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ORIGINAL ARTICLE

Multimodality Treatment of Craniopharyngioma: Aspiration of Cystic Contents and Placement of Ommaya Reservoir Stereotactically Followed by Gamma Knife Radiosurgery – Single Center Study of 81 Cases

AURANGZEB KALHORO[1], SANAM B. RAJPER[2], ABID SALEEM[2], A. SATTAR M. HASHIM[2]
[1]Neurospinal and Cancer Care Institute, Karachi Pakistan & Jinnah Medical Dental College
[2]Neurospinal and Cancer Care Institute, Karachi –Pakistan

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ABSTRACT

Objective: *The aim of the current study was to define the outcome of the Craniopharyngioma by available multiple treatment options.*

Material and Methods: A *Retrospective study was Neurospinal and Cancer Care Institute Karachi. A total of 81 consecutive patients who underwent treatment were included. Information regarding the treatment parameters like volume, prescribed dose, maximum dose was noted along with the baseline characteristics like age and gender of the patients. The 24-months survival was also observed in these patients after stereo tactically reservoir placement, aspiration and Gamma knife radiosurgery.*

Results: *The median age was 18 (IQR: 12-33) years. The median volume, prescription dose and maximum dose was 9.2 (IQR: 5.35-17.40) ml, 12 (IQR: 10-12) Gy, and 24 (IQR: 22-26) Gy respectively. 24-months follow-up showed that complete response was observed in 59 (72.8%), mild to moderate reduction in 20 (24.7%) whereas mortality in 2 (2.5%) patients. Amongst the two patients in whom mortality was observed, one patient had increased the size of tumor, whereas another patient showed a static tumor in size. The overall survival rate was 97.5%.*

Conclusion: *Craniopharyngioma is a tumor can be managed by multiple treatment options dueto its presentation and attachments. The multimodality management is associated with improved tumor control with acceptable complications.*

Keywords: *Craniopharyngioma, Ommaya Reservoir, Stereotactic, Gama Knife Radiosurgery Surgery.*

INTRODUCTION

The ideal management of Craniopharyngioma (CP) is challenging due to their location, it's a slow growing benign tumor. The emergence of CPs is observed from Rathke's cleft or craniopharyngeal duct.[1] Between the age group, these tumors occur children and adults with a bimodal age distribution.[2] The location of these tumors is considered with pituitary stalk, visual apparatus, vasculature from the Willis circle and 3rd ventricle.[3] In selected patients, gross total resection (GTR) deemed to be effective about the local tumor control as compared to subtotal resection. Thereby, the mainstay therapeutic approach is represented by GTR.[4] The purpose GTR can be complex to achieve due to the intimate correlation between the neural and vascular structures and tumor, regardless of any endocrine, surgery-related visual and neurologic complications.[5]

High operative mortality and morbidity implies formidable difficulties in order to treat these tumors, although the progression in endoscopic and microsurgical techniques offer better surgical

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outcomes to neurosurgeons in the form of success rate and the GTR rate of repeat surgeries.[6]

The use of Gamma Knife surgery (GKS) has been demonstrated recently for residual or recurrent Craniopharyngioma associated with local progression or tumor control free survival. It has been used increasingly for treating recurrent or residual Craniopharyngioma by zero mortality and lower morbidity.[7]

The study intended to determine progression free survival among Craniopharyngioma patients treated with multiple available options as cystic aspiration and GKS. This would be its kind of study from Pakistan to report the outcome of Craniopharyngioma patients treated with multiple treatment option including gamma knife surgery as an in-depth literature.

MATERIALS AND METHODS

Study Design

Retrospective analytic study. This study was conducted at the Neurospinal and Cancer Care Institute, Karachi, Pakistan from June 2012 and January 2018. A total of 81 consecutive patients who underwent treatment were included.

Inclusion Criteria

The age above 5 years, clinical and imaging favoring the diagnosis of Craniopharyngioma having cystic and sold component on imaging.

