Preservation of endocrine function after Ommaya reservoir insertion in children with cystic craniopharyngioma

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Received: 25 May 2022 / Accepted: 16 July 2022 / Published online: 4 August 2022
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Abstract

Introduction Children with craniopharyngiomas (CP) can experience significant morbidities caused by extensive surgery and/or radiation. Ommaya reservoir insertion (ORI) into cystic CP represents a minimally invasive approach allowing immediate decompression and aims to avoid additional injuries. The purpose of this study was to determine the surgical outcome and relevance of upfront ORI (± intracystic treatment) for preservation of endocrine function.

Methods We performed a retrospective chart review of children with CP treated at the Hospital for Sick Children between 01/01/2000 and 15/01/2020. Endocrine function was reviewed at the time of initial surgery and throughout follow-up. New endocrinological deficits related to the index procedure were defined as immediate failure (IF), whereas postoperative duration of endocrinological stability (ES) was analyzed using the Kaplan-Meier method. The rate of IF and ES was compared between the treatment groups.

Results Seventy-nine patients were included and had a median age of 8.3 years (range 2.1–18.0 years); 31 were males. Fifty-three patients with upfront surgical treatment, including 29 ORI and 24 gross total or partial resections had sufficient endocrinological follow-up data. Endocrine dysfunction occurring immediately after the index procedure (IF) was observed in 15 patients (62.5%) in the resection group compared to two patients (6.8%) in the ORI group, odds ratio: 0.05 (CI: 0.01–0.26, p < 0.0001). Excluding those with immediate endocrinological deficits, mean ES after ORI was 19.4 months (CI: 11.6–34.2), compared to 13.4 months (CI:10.6-NA) after surgical resection.

Conclusions Endocrine function was preserved in patients with upfront ORI (± intracystic treatment), which was confirmed as a minimally invasive procedure with an overall low morbidity profile.

Keywords Ommaya reservoir · Craniopharyngioma · Cystic · Resection · Endocrine function
Abbreviations

ACTH  Adrenocorticotropic hormone  
BX   Biopsy  
CT  Computerized tomography  
CCT  Cranial computerized tomography  
cMRI  Cranial magnet resonance imaging  
DI  Diabetes insipidus  
ES  Endocrinological stability  
FSH  Follicle-stimulating hormone  
GH  Growth hormone  
GTR  Gross total resection  
HSC  Hospital for Sick Children  
IF  Immediate failure  
IFN-α  Interferon-alpha  
LH  Luteinizing hormone  
MRI  Magnet Resonance Imaging  
PFS  Progression-free survival  
QoL  Quality of Life  
STR  Subtotal resection  
TSH  Thyroid-stimulating hormone

Introduction

Craniopharyngiomas (CP) are the most common non-glial CNS tumors in children representing 1.2–4% of all intracranial tumors [1]. Being classified as WHO grade 1 tumor, its predominant histological variant in childhood and adolescence is adamantinomatous with cyst formation, recognized as separate tumor entity [2, 3]. Theoretically, the benign nature of CP implies that complete tumor resection would provide a sustainable cure [4]. However, complete resection comes with a price due to the lesional intimacy with critical structures, imposing a significant risk to neurological, visual, and endocrinological function [5–8]. Given the morbidity related to surgery and radiation, which often results in severe long-term consequences with injury and impaired function of the hypothalamus, the management of CP in children remains controversial [4, 7, 9–11]. Other therapies, such as systemic chemotherapy haven’t proven a substantial value in the treatment of CP [12, 13]. With this in mind and acknowledging the need for a paradigm change away from radical surgery, efforts have been made over the last 2 decades to develop alternative treatment strategies, which allow for less extensive resection whilst protecting structures at risk and still provide efficacy [14, 15]. In this context, intralesional therapies via Ommaya reservoir insertion (ORI) into the cystic component of the CP have been established. ORI represents a minimally invasive intervention, which allows cystic decompression via aspiration and/or intracystic installation of agents, both designed to obtain durable cyst shrinkage with minimal overall toxicity [16–18]. Previous studies have addressed the efficacy of different agents, including bleomycin and interferon-alpha (IFN-α) [19–22]. IFN-α, especially, was found to delay disease progression and potentially offers a protracted time to definitive surgery or radiotherapy with a favorable toxicity profile compared with other therapeutic modalities [23–26]. The purpose of this study was to assess the overall morbidity of ORI in pediatric CP patients and its potential influence on endocrine function.

Material and methods

We performed a single center, retrospective observational study including pediatric patients with diagnosed CP between January 1, 2001, and January 15, 2020, at the Hospital for Sick Children (Sickkids) Toronto, Canada. The study subjects were identified using an electronic database of all craniopharyngioma patients and demographic, clinical, surgical and radiographic data were obtained through a retrospective chart review. The study was approved by the Research Ethics Board at Sickkids and conducted in accordance with their ethics guidelines and those of the University of Toronto. Due to the retrospective design of the study, the requirement for informed consent was waived by the REB.

