Quality of Life and Clinical Features of Long-Term Survivors Surgically Treated for Pediatric Craniopharyngioma

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■ OBJECTIVE: **Several studies have reported treatment methods and results for pediatric craniopharyngiomas; however, few have evaluated patients' quality of life (QOL) after long-term follow-up. To evaluate treatment options, we assessed the QOL of patients with pediatric craniopharyngioma approximately 19 years after surgery and analyzed factors affecting QOL.**

■ METHODS: **Twenty-six survivors who underwent resection of craniopharyngiomas at <15 years of age enrolled in this study and their physical condition was assessed. QOL was assessed by a short-form health survey (SF-36 version 2) for patients older than 19 years of age or by Child Health Questionnaire Parent Form-50 for patients 18 years of age and younger. Patients were divided into good and fair QOL groups according to their physical and mental summary scores. Factors affecting the QOL of both groups were evaluated.**

■ RESULTS: **Median follow-up time was 19.1 years (range, 2.8–44.1 years). Twenty-two (84.6%) patients were employed or in school; 14 (53.8%) had visual deficits. Panhypopituitarism was diagnosed in 22 of 26 (84.6%) subjects. SF-36 analysis indicated that patients had significantly lower scores for general and mental health. Visual deficits, obesity, and complications during follow-up significantly affected the fair QOL group long-term. Patients' basic characteristics, initial resection rates, times of operation or irradiation did not significantly affect long-term QOL.**

■ CONCLUSION: **Long-term survivors lived independently but had a lower overall QOL. Not only monitor short-term results based on estimation of the initial resection or recurrence rate, it is important to preserve visual and hypothalamic function and monitor arising complications for extended periods to improve patients' long-term QOL.**

INTRODUCTION

Craniopharyngiomas are rare pediatric brain tumors arising from the remnants of the Rathke pouch. Although histologically benign tumors, they are challenging to treat because of their location. Typically, these tumors are surrounded by the optic pathway, pituitary stalk, hypothalamus, third ventricle, and important blood vessels. Compression of these neural and vascular structures can cause visual impairment, endocrine disturbance, and hydrocephalus. Hypothalamic–pituitary function deficit, visual impairment, and obesity are common complications in the postoperative period after treatment for pediatric craniopharyngioma,[1] and despite high rates of survival, reportedly reduce quality of life (QOL).[2-5]

The optimal treatment of childhood craniopharyngioma remains a controversial subject. Total resection is advocated by many groups[6] because of the high local recurrence rates that have been reported after partial surgical resection[7,8]; however, radical surgery and irradiation can result in severe damage to the optic pathway and hypothalamic–pituitary axis, decreasing patients' QOL.[6,9] Therefore, some groups have advocated limited surgery

Key words
- Craniopharyngioma
- Long-term follow-up
- Pediatrics
- Quality of life

Abbreviations and Acronyms
BMI: Body mass index
CHQ-PF50: Child Health Questionnaire Parent Form-50
MCA: Mental component summary
MRI: Magnetic resonance imaging
PCA: Physical component summary
QOL: Quality of life

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without radiotherapy to minimize hypothalamic damage[10,11] even though this procedure increases the risk of local tumor recurrence.

Although irradiation may affect the visual and cognitive function for pediatric patients, the effectiveness and tolerability of irradiation as a salvage therapy in cases of progressive residual craniopharyngioma has been reported.[12] On the basis of previous reports, when selecting the best treatment option for pediatric craniopharyngiomas, it is important to consider not only the functional outcome after resection but also the long-term QOL of patients. In this study, we investigated the QOL of patients with childhood-onset craniopharyngioma after long-term follow-up and identified factors affecting fair QOL.

MATERIALS AND METHODS

Patients

Between 1968 and 2013, 35 patients with craniopharyngioma younger than 15 years of age were treated surgically at Kumamoto University. Two patients died in the early postoperative period as the result of hypothalamic dysfunction or severe liver dysfunction, and 1 died as the result of adrenal insufficiency during the follow-up period. All 3 patients were operated on earlier than 1983. Two patients were lost to follow-up. Thirty patients were confirmed to be alive at the end of 2013, and 26 of them (86.7%) who were available to estimate the QOL were enrolled in this study. Their surgical outcomes, irradiation parameters, visual and endocrinologic outcomes, and clinical course were investigated through the use of clinical records.

