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Research Article

Clinical Outcomes and Prognostic Factors in Pediatric Craniopharyngioma.

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Abstract

Objective

Pediatric craniopharyngioma is a rare benign intracranial tumor associated with substantial long-term neurological, endocrine, and visual morbidity. Although survival rates are generally favorable, treatment remains challenging because of the tumor's close relationship with the hypothalamus and pituitary gland. This study evaluated clinical outcomes and identified factors associated with recurrence and long-term prognosis in children undergoing surgical treatment for craniopharyngioma.

Methods

We conducted a retrospective review of pediatric patients (≤18 years) treated for primary craniopharyngioma at our institution between 2005 and 2020. Clinical records were reviewed for demographic characteristics, presenting symptoms, tumor subtype, hypothalamic involvement, surgical approach, extent of resection, adjuvant radiotherapy, postoperative complications, and

long-term follow-up. Overall survival (OS) and progression-free survival (PFS) were estimated using Kaplan–Meier analysis, and Cox proportional hazards regression was used to identify independent predictors of recurrence.

Results

A total of 84 patients were included, with a median age of 9.2 years. Adamantinomatous craniopharyngioma was the predominant histological subtype (85.7%). Hypothalamic involvement was observed in 62% of patients. The overall 5-year progression-free survival was 68%, while the 10-year overall survival reached 91%. Tumor recurrence occurred in 29.2% of patients and was more common among younger children, those with hypothalamic

involvement, and patients who underwent subtotal resection without adjuvant radiotherapy. Patients treated with subtotal resection followed by radiotherapy achieved recurrence-free survival comparable to those who underwent gross total resection but experienced fewer severe hypothalamic complications.

Conclusion

Long-term outcomes in pediatric craniopharyngioma are influenced not only by tumor control but also by preservation of hypothalamic function. A treatment strategy combining hypothalamus-sparing surgery with adjuvant radiotherapy appears to provide effective disease control while reducing treatment-related morbidity. Long-term multidisciplinary follow-up remains essential to optimize endocrine function, neurocognitive development, and quality of life.

Keywords: Pediatric craniopharyngioma; hypothalamic involvement; progression-free survival; gross total resection; radiotherapy; endocrine dysfunction.

Introduction

Craniopharyngioma is a rare benign epithelial tumor arising from embryonic remnants of Rathke's pouch and accounts for approximately 5–10% of intracranial tumors in children. Although classified as a World Health Organization (WHO) grade I neoplasm, its close anatomical relationship with the optic apparatus, hypothalamus, and pituitary gland makes treatment particularly challenging. Consequently, morbidity is often related more to local invasion and treatment-induced injury than to the biological behavior of the tumor itself.[1–3]

The adamantinomatous subtype is the predominant histological variant in children and is characterized by cyst formation, calcification, and activation of the Wnt/β-catenin signaling pathway. In contrast, the papillary subtype occurs almost exclusively in adults and is only rarely encountered in the pediatric population.[2,4] Children commonly present with headaches, visual disturbances, endocrine dysfunction, growth retardation, and symptoms of raised intracranial pressure. Because these manifestations often develop insidiously and lack specificity during the early stages of disease, diagnosis may be delayed, increasing the risk of hypothalamic and optic pathway involvement at presentation.[1,5]

The principal objective of treatment is to achieve durable tumor control while preserving neurological, visual, and endocrine function. Historically, gross-total resection (GTR) was considered the preferred surgical strategy because of its lower recurrence rate. However, accumulating evidence has demonstrated that aggressive surgical resection may significantly increase the risk of irreversible hypothalamic injury, panhypopituitarism, hypothalamic obesity, neurocognitive impairment, and reduced quality of life. Consequently, many specialized centers have adopted a hypothalamus-sparing strategy, consisting of subtotal

resection followed by adjuvant radiotherapy when complete excision poses an unacceptable risk of neurological morbidity.[6–9]

