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Minimally invasive management of adult craniopharyngiomas: An analysis of our series and review of literature

Gazanfar Rahmathulla[1,2], Gene H. Barnett[1]

Departments of Neurosurgery, [1]The Rose Ella Burkhardt Brain Tumor and Neuro-Oncology Center, Neurological and Taussig Cancer Institutes, Cleveland Clinic, Cleveland, Ohio, United States, [2]Mayo Clinic, Jacksonville, Florida

E-mail: Gazanfar Rahmathulla - rahmathulla.gazanfar@mayo.edu; *Gene H. Barnett - barnetg@ccf.org
*Corresponding author

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Abstract

Background: Craniopharyngiomas (CPs) are slow growing tumors with an incidence of between 1.2% and 4.6%, having a bimodal age distribution typically peaking in childhood and in adults between 45 and 60 years. Recurrences occur even after documented gross total resections necessitating a combination of therapeutic strategies. Obtaining a cure of this tumor in adults without producing major side effects continues to remain elusive.

Methods: We describe our results in 11 patients with CP treated in a minimally invasive fashion using a combination of techniques like burr hole aspiration, Ommaya reservoir placement, ventriculo-peritoneal (VP) shunting and focal radiation (Gamma Knife stereotactic radiosurgery/Intensity modulated radiotherapy [GKRS/IMRT]).

Results: Visual function remained intact in all patients; endocrine status remained stable with two patients developing new postoperative diabetes insipidus. There was no periprocedural morbidity or mortality, with hospital stays for any in-patient procedure being 48 hours or less.

Conclusions: Minimally invasive techniques such as cyst aspiration, insertion of a catheter with Ommaya reservoir, when combined with stereotactic radiosurgery/IMRT is an effective and safe option for management and long-term control of adult CPs. We believe the Ommaya catheter by itself could act as a stent, creating a tract allowing gradual drainage of cyst fluid and stabilization without necessitating any further interventions in selected cases.

Key Words: Craniopharyngioma, focal radiotherapy, minimally invasive, radiosurgery

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INTRODUCTION

Craniopharyngiomas (CPs) are benign, slow growing tumors whose ideal management remains controversial and challenging. They arise from remnants of the craniopharyngeal duct and/or Rathkes cleft. These tumors have an incidence of between 1.2% and 4.6%[8,48] with a bimodal age distribution, one peak occurring in children and the other in adults between the 4th and 6th decades. These tumors are located close to the visual apparatus, hypothalamus, pituitary stalk, 3rd ventricle, and vasculature from the circle of Willis. The proximity

of the tumor and its adherence to these critical structures makes complete microsurgical removal without neurological deterioration difficult.[17,87] Although these tumors are histologically benign, recurrence rates up to 57% have been reported even after surgical gross total resections, due to their invasiveness.

Traditional management of these tumors is microsurgical total resection. However, their propensity to recur had necessitated a combination of strategies such as local chemotherapy (e.g., bleomycin)[86] and frequent cyst aspirations. The good outcomes seen in the 1990s with minor surgical interventions followed by radiotherapy brought an alternative paradigm to the management of these tumors.[26,65] With technological improvements and better platforms for conformal radiation delivery, stereotactic radiosurgery (SRS) has been used to manage recurrent or residual tumors and has been reported to be an effective and safe addition in the treatment of these tumors.[11,61,64] With a median 10-year survival rates for these patients being as high as 85-93%,[83] safe therapeutic interventions are essential in order to maintain the quality of life of these patients. Individualized treatment strategies have to be used depending on the size, location, calcification, relation to adjacent vascular and neural structures, and the presence of a cystic component. The low incidence of these tumors coupled with the above mentioned tumor factors, along with numerous available interventions make it difficult to statistically quantify the efficacy of either an initial radical resection or graded sequential multi-modality treatments, making it difficult to produce guidelines for managing these tumors.

The aim of this study was to present our outcomes treating adult CP patients using a combination of minimally invasive strategies including cyst aspiration (with or without Ommaya reservoir system insertion), ventriculo-peritoneal (VP) shunting and either upfront or adjuvant conformal radiotherapy and a review of current literature.

MATERIALS AND METHODS

An institutional review board (IRB) approved retrospective chart review of all patients undergoing treatment for CPs between 1995 and 2010. Fifty-two patients with a diagnosis of CP underwent management at our institute between 1995 and 2010. We included all adult patients (>21 years) with an imaging diagnosis of CP with a predominantly cystic component, had undergone either a biopsy with cyst drainage, insertion of a catheter or Ommaya reservoir system, VP shunt or radiation therapy (RT) as their procedures, without any prior surgical intervention categorizing all these procedures together as minimally invasive. Out of the 52 patients, 11 patients were treated using the minimally invasive strategy. The median age for all CP patients at diagnosis was 49 years (range 24-80) with an equal number of male and female patients. In the minimally invasive treated group there were five male and six female patients with a median age of 58 years (range 24-80 years). Seven patients had histologically proven CPs with stereotactic biopsy (4 adamantinomatous, 2 WHO grade I, and 1 papillary) and of the remaining four patients, two underwent a stereotactic biopsy aspiration with characteristic machine oil fluid but no tissue sample and two patients in the cohort had undergone VP shunting elsewhere. For these 4/11 patients' clinical findings, laboratory workup, and neuroimaging was the basis for further management. In most cases after biopsy-cyst aspiration, patients were followed with magnetic resonance imaging (MRI) studies initially at 1 month, then every 3 months for a year and then every 6 months for a year, and subsequently at yearly intervals to evaluate tumor size and to determine the feasibility of early intervention with focal RT (Gamma knife radiosurgery or Intensity modulated radiotherapy [IMRT]). Detailed neuroendocrinological assessment was done prior to and following treatment. A brief description of three representative cases is presented.

