Microsurgical treatment of craniopharyngioma
Experiences on 183 consecutive patients

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Abstract
This study aimed to summarize the clinical experiences and postoperative effects of microsurgical approaches for craniopharyngioma.

A total of 183 craniopharyngioma patients who underwent microsurgical treatment since March 2009 to March 2015 in our hospital were included in current research. Surgical approaches were selected based on preoperative evaluations, including tumor locations, sizes, and growth patterns. Active measurements to manage water-electrolyte disorder and insipidus were taken for postoperative treatments. During the follow-up, patients were monitored for residual or recurrent tumor by postoperative contrast MRI scans done 1 to 3 months after surgery.

The used surgical approaches were as follows: frontopterional approach (76 cases), anterior interhemispheric approach (58 cases), transcallosal approach (10 cases), transsphenoidal approach (15 cases), unilateral subfrontal approach (15 cases), and combined approaches (9 cases). Around 124 cases (72.7%) received total tumor resection, 37 patients (20.2%) underwent subtotal resection, and 13 patients (7.1%) underwent partial removal. No significant difference was found on the postoperative complications among the different microsurgical approaches (all, P > .05). A total of 111 cases had an intact pituitary stalk preservation and 26 cases had partially preserved stalks during surgery. Visual improvement was achieved in 54 patients and visual deterioration occurred in 22 cases. Postoperative insipidus appeared in 114 cases and water-electrolyte disorder occurred in 99 cases. The postsurgical follow-up ranged from 3 to 69 months with a mean duration of 27.3 months and 23 patients suffered recurrence.

Based on careful preoperative evaluation, microsurgical treatments may be safe and effective approach to improve postoperative outcomes of craniopharyngioma patients.

Abbreviations: CT = computed tomography, MRI = magnetic resonance imaging, NMR = nuclear magnetic resonance.

Keywords: craniopharyngioma, microsurgery, postoperative effects, surgical approaches

1. Introduction
Craniopharyngioma is a type of embryo-epithelium tumor which originates from the remnant tissue of Rathke’s pouch, and the tumor mostly grows in saddle.[1–3] During growth, the tumor usually influences important tissue structures such as hypothalamus, visual pathway, stalk hypophysial and internal carotid. Besides, tumor removal may cause many complications, with low total removal and high recurrence rates. Thus, the resection of craniopharyngioma has always been a changeable operation in neurosurgery.[4–7]

With the application of microsurgical treatments, the transcranial approaches have been considered as safe and effective treatments for craniopharyngioma. The commonly used transcranial routes include midline anterior and frontolateral approaches, as well as other approaches.[8] The former usually includes transsphenoidal interhemispheric, unilateral subfrontal/bifrontal transbasal, while the latter mainly includes periorbital-frontotemporal and modified orbitozygomatic.[9] In order to preserve the quality of life and long term of tumor control and survival, surgical approaches selection must be based on careful preoperative evaluation, especially the anatomic location of the tumor.[10] There were a total of 183 craniopharyngioma patients who underwent microsurgical treatment in the Neurosurgery Department of PLA General Hospital since March 2009 to March 2015. We summarized the clinical experiences of microsurgical treatments for these 183 patients, and the report is as follows.

2. Materials and methods
This study was approved by the Ethics Committee of the PLA General Hospital. The written informed consent was obtained from each patient.

2.1. Materials
Among the 183 patients, there were 110 males and 73 females. All the patients ranged from 3 to 77 years with a mean age of 36.2 years. Among them, 29 of them were 3 to 14 years old. The course of disease was from 21 days to 10 years with an average duration of 17.3 months. Around 23 cases had a past surgery history. Admission symptoms: headache (n = 95), impaired vision (n = 113), defect of visual field...
(n = 91), diabetes insipidus (n = 29), epilepsy (n = 3), preoperative endocrine symptoms (n = 29), and hypovolutism (n = 16).

2.2. Examination of imaging

Before microsurgery, all patients underwent magnetic resonance imaging (MRI) plain and enhanced scan, and 135 cases received computed tomography (CT). Eighty cases were diagnosed with imaging (MRI) plain and enhanced scan, and 135 cases received before microsurgery, all patients underwent magnetic resonance foramen or aqueductus mesencephali. Around 30 patients presented moderate to severe hydrocephalus. The maximum diameter of tumor was 1.5–7.8 cm. Of all the cases, 25 cases were cystic, 135 cases were solid cystic and the rest 23 cases were parenchymatous. The obvious reinforcement of cystic wall and parenchymatous part was observed through enhanced scanning. There are 18 cases with the tumor body locating within the saddle, 55 cases on the saddle but not invading the third ventricle, 104 cases on the saddle and invading the internal and external of the third ventricle, 5 cases intruding into the lateral ventricle. In 6 cases, the tumor bodies were completely in the third ventricle.

