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ORIGINAL ARTICLE

Transsphenoidal microsurgical treatment of infradiaphragmatic craniopharyngioma*

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Abstract

Objective Typically, the transcranial approach has been used for the treatment of craniopharyngiomas with suprasellar extension, whereas the transsphenoidal approach has been used mostly for infradiaphragmatic craniopharyngioma. Total resection of craniopharyngioma can reduce the recurrence rate, especially in young children, but it may lead to severe complications. Therefore, any benefit of the degree of resection must be weighed against the risk of complications by the surgeons. The purpose of this study was to explore the therapeutic outcome after transsphenoidal microsurgical treatment of infradiaphragmatic craniopharyngioma and share our experiences.

Methods Between January 2003 and June 2013, 30 patients with infradiaphragmatic craniopharyngioma underwent transsphenoidal microsurgical resection in our hospital. The neurological, visual, and endocrine functions, and extent of resection were analyzed retrospectively. Recurrence or growth of residual tumor tissue during follow-up was assessed using magnetic resonance imaging (MRI).

Results Total resection was achieved in 25 patients (83.3%), subtotal resection was achieved in 4 patients (13.3%), and partial resection was achieved in 1 patient (3.4%). There were no perioperative deaths. Cerebrospinal fluid (CSF) leakage occurred in 6 patients, and among them, 2 required surgical repair of the sella. New-onset postoperative diabetes insipidus (DI) developed in 8 patients. Vision and visual fields were improved at different levels in 13 out of 16 patients who had sight impediments before treatment. Tumor recurrence and regrowth was observed in 2 patients; 1 patient underwent transsphenoidal reoperation, the condition of the other patient who had undergone several craniotomies grew worse over the 6-month follow-up period.

Conclusion Transsphenoidal surgery is an ideal choice in treating infradiaphragmatic craniopharyngioma. The transsphenoidal approach, which preserves pituitary function and avoids damage to the hypothalamic structures and optic nerve, is associated with fewer complications than the transcranial approach and a low mortality rate.

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Key words: craniopharyngioma; transsphenoidal approach; therapeutic effect

Craniopharyngiomas are epithelial tumors that arise from embryonic epithelial cells of the craniopharyngeal duct. They account for 1% of all primary intracranial neoplasms in adults and 1%–3% of intracranial tumors in children [1]. Despite their benign histological nature, craniopharyngiomas have a tendency to invade critical neurovascular structures, particularly the visual pathways and hypothalamus, resulting in high morbidity and mortality.

Craniopharyngiomas are localized to the sella or under the diaphragma sellae, where it is referred to as an infradiaphragmatic craniopharyngioma. The choice of surgical approach for craniopharyngiomas is closely associated with the tumor position, size, and texture. Typically, the transcranial approach has been used for the treatment of craniopharyngiomas with suprasellar extension, whereas the transsphenoidal approach has been used mostly for infradiaphragmatic craniopharyngiomas [2]. Total resection

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Table 1 Clinical characteristics of 30 patients who underwent transsphenoidal surgery for infradiaphragmatic craniopharyngioma

Variable	Children		Adults		Total	
	n	%	*n*	%	*n*	%
Number of patients	8		22		30	
Mean age (years) at surgery	13.4		32.7		27.6	
Female	4	50	13	59.1	17	56.7
Previous surgery	0		2	9.1	2	6.6
Headache	3	37.5	16	72.7	18	63.3
Adrenal function deficit	2	25	8	36.4	10	33.3
Menstrual disorder	1	12.5	7	31.8	8	26.7
Hypogonadism			1	4.5	1	4.5
Growth delay	3	42.9			3	42.9
Hyperprolactinemia	4	50	4	18.2	8	26.7
Polyuria and polydipsia	2	25	2	9.1	4	13.3
Visual deficit	4	50	12	54.5	16	53.3

* Values given as number of patients (%) unless otherwise indicated. Children is defined as <18 years old, adults as ≥ 18 years old

can reduce the recurrence rate, especially in young children, but it may lead to severe complications. Therefore, any benefit of the degree of resection must be weighed against the risk of complications by the surgeons. In this paper, we present our experiences and the therapeutic effects of 30 cases of infradiaphragmatic craniopharyngioma treated with transsphenoidal surgery.

