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ORIGINAL ARTICLE

Management of pediatric craniopharyngioma: 10-year experience from high-flow center

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Abstract

Purpose To report our experience and management strategies during 10 years for 137 childhood craniopharyngiomas treated at a single institution.

Methods Medical records of children with craniopharyngioma treated at Children's Cancer Hospital Egypt (CCHE-57357) from July 2007 to December 2017 were retrospectively reviewed. Beta-catenin as an immunohistochemical marker was assessed also in available specimens.

Results Our registry included 137 patients. Headache ($n = 122$), visual failure ($n = 118$), and hypothyroidism($n = 78$) were the most common findings on presentation. Three management protocols were identified; 65 patients were primarily followed up after surgery, 71 patients had radiotherapy after surgery, and one patient underwent surgery for Ommaya insertion with intracystic interferon injection. Overall, gross total resection/near total resection was achieved in 48 cases (35.04%), subtotal resection was achieved in 58 patients (42.33%), 29 (21.16%) had biopsy and Ommaya reservoir, and two patients with calcified lesions had no operations. Fifty-four patients showed recurrence/progression of their lesions. Allover, 5-year progression-free survival (PFS) was 52.3%, while it was 34.49% and 72.25% for the follow-up group and the radiotherapy group, respectively. Beta-catenin mutations were positive in 61/95 patients; 5-year PFS for beta-catenin negative and positive cases was 65.5% and 39.4% respectively ($p = 0.087$). Mortality was reported in eight patients. Intraoperative endoscopy-assisted assessment was the cornerstone of tailored decision-making.

Conclusion The concepts of conservative surgery and multimodal management should be applied to reach the perfect balance between the quality of life and the best tumor control rates. Beta-catenin mutations more than 5% are associated with statistically trending aggressive clinical behavior. The CCHE-57357 algorithm of individualized management protocol was presented.

Keywords Beta-catenin · Brain tumor · Conservative surgery · Endoscopy-assisted microsurgery · Pediatric craniopharyngioma

Introduction

Craniopharyngiomas are rare pediatric brain tumors which do not exceed 2.2 cases per million per year in most publications [1–8] and represent about 1–4% of pediatric brain tumors [9, 10]. Being in close proximity to the pituitary stalk, hypothalamus, and optic apparatus, they usually present with visual, endocrine, and cognitive disturbance. Pediatric craniopharyngioma represents a different pathological and genetic variant from the adult type; it is almost always adamantinomatous in contrast to papillary craniopharyngioma in adults. Also, underlying molecular and cellular pathogenesis of the adamantinomatous type was recognized as mutations in the CTNNB1 gene, which encodes β-catenin, leading to the overactivation of the WNT pathway, in contrast to BRAF V600E mutations identified in papillary

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craniopharyngioma [11–14]. There is a continuing debate around the merits and demerits of attempted gross total resection (GTR) as compared with subtotal resection (STR) or biopsy followed by adjuvant therapies [4, 10, 15–18].

We hereby report our experience and management strategies during 10 years for 137 childhood craniopharyngiomas treated at a single institution.

Patients and methods

The medical records of all children with the diagnosis of craniopharyngioma treated at Children's Cancer Hospital Egypt (CCHE-57357) during the period from July 2007 to December 2017 were retrospectively reviewed. All patients had at least 2 years of clinical follow-up. The study was approved by our hospital board review committee.

Clinical records, operative documentations, and radiological studies were reviewed. All patients had complete preoperative visual, endocrinal, and clinical assessment. Computed tomography (CT) and magnetic resonance imaging (MRI) were done as well for all patients preoperatively to assess the extensions of the lesions, their consistencies, and presence of calcifications, the data that guided the main surgical strategy. Postoperative MRI was performed within the 48 postoperative hours, then every 3 months in the first 2 years of follow-up and every 6 months thereafter unless there was progression or recurrence.

All of the surgeries that were done aiming for excision were performed through a pterional approach, while Ommaya insertion was done either through open craniotomy surgery, through stereotactic guidance, or under endoscopic visualization. Surgeries were performed by the senior author (M. El B.).

Extent of surgical resection was decided intraoperatively according to the relations of the lesion to the surrounding structures and its dissectability from the hypothalamus, pituitary stalk, and optic pathways, and it was aided by endoscopic visualization as well. An endoscope was introduced in craniotomy surgeries below the optic apparatus and the internal carotid artery and through opened lamina terminalis for full assessment of the microscopic blind areas; also, assessment of cerebellopontine angle, prepontine cistern, basilar artery, pituitary stalk, and perforators was performed by endoscopy as well. GTR was defined as no residual tumor on intraoperative endoscopic or microscopic inspection, with no remnant of the tumor on the early postoperative MRI. A near total resection (NTR) was considered when tumor capsule remnant was intentionally left behind as reported by the surgeon and when tumor residual was less than 1 cm in postoperative images. STR was considered when more than 1 cm of the tumor was left behind.