Patients

Patients younger than 18 years at the time point of diagnosis with clinically and radiographically confirmed diagnosis of CP, who completed their entire treatment course at HSC were included in this retrospective study. Patients not treated at Sickkids and with incomplete clinical, surgical, radiographic, endocrine and follow-up data were excluded.

Surgical treatment and outcome analysis

A dedicated review of ORI procedures was performed. The patient’s chart, OR reports and postoperative MRIs were assessed for the anatomical approach, the technical approach, including the use of technical devices, intra- and postoperative complications, the indication and number of revision surgeries, as well as the indications for secondary ORI. Intraoperative and postoperative complications related to ORI as well as delayed events requiring revision, or additional resection surgery were defined as secondary outcome.

Endocrinological data and outcome analysis

Endocrine data were retrieved via chart review from documentations of our endocrine clinic, including diagnosis, follow up data as well as the need for substitution. Endocrine function was assessed preoperatively, peri-operatively and followed every 3–6 months postoperatively by
paediatric endocrinology. The following diagnostic criteria and values were applied for determination of endocrine function: growth hormone (GH) deficiency was diagnosed based on low growth velocity (< 5 cm/year), an IGF-1 that is low for sex and age, and provocative GH stimulation testing with arginine and clonidine yielding peak GH levels of <0.3 IU/L. Central hypothyroidism was defined by FreeT4 < 10 mmol/L with inappropriately low or normal TSH (<4.0 mIU/L). Central adrenal insufficiency was diagnosed with an ACTH stimulation test resulting in 60 min cortisol level of <420 nmol/L. Delayed puberty is diagnosed in girls with no breast development by age 13 years and boys with testicular volume < 4 mL at age 14 years or older and in both girls and boys, luteinizing hormone <0.3 IU/L. Central diabetes insipidus was diagnosed when there is evidence of plasma hyperosmolality (greater than 300 mmol/kg H2O), urine hypoosmolality (less than 300 mmol/kg H2O or urine/plasma osmolality less than 1), with ongoing polyuria (urinary volume greater than 4–5 ml/kg/hr). These definitions are consistent with guidelines from Endocrine Society, Pediatric Endocrine Society and European Society for Pediatric Endocrinology.

Charts were equally reviewed for documented presence of diabetes insipidus (DI) and for the need of hormone substitution or medical treatment of DI. Endocrinological deficits were classified as incomplete or complete depending on the number of dysfunctional axes and the type of required substitution or hormonal replacement medication. Endocrine deterioration was defined as dysfunction of any additional hormone axis and the need for substitution or hormonal replacement medication of any new or pre-existing dysfunction. Transient endocrinological deficits occurring in the early post-operative period were recorded, but not integrated in the outcome analysis. The diagnostic time point of a persisting endocrinological deficit after the index procedure was used for calculation of ES and correlated to any potential event, including radiographical tumor progression and secondary interventions. Any secondary intervention was considered as indicator for tumor progression with potential worsening of endocrine function. Accordingly, the primary outcome was endocrinological stability, defined as ES, and describing the time period between the primary treatment event and first post-operatively detected endocrinological deterioration. Follow up data of our patients, which were available after the age of 18 were also included in the outcome analysis.

Statistical analysis

A two-staged survival model was applied to determine the rate of IF (an ES of zero) in both treatment groups using Fishers exact test. P-value and estimated odds ratio are presented. For those patients with a positive ES time, Kaplan–Meier curves of ES were fitted and median ES times for each treatment group are presented along with 95% confidence intervals. A cox-proportional hazard model was used to estimate the hazard ratio between ORI and resection in those with a positive endocrinological stability time. Statistical significance was reached at a p-value equal or less than 0.05. All tests were performed using IBM SPSS Statistics Version 26.0 (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp, USA).

Results

Demographic data

Seventy-nine patients were diagnosed and treated with CP at the Hospital for Sick Children between 01/01/2000 and 15/01/2020. The median age at diagnosis was 7.8 years (range 0.8–18.0 years), the median follow-up duration 6.1 years (range 0.02–17.2 years) and the gender ratio was 1.3 (males/females). The diagnosis was obtained clinically, including endocrinological and ophthalmological examination, and radiographically via CT and MR imaging (+ contrast). Additional histopathological results, confirming the adamantinomatous CP diagnosis, were available from 45 patients. The choice of the primary treatment was determined within an interdisciplinary tumor board, which included neurooncologists, neurosurgeons, neuroradiologists, neuropathologists and radiation oncologists and based on the patient’s clinical and neurological presentation, the tumor size and configuration (with/without cystic component).