CASE REPORTS

Case 1

HS, a 46-year-old male presented with decreased vision in his left eye along with impotence and diminished energy levels of about 3 months duration. His endocrine evaluation revealed pan-hypopituitarism. He was diagnosed with a suprasellar mass, mixed solid-cystic [Figure 1a and b] and underwent an image-guided stereotactic (using skull fiducials) brain biopsy and aspiration of the cyst, which contained about 4 cc of oily fluid. Histologic review revealed a papillary CP. One month later he underwent Gamma Knife radiosurgery on the residual tumor [Figure 2]. Postoperatively he did well with a gradual improvement in his vision and a decrease in tumor size as seen on imaging 5 years following initial treatment [Figure 3a and b]. His pan-hypopituitarism remained stable and he is currently being managed with hormone replacement therapy. Six years following Gamma Knife stereotactic radiosurgery (GKRS) treatment, his tumor recurred and he underwent an extended transphenoidal surgery presently remaining free of radiographic tumor.

Case 2

MO, a 24-year-old male presented at an outside hospital with headaches of a few months in duration with a loss of libido and decreased energy levels. His endocrine workup revealed hypopituitarism and imaging showed a 2.5 cm sellar-suprasellar solid cystic mass for which he underwent

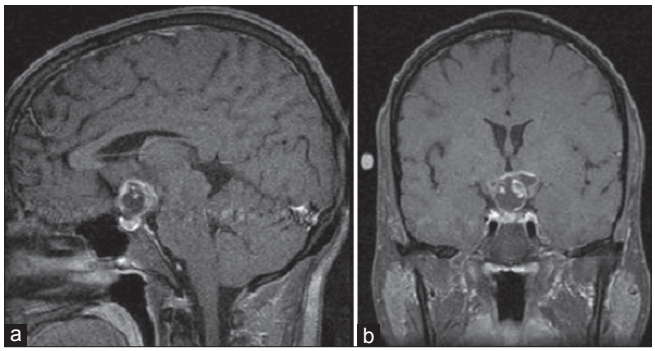

Figure 1 (a and b): HS, a 46-year-old male presented with symptoms of visual and endocrine dysfunction. T1-MR postcontrast images on presentation with sagittal (a) and coronal (b) sequences revealing a mixed tumor with sellar-suprasellar involvement, contrast enhancement at the periphery and mass effect over the optic chiasm

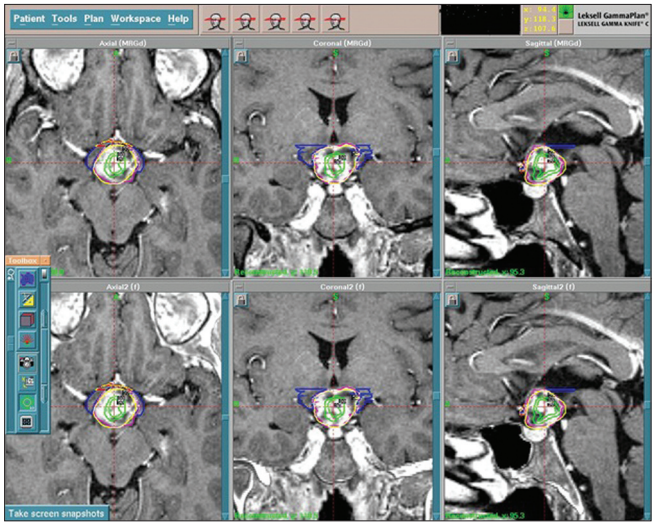

Figure 2: Leksell GKRS plan for the patient HS. The blue outline represents the optic apparatus and is the organ at risk in the treatment plan. The red outlines the tumor contour, with the green line representing the 90% IDL and the yellow 55% IDL

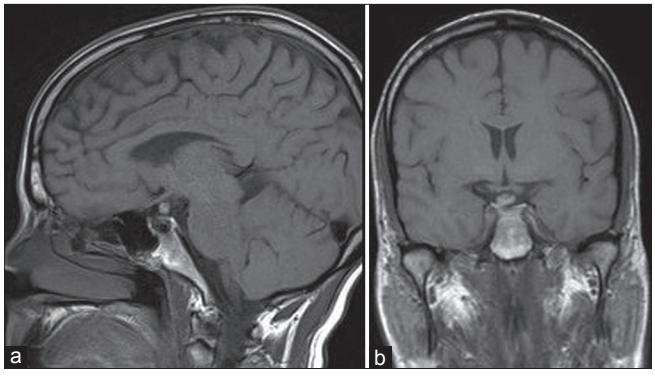

Figure 3 (a and b): T1-MR postcontrast images on follow-up at 5 years revealing a significant reduction in the size of the tumor on both the sagittal (a) and coronal (b) images without any mass effect on the optic chiasm

a cyst aspiration and biopsy. He subsequently had tumor progression and was treated with GKRS. Long-term follow-up at 9 years continues with the patient remaining stable and requiring no further interventions.