Patients who presented with clinically overt acute hydrocephalus were managed by ventriculo-peritoneal shunt insertion, either as a standalone procedure or in conjunction with endoscopically and stereotactically guided procedures such as Ommaya insertion, septostomy, and biopsy. On the other hand, patients who presented with radiological evidence of hydrocephalic changes but without obvious manifestations of increased intracranial tension were scheduled for tumor excision surgery as soon as possible.

Regarding focal postoperative irradiation, gross target volume was defined as any residual tumor and/or the tumor bed, and all cystic areas were included in it as tumor cells could be present in the cyst walls. Most of the patients were treated with intensity-modulated radiotherapy or volume-modulated arc therapy applying radiotherapy (RTH) dose ranged from 50.4 to 54 Gy delivered at 1.8 Gy per fraction.

Beta-catenin mutations were assessed retrospectively in the available specimens and included 95 cases and were examined as an immunohistochemical tumor marker through immunostaining by using the Benchmark Ventana system.

Follow-up surveillance included the follow-up imaging, hormonal profile, visual acuity, fundus and perimetry, and neurological examination, and this surveillance was conducted by a multidisciplinary team which included neurosurgeons, neurologists, oncologists, endocrinologists, and ophthalmologists.

Statistical analysis

Overall survival (OS) was calculated from the date of registration to the date of death from any cause or last follow-up. Progression-free survival (PFS) was calculated from the date of registration to the date of tumor progression, death, or last follow-up. The Kaplan–Meier method was used for survival analysis with 95% confidence intervals calculated using Greenwood's formula and p values reported from the two-sided log rank test.

The chi-square and Fisher's exact tests were used for categorical variables, while the t test and ANOVA (or their non-parametric counterparts) were used for continuous variables. The statistical significance threshold was determined at a p value of ≤ 0.05. All statistical analyses were performed using IBM SPSS version 22.

Results

Our registry included 137 patients. Headache (122 patients) and visual deterioration (118 patients) were the most common presentations. Endocrine deficits were detected preoperatively in 104 patients; the commonest of which was hypothyroidism (78 patients). Diabetes insipidus was present initially in 24 patients (Table 1).

Table 1 Initial clinical findings in our patients

Clinical findings	Number of patients	Percentage from the whole series
Headache	122	89.05%
Increased intracranial pressure due to hydrocephalus	48	35.03%
Visual affection	118	86.13%
Endocrine affection	104	75.91%
Hypothyroidism	78	56.93%
Hypocortisolism	60	43.79%
Decreased GH	40	29.19%
Panhypopituitarism	7	5.10%
Diabetes insipidus	24	17.51%
Motor deficits	3	2.18%
Fits	7	5.10%

Overall, GTR was achieved in 48 cases (35.04%), while STR (more than 1-cm residual) was the case in 58 patients (42.33%), 29 (21.16%) had biopsy and Ommaya reservoir, and two patients were not operated upon presentation because they had totally calcified lesions.

The patients were categorized into three groups according to their management protocol; 65 patients were primarily followed up after their surgery, and they represent most of our early cases, those will be referred to as the "follow-up group"; 71 patients had RTH after surgery, those will be referred to as the "radiotherapy group"; and one patient underwent surgery for Ommaya insertion then received interferon injection in it. The extent of surgical intervention in each group is summarized in Table 2.

Median follow-up period was 43.95 months (95% CI: 38.16–54.93; IQR 29.77–75.16); 54 (39.41%) patients showed recurrence or progression of their lesions. Allover, 5-year PFS was 52.3%, while its sub-categorization was 34.49% (95% CI: 23.9–49.79%) and 72.25% (95% CI: 59.16–88.25%) for the follow-up group and the radiotherapy group, respectively (log rank $p = 0.0000122$). Median time to progression in the follow-up cohort and the radiotherapy cohort was 20.5 months and 44.3 months, respectively.

Mortality was reported in eight patients; four cases presented with aggressive recurrence invading the hypothalamus for 3 to 8 years of follow-up and led to disturbed level of consciousness and severe electrolyte disturbance; one of them died after trial of NTR of the recurrence. One patient died postoperatively following GTR that was complicated by operative bed hematoma which was evacuated, hypothalamic affection, and severe electrolyte disturbance; the remaining three cases were lost to regular follow-up in the hospital and were found to be dead of remote complications of hypothalamic affection and electrolyte disturbance.

In the first group (follow-up group), 40 patients showed progression with a total of 74 progression events (details are summarized in Table 3), while 25 did not. Progressions were managed on individual basis according to the different conditions of the patients and are summarized in Table 4. A total of 37 progression events in the follow-up group received RTH for progression management. Only six out of 37 progressed after RTH with 5-year PFS of 88.3%. In one patient, two progressions were recorded, but his parents refused RTH and his general and endocrinological status precluded surgical interventions.

Regarding the radiotherapy group, 14 patients showed progression with a total of 33 progressions events, while 57 patients did not. Univariable regression shows that RTH (as an initial management) decreases the risk of progression by 70.38%, i.e., HR = 0.2962 (95% CI: 0.166–0.529, $p = 0.0000381$). The number of progressions in every patient is variable and summarized in Table 3. Different modalities for management of these progressions are detailed in Table 4.