Treatment overview

A total of 66 out of 79 patients underwent initial surgical treatment. The remaining 13 patients received either nonsurgical treatments (irradiation, observation) or were followed elsewhere. ORI was performed in total in 41 patients and was the primary treatment in 32 patients, alone (n = 20) or in combination with cyst fenestration (n = 6), tumor resection (n = 2), biopsy (n = 2) or biopsy and cyst fenestration (n = 2). The remaining 34 patients underwent surgery, including two ventriculoperitoneal shunt insertions, six subtotal resections (STR), one subtotal resection combined with cyst fenestration, 19 gross total resections (GTR), two biopsies (BX), three biopsies with cyst fenestration and two cyst fenestrations alone. Secondary ORI was performed in nine of those patients at a later time point (Table 1). The surgical and endocrinological outcome after ORI will be reported.
separately in the following sections and according to the available follow-up (FU) data. A comprehensive overview of all treatments is illustrated in Fig. 1.

| Index surgery                        | Patient number (n) | Secondary ORI | Total n = 66 | Secondary ORI | Total n = 9 |
|-------------------------------------|--------------------|---------------|--------------|---------------|-------------|
| BX                                  | 2                  | –             |              |               |             |
| BX and cyst fenestration            | 3                  | –             |              |               |             |
| Cyst fenestration                   | 2                  | 2             |              | 2             |             |
| GTR                                 | 19                 | 3             |              | 3             |             |
| ORI                                 | 20                 | –             |              |               |             |
| ORI and BX                          | 2                  | –             |              | 2             |             |
| ORI and cyst fenestration           | 6                  | –             |              | 6             |             |
| ORI and tumor resection             | 2                  | –             |              | 2             |             |
| ORI, BX and cyst fenestration       | 2                  | –             |              | 2             |             |
| STR                                 | 5                  | 2             |              | 2             |             |
| STR and cyst fenestration           | 1                  | –             |              | 1             |             |
| VP shunt                            | 2                  | 2             |              | 2             |             |

Surgical outcome after ORI

ORI was performed in 41 patients, including 22 females and 19 males. These patients underwent a total of 75 Ommaya reservoir (OR) related surgeries, comprised of 62 new catheter insertions (83%) and 13 revisions (17%). For 32 patients ORI was the initial treatment and 21 patients required multiple catheter insertions: 15 patients underwent two catheter insertions, five patients three and one patient four, respectively (Fig. 2A).

The surgical approaches for new catheter insertions were mainly performed as a burr hole technique (n = 45) in the frontal (n = 40) or temporal region (n = 5). Seventeen surgeries used an open craniotomy for catheter insertion, equally with a preference for the frontal (n = 15) versus temporal (n = 2) region. Technically, ORI was supported using ultrasound (n = 49), navigation (n = 32) and the endoscope (n = 24), often in a combined fashion. In 6 of 17 open craniotomies the microscope was introduced during ORI (Fig. 2B). Catheter function was tested post-operatively by manual aspiration from the Ommaya reservoir. In case of considered intracystic treatment a permeability study was performed to assess the contrast distribution within the cystic portion of the CP after direct contrast injection into the Ommaya reservoir and to rule out leakage (Fig. 3).

The reasons for additional ORI were diagnosis of a new cystic CP component (n = 15), or the need for revision
surgery in the presence of catheter dysfunction \((n = 6)\). Complications related to ORI occurred in 11 patients (27%): five patients (12%) required one or more immediate revisions due to mispositioning of the catheter \((n = 3)\) or infection \((n = 2)\). Intraoperative bleeding occurred in two patients and four patients showed transient visual deficits after the surgery (Table 2). There were no permanent neurological deficits observed following ORI.

Postoperative treatments via the OR were variable and included intracystic administration of chemotherapy. Bleomycin was administered in nine patients (22%) and IFN-α in 18 patients (44%). Intermittent cyst fluid aspiration was performed in two patients (5%). Twelve patients did not receive any OR-related treatments (29%) (Fig. 2C).

### Endocrinological outcome after ORI

Fifty-five surgical patients had sufficient endocrine FU information (follow-up provided at Sickkids and minimum of 3 months post-OP), including 29 patients with upfront ORI and 24 patients with GTR or STR, and two patients with VP-shunt insertion. The median duration of follow up in the surgical cohort was 6.5 years (range 0.3–17.6 years). Sixteen patients were diagnosed with endocrine deficits pre-operatively, seven patients undergoing resection, nine patients ORI, respectively. One patient in the ORI group presented with panhypopituitarism at the time point of diagnosis. The remaining 39 patients had normal endocrine function at the time point of their index surgery and were monitored for endocrine changes throughout the follow up period.