Exclusion Criteria

Age less than 5 years, previously operated cases, recurrent cases.

Surgical Technique

Gamma knife technique in adults was performed using a Leksell frame which was placed under local anesthesia exceptionwas considered for the GKS procedure in pediatric patients,especially under the age of 14 for placement of the frame was done under general anesthesia, which was retained during the GKS procedure. Thereafter, MRI brain was donewith a stereotactic frame to proceeds further treatment plans. When due to implants or other reason MRI was not possible, CT scan brain was choice for target selection. The main purpose of planning the dosage in GKS for Craniopharyngioma was to maximize the effect in the solid portion of the tumor without causing irradiation of the surrounding normal brain structure or with minimal effect especially deep structures which were sensitive to radiation notable structure were hypothalamus, brainstem, optical apparatus and thalamus. When the optical apparatus was in close range to Craniopharyngioma was treated with lower doses, resulting in a maximum dose of less than 12 Gy for the visual pathway structures. Cystic components were treated on the same day or a few days before with stereotactic aspiration followed by radiosurgery.

Follow-up

After GKS, all patients underwent on average 24-months intervals of clinical evaluations.

Information regarding the treatment parameters like volume, prescribed dose and maximum dose were noted along with the baseline characteristics like age and gender of the patients. The 24-months survival was also observed in these patients after aspiration and reservoir placement stereotactically and Gamma knife radiosurgery.

Data Analysis

Statistical analysis for Social Sciences (SPSS) version 22 was used for the purpose of statistical analysis. Median and interquartile ranges were reported for quantitative variables like age and treatment parameters like volume, prescribed dose and maximum dose. Frequency and percentages were calculated for quantitative variables like gender, complete response, and 12-months survival. Statistical analysis was carried out using Mann-Whitney U test and chi-square test. P-value < 0.05 was taken as significant.

RESULTS

Out of total 81 patients, the median age was 18 (interquartile range-IQR: 12-33) years, while minimum age was five years and maximum age was 53 years. There were 60 (74.1%) males and the remaining 21 (25.9%) were females. The median volume of the Craniopharyngioma was 9.2 (IQR: 5.35-17.40) ml; ranges from 0.98 ml as the minimum and 57.40 as the maximum. The median prescription dose was 12 (IQR: 10-12); ranges from 1 as the minimum and 23 as the maximum. The maximum dose was 24 (IQR: 22-26).

All patients were clinically followed-up by neuroimaging, complete response was observed in 59

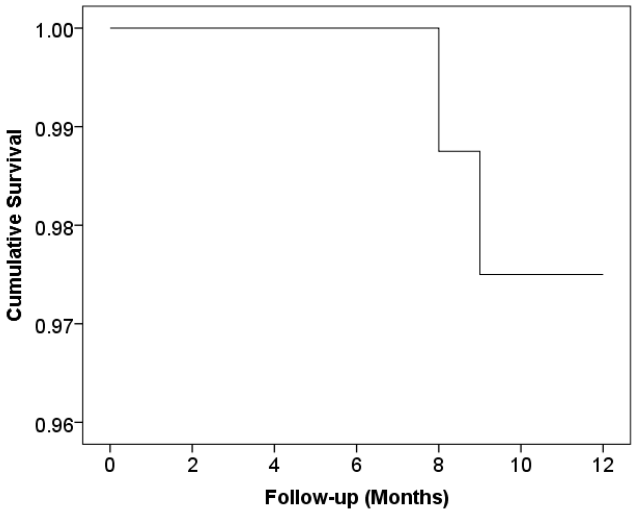

Fig. 1: *Survival Curve Demonstrating Overall Survival Following GKS.*

(72.8%), mild to moderate reduction in 20 (24.7%) whereas mortality in 2 (2.5%) patients. Amongst the two patients in whom mortality was observed, one patient had increased the size of the tumor, whereas another patient showed a static tumor in size. The overall survival rate was 97.5% (Figure 1).