Ninety-five specimens were available for β-catenin assessment. Positive mutations were detected in 61 cases (64.2% of studied cases), and 5-year PFS for β-catenin-preserved

Table 2 Surgical intervention in each group of patients

Extent of surgery	Postoperative follow-up protocol	Radiotherapy protocol	Interferon protocol	Total
GTR/NTR	39	9 (all are NTR)	0	48
STR	21	37	0	58
Ommaya/biopsy	5	23	1	29
No surgery	0	2	0	2
Total	65	71	1	137

Table 3 Progression events in each group of patients

Number of progressions in the same patient	Follow-up group (group 1)	Radiotherapy group (group 2)	Interferon group (group 3)	Total
1	21 patients	5 patients	None	26
2	12 patients	3 patients	None	15
3	4 patients	4 patients	None	8
4	None	1 patient	None	1
5	1 patient	None	None	1
6	2 patients	1 patient	None	3
Total	40 patients	14 patients	None	54

(negative) cases was 65.5% (95% CI: 48.9–82.1%), while it was 39.4% for β-catenin-aberrant (positive) cases (95% CI: 19.41–59.39%, $p = 0.087$, hazard ratio = 1.78; 95% CI: 0.91–3.49). Among those 61 patients, 22 showed progression and most of them were in the follow-up group (81.8%, $n = 18$). Moreover, 74.3% ($n = 29$) of those with positive mutations and did not have progression through the follow-up period were in the radiotherapy group, and these results may point to the protective value of upfront RTH when there is β-catenin mutations. Five-year PFS for ≤ 5% mutations versus > 5% was 92.3% and 85.7%, respectively ($p = 0.22$).

The visual status remained stationary in 53 and 48 patients in the radiotherapy group and follow-up group, respectively, while it deteriorated in five cases (7%) in the radiotherapy group and in nine cases (13.8%) in the follow-up group, respectively (Table 5). Endocrinologically, 65 patients in the radiotherapy group and 58 in the follow-up group were clinically good (details are in Table 5), and 116 (84.67%) patients are on hormonal replacement therapy (58 patients in each group). Eleven patients in the radiotherapy group did not need replacement as compared with four patients only in the follow-up group (Table 5).

Discussion

Craniopharyngioma management is debatable. Debate revolves around the quality of life of these children, where some adopted complete resection aiming for complete cure owing to its benign histological nature [19–24], while less-invasive surgeries gained acceptance by others for better endocrinal and visual outcome with this longstanding disease in such an eloquent location [10, 15–17, 25]. Having this concern and based on the aim of achieving the best balance between tumor control and quality of life for children with craniopharyngiomas, our main management protocol had shifted from the radical surgical attitude to the concept of adopting more conservative surgical approaches. The benefits of this conservative surgery and hypothalamus-sparing surgery are recently well-established in the literature [17, 26, 27].

It is worth mentioning that conservative surgery here is not a synonym to subtotal resection. However, we adopted a planned individualized surgical approach where the decision-making was guided mainly by the preoperative imaging and the intraoperative assessment and findings. According to this concept we have adopted, GTR should be

Table 4 Multimodal management of progression events in the follow-up and radiotherapy groups

Management modality	Number of progressions managed by this modality in the follow-up group	Number of progressions managed by this modality in the radiotherapy group
Follow-up as there was no clinical progression or minimal progression radiologically	8	6
Re-excision or debulking only	1	4
Insertion of new Ommaya only	18	18
Re-excision and Ommaya insertion in residual cyst	2	2
Re-excision and Ommaya insertion and interferon injection	1	0
Debulking and radiotherapy	7	0
Insertion of Ommaya and radiotherapy	10	0
Ommaya revision only	5	1
Endoscopic fenestration of a cyst	0	2
Radiotherapy only without intervention	20	0

Table 5 Visual and endocrinal outcomes

Outcome		Radiotherapy group		Follow-up group	
Visual outcome	Stationary	53 (74.6%)		48 (73.8)	
	Improved	11 (15.5%)		3 (4.6%)	
	Deteriorated	5 (7%)		9 (13.8%)	
	Not available	2		5	
Endocrinal outcome	Clinically good and normal labs	41		49	
	Clinically good but still some labs are abnormal	24		9	
	Clinically not good (other than diabetes insipidus)	4		4	
	Diabetes insipidus	44		50	
	Replacement therapy (Eltroxin, hydrocortisone, and growth hormone)	58	17 (three drugs) 41 (one or two drugs only)	58	21 (three drugs) 37 (one or two drugs only)
	No replacement	11		4	
	Not available	2		3	

the goal when the tumor, intraoperatively, is safely dissectible from the surroundings especially the hypothalamus and the pituitary stalk; otherwise, STR should be done with the least possible tumor residual being intentionally left behind. For completely cystic craniopharyngiomas, an Ommaya reservoir is inserted guided by frameless stereotaxy, by endoscopy, or through craniotomy.