A survival model using a two-stage process was applied to compare the rate of IF (defined as an EFS of zero) and endocrinological stability (defined as ESS) between the treatment groups (Fig. 4A). Endocrine dysfunction (partial or complete) occurring immediately after the index procedure was observed in 15 patients (62.5%) in the resection group compared to two patients (6.8%) in the ORI group, odds ratio: 0.047 (CI: 0.004–0.263, \(p < 0.0001\)). In the remaining patients with no IF, endocrine stability after the index procedure (EFS, median) was 13.4 months (CI: 10.6–NA, we are unable to accurately estimate a 95% CI in this group due to the low sample size of 9) in the resection group compared to two patients (6.8%) in the ORI group, odds ratio: 0.047 (CI: 0.004–0.263, \(p < 0.0001\)). In the remaining patients with no IF, endocrine stability after the index procedure (EFS, median) was 13.4 months (CI: 10.6–NA, we are unable to accurately estimate a 95% CI in this group due to the low sample size of 9) in the resection group compared to two patients (6.8%) in the ORI group, odds ratio: 0.047 (CI: 0.004–0.263, \(p < 0.0001\)). In the remaining patients with no IF, endocrine stability after the index procedure (EFS, median) was 13.4 months (CI: 10.6–NA, we are unable to accurately estimate a 95% CI in this group due to the low sample size of 9) in the resection group compared to two patients (6.8%) in the ORI group, odds ratio: 0.047 (CI: 0.004–0.263, \(p < 0.0001\))
Substitution or hormonal replacement was indicated in 50 out of the 55 (91%) surgical patients over the entire course of disease.

In patients with pre-existing endocrine deficits, comparative analysis of their perioperative endocrine function showed an increase in the number of dysfunctional axes and the need for substitution in the resection group whereas it remained stable after ORI (Fig. 4C). We could not detect any difference in endocrine function in patients with intracystic treatment after ORI compared to those without or intermittent aspiration only.

**Discussion**

In this study we analyzed the surgical impact of ORI and its effect on endocrine function in children with CP. Surgical tumor resection lead in 62.5% of the patients to immediate post-operative endocrinological dysfunction, compared to 6.8% after ORI. Furthermore, we saw that upfront ORI (± intracystic treatment) maintained endocrine stability with a median duration of 19.4 months (CI: 11.6–34.2) until the next intervention/ tumor progression, compared to a shorter, albeit not significantly shorter ($p = 0.063$) duration in most of the patients after GTR or STR. Also, in patients with pre-existing deficits, we could observe that the number of dysfunctional endocrine axis remained stable after ORI, however, increased in patients, who underwent upfront resection. The ORI-related treatments were variable and included intracystic administration of bleomycin or IFN-α.
Fig. 4 (A) Numbers of immediate failure and endocrinological stability (B) Endocrine stability after ORI versus resection (C) Pre- and postoperative (6 months) endocrine status
but also consisted of intermittent cyst fluid aspiration or no ORI-related treatment at all.

Previous studies have addressed variable effects of ORI-related therapies in CP disease. The stereotactic or open surgical implantation of an intracystic catheter with a subcutaneous reservoir was found to be a useful means of reducing the volume of the cyst and to prolong the interval until radiotherapy or surgical resection, in particular, in patients with large cysts exerting mass effect [27]. Accordingly, Moussa et al. observed a significant improvement of the clinical status and visual acuity in symptomatic patients after cyst drainage via ORI [28]. Similar effects were seen in patients after cyst drainage with subsequent radiosurgery of the solid tumor component and/or cyst remnants [29–31]. Another report by Schubert et al. indicates the superiority of stereotactic ORI placement, cyst drainage and radiotherapy over tumor resection with respect to progression-free survival (PFS) [32]. Beyond the drainage-related, mechanical decompression of critical anatomical structures, intracystic treatments, such as bleomycin and IFN-α have shown effectiveness with respect to cyst size reduction [3, 20, 23, 24, 33–36]. Only one study focused on the endocrinological outcome after open microsurgical resection versus minimally invasive drainage procedures and systematically analyzed the tumor control rates and functional scores in a cohort of 79, mainly adult CP patients [37]. The minimally invasive procedure included a stereotactic catheter implantation in cystic CP, providing continuous bidirectional cyst drainage into the supratentorial ventricular system and the basal cisterns. They could show that the endocrinological deterioration rate was significantly lower for cystic tumors undergoing stereotactic treatment (23.1%) than after microsurgery (85.7%), (p < 0.001) [37]. Despite the technical differences in drainage and catheter implantation, we could demonstrate, that, in line with their results, ORI leads to preservation of endocrine function compared to other types of microsurgical intervention. A longer duration of anatomical decompression of the cyst correlated with longer endocrinological function preservation and if ORI resulted in a maintained decompression, intracystic therapy was unnecessary. Given that more than 30% of our patients did not receive any intracystic agent after ORI, and that we did not observe any difference in endocrine outcome in relation to the type of ORI-associated treatment, we presume that already cyst drainage alone via ORI contributes significantly to the preservation of endocrine function, analogous to the observation of Rachinger et al. [37]. It was reported that in some cases single cyst drainage leads to changes in local pressure resulting in enlargement of neighboring small cysts [28]. We did not observe this condition in our patient cohort but arising of new cysts in different locations at the time point of tumor progression. Immediate changes or occurrences of separate cysts, however, did not occur during the initial cyst decompression period, emphasizing the hypothesis of duration-dependent benefit of the initial cyst decompression effect via ORI.

