalamic involvement is limited surgery (partial/subtotal resection or Omaya implantation). In these cases RT/RS may be postponed to the moment of tumor progression due to later peak of relapse.

Cyst enlargement within 6 months after RT/RS is usually transient and rarely requires surgical treatment.

Conformal RT/RS is effective and relatively safe in terms of visual outcome and endocrine function.
Challenges, pitfalls and surgical limits in childhood craniopharyngioma

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Craniopharyngioma defines an intracranial embryonal, non-glial dysplastic tumor of perisellar region including the 3rd ventricle. In the realm of close anatomical vicinity – e.g. hypothalamus, brain stem, optic nerve and pituitary gland as well as the circle of Willis – operative management implies experience beside challenges including surgical limits to avoid operative pitfalls.

Neuroendoscopic routes in craniopharyngioma surgery are known as transnasal-transsphenoidal, transventricular and supraorbital assisted by endoscopy. Beside the classic fronto-pterional approach, neuroendoscopic procedures claim an increasing field of neurosurgical procedures for being both minimally invasive and less traumatic.

The transnasal-transsphenoidal route proves value not only as first time surgery but for recurrent solid and cystic lesions as well. In addition the transsphenoidal endoscopic approach is regarded superior to the microsurgical technique because peri- and suprasellar resectable tumor remnants can be identified by a 30 degree lens, in a so called looking around the corner fashion.

Meticulous anatomic pre-operative consideration is mandatory due to age related development of pneumatized sinuses including shaping of turbinates especially in children. Special interest should be given to the carotid eminences defining the lateral framing of the sella. It is crucial to be aware of their width at least around 0.8 cm defining the surgical corridor into the sellar. Otherwise surgery cannot be done endoscopically via this approach in children. All major lesions should be done by a binostil approach in liason with an experienced ENT surgeon sharing experience with the so-called naso-septal flap. As all craniopharyngioma are anatomically located in the subarachnoidal space water-tight closure of the dura is essential to avoid postsurgical CSF leakage risking meningitis.

Transventricular routes, using the physiological ventricular cavity suit nicely for intraventricular lesions especially cystic components. When entering the lateral ventricles one must be aware of the fornix because otherwise severe mnemonic deficits, or left/ right confusion might be clinically evident. When lesioning the hypothalamus, patients suffer from derangement of electrolytes, endocrine disturbances, coma and hypothalamic obesity.

If surgery is performed too close to the infundibular recess, diabetes insipidus can occur temporarily or continously. Special care must be taken with distorted anatomy to avoid vascular injury in close vicinity to the basilar artery and its prepontine branches to not run the risk of potentially lethal ICH/SAH. Prepontine cysts even can invade the brain stem to make neuroendoscopic procedure very limited in terms of cardiac arrest by brain stem irritation. Growing burr holes with herniating parenchyma after surgical closure have been reported in literature due to improper wound and dural closing. More solid tumor margins can be resected with endoscopic CUSA application or LISA laser.

After surgical pterional resection and postoperative radiation fusifom dilatation of the internal carotid artery (ACI) can be seen from time to time needing interventional treatment through neuroradiology.