Case 3

MC, a 69-year-old female who following a head injury, was diagnosed with an incidental suprasellar cystic-solid mass. She remained asymptomatic for 4 years, subsequently developing diminished vision along with weight gain with an increase in lesion size. She underwent biopsy-aspiration of the cyst followed by Gamma Knife radiosurgery a month later. Subsequently 4 months later she developed a cyst recurrence on imaging and underwent Ommaya reservoir insertion , having no associated clinical changes. On follow-up, her MRI revealed an increase in the size of the cyst. Although further aspiration of the cystic component via the Ommaya reservoir was advised, she declined any intervention. Repeat imaging revealed a spontaneous decrease in the size of the cystic component that remained stable over time and required no further intervention.

RESULTS

All the patients were evaluated clinically for their neurological, endocrine status, and MRI imaging at our institution. Initial follow-up imaging was obtained at 1 month, then every 3 months for a year, subsequently at 6 months intervals for a year, and then at yearly intervals. Earlier imaging was done in cases of symptomatic worsening or if progression was observed on their MRIs. In patients with stable disease yearly clinical and neuroimaging follow-up was performed.

Clinical response

There were no procedural or perioperative associated morbidity or mortality. The mean follow-up period in these patients was 66 months (range 2-144 months) and the median was 60 months. There was always a residual component on posttreatment MRI scans because the interventions did not include gross surgical resection. Two patients who were 77 and 78 years at the time of initial diagnosis and treatment were lost to follow-up after a period of 11 and 9 years, respectively. On the last clinic visit, they had no progression of their disease and were 88 and 87 years old. The remaining patients continue to be observed with regular clinic visits and with no mortalities in this group.

Of the 11 patients, 8 underwent stereotactic biopsy aspiration followed by clinical and neuroimaging follow-up, 4 patients had insertion of an Ommaya reservoir and aspiration of the cystic component either as an initial or subsequent procedure. Duration of in-hospital stay for these procedures ranged from 24 to 48 hours. Four (4/11) patients had GKRS, and three (3/11) had IMRT following tumor cyst decompression. The choice of RT was determined by the dose constraints and proximity

of the tumor to the optic nerves. One patient (1/11) in the cohort was treated at an outside facility with upfront GKRS (case no. 7). This patient subsequently developed visual deterioration associated with tumor progression and was treated with an IMRT boost [Table 1]. At our Institute ($N = 4$), the patients who had GKRS for tumor control had tumor volumes ranging from 1.6 to 4.1 cc (mean 2.33 cc). Maximum dose to the optic apparatus was less than 9 Gy, with a mean maximum tumor dose of 19.2 Gy, and a mean marginal dose of 10.75 Gy using 6-22 isocenters [Table 2]. The three patients who underwent initial IMRT received a standard dose of 54 Gy in in daily fractions of 1.8-2.0 Gy. One patient (9) treated early in the series received ^{32}P intracavitary irradiation for tumor control.

Serial neuroendocrine evaluations revealed anterior pituitary hormone dysfunction in 8/11 of the patients. Two patients had improvement of their preexisting partial DI after intervention. Two patients (7 and 10) underwent VP shunts for obstructive hydrocephalus as the only invasive procedure prior to initiating RT. There was no formal neuropsychological evaluation prior to or after radiation treatments, making it difficult to objectively assess cognitive decline or improvement.

Response of the tumor to minimally invasive interventions

The tumors treated, were mixed tumors having both a solid as well as a predominantly cystic component. In our series, we defined progression as a symptomatic worsening with corresponding changes in neuroimaging after the last intervention, stable disease in cases where there was no symptomatic worsening but there could be fluctuation in the size of the cyst on MRI, and a complete response when there was neither symptomatic nor neuroimaging changes in the tumor. According to our criteria, there was one patient (1/11) in whom symptomatic progression occurred, along with radiological worsening of the solid component about 6 years following his treatment, at which time the tumor was amenable to surgical intervention (case 1). There were five (5/11) patients with stable disease, in whom two (2/11) had a fluctuation in cyst size on follow-up imaging. These

Table 1: Summary of clinical interventions and duration of follow-up

Patient	Age/sex	Biopsy-aspiration	Ommaya insertion	GKRS	No of invasive interventions	IMRT	Chemo	Follow-up (months)
1	46/M	+	-	+	2	-	-	72
2	24/M	+	-	+	1	-	-	120
3	69/F	+	+	+	2	-	-	48
4	58/M	+	-	+	1	-	-	60
5	31/M	+	+	-	4	+	-	53
6	49/F	+	-	-	1	-	-	2
7	62/F	-	-	+	1 (VP shunt)	+	-	84
8	55/M	+	+	-	2	-	-	12
9	78/F	+	+	-	2	32P	-	108
10	77/F	-	-	-	1 (VP shunt)	+	-	144
11	66/F	+	-	-	1	+	-	24