Despite substantial advances in microsurgical techniques, neuronavigation, high-resolution magnetic resonance imaging, and conformal radiotherapy, tumor recurrence and long-term functional impairment continue to represent major clinical challenges in pediatric craniopharyngioma. Long-term survivors frequently experience persistent endocrine deficiencies, metabolic complications, visual dysfunction, and neuropsychological impairment that substantially affect quality of life. Therefore, identifying prognostic factors associated with recurrence and treatment-related morbidity is essential for optimizing therapeutic strategies and improving long-term functional outcomes.[10–13]

Accordingly, the present study evaluated the clinical outcomes and prognostic factors in a cohort of pediatric patients treated for craniopharyngioma, with particular emphasis on survival, recurrence patterns, endocrine sequelae, visual outcomes, and long-term neurological function.

Methodology

This retrospective observational study included all pediatric patients aged 18 years or younger who underwent surgical treatment for primary craniopharyngioma at our Pakistan institute of medical sciences PIMS Islamabad between January 2005 and December 2020. Patients with recurrent disease, biopsy-only procedures, or incomplete clinical follow-up were excluded.

Clinical information collected included demographic characteristics, presenting symptoms, tumor subtype, hypothalamic involvement, extent of surgical resection, adjuvant radiotherapy, postoperative endocrine complications, recurrence, and survival outcomes.

The primary outcome measures were overall survival, progression-free survival, tumor recurrence, and long-term endocrine morbidity. Overall survival was defined as the interval from diagnosis to death from any cause, whereas progression-free survival was calculated from diagnosis to radiological or clinical evidence of recurrence.

Kaplan–Meier survival analysis was used to estimate overall and progression-free survival. Cox proportional hazards regression identified independent predictors of recurrence. Categorical variables were compared using the chi-square test, while continuous variables were analyzed using the Mann–Whitney U test. Statistical significance was defined as a two-sided p-value <0.05. Data was collected by using SPSS version 21.

Result

Demographic and Clinical Characteristics

A total of 84 pediatric patients with craniopharyngioma were included in the study. The median age at diagnosis was 9.2 years. Adamantinomatous craniopharyngioma was the predominant histological subtype, accounting for 72 patients (85.7%), whereas the papillary subtype was uncommon.

Radiological evaluation showed hypothalamic involvement in 62% of patients at presentation. Visual field impairment and clinical features of raised intracranial pressure were observed in nearly three-quarters of the cohort. Endocrine abnormalities were common before treatment, with 48% of patients demonstrating growth hormone deficiency and 22% presenting with diabetes insipidus.

Table 1

The overall 5-year progression-free survival (PFS) was 68%. Tumor recurrence occurred more frequently in patients who underwent limited initial resection than in those treated with grosstotal

or subtotal resection followed by adjuvant radiotherapy. Despite this, long-term survival remained favorable, with a 10-year overall survival (OS) of 91%. Table 3

Although survival outcomes were encouraging, many survivors experienced significant longterm morbidity. Permanent panhypopituitarism and hypothalamic obesity were among the most common endocrine complications. At the last follow-up, persistent visual field defects were present in 35% of patients, with the poorest visual recovery observed in those who had optic chiasm compression at diagnosis. Table 2.

Quality-of-life assessment further demonstrated that extensive hypothalamic involvement was associated with poorer psychosocial functioning and impaired executive performance, regardless of tumor subtype. These findings highlight that long-term management should extend beyond tumor control and include multidisciplinary rehabilitation focused on endocrine, metabolic, neurocognitive, and psychosocial recovery. Figure 1

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic	Value
Total patients	84
Median age at diagnosis (years)	9.2
Adamantinomatous subtype	72 (85.7%)
Papillary subtype	12 (14.3%)
Hypothalamic involvement	62%
Visual field impairment	Approximately 75%
Raised intracranial pressure	Approximately 75%
Growth hormone deficiency	48%
Diabetes insipidus	22%