The comparison of treatment parameters of Craniopharyngioma patients with age and gender has showed significant difference of maximum dose with age (p-value 0.014) only (Table 1).

An insignificant association of gamma knife surgery was observed with prognostic factors like age (p-value 0.117), gender (0.191), volume (p-value 0.767), prescribed dose (p-value 0.494) and maximum dose (p-value 0.168 (Table 2).

Table 1: *Comparison of Treatment Parameters of Craniopharyngioma Patients with Age and Gender.*

	Volume, ml	**Prescribed Dose, Gy**	**Maximum Dose, Gy**
Total (n = 81)	9.2 (5.4 – 17.4)	12 (10-12)	24 (22-26)
Age, Years			
≤ 18 (n = 41)	10.2 (6.2 – 17.4)	12.0 (10.0-12.0)	24 (20-24)
> 18 (n = 40)	8.1 (4.7 – 18.5)	12.2 (10.0-13.0)	24 (24-27)
p-value	*0.527*	*0.109*	*0.014**
Gender			
Male (n = 60)	13.4 (5.0 – 17.7)	12 (10.0-12.0)	24 (22.1-25.8)
Female (n = 21)	8.5 (6.5 – 17.8)	12 (10-13.5)	24 (22.5-28.0)
p-value	*0.901*	*0.340*	*0.578*

All data presented as median (IQR), Mann-Whitney u test applied, p-value < 0.05 taken as significant, *significant

Table 2: *Comparison of Outcome of GKS among Craniopharyngioma Patients with Prognostic Factors.*

Variables	**Total**	**Complete Response**		**p-value**
		Yes	**No**	
		n (%)	**n (%)**	
Age, years				
≤ 18	41	33 (81)	8 (20)	0.117
> 18	40	26 (65)	14 (35)	
Gender				
Male	60	46 (77)	14 (23)	0.191
Female	21	13 (62)	8 (38)	
Volume, ml				
≤ 19	39	29 (74)	10 (26)	0.767
> 19	42	30 (71)	12 (29)	
Prescribed Dose, Gy				
≤ 12	62	44 (71)	18 (29)	0.494

> 12	19	15 (79)	4 (21)	
Maximum Dose, Gy				
≤ 24	57	39 (68)	18 (32)	0.168
> 24	24	20 (83)	4 (17)	