We have only one patient included in this study with cystic craniopharyngioma in the interferon group. Moreover, we are following another 3 cases in our hospital lately, but we are usually faced with its limited availability in the pharmaceutical market. Our patient who is 12 years old with positive β-catenin mutation is being followed for more than 3.5 years with stationary course and good clinical state which goes in hand with series reported in the literature [28–30] that showed promising results regarding the control of disease progression and delay or abandon complex surgery or radiotherapy. However, it is too early for us to have definitive results.

Our series incorporated two main large groups of patients; the first one, the follow-up group, included those whose main management was follow-up after surgery, and it represented most of our early experience cases; and the second one, the radiotherapy group, included those who received postoperative RTH, and it included most of the cases managed after changing our protocols to embrace more conservative surgical approaches. In the follow-up group, the 5-year PFS was 34.49%, while the 5-year PFS in those who received immediate RTH after surgery was 72.25%. Moreover, among those in the follow-up group and received RTH for progression management ($n = 37$), only six out of 37 progressed after RTH with 5-year PFS of 88.3%. This points out the beneficial value of giving RTH for lesions not totally excised, which ensures better rates of control of the lesions, and this was concluded also by other investigators [10, 18, 31–33]. Our statistics also showed that univariable regression shows that RTH (as an initial management) decreases the risk of progression by 70.38%, i.e., HR = 0.2962 (95% CI: 0.166–0.529, $p = 0.0000381$).

As the first surgical approach carries the only best chance for the patient and based on our experience and the outcome of our patients, our algorithm (Fig. 1) for initial management of pediatric craniopharyngioma was proposed with a multimodal tailored approach aiming for the best possible quality of life and best tumor control. A tailored individualized approach with adoption of conservative surgery was recognized in some studies in the literature, where patients were categorized according to the degree of hypothalamic invasion as detected in preoperative MRI and clinical data that led the authors to stratify the treatment protocols and build their algorithm of management to reduce morbidity [10, 15, 20]. Moreover, other authors had attempted to develop grading criteria for hypothalamic involvement by craniopharyngioma in the MRI to serve as a prognostic objective factor to guide treatment plan [25]. Not only does our algorithm incorporate preoperative MRI findings but also it takes into consideration the most important cornerstone for surgical and subsequent management which is the "intraoperative assessment" of relations, extensions, and dissectability of the tumor from the hypothalamus, pituitary stalk, and the optic apparatus because such parameters can be only ensured intraoperatively. In many instances, lesions assumed to be invading the hypothalamus in MRI may be found compressing or stretching it only and can subsequently be safely dissected free, and this careful assessment can be only performed under the microscope or even only after endoscopic assistance. This concept was emphasized by some authors who discouraged intentional incomplete removal of all retrochiasmatic tumors without knowing the true relationship with the hypothalamus and asserted that final decision about the optimal extent of tumor removal should be made during the surgery [34]. This was clearly

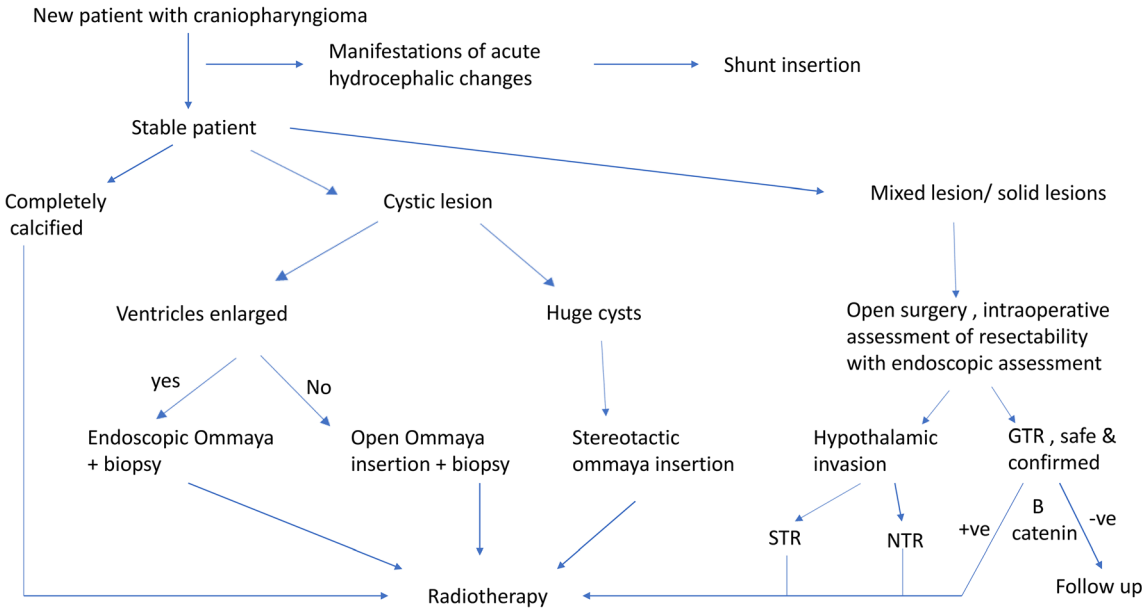

Fig. 1 Our CCHE-57357 proposed algorithm for the initial management of pediatric craniopharyngiomas

evident in our series, where hypothalamic invasion present in the preoperative MRI was intraoperatively confirmed with the aid of the concomitant endoscopic assistance, and the least possible residual was thereafter intentionally left behind. On the other hand, other lesions were found to be resectable from the chiasm and the hypothalamus safely under endoscopic vision.