VP: Ventriculo-peritoneal, IMRT: Intensity modulated radiation therapy, GKRS: Gamma knife radiosurgery

Table 2: Radiosurgery/IMRT treatment data with pre- and posttreatment dimensions and endocrine status

Patient	Max dose Gy	Margin dose Gy	IDL (%)	Vol (cc)	Visual status pretreatment	Visual status on follow-up	IMRT dose	Endocrine status on follow-up
1	16	9	55	4.1	VA/VF ↓	↔/↓	-	Panhypopituitarism
2	29.4	15	51	1.6	↔	↔	-	Hypothyroid
3	15.9	9	57	1.8	↓	↔/↑	-	Hypothyroid and hypogonadism
4	15.4	10	65	1.8	↓	↑	-	Panhypopituitarism
5	-	-	-	-	↓	↑	54 Gy	Panhypopituitarism
6	-	-		-	↓	↑		Stable
7	-	15	50	2.5	↔	↔	51 Gy	Stable
8	-	-		-	↓	↑		Hypogonadism
9	-	-	-	-	↓	↔	32 P	Stable
10	-	-	-	-	↔	↔	54 Gy	Stable
11	-	-	-	-	↓	↑	54 Gy	Stable

↓: Has visual deterioration on presentation, ↑: Vision improved to normal after treatment, ↔: Vision remained stable, IMRT: Intensity modulated radiation therapy, Gy: Gray,

two patients continue to remain clinically stable from their baseline initial evaluations, and at present have reduced cystic components without the need for further intervention. One (1/11) patient has progressed on imaging without symptomatic clinical worsening and continues to be observed. Two (2/11) patients have stable tumors on imaging following biopsy-cyst aspiration without radiation (case no. 6 and 8) and continue to be observed. Five (5/11) patients have been defined as having a complete response according to our criteria (case nos. 4, 7, 9, 10, 11), as they have no clinical or MRI changes after receiving focal RT (GKRS/IMRT or ^{32}P). A fluctuation in the cyst dimensions is a common occurrence, subsequent to radiotherapy and although patients may not be symptomatic, they requiring diligent follow-up. Hence according to our criteria, only one patient (case no. 1) had a true progression, whereas the others are either stable or improved.

Endocrine outcomes

Eight patients (73%) had one or more endocrine deficits on presentation, hypogonadism being the most common at presentation five (5/11, 45%). There were two (2/11, 18%) who presented with hypothyroidism and (3/11, 27.2%) had pan-hypopituitarism. Diabetes insipidus was seen at presentation in one (1/11, 9%) patient (case 5).

In the course of their treatments, two new patients had developed pan-hypopituitarism and required hormone supplementation (preoperatively 3/11 (27.2%); postoperatively 5/11 (45%)) following intervention. The patients with hypothyroidism required hormone replacement during their follow-up. Transient diabetes insipidus was seen in one patient following a biopsy (case no. 8) and was permanent in one (case no. 5). The endocrine evaluation and management was performed by the neuroendocrinologist in the pre- and postoperative periods.

Visual outcomes

Eight patients (73%) had a visual field defect at presentation. Visual deficits included blurring of vision, diplopia, and field cuts and all affected patients were symptomatic. Six (6/8) of these patients had improvement in vision at last follow-up irrespective of the type of intervention, one had no change and one patient had a worsening of vision. Although one patient (case 7) did undergo GKRS and subsequently IMRT, her vision remained stable on follow-up.

Discharge time and associated medical morbidity

In-hospital stay was required for performing a biopsy, insertion of an Ommaya reservoir or placement of a VP shunt. Patients who underwent any of these procedures were discharged within 48 hours, with no associated complications related to hospital stay. Endocrine issues were taken care of by the neuroendocrinologist on an out-patient follow up basis. For adjuvant radiation procedures no hospital admission was required.

DISCUSSION

CPs are histologically benign tumors involving the sellar-suprasellar region, but often invading or adherent to adjacent critical structures. The intimate association between the tumor and the optic apparatus, hypothalamus, and pituitary gland makes treating them challenging. In reports published prior to the 1980s, recurrence rates for PCs varied from 30% to 50%.[9,10,28,87] Although numerous technological advances in image-guided surgical systems and micro-techniques have been made since then, the results are only slightly better.[6,17,18,39,41,42,59,81] With a variety of therapeutic options available to treat these patients, do select subgroup adult patients with PCs need aggressive microsurgery with a gross resection as a goal?