Cyst fenestrations in addition to the surgical intervention were performed in both groups: eight in the ORI group and six and the surgery group. The cyst fenestration per se could theoretically have an independent impact on endocrinological function via increased manipulation on the tumor/cyst and the pituitary gland. However, as cyst fenestrations were performed nearly equally often in both groups, cyst fenestration as outcome determining factor was not included in our analysis.

Despite the sparsity of studies comparing the effect of ORI and open microsurgery on endocrine function, we have learned from previous studies, that open tumor resection in CP carries a significant risk of secondary morbidity and mortality related to endocrinological deterioration [7, 9, 38, 39]. Clark et al. found in their analysis, that postoperative endocrine function is the main morbidity outcome that varies with respect to extent of resection and adjuvant therapy in pediatric craniopharyngioma [40]. Irreversible DI was reported by Mueller et al. in 80–93% of all complete resections and growth hormone deficiency in 75% of cases [41]. Elsewhere it was shown that radical surgical strategies are associated with poor hypothalamic and endocrine outcome and furthermore substantially reduced the quality of life (QoL) of approximately 50% of long-term survivors [8]. Another study by Merchant et al. confirmed the strong relationship between endocrine deficiency and its impact on the quality of life. They stratified a cohort of 30 CP patients into two groups: those who had aggressive resection compared with those who had a limited resection combined with radiotherapy. Both groups demonstrated a similar rate of tumor recurrence, but a higher rate of diabetes insipidus and lower QoL in the aggressive resection group [42]. Therefore, we consider a delay of endocrine deterioration after ORI, as experienced in our cohort, a substantial benefit for patients with cystic CP.

Although ORI is a minimally invasive approach and preserved endocrine function, we experienced surgical complications in 11 out of 41 patients, including three mispositioned catheters, two infections, two minor hemorrhages as well as four transient visual deficits. Catheter revisions or multiple ORI were required in patients with catheter blockage or complex, multi-cystic lesions. Zuccarelli et al. reported a very rare case of delayed bilateral, right greater than left hemiballismus in a CP patient 2 years following ORI due to position change of the catheter after cyst decompression [43]. Searching for optimization of the ORI procedure, Zanon et al. performed different techniques of catheter insertion. They experienced complications, namely misplacement or leakage in 16.3% of their patients, independent of the technical approach. These observations of
misplacement of the catheter or contrast leakage in 7–16% of ORI procedures have been summarized by Pettorini and colleagues [44]. Different outcomes have been reported by Peyrl et al. Their overall complication rate was 1% in 98 patients with ORI undergoing repetitive administration of chemotherapeutic agents into the cerebrospinal fluid, concluding that Ommaya reservoirs are safe and complications infrequent when provided by a well-trained team and under strict aseptic conditions [45]. In comparison to this study, our perioperative complication rate is slightly elevated. However, there is a difference between their surgical approach, namely the catheter insertion into the ventricular system, and our approach, which intends to place the catheter directly into the CP cyst. The latter one is more challenging and therefore may be related to a higher complication rate. Furthermore, complications, such as catheter blockage are more frequent in cystic ORI given the higher protein content of the CP cyst fluid compared to the CSF. However, only 5 out of 41 patients required further complication-directed treatments, indicating an acceptable morbidity profile, but room for improvement according to the protocol of Peyrl et al. [45].

Despite its comprehensive results, this retrospective study suffers several limitations. One is the high variability within the performed surgical approaches, predominantly concerning the technical aspects, the combination of procedures and the use of guidance tools, such as the endoscope, navigation or ultrasound. We acknowledge that the neurosurgical decision making in our cohort was dependent on the expertise and preference of the surgeon and related to the clinical urgency, but not necessarily following any internal standards, which are usually in place for outcome optimization and minimalization of complications, respectively. Given the relatively small patient number, we could not systematically analyze the impact of these different technical approaches. Similarly, the fact that we did not observe any difference in the endocrine function after either IFN-α, bleomycin, cyst aspiration or no treatment at all must be interpreted in the context of a small patient cohort and emphasizes the need for evaluation in prospective studies. Another limitation with respect to the patient numbers can be observed in the statistical analysis of the ES in the resection group. Only nine patients showed ES after elimination of the patients with IF, which did not allow the determination of the confidence interval. Lastly our study lacks analysis of radiographic measurements on the initial cyst volumes and their change over time. This could represent a complementary outcome correlate for the explanation of the endocrine changes and may be worthwhile investigating in a separate study.