The concept of conservative surgery for craniopharyngioma included in our proposed algorithm was greatly aided by the advancement in neuroendoscopy, where safe and less-invasive management could be accomplished. Endoscopy-assisted microsurgical excision of mixed or solid lesions has gained interest in the literature being a tool that increased the extent of tumor resection safely [35–37]. Similarly, this technique enabled us to fulfill the concept of conservative surgery, where the goal of GTR was reached by introducing the endoscope underneath the internal carotid artery and optic apparatus or through the lamina terminalis (Fig. 2) to visualize unrecognized residuals in hidden corners or microscopically blind areas, such as the ventral aspect of the chiasm, contralateral optic nerve and tract, and pituitary stalk, and helped careful non-blind dissection of the tumor from the critical neurovascular surrounding structures such as the chiasm, hypothalamus, and perforators. Also, endoscopic assistance justified the subtotal resection in those patients, where the mass was adherent or invading the hypothalamus and helped to leave the smallest residual (1 cm or less) for a better response and a less burden of the adjuvant RTH. It is worth mentioning that intraoperative endoscopic visualization was helpful in assessment of the lesions extending into the cerebellopontine angle and the third ventricle, where the detailed anatomy of the critical structures was clarified and tumor extensions in these remote areas were assessed. So, all of these benefits of neuroendoscopy in craniopharyngioma management solidify the concepts of conservative surgery and maximum safe resection especially in the first surgery which is the best chance for those patients. In case of completely cystic lesions, endoscopic biopsy and Ommaya insertion were performed, and this was followed by interferon injection or RTH, thus achieving confirmation of diagnosis and decompression of the hypothalamus and visual pathway in a less-invasive manner with good functional outcome and tumor control.

Regrowth or recurrence of craniopharyngioma is a commonly reported event in the literature during the follow-up periods, and the incidence of occurrence ranged from 18 to 52% even after GTR and/or RTH [1, 2, 13, 15, 21, 38–40]. Different risk factors for regrowth or recurrence were detected by some authors such as younger age [15], size of the lesion [38, 41], cystic nature [38], presence of hypothalamic adhesions, high Ki-67 and p53 levels [41, 42], extent of surgical excision, and use of RTH [10, 18]. Some recent studies referred to the strong correlation between beta-catenin mutations and recurrence of adamantinomatous craniopharyngioma and the poor outcome [43, 44].

As a result, management of craniopharyngioma progressions should be multimodal and individualized according to each case's scenario in order to reach the best possible quality of life by stabilizing visual and neurological states as well as pituitary and hypothalamic axis integrity (Fig. 3), and this was apparent in our series, where multiple progressions were managed differently (Table 4). We had progressions in 39.41% of our cases during the whole follow-up period, and median time to progression in the follow-up cohort and radiotherapy cohort was 20.5 months and 44.3 months, respectively. The value of RTH in the control of craniopharyngioma progression was apparent in our study from the 5-year PFS for both groups,