Of the various therapeutic strategies available, microsurgical resection is still considered to be the mainstay of management for adult patients with PCs.[27] Gross total resections may give rise to a cure, but major series reported have a success rate ranging between 30% and 97%.[28,35,38,68,75,78,79] Recurrence rates vary between 5% and 10% in some series to as high as 50% following so called "gross total" resections. The success rates of gross total resections reported in a large recently reported single center series is 95.6% for tumors with a diameter of less than 6 cm and 58.8% for those with diameters greater than 6 cm.[72] Other early primarily operative series such as that of Konovolov *et al*.[35] report complete resection rates of 64% with other series of Sweet *et al*.[75] and Samii *et al*.[68] reporting 93% and 97%, respectively. The recurrence rates for these tumors range from 0% to 26% following gross total resections,[15,46] with the highest risk of recurrence being in the first 3 years following surgery.[31,88] Prasad *et al*.[64] in their 30-year review reported only 11 (35.5%) of the 31 series achieved more than a 50% radical resection rate. The operative mortality in published large series ranges from 0% to 5.4%,[18,29,83] especially after resecting tumors invading the hypothalamus,[67] with Yasargil[87] in his series reporting 16.7% mortality due to more aggressive total removal in all their cases. The morbidity rates range from 12% to 60% and include hormonal deficiency, cerebrospinal fluid (CSF) leaks, visual dysfunction, hypothalamic–metabolic dysfunction, and cognitive dysfunction.[21,47,88] Recurrent tumors are more difficult to operate upon and are associated with significantly lower progression-free survival rates as well as higher mortality and morbidity rates. Patients who undergo transphenoidal surgery have lower mortality rates when compared with the transcranial route.[18] The results of the outcomes with various major microsurgical series reported in literature are described in Table 3.

Although our cohort of patients is small, we observed good long-term control rates as seen by the duration

of follow-up [Table 1]. The absence of procedural and periprocedural morbidity, good long-term tumor control, minimal acute and late endocrine, visual toxicity, and early hospital discharge make these minimalistic procedures a viable option in the multi-modality treatment of CPs in adult patients. These patients can resume their baseline activities, being mobilized early following these interventions, thus preventing the associated complications of longer hospital stay. Although in our series, the number of patients is small and formal neuropsychological testing was not done, there were no neurocognitive complaints following treatment. We observed that patients aged over 60 years have better long-term control, with fewer cyst recurrences or tumor progression.

Moussa *et al.* treated 52 patients with cystic CPs using an Ommaya reservoir catheter to aspirate the cyst contents.[59] In their series, 73% were stable over a follow-up period of 7 years and they hypothesize that collapse of the cyst enables communication of the terminal holes with the outside CSF spaces allowing egress of cyst fluid. The use of an Ommaya reservoir for drainage of cystic contents has been described in similar reports by Spaziante *et al.*[73] and Al Abyad *et al.*[1] In our cases, the tumor cysts also appear to stabilize after catheter placement without the need for repeated aspirations. Although this could be related to a delayed effect of radiation on tumor fluid production, we believe it could be a combination of radiation, the above phenomenon and additionally the act of perforating the cyst wall, and insertion of the catheter, which by itself acts as a stent allowing cyst fluid to egress along its sides via capillary forces into the subarachnoid space [Figure 4a-e]. The catheter in our cases is placed at the deepest point within the cyst in our cases and even though the wall collapses around the catheter, it appears to be inadequate for a direct communication via the holes at the tip. Our algorithm for selecting and managing this subgroup of CP patients has been outlined [Figure 5]. The infrequent occurrence of these tumors, their varying presentation characteristics, and behavior makes it difficult to perform prospective randomized trials.

In literature, control rates appear to be better for solid or cystic tumors compared with mixed, large, and multi-cystic tumors, factors that predict poorer outcomes.[55] Additionally cystic recurrences more frequently occur following GKRS,[33,61] rather than progression of the solid tumor component, similar to what is seen in our patient cohort. In reports published prior to the 1980s, recurrence rates for CPs varied from 30% to 50%.[9,28,87] Although numerous technological advances in image guided surgical systems and micro-techniques have been made since then, the results are only slightly better.[18,42,81]

With variable results from surgery, data from the Royal Marsden hospital[65] and Children's hospital in Boston[26]