Materials and methods

Patients

From January 2003 to June 2013, 30 patients with infradiaphragmatic craniopharyngioma were treated using transsphenoidal microsurgery in our hospital. Patient consent and approval from the Institutional Review Board of Tongji Hospital were obtained for this study. The patient group consisted of 22 adults (9 men and 13 women) and 8 children (4 boys and 4 girls). The age of the patients ranged from 4 to 50 years (mean 27.6 years). Twenty-seven patients had received no previous treatments. One patient had undergone two craniotomies and one γ-knife treatment elsewhere. One patient presented with recurrence after undergoing a transsphenoidal operation elsewhere. One patient had undergone one γ-knife treatment elsewhere.

Clinical symptoms

The main clinical characteristics of the 30 patients are summarized in Table 1. The preoperative duration of symptoms due to the tumor varied between 1 week and 17 years (mean 2.1 years). Principal complaints and symptoms included decreased vision and/or temporal hemianopsia in 16 cases, headache in 19 cases, hypogonadism in 1 case, growth delay in 3 cases, polyuria and polydipsia in 4 cases, menstrual disorder in 8 cases, and hyperprolactinemia in 4 cases.

Neuroimaging evaluation

Location, size, degree of cystoid variation, calcification, and sellar enlargement of the tumor were evaluated on films of computed tomography (CT) and magnetic resonance imaging (MRI). The masses measured between 5 mm and 35 mm in diameter. The principal mass was located exclusively in the sella in 23 cases, partially in the sella and suprasellar region in 7 cases. Calcifications were found in 16 craniopharyngiomas, and cysts were observed in all cases.

Endocrinological evaluation

During the preoperative period, the prolactin level increased (from 28.07 ng/mL to 76.19 ng/mL) in 8 patients (2 men and 6 women), thyroid function decreased in 6 patients. An adrenal function deficit occurred in 10 patients.

Surgical procedure

The transsphenoidal approach, which has the advantage of offering better exposure of the bottom of the sphenoid sinus, can be used for infradiaphragmatic craniopharyngiomas located in the sella. The sphenoid sinus was opened; using rongeurs and a drill, the sinus opening was widened and its septum removed, especially exposing the window to the slope. Since most of the bony wall of the sphenoid sinus was eroded by the tumor, and the mucus membrane laid directly against the dura mater. It was important to keep the dura intact during mucus membrane and bony dissection. After the dura of the sellar floor was widely opened according to the size of the tumor using micro scissors, a tumor with capsule of variable thickness was often exposed immediately. Subsequently, subcapsule tumor debulking was undertaken gently using aspiration. The capsule of the tumor could be dissected in 3 planes as follows. First, capsular adhesion of the slope was dissected from the dura after coagulation. Capsular

adhesion near the normal pituitary gland was then dissected. Since the normal pituitary gland acted as a barrier, tumor adhesion in this area could be easily detached. Subsequently, the contralateral tumor was dissected. In cases of tight adhesion, it was treated by coagulating the walls of tumor along the cavernous sinuses and then cutting. If the adhesion was difficult to detach, the plane of the diaphragma sellae could be dissected in advance. Finally, dissection of tumor adhesion located in the plane of the diaphragma sellae. The normal pituitary gland was protected cautiously, because it was often seen at the surface. Meanwhile, due to the different levels of collapse, the diaphragma sellae was dissected gently along the capsule, and then the capsule was cut after coagulating the base of capsule. Intraoperative CSF leakage might occur during the dissection, which was controlled either with hemostatic gauze or with a small cotton pad. The resection of the calcified part of the tumor was slow and meticulous. Since the diaphragma sellae was involved with the tumor, it could be deficient to differing extents. Therefore, repair of the diaphragma sellae was crucially important. In our cases, all sellar floor repairs were performed with autogenous fascia and fat.

Follow-up review

Postoperative endocrinological and ophthalmological evaluations were performed 1 week after surgery. MRI and endocrinological evaluation were performed 3 months after surgery. Subsequently, MRI was repeated annually. The duration of follow-up in this study was from 6 months to 116 months. Fig. 1 and 2 present two representative cases.

Results

Extent of resection

The tumors were totally resected in 25 (83.3%; 2 representative cases shown in Fig. 1 and 2), subtotally resected in 4 (13.3%), and partially resection in 1 (3.4%). During the follow-up period, 2 patients demonstrated a recurrence.