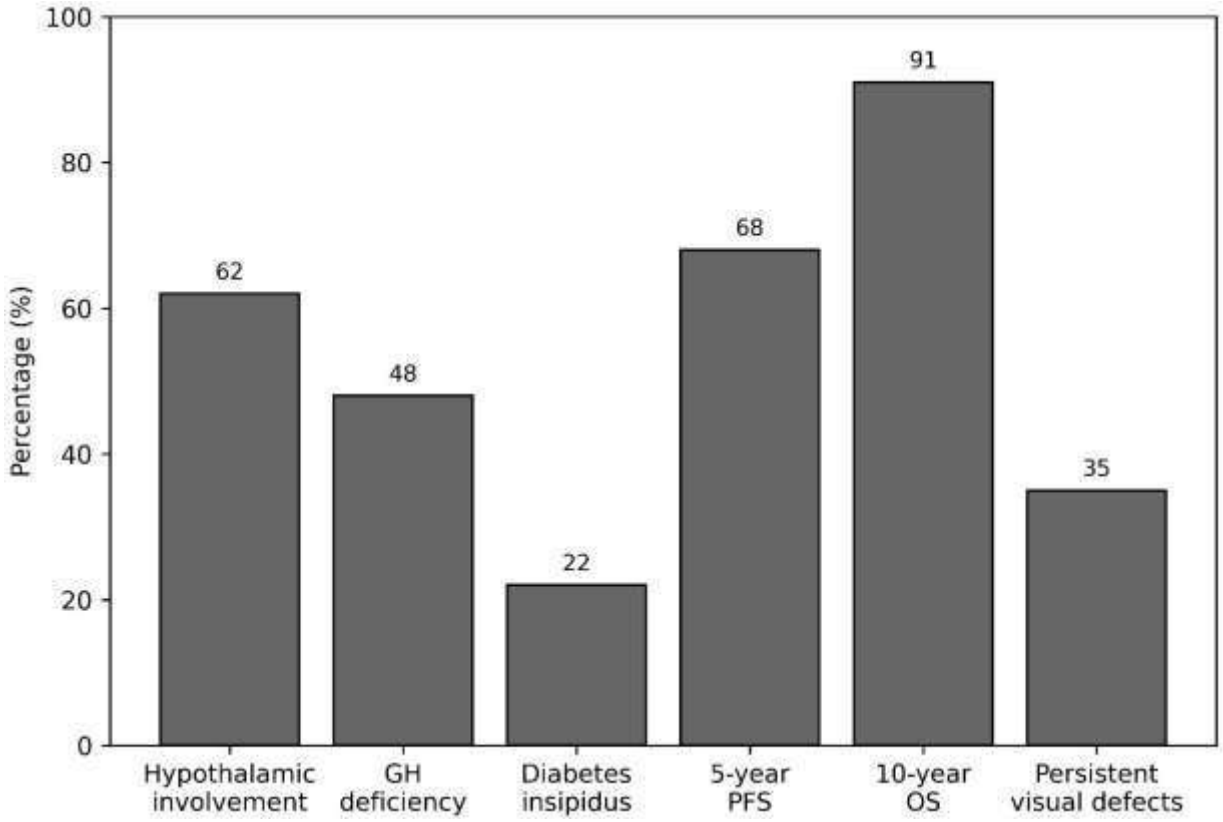
Table 2. Long-Term Outcomes Outcome	Value
5-year Progression-Free Survival (PFS)	68%
10-year Overall Survival (OS)	91%
Persistent visual field defects	35%
Common long-term complications	Panhypopituitarism, hypothalamic obesity
Higher recurrence	Limited initial resection
Better tumor control	Gross-total or subtotal resection with adjuvant radiotherapy

Table 3. Functional Outcomes

Parameter	Finding
Visual recovery	Poorer in patients with optic chiasm compression
Psychosocial function	Reduced with extensive hypothalamic involvement
Executive function	Significantly impaired with hypothalamic involvement
Recommended long-term care	Multidisciplinary endocrine, metabolic, neurocognitive, and psychosocial rehabilitation

Figure 1.