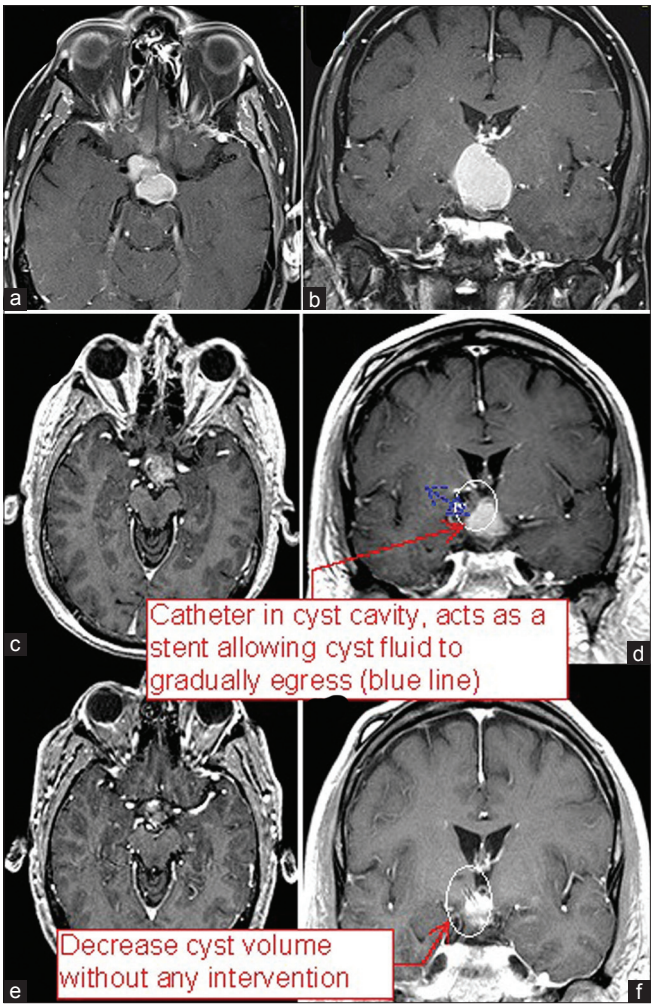

Figure 4: Patient, a 55-year-old male presented with visual blurring and diplopia. MR imaging, T1WI axial and coronal preoperative (a and b) postcontrast shows a suprasellar cystic lesions measuring 2.8 × 2.5 × 3.3 cm. He underwent an Ommaya insertion with aspiration of the cystic component and was discharged a day later. His vision improved and he had no DI, neurological, or endocrine worsening. Follow-up MR imaging at 6 weeks, T1WI postcontrast axial and coronal (c and d) reveal the catheter in the cavity. At 1 year follow-up without any intervention his MRI T1WI axial and coronal (e and f) show a smaller cyst. The catheter may act as a stent gradually allowing cyst fluid to egress.

treating patients with conventional radiotherapy (CRT), reveal that a combination of surgery and radiotherapy or radiotherapy alone achieves excellent tumor control and survival. These early studies indicated the radiosensitive biology of these tumors. There was no significant difference seen in outcomes or survival in those patients who received upfront adjuvant RT and RT at the time of progression.[54,62,65] Doses for CRT have ranged between 50 and 60 Gy[20,23,50,66] with several authors reporting better control rates at doses >54 Gy.[23,66] Karavitaki *et al.*[31] and Stripp *et al.*[74] found comparable 10-year survival in patients treated with either gross surgical removal or by surgery followed by CRT. CRT had risks of optic neuropathy ranging from