Surgical complications

Postoperative CSF leakage occurred in 6 patients. Among them, 2 patients required transsphenoidal sellar repair. In 4 patients, CSF leakage was successfully resolved after continuous lumbar drainage. Other compli-

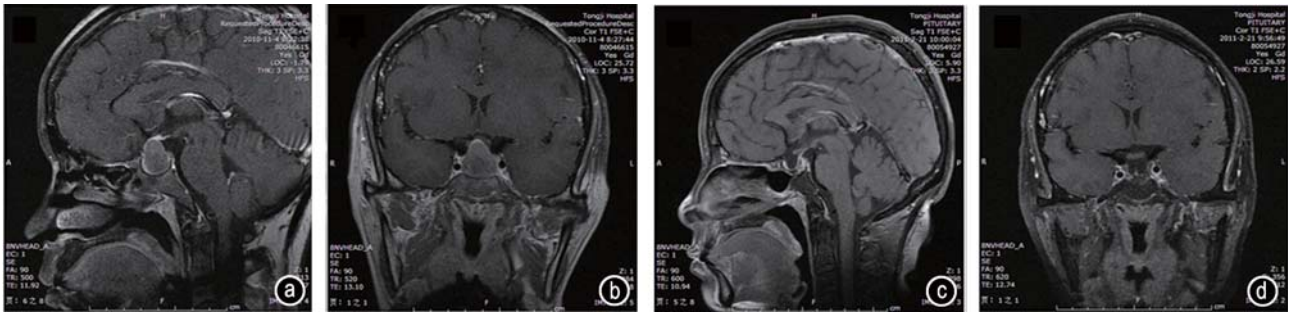

Fig. 1 Preoperative and postoperative enhanced magnetic resonance (MR) images of the treatment of infradiaphragmatic craniopharyngioma. Preoperative sagittal (a) and coronal (b) MR images showing that the sella was enlarged, diaphragma sellae was raised, and tumor was separated from suprasellar structures by the diaphragma sellae. Postoperative sagittal (c) and coronal (d) MR images showing that the diaphragma sellae was collapsed and the pituitary gland together with the pituitary stalk were well preserved

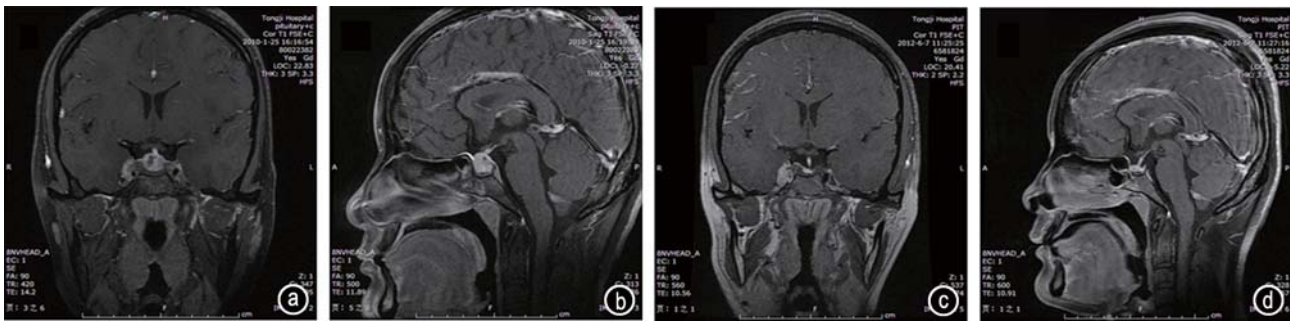

Fig. 2 Preoperative and postoperative enhanced magnetic resonance (MR) images of the treatment of infradiaphragmatic craniopharyngioma. Preoperative coronal (a) and sagittal (b) MR images showing that the tumor was mainly located in the sella and the diaphragma sellae was raised. Postoperative coronal (c) and sagittal (d) MR images showing that the diaphragma sellae was collapsed and the pituitary gland together with the pituitary stalk were well preserved

cations included 7 cases of diabetes insipidus and 2 cases of electrolyte disturbance, which resolved after 3 months. The condition of 1 patient who had undergone several craniotomies grew worse during the follow-up period of half a year.

Visual evaluation

Vision and visual fields improved at different levels in 13 out of 16 patients who had sight impediments before the operation. There were no permanent visual deficits.

Postoperative endocrinological evaluation

A postoperative normalization of excessive prolactin secretion was found in eight patients. Preoperative adrenal function deficit in one patient was back to normal after surgery. Normal thyroid function decreased after surgery in 4 patients. The normal level of cortisol was reduced after surgery in 2 patients. The newly disturbed functions normalized after 3 months.

Discussion

Morbidity characteristic

No significant sex difference was found to exist in terms of the incidence of craniopharyngiomas. However, in an analysis of a large sample of cases, craniopharyngiomas were detected more frequently in male rather than female patients [3]. Seventeen (56.7%) female patients were included in this group. Children aged between 5 and 9 years and adults aged between 40 and 44 years had the highest incidence of this disease. Of the 30 patients, 11 (36.7%) patients were aged between 18 and 30 years; 8 (26.7%) patients aged between 40 and 50 years; 8 (26.7%) patients were younger than 18 years and 2 (6.7%) patients were aged between 30 and 40 years.