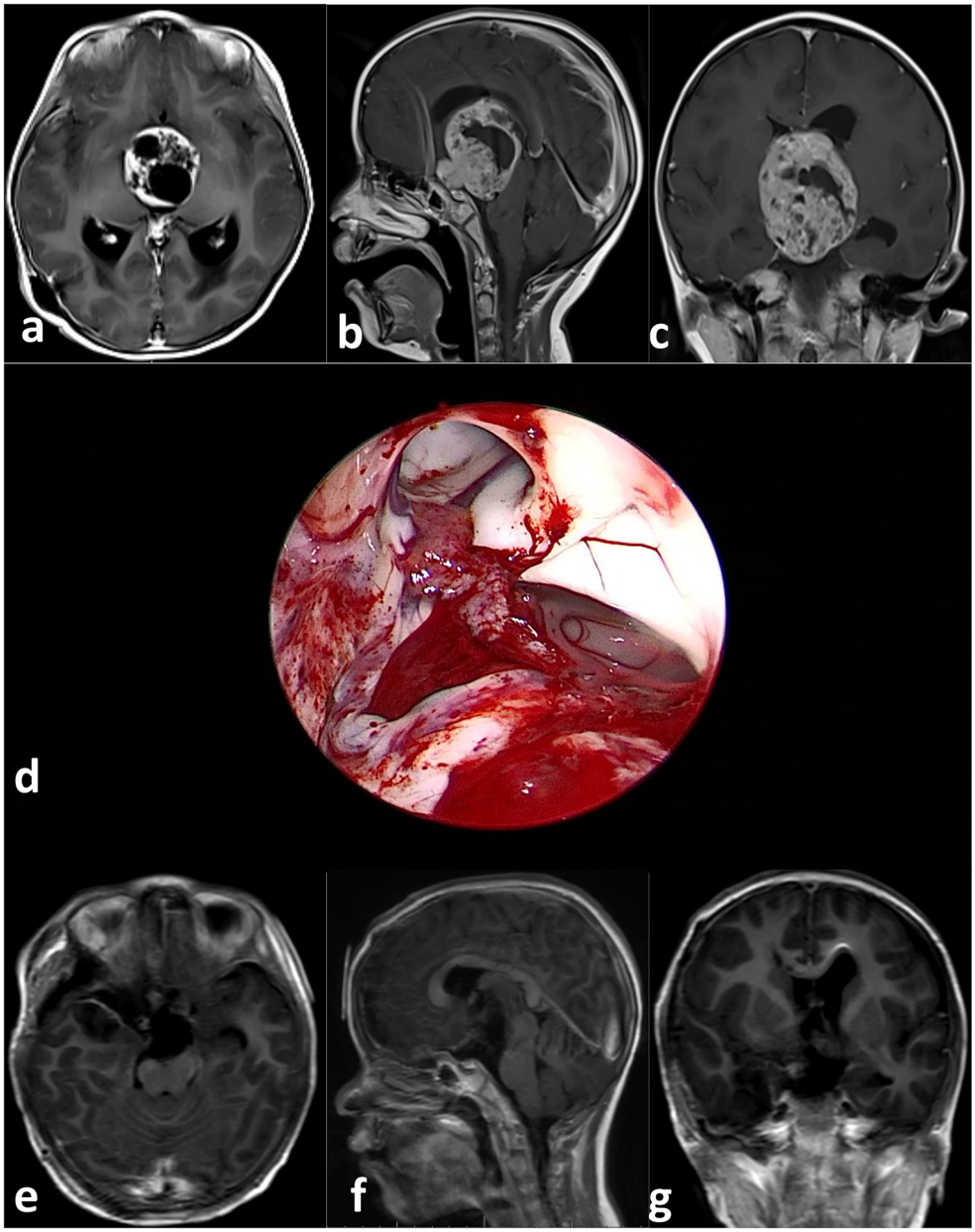

Fig. 2 A 4-year-old female presenting with visual failure in the right eye and manifestations of increased intracranial pressure. **a**–**c** Preoperative axial, sagittal, and coronal MRI with contrast. **d** Intraoperative endoscopic view showing complete excision out of the third ventricle. **e**–**g** Postoperative MRI showing complete excision of the lesion and the patient clinically stable on thyroid replacement and desmopressin for diabetes insipidus

number of progressions in each group, and univariable regression, which collectively show that RTH decreases the risk of progression by 70.38%.

Beta-catenin mutations were assessed in 95 patients in our series, and positive mutations were found in 61 cases (64.2%), which points to the role of these mutations in pathogenesis. Five-year PFS for β-catenin-preserved (negative) cases was 65.5%, while it was 39.4% for β-catenin-aberrant (positive) cases (Fig. 4), and although not statistically significant ($p = 0.087$), this trend may have a prognostic value and correlates with others who demonstrated strong correlation between β-catenin mutations and recurrence [43]. Also, an interesting finding in our patients was that 74.3% of those with positive mutations and did not have progression through the follow-up period were in the radiotherapy group, and these results may point to the protective value of upfront RTH when there is β-catenin mutations (Fig. 5), and this should be considered in the management of these cases as suggested in our algorithm, where in cases with positive mutations, GTR can be followed by RTH especially if there is doubt by the surgeon about minimal residual capsule that is not evident in the postoperative MRI. Among those where the degree of mutation was available ($n = 43$), three out of four progressed tumors had mutations more than 5%. Also, 5-year PFS for patients who