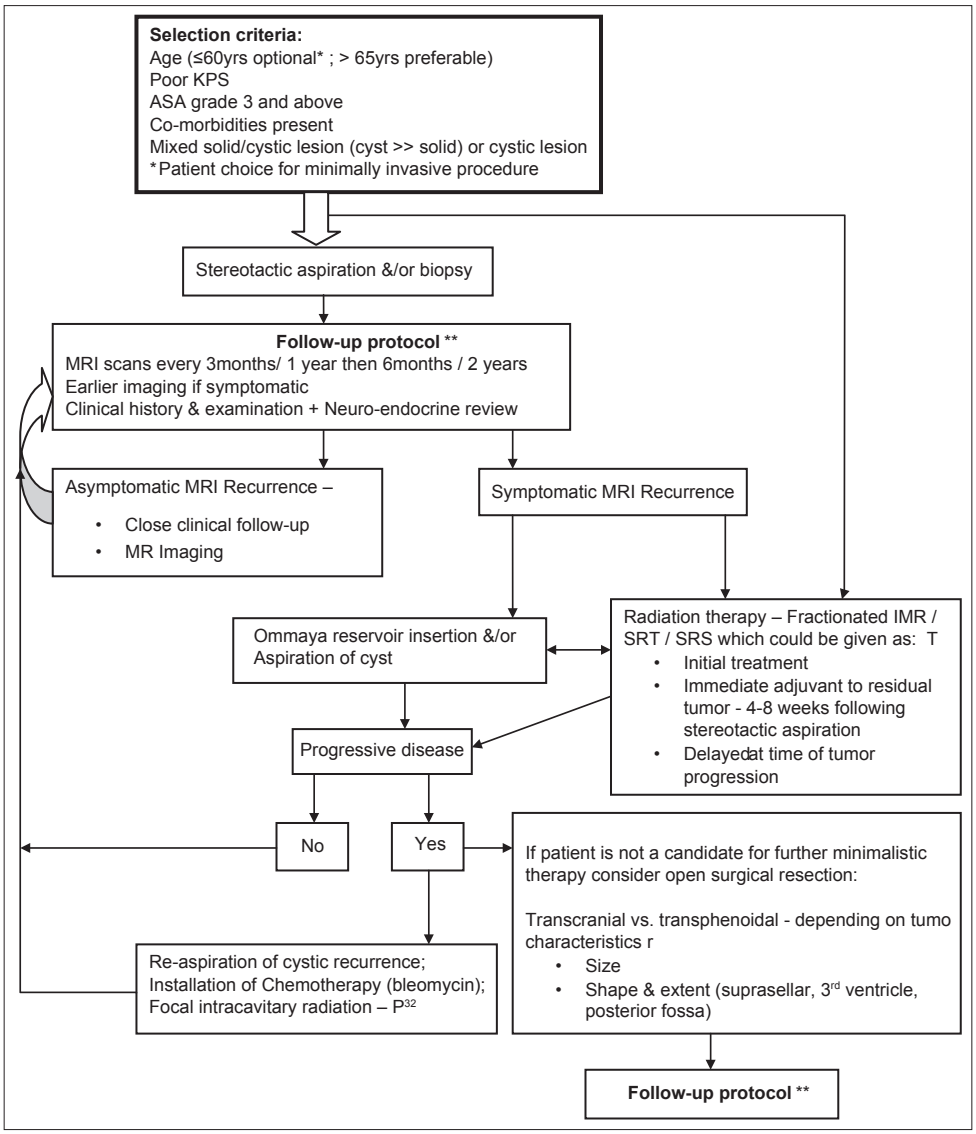

Figure 5: Algorithm outlining our decision pathway in the minimally invasive management of the patients included in this study with craniopharyngiomas. Our preferred choice for this subset is an initial aspiration and biopsy of the wall, although in the elderly, if the lesion is not amenable to any intervention, radiosurgery or radiation therapy may be a first line option There is no 'one size fits all' paradigm, as each patient presents with their own clinical and imaging findings upon which further treatment decisions should be based.

9% to 30%,[20,24,66] neuropsychological sequel in 10-12.5% patients, and delayed hypothalamic-pituitary damage in up to 23%. Fractionated radiotherapy has been used since the 1990s[20,65] for the postoperative management of these tumors with good tumor control rates. The early series using CRT are described in Table 4.

Evolution in conformal RT techniques such as intensity modulated radiation therapy (IMRT), stereotactic fractionated radiotherapy, proton beam therapy, and SRS has been used more frequently for treating these tumors.[11,19,34,53,54,61,64] Local tumor control using fractional conformal RT is best achieved with radiation doses of between 54 and 61 Gy[66] with diminished radiation-induced side effects of visual, pituitary dysfunction, cognitive changes, and development of secondary malignancies.[51] Tumor control rates after SRS range from 33% to 90%.[11,30,34,61,64] Niranjan *et al.*[61] in their series of 46 patients report overall survival rates and control rates at 5 years of 97.1% and 68%, respectively. Complications with SRS include radiation-induced optic neuropathy that has been reported at doses of greater than 8-10 Gy[43,57,80] with factors like previous radiation in the region, volume of the optic apparatus exposed playing a role in the development of this complication.[25] Although SRS avoids the long-term complications associated with fractionated RT, mean morbidity rates are around 4%.[22] Kobayashi[33] and Chung[12] noted favorable quality of life outcomes in patients who responded to SRS. The various reported series using both GK are reported in Table 5.

Table 3: Review of results for microsurgical excision and radiotherapy for craniopharyngiomas

Series	Year	No.	Complete %	Recurrence %	Partial	Partial %	Partial resection and RT	Partial resection and RT %	Recurrence %
McKissock and Ford[37]	1966	45	0	0	0	0	45	100	27
Kramer[36]	1968	16	0	0	0	0	16	100	19
Tandon Sharma[71]	1974	18	0	0	0	0	18	100	0
Katz[32]	1975	34	100	26	0	0	0	0	0
McMurry[49]	1977	30	33	20	9	30	11	37	18
Shapiro[70]	1979	38	58	23	9	24	7	18	0
Laws[40]	1980	26	35		15	58	2	8	
Carmel[9]	1982	43	33	50	14	33	14	33	21
Symon[76]	1985	20	100	5	0	NA	0	NA	NA
Sweet	1988	43	93	10	3	7	NA	NA	NA
Yasargil[87]	1990	144	90	7	NA	NA	NA	NA	NA
Samii[68]	1991	34	97	9	1	3	NA	NA	NA
Konovalov[35]	1992	198	64	NA	71	36	NA	NA	NA
Regine[66]	1993	56	21	NA	5	9	39	NA	33
Duff[15]	2000	121	57	17	NA	43	NA	NA	NA
Van Effentere and Boch[83]	2002	122	NA	59	13	NA	18	NA	NA
Minamida[52]	2005	37	NA	70	15	NA	30	NA	NA

NA: Not available, RT: Radiation therapy

Table 4: Summary results of main series using conventional radiation therapy for the treatment of craniopharyngiomas

Authors	No. treated	Year	Modality	Median dose (Gy)	Tumor size (ml)	Follow-up (months)	Control	Morbidity%
Regine[66]	58	1993	CRT	56-62	NA	17 years	82 at 10 years	NA
Rajan[65]	173	1993	CRT	50	NA	12 years	83 at 10 and 79 at 20 years	50
Hetelekidis[26]a	37	1993	CRT	54	NA	49	86 at 10 years	60
Habrand[23]a	37	1999	CRT	50	NA	NA	78 at 5 and 56.5 at 10 years	40
Merchant[50]a	15	2004	CRT	54	NA	72	94 at 5 years	80
Varlotto[84]	24	2002	CRT	60	NA	12 years	89 at 10 and 54 at 20 years	20
Stripp[74]	76	2004	CRT	55	NA	7.6 years	84 at 10 years	20
Pemberton[62]	87	2005	CRT	43	NA	8 years	77 at 10 and 66 at 20 years	10
Moon[56]	50	2005	CRT	54	12	12.8 years	96 and 91 at 5 and 10 years	15
Merchant[51]a	28	2006	CRT	55	NA	36	90 at 3 years	NA