2.3. Examination of visual acuity and endocrine

Before the microsurgery, the patients came to Ophthalmology Department of our hospital for routine examination of visual acuity and visual field to make clear the existence and extent of the vision and field damages. All the patients underwent comprehensively preoperative endocrine examination related to pituitary and hypothalamus, including checks for blood prolactin, thyroid hormones, gonadal hormones, growth hormone, adrenocorticotropic hormone, cortisol etc. There were 55 cases of cortisol decline and 42 cases of thyroid function decline in the laboratory preoperative examination.

2.4. Preoperative evaluation

After hospital admission, patients took the routine examination for cranial NMR, visual field and hormone, etc. We comprehensively analyzed and evaluated the size and growth pattern of craniopharyngioma as well as the influence on optic nerve, hypothalamus function and patients status, and then selected the most appropriate microsurgical approach and tried to achieve total-tumor resection with minimal-trauma if the patients’ condition allowed. Patients who were in low cortisol levels were supplemented with corticosteroids 1 to 3 days before the operation. Intraoperative navigation and magnetic resonance could be used for the resection of giant craniopharyngioma.

2.5. Postoperative treatments and follow-up

The electrolyte levels and 24 hours quantity of the electrolyte were routinely monitored after operation. Within postoperative 24 hours, the intracranial CT was rechecked to gain acquaintance of intracranial situation, and the endocrine hormone level was also reviewed. In the early postoperative time, patients were given cortisol and thyroid hormone to supplement or replace the treatments, pituitrin to control diabetes insipidus and redress water-electrolyte disorder in time. Generally speaking, diabetes insipidus was temporary that could return to the normal levels within 3 weeks. A postoperative review within 1 month was performed all the patients with diabetes insipidus. If the diabetes insipidus was not improved within 1 month; moreover damages were observed above the median protuberance of the stalk of the pituitary gland through MRI, the patients were diagnosed with persistent diabetes insipidus. The cranial MRI, endocrine, visual acuity and visual field were rechecked 1 to 3 months after surgery. And if residual tumors were found in the cranial MRI, patients would be instructed to undergo gamma knife treatment; thereafter patients were reviewed every 6 months with MRI to observe the changes of tumor. Patients with no residual tumor were followed up every 8 to 12 months.

3. Results

3.1. The general information of patients with different approach

The 183 tumor cases were operated with different approaches, including frontopterional approach in 76 cases, anterior interhemispheric approach in 58 cases, transcallosal approach in 10 cases, transsphenoidal approach in 15 cases, unilateral subfrontal approach in 15 cases, and combined approaches in 9 cases. The general information of patients with different microsurgery approaches was summarized in Table 1.

3.2. Operation results in different approach group

In this study, there were no cases died during operations. The extents of tumor resection were determined by intraoperative judgments and postoperative iconography (Figs. 1 and 2). There

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### Table 1

| Factor                      | Frontopterional (n = 76) | Anterior interhemispheric (n = 58) | Transcallosal (n = 10) | Transsphenoidal (n = 15) | Unilateral subfrontal (n = 15) | Combined (n = 9) |
|-----------------------------|--------------------------|-----------------------------------|------------------------|--------------------------|-------------------------------|-----------------|
| Gender (male/female)        | 46/30                    | 31/27                             | 6/4                    | 10/5                     | 10/5                          | 7/2             |
| Age                         | 38.4 ± 2.1               | 36.2 ± 2.3                        | 35.8 ± 1.6             | 37.4 ± 2.2               | 41.0 ± 2.9                    | 43.5 ± 3.2      |
| Tumor diameter (range, cm)  | 1.2–6.7                  | 1.5–4.6                           | 2.2–3.8                | 2.1–4.2                  | 1.7–5.9                       | 1.6–6.9         |
| Preoperative symptoms       |                          |                                   |                        |                          |                               |                 |
| Headache                    | 32                       | 28                                | 6                      | 11                       | 9                             | 9               |
| Impaired vision             | 46                       | 37                                | 8                      | 12                       | 6                             | 4               |
| Defect of visual field      | 30                       | 26                                | 7                      | 10                       | 12                            | 6               |
| Diabetes insipidus          | 13                       | 9                                 | 1                      | 2                        | 2                             | 2               |
were 133 cases (72.68%) experiencing total tumor removal, 37 cases (20.22%) undergoing subtotal resection, and 13 cases (7.1%) suffering partial removal. The distribution of total, subtotal, and partial removal in different surgical approach groups were shown in Table 2. There was no statistically significant on total removal rate between the 2 major surgical approaches (frontopterional approach vs anterior interhemispheric approach). The postoperative hospitalization was 8 to 85 days with an average of 16.9 days. During the microsurgery, intact pituitary stalks presented in 111 cases, partially preserved stalks showed in 26 patients. Besides, 23 stalks were resected with tumors and 24 cases had no stalks. 5 cases of anterior interhemispheric approach had cut off the anterior communicating artery, without adverse postoperative complications. 9 cases of giant craniopharyngioma (maximum diameter > 6cm) were removed with the assistance of magnetic resonance, including total resection in 6 cases and subtotal resection in 3 cases.