Although the surgical outcome in our study confirms a low to moderate morbidity profile of ORI, the benefits of endocrine function preservation are multifold. Endocrine stability was maintained after ORI in 93.2% of the patients with a mean ES of 19.4 months (CI: 11.6–34.2), compared to 37.5% (odds ratio: 0.047 (CI: 0.004–0.263, p < 0.0001) with a mean ES of 13.4 months (CI: 10.6–NA) after resection, hazard ratio: 0.460 (CI: 0.203–1.044, p = 0.063). The maintenance of physiologic regulation of the endocrine system is especially important in the pediatric age range when rapid changes in growth and pubertal development occur. Although hormonal replacement is available for all of the endocrine axes, it cannot mimic the fine-tuned feedback system of normal physiology, so a delay of endocrine deterioration is beneficial. Taking these aspects into account, ORI represents a valuable procedure and was shown to have a comparably good safety profile as VP-shunts [46]. Further studies are required to elucidate the implications of ORI with respect to hypothalamic, ophthalmological, vascular and neurocognitive long-term outcome.

Conclusions

ORI is a minimal invasive procedure in pediatric CP patients with a low overall morbidity. Catheter revisions are not uncommon due to blockage and multiple catheters may be necessary to address recurrent cystic lesions at new locations. Endocrine function was preserved in patients with upfront ORI (± intracystic treatment). Further studies are required to elucidate the implications of ORI with respect to ophthalmological, vascular and neurocognitive long-term outcome.

Acknowledgements We thank the entire interdisciplinary team, including our nurses, nurse practitioners and social workers, who were involved in the care of these patients.

Author contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by LNL. The first draft of the manuscript was written by LNL and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding The authors declare that no funds, grants, or other support were received for this study nor during the preparation of this manuscript.

Data availability The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethical approval The study was approved by the Research Ethics Board at Sickkids and conducted in accordance with their ethics guidelines and those of the University of Toronto.
Consent to participate  Due to the retrospective design of the study, the requirement for informed consent was waived by the REB.