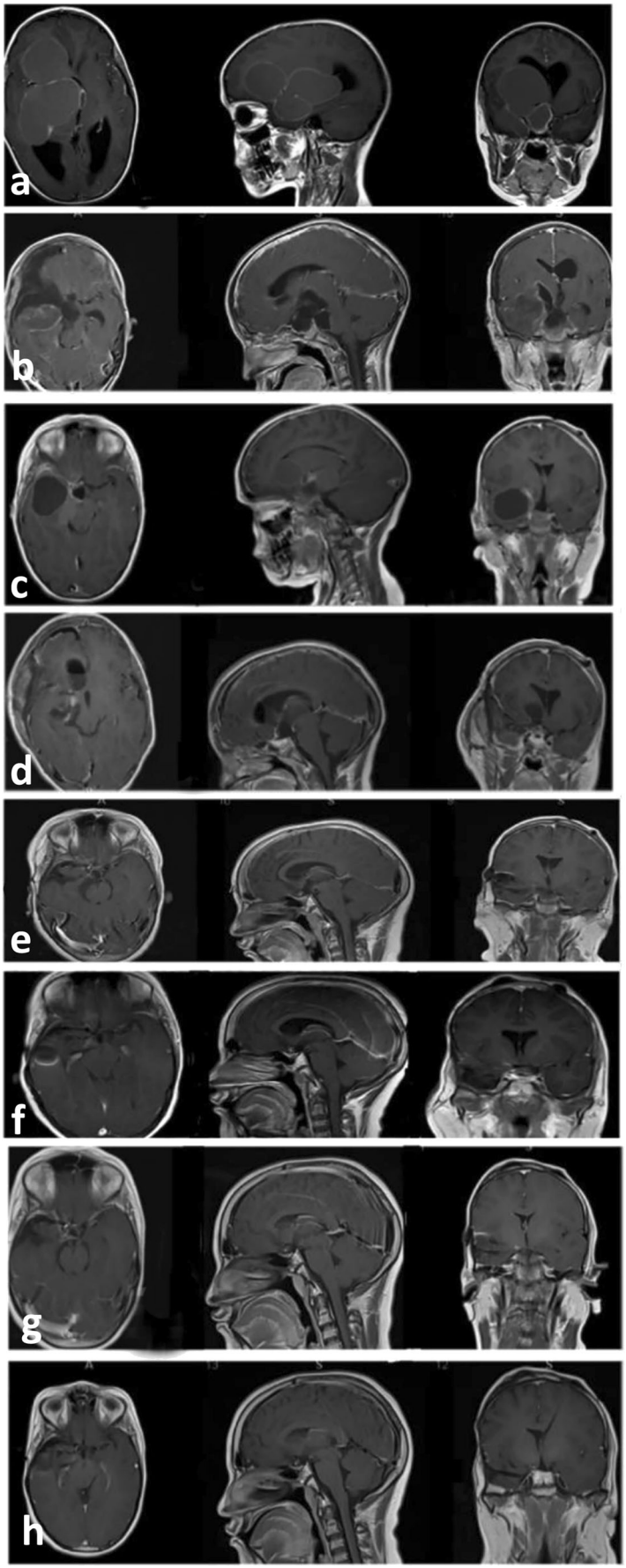

Fig. 3 A 10-year-old male presented with headache, vomiting, and poor vision in the right eye with positive β-catenin mutations. **a** Preoperative MRI showing huge multilocular cystic craniopharyngioma with complex tumor extensions and obstructive hydrocephalus. **b** Postoperative MRI showing NTR. **c** Follow-up MRI after 1 year showing a right temporal cystic tumor recurrence with a significant mass effect. **d** MRI after operation for evacuation of the cyst and insertion of an Ommaya, and then the patient received radiotherapy. **e** MRI follow-up after 2 years. **f** MRI follow-up after 4 years. **g** MRI follow-up after 7 years. **h** MRI follow-up after 9 years showing no further progression, and the patient is clinically stable

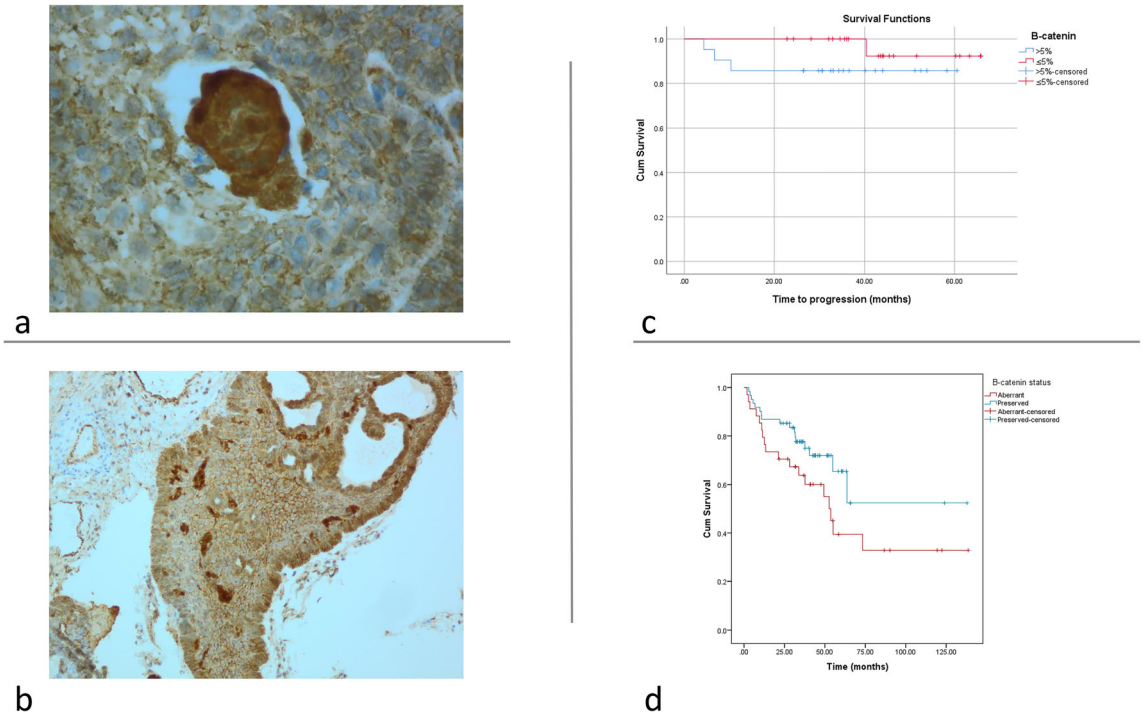

Fig. 4 **a**, **b** Positive nuclear reaction to beta-catenin is noted commonly in squamous epithelial morules (nests) among the stratified squamous epithelial lining. Rest of the epithelium shows cytoplasmic and membranous reaction to beta-catenin. **c** Kaplan–Meier curve showing survival for β-catenin mutation ≤ 5% and > 5%. **d** Kaplan–Meier curve showing the effect of β-catenin mutations on survival