Surgical Approaches and Treatment Strategies

The 26 surgeries were performed by various surgeons at Kumamoto University Hospital. Between 1968 and 1983, 5 patients were operated upon via the subfrontal approach and partial tumor removal was performed with or without intratumoral administration of colloidal gold (Au^{198} colloid) or bleomycin. After 1984, total removal was attempted for 18 patients via the subfrontal, transsylvian, or basal interhemispheric approaches. Since 2005, the endoscopic transsphenoidal approach has been performed on 3 patients as the primary treatment to attempt the total removal. The removal rate was determined by a comparison of the pre- and postoperative findings with computed tomography or magnetic resonance imaging (MRI) scans of 22 patients and the operative records of 4 patients. The removal rate was defined as follows: total removal, no enhancement lesion; subtotal removal, residual small enhancement lesion but no apparent mass (more than 95% of the tumor was removed); and partial removal, obvious residual mass. Although the removal rates in 4 patients who have been estimated by the medical records were not able to be measured accurately, it was determined to partial removal from the description of the obvious residual mass in the record. In this study, aggressive treatment refers to total or subtotal removal and conservative treatment refers to partial removal or irradiation.

QOL Investigation

A QOL questionnaire was sent to confirmed survivors from December 2013 to July 2015. Twenty-six of 30 (86.7%) patients returned the questionnaires. QOL was assessed using a short-form health survey (SF-36 version 2) composed of 36 items that determine general well-being during the past 30 days[13] for 22 patients 19 years and older. The items were formulated as statements or questions to assess the following 8 health concepts: 1) physical function, 2) social function, 3) limitations in usual activities because of physical health problems, 4) pain, 5) general mental health (psychological distress and well-being), 6) limitations in usual activities because of emotional problems, 7) vitality (energy and fatigue), and 8) general health perceptions and change in health. On the basis of the score on each subscale, the physical component summary (PCS) and mental component summary (MCS) were calculated according to the manual for the SF-36.

For 4 patients 18 years of age and younger, QOL was assessed by parent reporting on the Child Health Questionnaire Parent Form-50 CHQ-PF50; (HealthActCHQ Inc., Boston, Massachusetts, USA). It consists of 10 health concepts: physical functioning; general health; pain; mental health; self-esteem; behavior; role/social limitations due to emotional or behavioral difficulties; role/social limitations due to physical health; emotional impact on parent; and time impact on parent. Physical summary score and psychosocial summary score were calculated according to the manual for the CHQ-PF50 and compared with the standard scores.

If any of patients' PCS or MCS scores in SF-36, or any of the physical summary score or psychosocial summary score in CHQ-PF50 were more than one standard deviation lower than the standard value, their QOL was estimated to be fair.

Statistical Analysis

Average of age, tumor size, and body mass index (BMI) were compared between the good and fair QOL groups and analyzed by the Welch's *t*-test. Mean values from the 8 health concepts of SF-36 and the calculated PCS and MCS were compared with national standard data and analyzed by the Welch's *t*-test. Fisher's exact test was used to assess associations between the good and fair QOL groups. A Mann-Whitney U test was used to analyze continuous variables. A *P* value of less than 0.05 was considered significant.

RESULTS

Patient Characteristics at Initial Treatment

Clinical characteristics at the initial treatment of the 26 patients are summarized in **Table 1**. The mean age at initial treatment was 7.3 years (range, 4–14 years), and the male-to-female ratio was 10:16. The mean tumor diameter was 39.4 ± 13.8 mm and 22 of 26 (84.6%) tumors were cystic. Preoperative symptoms of visual disturbance, hydrocephalus, hormonal deficit, and headache were observed in 14 (53.8%), 9 (34.6%), 7 (26.9%), and 2 (7.7%) of 26 patients, respectively.

At initial surgery, total removal was achieved in 7 patients, subtotal removal in 9 patients, and partial removal in 10 patients. Of the 10 patients with partial removal, 5 were subjected to irradiation. The details of the irradiation techniques used are as follows, 50–55 Gy conventional local radiation (3 patients), intratumoral administration of Au^{198} colloid (1 patients), and stereotactic radiotherapy with Novalis (BrainLAB, Feldkirchen, Germany; 1 patient). One patient was subjected to intratumoral administration of 2 mg bleomycin immediately after the surgery.