3.3. Postoperative complications
The major complications in different surgical approach groups were summarized in Table 2. After the microsurgery, 114 cases had diabetes insipidus, including 71 cases of temporary insipidus (urine volume returned to normal level in 1–3 weeks) and 43
cases of persistent insipidus. 99 cases had electrolyte disturbances. Within 1 month after surgery, 54 cases showed visual improvement, 107 cases had no visual change and 22 cases appeared visual deterioration (7 cases of anterior interhemispheric approach and 15 cases of frontopterional approach, of which 1 case was side blind). A total of 6 cases presented with intracranial hematoma, including 3 cases with epidural hematoma (2 cases of frontopterional approach and 1 case of transcallosal approach), 3 cases with frontal intracerebral hematoma (interhemispheric approach). All the above 6 cases suffered reoperation to remove hematoma and then recovered. 6 cases had oculomotor paralysis, and 5 cases recovered after half a year and 1 case partially recovered. About 2 cases showed cerebrospinal fluid leakage, including 1 case of transsphenoidal approach and 1 case of anterior interhemispheric approach, and the former recovered after repair. Intracranial infection occurred in 15 cases, which all recovered after lumbar cistern drainage, including 1 case of combined incision infection. Thyroid function decreased in 58 cases and cortisol declined in 75 cases, which needed hormone for replacement therapy. Moreover, no significant difference was found on the postoperative complication among the different microsurgical approaches (all, \( P > .05 \)).

### 3.4. Follow-up

Around 160 cases were followed up while 23 cases were lost. The follow up ranged from 3 to 69 months with an average of 27.3 months. In this period, tumor recurrence occurred in 23 cases, including 19 with reoperation and 4 cases with radiosurgical treatment. Among the followed patients, 120 cases could return to orthobiosis, 28 cases had mild neurological dysfunction but could live independently, and 12 cases were not able to take care of themselves.

### 4. Discussion

With the development of microsurgery, the selection of surgical approach for craniopharyngioma still remains a great challenge.

### Table 2

| Tumor removal | Front-opterional \( (n=76) \) | Anterior interhemispheric \( (n=58) \) | Transcallosal \( (n=10) \) | Transsphenoidal \( (n=15) \) | unilateral subfrontal \( (n=15) \) | Combined \( (n=9) \) |
|----------------|-------------------------------|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Tumor removal  |                              |                                 |                 |                 |                 |                 |
| Total          | 57                            | 51                              | 6               | 2               | 14              | 3               |
| Subtotal       | 16                            | 6                               | 4               | 8               | 1               | 2               |
| Partial        | 3                             | 1                               | 0               | 5               | 0               | 4               |
| Complications  |                               |                                 |                 |                 |                 |                 |
| Diabetes insipidus | 44                            | 31                              | 9               | 13              | 12              | 5               |
| Temporary insipidus | 30                            | 20                              | 6               | 6               | 6               | 3               |
| Persistent insipidus | 14                            | 11                              | 3               | 6               | 6               | 2               |
| Electrolyte disturbances | 35                            | 28                              | 7               | 13              | 11              | 5               |
| Intracranial hematoma | 2                             | 3                               | 1               | 0               | 0               | 0               |
| Epidural hematoma | 2                             | 0                               | 1               | 0               | 0               | 0               |
| Frontal intracerebral hematoma | 0                             | 3                               | 0               | 0               | 0               | 0               |
| Oculomotor paralysis | 2                             | 1                               | 0               | 0               | 0               | 2               |
| Cerebrospinal fluid leakage | 0                             | 1                               | 0               | 1               | 0               | 0               |
| Intracranial infection | 3                             | 3                               | 2               | 3               | 2               | 2               |
On the basis of tumor size, location, direction and other aspects, we select the approach that causes small wounds, fewer complications and less influence on hypothalamus, optic nerve as well as carotid artery system. Part of frontotemporal approaches were replaced by unilateral subfrontal approach, and part of transcallosal approaches by anterior interhemispheric approach. Besides, ventriculoscope was applied in 5 cases to cope with the craniopharyngioma in third ventricle.