CRT: Conventional radiotherapy, a: Pediatric series included, NA: Not applicable, Gy: Gray

Our patients receiving IMRT were treated with a standard dose of 54 Gy and the GKRS patients received marginal doses varying from 9 to 15 Gy with various series report marginal doses ranging from 3 to 25 Gy for long-term tumor control. Alternative dose plans prescribing lower margin doses with a high central dose at the same time avoid adverse radiation effects to adjacent organs at risk with good tumor control.[33] We prefer treating the tumor to the 50% isodose line and in cases where in the tumor and optic apparatus are in close proximity, the patients preferentially receive IMRT.

Alternative treatment options include intracavitary radiation and chemotherapy,[11] mainly used to treat recurrent cystic tumors. Pollock *et al.*[63] reported cyst control in 90.6% of patients using this treatment modality, however, Lunsford *et al.*[44] reported the ineffectiveness of intracavitary radiation for treating CPs with a more solid component. Installation of bleomycin into the cyst cavity has been advocated by Savas[69] and Takahashi[77] as an alternative, using its antineoplastic properties that interfere with DNA production, to suppress cyst fluid, and obliterate the cyst cavity.[11]

Although we tried to obtain histology in all our cases prior to treatment, this was not possible in four (4/11) patients. In two (2/4) of these patients, we attempted to biopsy the wall, however, doing a stereotactic biopsy of the cyst wall is technically challenging because of capsule shift after puncturing the wall, the associated adjacent vessels

Table 5: Summary of major reported GKRS/FSRT series for craniopharyngiomas

Authors	No. of patients	Year	Prior surgery%	Treatment modality	Marginal dose (Gy)	Follow-up (months)	Tumor control rates %	Morbidity/ mortality %
Backlund[4]	9	1979	22.2	GKRS	20-30	NA	100	11.1/0
Lunsford[45]	3	1993	33.3	GKRS	16.7-20	NA	67	33.3/0
Prasad[64]	9	1995	67	GKRS	12.9	NA	62.5	0/0
Mokry[55]	23	1999	39	GKRS	7.8-9.7	24	74	0/0
Chung[12]	31	2000	74	GKRS	12.2	36	87.2	3.2/0
Chiou[11]	10	2001	50	GKRS	16.4	67	58	10/0
Amendola[3]	14	2002	86	GKRS	14	39	86	0/0
Ulfarsson[82]	21	2003	56	GKRS	3-25	13.6 years	36	19/0
Kobayashi[34]	98	2005	100	GKRS	11.5	66	79.6	6/5
Barua[5]	7	2003	100	GKRS	14.2	50	100	NA
Albright[2]	5	2005	0	GKRS	NA	29	80	0/0
Combs[13]	40	2007	100	FSRT	52	98	100 at 10 years	10
Minniti[54]	39	2007	100	FSRT	50	40	92 at 5 years	32

GKRS: Gamma knife radiosurgery, FSRT: Fractionated stereotactic radiation therapy, NA: Not applicable, Gy: Gray

and the deep seated location of the tumor mass. Of the remaining two (2/11) patients, one patient had undergone VP shunting elsewhere and another had undergone shunt insertion and GKRS following which they had presented to us for further management. Even though other lesions have to be considered in the differential diagnosis of sellar–suprasellar neuroimaging,[7,68] with the age of the patient, clinical and laboratory findings along with computed tomography (CT) evidence of calcification and MRI imaging revealing heterogeneous enhancement of the solid component with a mixed solid-cystic sellar–suprasellar lesion, following a detailed discussion with the patient, both the patient and treating team decided to go ahead with our management strategy. Additional technical challenges associated with the stereotactic procedure are the appropriate placement of the Ommaya catheter accurately within the depth of the cyst. While histologically, papillary CPs are less likely to recur,[15,86] we could not analyze our outcome based on histology because of the absence of adequate specimens in many of our cases. In our series we used a combination of RT techniques, including IMRT and GKRS and have observed good long-term outcomes.

The overall 10-year survival rates for CPs presently range from 85% to 90%[31,83] and 62% to 76%[14,85] at 20 years, with mortality beyond that infrequently due to disease progression.[16] Mortini *et al.*[58] recently reported a loss of independence in activities of daily living and a decreased quality of life on long-term follow up after surgery in CPs. Thus, in the treatment of carefully selected adult patients, alternative minimalistic treatment options have to be integrated into the management plan in order to avoid major morbidity related to surgery. Additional advantages include shorter hospital stays, maintaining their activity level, quality of life, and immediately resume their active lifestyle.

CONCLUSION

CP management requires an individualized, multi-disciplinary approach. Radical surgery is not justified in all cases, especially with adjunct treatment modalities now readily available. The good long-term control rates, low endocrine, visual and cognitive morbidity and minimal to no mortality, and short hospital stays make minimally invasive strategies a viable option for the long-term control of these tumors in the elderly and other well-selected patients.

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