Our series, consisting of n=34 pediatric patients, operated upon from April 2008 to December 2016. The youngest child was 2, the oldest 18 years, showing a mean age of 5,6 years. N= 7 patients faced surgery via a pterional approach, while all of them had intraoperative neuroendoscopic rectification of the resectional tumor amount, including visualisation of potential remnants, e.g. around the hypothalamus. N= 8 of them presented with craniopharyngioma as first time diagnosis, whereas n= 5 were referred to as recurrent cases. N=9 patients underwent transventricular endoscopic surgery alone, consisting of mainly cystic tumorous lesions. Unfortunately, only one patient, 14 years old, was followed in excellent clinical condition without hormonal substitution. The transventricular approach fitted
best for a child suffering complex heart failure, hemiparetic, blind due to chiasmatic cystic
tumor compression and on complete hormonal substitution. This case highlights nicely the
value of minimally invasive neuroendoscopy being highly effective.
Sometime histology can be difficult. N=1 patient had gross total resection of a supposed
solid craniopharyngioma via pterional surgery. She was operated upon in a transsphenoidal
technique only two months later presenting acute loss of vision due to chiasmatic
compression deriving from tumor progress. The histologic specimen came up with an
immature teratoma finally.
Taking into account minimally invasive endoscopic procedures, the pterional approach
warrants still its value without doubt. We feel all microsurgical cases should be reviewed
intraoperatively via endoscope, including 30 degree optics. The resectability of calcified
remnants around the hypothalamus and prepontine area can be controlled easily through
the endoscope.
To our understanding preoperative hypothalamic involvement by craniopharyngioma,
especially invading the posterior part of hypothalamus predicts a limited tumor resection to
avoid focal deficits both neurological and endocrinological. The hypothalamus represents the
neurosurgical landmark limiting surgical procedures to preserve neurological integrity.
Self- and Informant-rated Apathy in Childhood-Onset Craniopharyngioma Patients

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Introduction. The current study aimed to assess whether childhood-onset craniopharyngioma (CP) patients suffer from symptoms of apathy, and whether apathy scores, obtained from patients and members of their family(?), are related to depression.

Methods. Patients with childhood-onset craniopharyngioma (n=35) and matched healthy controls (each n=35) were asked to complete self-ratings of the Apathy Evaluation Scale, whereas informant-ratings were obtained from their close others. Depression was assessed using the German version of the Center for Epidemiological Studies Depression Scale. Apathy and depression were compared between patients and healthy controls using the nonparametric Mann-Whitney U test. Differences between self- and informant-rated apathy within the single groups were analyzed using the Wilcoxon Signed-Rank test.

Results. Compared to healthy controls, patients displayed significantly higher apathy levels in informant-ratings, but not in self-ratings. There was a significant discrepancy between self- and informant-rated apathy in patients. In addition, there was a tendency towards higher depression scores in patients compared to healthy controls.

Conclusions. This is the first study to show that patients with childhood-onset craniopharyngioma may be at high risk for apathy. Noteworthy, apathy levels in the patient group were judged to be high by their close others but not by the patients themselves, indicating that many patients were not fully aware of their impairments. Moreover, apathy was shown to be related to symptoms of depression. As apathy is associated with numerous adverse outcomes, affecting everyday life and vocational opportunities, future investigations are needed to identify specific risk factors for apathy.
Eating Behavior and Oxytocin in Childhood-onset Craniopharyngioma Patients

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**Background:** Severe obesity due to disease and/or treatment-related hypothalamic lesions (HL) frequently impairs quality of life in childhood-onset craniopharyngioma patients (CP). CP often show eating restraints or binge eating. Oxytocin, a peptide hormone produced in the hypothalamus and secreted by posterior pituitary gland, plays a major role in the regulation of eating behavior and body composition.

**Subjects and methods:** 34 CP and 73 healthy controls participated in a cross-sectional case-control study which aimed to investigate the associations between eating behavior/eating disorders, HL and OSC (oxytocin saliva concentrations). OSC were measured before and after standardized breakfast by immunoassay. Eating behavior was assessed using the Inventory for Eating Behavior and Weight Problems and the Inventory for Eating Disorders.

**Results:** CP with anterior plus posterior HL (grade 2) scored more pathological with regard to eating behavior and eating disorders associated with obesity than CP with a lower HL grade and healthy controls. Eating behavior in CP with anterior HL (grade 1) was more similar to that of healthy controls except their tendency for high dietary restraints. Decreases in postprandial compared to fasting OSC were associated with adverse eating behavior in both CP and healthy controls and with higher BMI SDS in CP.

**Conclusions:** This is the first study to show that different grades of HL are associated with distinct patterns of eating behavior. In addition, our results suggested that reduced postprandial compared to fasting OSC is associated with weight problems in CP and with adverse eating behavior and eating disorders in both CP and healthy controls.