had ≤ 5% mutations versus those with > 5% mutations was 92.3% and 85.7%, respectively ($p = 0.22$). Among the four mortality cases due to aggressive recurrence, β-catenin mutations were present in three of them and were more than 5%.

This aggressive clinical behavior of tumors possessing more than 5% β-catenin mutations may direct the management plan towards the immediate postoperative RTH even in cases in which GTR has been achieved and prove to possess more than 5% β-catenin mutations. These findings although statistically non-significant are trending and clinically significant, and of course, they direct further future studies with larger scales for thorough assessment of these mutations and their clinical significance.

Visual status follow-up showed stabilized vision in nearly the same percentage of patients in both cohorts and even with slightly more improvement and less visual deterioration in the

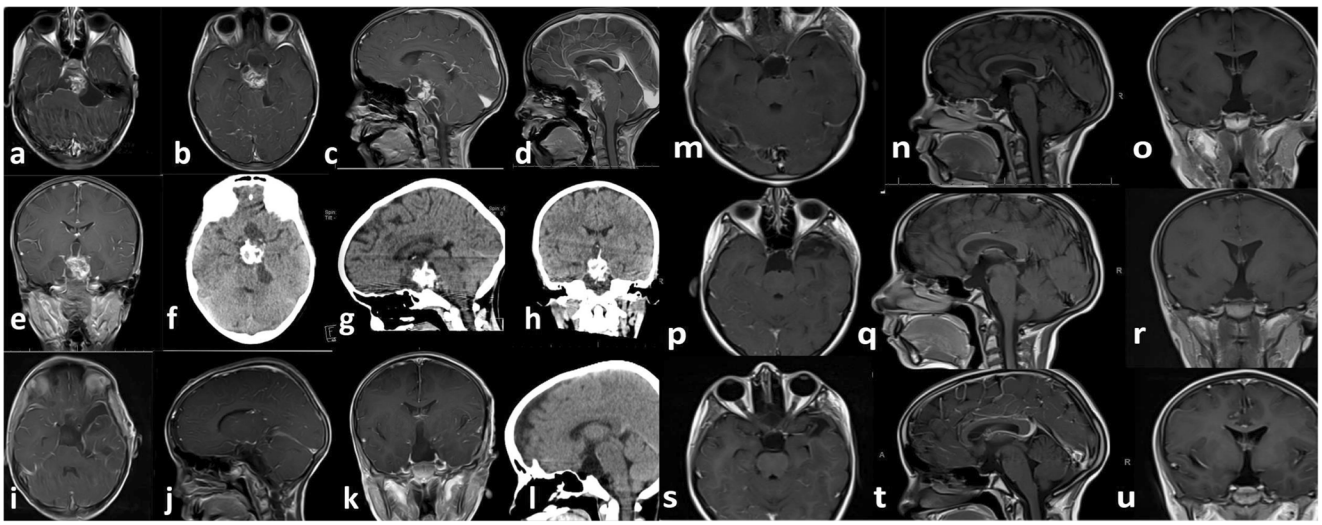

Fig. 5 An 8-year-old female presented with visual failure in the left eye and had positive β-catenin mutation (40%) who was operated upon presentation by near total resection followed by radiotherapy. **a**–**e** Preoperative MRI images. **f**–**h** Preoperative CT images. **i**–**l** Postoperative images. **m**–**o** MRI after 1 year. **p**–**r** MRI after 3 years. **s**–**u** MRI after 4 years showing no recurrence or progression of the lesion

radiotherapy group. In addition, endocrine outcome was almost comparable between the two groups, with more patients in the radiotherapy group that were not dependent on replacement therapy. This copes with what was previously reported by some authors [45, 46] about the minimal rate of long-term complications of RTH in recurrent and residual craniopharyngiomas, and this should encourage the use of RTH in these situations especially with the advancement in planning and delivery techniques.

Conclusion

The quality of life should be considered as a clinically important endpoint in the management of pediatric patients with craniopharyngioma. The concepts of conservative surgery and multimodal management should be applied to reach the perfect balance between the quality of life and the best tumor control rates. Beta-catenin mutations more than 5% are associated with statistically trending aggressive clinical behavior. The CCHE-57357 algorithm of individualized management protocol is presented.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest in personal, financial, institutional, or industry affiliations in any of the drugs, materials, or devices described in this article. The authors have no conflicts that may affect ethical adherence.

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