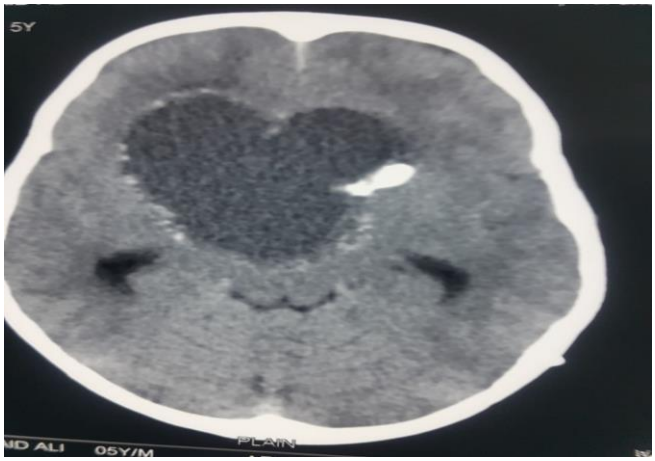

Fig. 2: *CT Brain showing that Ommaya Reservoir in Cystic Portion.*

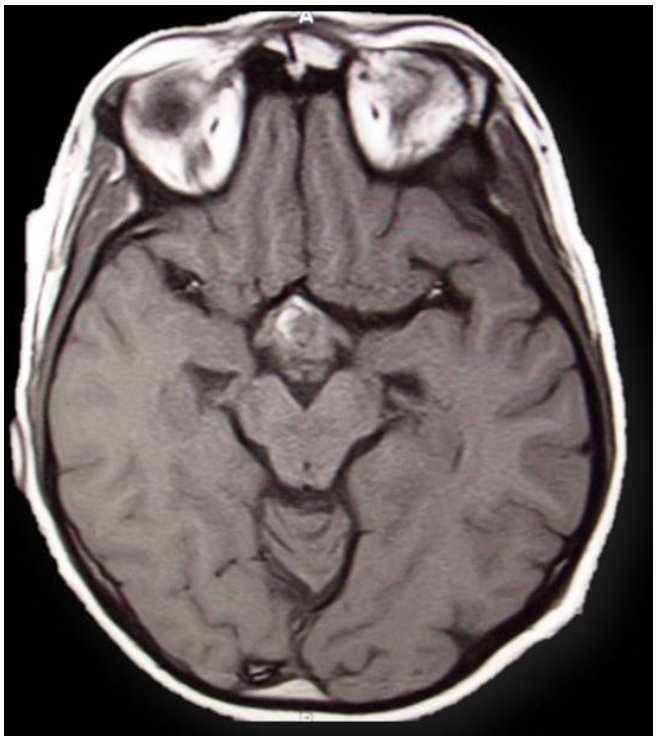

Fig. 3: *Result of Craniopharyngioma after One-Year Follow-up.*

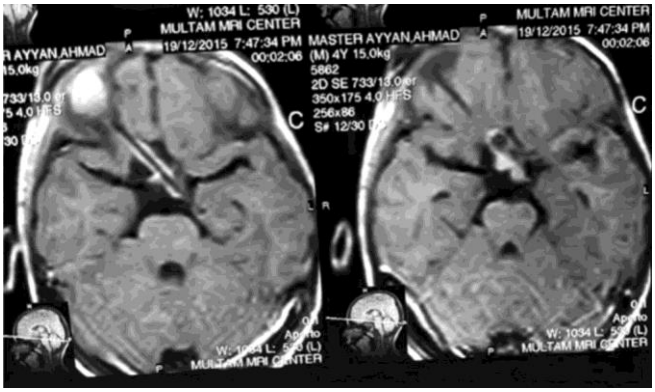

Fig. 4: *MRI Brain Axial View Showing Ommaya Reservoir in Situ.*

DISCUSSION

This study was conducted at neurospinal and cancer care institutes with Gamma knife and Stereotactic placement of the reservoir.In the current study, multiple modality options used to improve progression free survival among Craniopharyngiomas patients treated with GKS were studied. Previously, several studies have reported the use of Gamma Knife surgery among Craniopharyngioma patients.[8-10] The outcome of the study has showed a satisfactory response in the majority of the patients while mortality was observed in only 2 patients. Although this finding matched with a previous study of Bishop et al in which progression free survival was observed in almost 92% of the patients.[11] The only difference observed was that the follow-up in the current study was 2 years. However, in the study of Bishop et al, five-year survival was reported. A 10-year survival rate of 91% was also reported in a study by Kobayashi et al,[12] Control was seen in 90%, 80% and 59% solid, cystic and in mixed tumors, respectively, with a mortality of 0.5% conducted by Gopalan et al,[13] while in this study, 94% control was observed.

In the current study, of 2 patients in whom mortality was observed, 1 patient had increased the size of the tumor, whereas another patient showed a static tumor in size. In a previous study, mortality was reported in almost 9% patients.

The literature review revealed Craniopharyngioma series of differences in progression-free survival and overall survivalrates based on the different radiosurgical images. In the study, the overall 5-year survival was 75.5 percent and progression free survival rates was 67 percent[14]. Hasegawa et al. reported a 5-and 10-year progression of free survival

rates of 62 per cent and 52 per cent respectively [15]. Niranjan et al. reported a total 5-year survival rate of 97.5 percent and a 5-year progression-free survival rate of 91.6 percent.[16]

In the current study, the median prescription dose was 12 whereas the maximum dose was 24. Various studies have reported that a dose of 12 Gy may be adequate for tumor control,[12,17] and the dose to the optic apparatus in the vicinity should not exceed 8 Gy. A highly conformal plan should be tailored to minimize dosing to the optic apparatus, using smaller radiation doses. Cystic enlargement of Craniopharyngioma can occur after gamma knife surgery, leading to visual deterioration,[18] which may require aspiration of the cyst for immediate relief. In the study of Kobayashi et al.[12] the prescribed dose was 11.5 Gy.