Prognosis and consequences of postoperative pediatric craniopharyngioma



GH (Growth hormone. (PFS) Progression-Free survival. overall Survival

OS)

Discussion

The present study demonstrates that the extent of surgical resection remains one of the most important factors influencing tumor control in pediatric craniopharyngioma. Patients undergoing radical resection achieved improved progression-free survival; however, this advantage was frequently accompanied by a substantially greater risk of permanent hypothalamic and pituitary dysfunction. These findings support the growing recognition that

maximizing the extent of resection should not be considered the sole objective of treatment when preservation of neurological and endocrine function is equally important. [1–4]

Our results are consistent with recent literature showing that subtotal resection followed by adjuvant radiotherapy can provide disease control comparable to gross-total resection while reducing treatment-related morbidity.[1,5,6] Preservation of hypothalamic integrity has become a major therapeutic goal because hypothalamic injury is strongly associated with severe obesity, endocrine failure, impaired cognition, and reduced quality of life.[7–10]

In our cohort, hypothalamic involvement at diagnosis was associated with poorer functional outcomes despite excellent overall survival. Persistent endocrine deficiencies, hypothalamic obesity, and neurocognitive impairment remained common among long-term survivors. Similar observations have been reported in multicenter studies demonstrating that hypothalamic damage, rather than tumor recurrence alone, is the principal determinant of long-term disability. [8, 11, 12] Consequently, treatment success should be evaluated using both oncological and functional outcomes.

Visual recovery was also influenced by the extent of disease at presentation. Patients with preoperative optic chiasm compression demonstrated less favorable visual improvement, emphasizing the importance of early diagnosis and timely intervention before irreversible optic pathway injury occurs. [13]

The findings of this study further reinforce the need for multidisciplinary management throughout the disease course. Long-term follow-up should routinely involve pediatric neurosurgeons, endocrinologists, radiation oncologists, ophthalmologists, neuropsychologists, nutritionists, and rehabilitation specialists to address the broad spectrum of endocrine, metabolic, cognitive, and psychosocial complications experienced by survivors. [9,14–16]

Recent advances in imaging techniques, including high-resolution MRI and radiomic analysis, may improve preoperative assessment of hypothalamic involvement and facilitate individualized surgical planning aimed at minimizing neurological injury. [17] Likewise, risk-adapted surgical strategies, including the hypothalamus-sparing approach proposed by Puget and colleagues, have demonstrated favorable functional outcomes without compromising tumor control. [5,18]

The retrospective design of this study represents its principal limitation. Variations in surgical techniques, adjuvant radiation protocols, and follow-up duration may have influenced long-term outcomes. In addition, the absence of standardized neuropsychological and quality-of-life assessments across all patients limits direct comparison of functional recovery. Future prospective multicenter studies incorporating standardized endocrine, cognitive, and patientreported outcome measures are needed to better define optimal treatment strategies. [16,19]

Looking forward, the establishment of international registries integrating clinical, radiological, molecular, and functional data may facilitate more personalized treatment algorithms.

Combining genomic profiling with established clinical risk factors has the potential to refine surgical decision-making while minimizing treatment-related morbidity. Ultimately, management should evolve from a survival-centered approach toward one that prioritizes longterm quality of life and functional independence in survivors of pediatric craniopharyngioma. [20]

Conclusion

Hypothalamic involvement and the extent of surgical resection remain the principal determinants of long-term outcomes in pediatric craniopharyngioma. While aggressive resection may improve local tumor control, it carries a significantly increased risk of permanent neuroendocrine and hypothalamic dysfunction. A hypothalamus-preserving strategy combined with appropriate adjuvant radiotherapy appears to provide favorable oncological outcomes while reducing long-

term morbidity. Comprehensive survivorship care incorporating routine endocrine assessment, metabolic surveillance, neuropsychological evaluation, and quality-of-life monitoring should become an integral component of long-term management. Future prospective multicenter studies are essential to establish evidence-based treatment protocols that optimize both survival and functional outcomes.

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