For patients with craniopharyngioma, we performed rigorous preoperative assessments, selected treatment protocols and approaches according to individuation. These assessments include: the patients' systemic condition, making explicit whether the patients could tolerate the surgery and choosing optimal treatment for patients if conditions permit; endocrine and visual acuity: patients with low cortisol level should be supplemented with corticosteroids 1–3 days before the operation. Choose either frontotemporal approach or unilateral subfrontal approach in line with visual acuity; preoperative imaging: the most important basis for selecting the surgical approach. Tumor features, such as size, position, growth pattern, and the size and location of calcification, relationship between tumor with visual pathway and Circle of Willis, and relationship of tumor with the third ventricle and hypothalamus were identified in the study. The application of intraoperative navigation and magnetic resonance scanning is of great help for the total resection in giant tumor cases.

Unilateral subfrontal approach is propitious to resect craniopharyngioma which grows along the partial side or midline of middle and small sized saddles. This type of approach has small trauma, does not need to turn open the temporal muscle and middle and small sized saddles. This type of approach has small approach has blind zone for giant craniopharyngioma inside and needs to cut off the anterior communicating artery as well. Nevertheless, this approach has blind zone for giant craniopharyngioma inside and outside the third ventricle, especially for tumors at the high position or the rear protruding into the third ventricle. Meanwhile, the operation has great influence on internal carotid artery system and optic nerve. The lamina terminalis reveal of combined approach is inferior to the anterior interhemispheric approach. In recent years, we mainly use the anterior interhemispheric approach, which can remove the tumor that is in a higher position invading the third ventricle or just in the third ventricle in the saddle. After separating the longitudinal, there is a broad and direct line of vision from front to back, which makes it direct and easy to remove tumors invading the rear of the third ventricle through the angle adjustment of headstock, especially to protect the anterolateral hypothalamic nuclei. However, separating the longitudinal often needs to cut off the sagittal-sinus-abouchement bridge vein which may also increase the risk of frontal lobe hemorrhage, and sometimes it needs to cut off the anterior communicating artery as well. Transcallosal approach is mostly used to deal with saddle tumor which has intruded into the third ventricle, lateral ventricle and septum pellucidum. When the tumor grows up higher than the monro foramen plane or into the lateral ventricle, craniopharyngioma can be removed through the transcallosal-lateral ventricle-mono foramen, or by gyrus frontalis medius stoma via interventricular foramen after growing into the lateral ventricle. Transcallosal approach has difficulty in removing the craniopharyngioma which locates in the saddle or beneath the optic cross at saddle back. Moreover, dissecting corpus callosum and fornix will lead to silence, memory loss and other complications.

In recent years, craniopharyngioma which has protruded into the rear of third ventricle, was mainly removed by the interhemispheric approach. The approach could cut off tumors in saddles, anterior cranial fossa, even from the rear of third ventricle to interpeduncular cistern through adjusting the angle of headstock, and avoid complications such as silence, memory loss etc caused by dissecting corpus callosum and fornix. The report of Shi et al shows that the pituitary stalk preservation rate of anterior interhemispheric approach exceeds the frontotemporal approach. Around 15 cases of craniopharyngioma have been resected by endoscopic transphenoidal approach which is suitable for the tumor in or mostly in saddle. But we consider that the total resection rate of the approach is low and craniopharyngioma can recur easily. The main reason why we cannot totally resect the tumor is that the cystic wall of craniopharyngioma cannot be completely stripped, especially its tight adhesions with saddle diaphragm confirmed by pathological examination that most of the saddle diaphragm merges together with cystic wall. Five patients took the ventricle endoscopic resection of craniopharyngioma, and 1 patient who had solid-cystic craniopharyngioma in the third ventricle was in bad conditions with medical disease like hypertension and diabetes mellitus, thus the craniopharyngioma was mainly removed via the ventricle endoscopic resection followed by ventriculostomy of the third ventricle considering the patient’s nontolerance of craniotomy, and the patient recovered well without recurrence during the follow-up for 6 months. We think transventricular endoscopic resection is well suited for patients with small primary ventricle craniopharyngiomaoh or the third ventricle craniopharyngiomah without craniotomy tolerance. The procedure is to remove the contents in cystic first, and then to excise the parenchymatous part. After resection of most tumor, stoma fistula of the third ventricle or aqueduct plasty should be carried out to address the obstructive hydrocephalus. But it is hard to achieve total tumor resection because of the incomplete stripping of cystic wall under the endoscope. Fully peeling cystic wall under the endoscope is difficult and dangerous that may lead to reoccur. Small craniopharyngioma in the third ventricle can be treated with endoscopic resection.

The appropriate microsurgery approach should be selected on the basis of the preoperative evaluation including tumor location, size and growth pattern as well as the morphological characteristics. Microsurgery may be effective and safe for patients with craniopharyngioma.

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