The results of the study were also corroborated with the findings of other studies that revealed a strong association between marginal dose to the tumor and effect of GKS.[9,10,19,20] Tumor volume and proximity to vital structures are the factors that rely on the selection of marginal dose. Generally, the effective consequences were attained with marginal cystic aspiration resulting in decrease volume, followed by GKS. Paucity of VFG can be interpreted as that tumor was not reachable due to the substantial decrease from an appropriate decompression in tumor size.[9,21] Therefore; it allows an increase of marginal quantity to the solid component of the tumor, which results in an expanded in-field program for studies.

The finding of our study could be highlighted in the light of the limitation that the sample size was smaller and shorter follow-up period. Therefore, our data should be extrapolated to generalize the findings by undertaking larger sample size. Also, future studies should include hospital stays, patient's activity level, and quality of life as to be examined for the specific disease through the treatment used.

Because the Craniopharyngioma is a benign tumor and varied mode of presentation in both adults and in children; the treatment options of patients having such variable tumor are diverse and surgical treatment options range from aspiration of cystic contents and placement of the Ommaya reservoir to craniotomy and complete excision or partial debulking to chemotherapy or radiotherapy or radiosurgery. This tumor is more complicated and complex in its clinical presentation and position and in its connection to the medical and sensitive systems around it.

CONCLUSION

The current study suggests that Craniopharyngioma is a tumor that must be managed by multiple treatment options; initially debulk decrease pressure effects on the surrounding critical vital structures by aspiration of cystic contents and Ommaya reservoir placement followed by Gamma Knife radiosurgery. This multimodality management is associated with improved tumor control with acceptable complications.

REFERENCES

1. Himes BT, Ruff MW, Van Gompel JJ, Park SS, Galanis E, Kaufmann TJ, Uhm JH. Recurrent papillary craniopharyngioma with BRAF V600E mutation treated with dabrafenib: case report. Journal of Neurosurgery, 2018; 130 (4): 1299-303.
2. Chu C, Su Y, Lieu A, Lin C, Kwan A. Comparison Study of Clinical Presentation and Surgical Outcome between Children and Adults with Craniopharyngioma: A 22-Year Single-Center Experience in Southern Taiwan. J Neurol Disord. 2017; 5 (350): 2.
3. Attuati L, Picozzi P. Radiotherapy and Radiosurgery for Craniopharyngiomas. In Diagnosis and Management of Craniopharyngiomas, 2016: (pp. 101-112). Springer, Cham.
4. Kobayashi T, Tsugawa T, Hatano M, Hashizume C, Mori Y, Shibamoto Y. Gamma knife radiosurgery of craniopharyngioma: results of 30 cases treated at Nagoya Radiosurgery Center. Nagoya Journal of Medical Science, 2015; 77 (3): 447.
5. Müller HL. Craniopharyngioma and hypothalamic injury: latest insights into consequent eating disorders and obesity. Current Opinion in Endocrinology, Diabetes, and Obesity, 2016; 23 (1): 81.
6. Lania A, Spada A, Lasio G. Diagnosis and management of craniopharyngiomas. Springer International Publishing, 2016.
7. Lubuulwa J, Miao Z, Liu S, Chen J, Wang S, Jiang W, Shu K, Lei T. Clinical, Pathological and Surgical Risk Factors Associated with Craniopharyngioma Recurrence: A Literature Review. Neurosurgery, 2019; 9: 61-77.
8. Muskens IS, Najafabadi AH, Briceno V, Lamba N, Senders JT, van Furth WR, Verstegen MJ, Smith TR, Mekary RA, Eenhorst CA, Broekman ML. Visual outcomes after endoscopic endonasal pituitary adenoma resection: a systematic review and meta-analysis. Pituitary, 2017; 20 (5): 539-52.
9. Dho YS, Kim YH, Kim JW, Park CK, Chung HT, Kim SK, Paek SH, Wang KC, Kim DG. Optimal strategy of gamma knife radiosurgery for craniopharyngiomas. Journal of Neuro-Oncology, 2018; 140 (1): 135-43.