References

1. Bunin GR, Surawicz TS, Witman PA, Preston-Martin S, Davis F, Bruner JM (1998) The descriptive epidemiology of craniopharyngioma. J Neurosurg 89(4):547–551. https://doi.org/10.3171/jns.1998.89.4.0547
2. Louis DN, Perry A, Wesseling P et al (2021) The 2021 WHO classification of tumors of the central nervous system: a summary. Neuro Oncol 23(8):1231–1251. https://doi.org/10.1093/neoab/noab106
3. Bartels U, Laperriere N, Bouffet E, Drake J (2012) Intracystic therapies for cystic craniopharyngioma in childhood. Front Endocrinol 3:39. https://doi.org/10.3389/fendo.2012.00039
4. Puget S (2012) Treatment strategies in childhood craniopharyngioma. Front Endocrinol 3:64. https://doi.org/10.3389/fendo.2012.00006
5. Srinivasan S, Ogle GD, Garnett SP, Briody JN, Lee JW, Cowell CT (2004) Features of the metabolic syndrome after childhood craniopharyngioma. J Clin Endocrinol Metab 89(1):81–86. https://doi.org/10.1210/jc.2003-030442
6. Villani RM, Tomei G, Bello L et al (1997) Long-term results of treatment for craniopharyngioma in children. Child’s Nervous Syst 13(7):397–405. https://doi.org/10.1007/s003810050108
7. Kalapurakal JA, Goldman S, Hsieh YC, Tomita T, Marymont MH (2003) Clinical outcome in children with craniopharyngioma treated with primary surgery and radiotherapy delayed until relapse. Med Pediatr Oncol 40(4):214–218. https://doi.org/10.1002/mpo.10247
8. Müller HL (2011) Consequences of craniopharyngioma surgery in children. J Clin Endocrinol Metab 96(7):1981–1991. https://doi.org/10.1210/jc.2011-0174
9. Müller HL (2010) Childhood craniopharyngioma: current controversies on management in diagnostics, treatment and follow-up. Expert Rev Neurother 10(4):515–524. https://doi.org/10.1586/ern.10.15
10. Puget S, Garnett M, Wray A et al (2007) Pediatric craniopharyngiomas: classification and treatment according to the degree of hypothalamic involvement. J Neurosurg 106(1 Suppl):3–12. https://doi.org/10.1358/pen.2007.106.1.3
11. Pierre-Kahn A, Recassens C, Pinto G et al (2005) Social and psycho-intellectual outcome following radical removal of craniopharyngiomas in childhood: a prospective series. Child’s Nervous Syst 21(8–9):817–24. https://doi.org/10.1007/s00381-005-1205-6
12. Hargrave DR (2006) Does chemotherapy have a role in the management of craniopharyngioma? J Pediatric Endocrinol Metabol 19(Suppl 1):407–412
13. Jakacki RI, Cohen BH, Jamison C et al (2000) Phase II evaluation of interferon-alpha-2a for progressive or recurrent craniopharyngiomas. J Neurosurg 92(2):255–260. https://doi.org/10.3171/jns.2000.92.2.0255
14. Puget S, Grill J, Hahbrand JL, Sainte-Rose C (2006) Multimodal treatment of craniopharyngioma: defining a risk-adapted strategy. J Pediatric Endocrinol Metabol 19(Suppl 1):367–370
15. Flitsch J, Aberle J, Burkhardt T (2015) Surgery for pediatric craniopharyngiomas: is less more? J Pediatric Endocrinol 28(1–2):27–33. https://doi.org/10.1515/jpem-2014-0417
16. Frio F, Solari D, Cavallo LM, Cappabianca P, Raverot G, Jouanneau E (2019) Ommaya reservoir system for the treatment of cystic craniopharyngiomas: surgical results in a series of 11 adult patients and review of the literature. World Neurosurg. https://doi.org/10.1016/j.wneu.2019.07.217
17. Gutin PH, Klemme WM, Lagger RL, MacKay AR, Pitts LH, Hosobuchi Y (1980) Management of the unresectable cystic craniopharyngioma by aspiration through an Ommaya reservoir drainage system. J Neurosurg 52(1):36–40. https://doi.org/10.3171/jns.1980.52.1.0036
18. Rogers LR, Barnett G (1991) Percutaneous aspiration of brain tumor cysts via the Ommaya reservoir system. Neurology 41(2):279–82. https://doi.org/10.1212/wnl.41.2_part_1.279
19. Hukin J, Steinbok P, Layaf-Cousin L et al (2007) Intracystic bleomycin therapy for craniopharyngioma in children: the Canadian experience. Cancer 109(10):2124–2131. https://doi.org/10.1002/cncr.22633
20. Mottolese C, Stan H, Hermier M et al (2001) Intracystic chemotherapy with bleomycin in the treatment of craniopharyngiomas. Child’s Nervous Syst 17(12):724–730. https://doi.org/10.1007/s00381-005-0524-5
21. Zhang S, Fang Y, Cai BW, Xu JG, You C (2016) Intracystic bleomycin for cystic craniopharyngiomas in children. Cochrane Database System Rev 7:CD008890. https://doi.org/10.1002/14651858.CD008890.pub4
22. Steinbok P, Hukin J (2010) Intracystic treatments for craniopharyngioma. Neurosurg Focus 24(3):E13. https://doi.org/10.3171/2010.1.focus09315
23. Kilday JP, Caldarelli M, Massimi L et al (2017) Intracystic interferon-alpha in pediatric craniopharyngioma patients: an international multicenter assessment on behalf of SIOP and ISPN. Neuro Oncol 19(10):1398–1407. https://doi.org/10.1093/neoab/nox056
24. Ierardi DF, Fernandes MJ, Silva IR et al (2007) Apoptosis in alpha interferon (IFN-alpha) intratumoral chemotherapy for cystic craniopharyngiomas. Child’s Nervous Syst 23(9):1041–1046. https://doi.org/10.1007/s00381-007-0409-3
25. Cavalheiro S (2017) Intracystic interferon-alpha in pediatric craniopharyngioma patients. Neuro Oncol 19(10):1419. https://doi.org/10.1093/neoab/nox123
26. Dastoli PA, Nicacio JM, Silva NS et al (2011) Cystic craniopharyngioma: intratumoral chemotherapy with alpha interferon. Arq Neuropsiquiatr 69(1):50–55
27. Choux MLG, Genitori L., Children. Ci, Neurochirurgie 37(Suppl.1) (1991).
28. Moussa AH, Kerasha AA, Mahmoud ME (2013) Surprising outcome of ommaya reservoir in treating cystic craniopharyngioma: a retrospective study. Br J Neurosurg 27(3):370–373. https://doi.org/10.3109/02688697.2012.741732
29. Rahmathulla G, Barnett GH (2013) Minimally invasive management of adult craniopharyngiomas: an analysis of our series and review of literature. Surg Neurol Int 4(Suppl 6):S411–S421. https://doi.org/10.4103/2152-7806.121612
30. Reda WA, Hay AA, Ganc JC (2002) A planned combined stereotactic approach for cystic intracranial tumors: report of two cases. J Neurosurg 97(5 Suppl):610–2. https://doi.org/10.3171/jns.2002.97.supplement
31. Jarebi M, Coutte A, Bartier F, Khormi Y, Pellier J, Lefranc M (2019) A novel, hybrid, stereotactic approach (radiosurgery and dual Ommaya reservoirs) for the treatment of mixed (polycystic and solid) craniopharyngioma. Stereotact Funct Neurosurg 97(4):266–271. https://doi.org/10.1159/000503690
32. Schubert T, Trippel M, Tacke U et al (2009) Neurosurgical treatment strategies in childhood craniopharyngiomas: is less more? Child’s Nervous Syst 25(11):1419–1427. https://doi.org/10.1007/s00381-009-0978-4
33. Cavalheiro S, Di Rocco C, Valenzuela S et al (2010) Craniopharyngiomas: intratumoral chemotherapy with interferon-alpha: a...
multicenter preliminary study with 60 cases. Neurosurg Focus 28(4):E12. https://doi.org/10.3171/2010.1.focus09310
34. Mrowczynski OD, Langan ST, Rizk EB (2018) Craniopharyngiomas: a systematic review and evaluation of the current intratumoral treatment landscape. Clin Neurol Neurosurg 166:124–130. https://doi.org/10.1016/j.clineuro.2018.01.039
35. Takahashi H, Yamaguchi F, Teramoto A (2005) Long-term outcome and reconsideration of intracystic chemotherapy with bleomycin for craniopharyngioma in children. Child’s Nerv Syst 21(8–9):701–704. https://doi.org/10.1007/s00381-005-1208-3
36. Hukin J, Visser J, Sargent M, Goddard K, Fryer C, Steinbok P (2005) Childhood craniopharyngioma: Vancouver experience. Child’s Nerv Syst 21(8–9):758–765. https://doi.org/10.1007/s00381-005-1220-7
37. Rachinger W, Oehlenschlaegel F, Kunz M et al (2017) Cystic craniopharyngiomas: microsurgical or stereotactic treatment? Neurosurgery 80(5):733–743. https://doi.org/10.1012/000000000001408
38. Olsson DS, Andersson E, Bryngelsson IL, Nilsson AG, Johannsson G (2015) Excess mortality and morbidity in patients with craniopharyngioma, especially in patients with childhood onset: a population-based study in Sweden. J Clin Endocrinol Metab 100(2):467–474. https://doi.org/10.1210/jc.2014-3525
39. Lucas C, Benderitter T, Choux M (1982) Pre- and postoperative endocrine function in children with craniopharyngioma. Archives francaises de pediatrie 39(5):303–307
40. Clark AJ, Cage TA, Aranda D, Parsa AT, Auguste KI, Gupta N (2012) Treatment-related morbidity and the management of pediatric craniopharyngioma: a systematic review. J Neurosurg Pediatr 10(4):293–301. https://doi.org/10.3171/2012.7.Peds11436
41. Müller HLSN (2001) K, Multizentrische PB, mit vKuJ. Verlag KMIHE, Isensee O, Germany
42. Merchant TE, Kiehna EN, Sanford RA et al (2002) Craniopharyngioma: the St Jude Children’s Research Hospital experience 1984–2001. Int J Radiat Oncol Biol Phys 53(3):533–42. https://doi.org/10.1016/s0360-3016(02)02799-2
43. Zuccarelli B, Aalbers B, Grabb P (2016) Hemiballismus as a complication of an intratumoral chemotherapy catheter. J Clin Neurosci 30:129–131. https://doi.org/10.1016/j.jocn.2016.01.031
44. Pettorini BL, Tamburrini G, Massimi L, Caldarelli M, Di Rocco C (2009) Endoscopic transventricular positioning of intracystic catheter for treatment of craniopharyngioma. Technical note. J Neurosurg Pediatr 4(3):245–248. https://doi.org/10.3171/2009.4.peds0978
45. Peyrl A, Chocholous M, Azizi AA et al (2014) Safety of Ommaya reservoirs in children with brain tumors: a 20-year experience with 5472 intraventricular drug administrations in 98 patients. J Neurooncol 120(1):139–145. https://doi.org/10.1007/s11060-014-1531-1
46. Kramer K, Smith M, Souweidane MM (2014) Safety profile of long-term intraventricular access devices in pediatric patients receiving radioimmunotherapy for central nervous system malignancies. Pediatr Blood Cancer 61(9):1590–1592. https://doi.org/10.1002/pbc.25080

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