10. Losa M, Pieri V, Bailo M, Gagliardi F, Barzaghi LR, Gioia L, Del Vecchio A, Bolognesi A, Mortini P. Single fraction and multisession Gamma Knife radiosurgery for craniopharyngioma. Pituitary, 2018; 21 (5): 499-506.
11. Bishop AJ, Grosshans DR. Craniopharyngioma. InRadiation Oncology for Pediatric CNS Tumors, 2018: pp. 295-309. Springer, Cham.
12. Kobayashi T, Kida Y, Mori Y, Hasegawa T. Long-term results of gamma knife surgery in the treatment of craniopharyngioma in 98 consecutive cases. J Neurosurg. 2005; 103 (6 Suppl): 482-8.
13. Gopalan R, Dassoulas K, Rainey J, Sherman JH, Sheehan JP. Evaluation of the role of Gamma Knife surgery in the treatment of craniopharyngiomas. Neurosurgical Focus, 2008; 24 (5): E5.
14. Xu Z, Yen CP, Schlesinger D, Sheehan J: Outcomes of Gamma Knife surgery for craniopharyngiomas. J Neurooncol. 2011; 104: 305–313.
15. Hasegawa T, Kobayashi T, Kida Y: Tolerance of the optic apparatus in single-fraction irradiation using stereotactic radiosurgery: evaluation in 100 patients with craniopharyngioma. Neurosurgery, 2010; 66: 688–695.
16. Niranjan A, Kano H, Mathieu D, Kondziolka D, Flickinger JC, Lunsford LD: Radiosurgery for craniopharyngioma. Int J Radiat Oncol Biol Phys. 2010; 78: 64–71.
17. Ulfarsson E, Lindquist E, Roberts M, Rähn T, Lindquist M, Thorén M, et al. Gamma Knife radiosurgery for craniopharyngiomas: Long-term results in the first Swedish patients. J Neurosurg. 2002; 97 (5 Suppl): 613-22.
18. Chung WY, Pan DH, Shiau CY, Guo WY, Wang LW. Gamma knife radiosurgery for craniopharyngiomas. J Neurosurg. 2000; 93 (3 Suppl): 47-56.
19. Juloori A, Murphy ES. Pediatric Radiosurgery. In Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy, 2019: 331-343. Springer, Cham.
20. Saleem MA, Hashim AS, Rashid A, Ali M. Role of gamma knife radiosurgery in multimodality management of craniopharyngioma. InGamma Knife Neurosurgery in the Management of Intracranial Disorders, 2013: 55-60. Springer, Vienna.
21. Mortini P, Gagliardi F, Bailo M, Losa M. Surgical Approach to Craniopharyngiomas: Transcranial Routes. In Diagnosis and Management of Craniopharyngiomas, 2016: 85-99. Springer, Cham.

Additional Information

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Human Subjects: Consent was obtained by all patients/participants in this study.

Conflicts of Interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following.

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Address for Correspondence: Aurangzeb Kalhoro
Department of Neurosurgery, Jinnah Medical Dental College, Karachi
draurangzebkalhoro@gmail.com

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr.#	Author's Full Name and Affiliation	Intellectual Contribution to Paper in Terms of:
1.	Aurangzeb Kalhoro	Study design and methodology. Proposed topics and Basic Study Design, & data collection statistical analysis Data collection and calculations
2.	Sanam B Rajper	Referencing, data calculations and manuscript writing
3.	Abid Saleem	Analysis of data and interpretation of results etc.
4.	Abdul Sattar M. Hashim	Analysis of data and quality insurer Literature review