Clinical symptoms

Generally, the principal signs and symptoms of craniopharyngiomas included headache, visual impediments, diabetes insipidus, and hypopituitarism. The initial symptoms of young children were different from those of adult patients. Endocrine disorder, progressive loss of vision, and intracranial hypertension mostly occur in children, while impaired vision mostly occurs in adults [4–5]. In our series, 3 (37.5%) children complained of headache and 12 (54.5%) adult patients complained of decreased vision. In our cases, 25% of the patients with visual impediments were diagnosed with bitemporal hemianopsia. Intrasellar craniopharyngiomas can affect the function of the anterior pituitary, resulting in hypopituitarism and developmental delay in patients younger than 18 years of age. In our cases, 2 of 8 juvenile patients demonstrated developmental delay, while those older than 18 years exhibited hypogonadism. Craniopharyngiomas can also increase the occurrence of endocrine symptoms such as amenorrhea-galactorrhea syndrome in female patients and hypogonadism in male patients. In our group, 4 adult patients demonstrated excessive prolactin secretion causing menolipsis together with/ without lactation, other menstrual disorders, and hypogonadism. The tumor can also affect the function of the posterior pituitary, resulting in diabetes insipidus; 6.7% of the patients in our cases developed symptoms of diabetes insipidus.

Neuroimaging evaluation

On imaging studies, most tumors are of lobular shape, while a few are rounded with a clear border. According to their structure, tumors can be separated into 3 types: cystic, solid, and cyst-solid. As to the cyst-solid mass, the cystic region is typically located superiorly and the solid region is located inferiorly. MRI suggests that most regions of cystic change show high signal intensity on T1-weighted images. In tumors with two or more cystic areas, the signal intensity can be the same or different. The reason for the high signal intensity on T1-weighted images in cystic regions is that cystic fluid contains higher protein content, including one or more of the following: cholesterol, triacylglycerol, methemoglobin (with a history of bleeding), calcifications, and epithelial exfoliation. Areas of cystic change generally show high signal intensity on T2-weighted images, but a few regions may show low signal intensity, probably because they contain calcifications or hemosiderin. Solid craniopharyngiomas and the solid part of cystosolid craniopharyngiomas show uniform T1-weighted imaging signal intensity and uniform or high T2-weighted imaging signal intensity. A few lesions with calcifications and keratoprotein or sporadically located in trabecular bone show low signal intensity both on T1-weighted images and T2-weighted images. Both CT and MRI reveal that at times large cysts have an air-fluid level. MR enhancement scans show that the enhanced extent of normal glands is significantly higher than that of tumorous tissues. Normal glands crushed flat by medium-sized tumors appear as a lamellar band with high signal intensity. In general, they are pressed beneath the tumor or are unaffected.

Differential diagnoses

Craniopharyngioma in the sellar region should be distinguished from cystic pituitary adenoma, Rathke cleft cyst, pituitary abscess, and epidermoid cyst. Differential diagnoses are mainly made through imaging tests before surgery; calcification in craniopharyngiomas can be detected on CT imaging, but not in other tumors. MRI demonstrates that the principal differences are as follows:

(1) Cystic pituitary adenomas are always visibly connected with the pituitary gland or the normal pituitary gland is not visible. Due to the different contents of the

cystic fluid, the interface of the two signals frequently appears with an intracapsular air-fluid level. MR enhancement scans show that the capsule wall and solid part of the tumor are significantly enhanced.

(2) Rathke cleft cysts involve the intrasellar region and often extend upward. They usually have the following imaging features: a homogeneous signal intensity within the lesion, lack of internal enhancement, and small variance in the lesion during the follow-up period.

(3) The characteristics of pituitary abscess include a history of fever, lesions involving the whole pituitary gland, disappearance of the normal pituitary gland on imaging, and posterior pituitary symptoms.

(4) The typical signal intensity of epidermoid cysts is equal to that of cerebrospinal fluid. Enhancement scans show that the tumors are not enhanced.

Selection of surgical approach and results

The ideal surgical approach has been controversial since craniopharyngioma was first removed surgically. According to the tumor position, size, texture, and surgeon comfort, there are 3 major types of surgery: transcranial surgery, transsphenoidal surgery, and drainage. Among them, transcranial surgery includes the pterional approach, subfrontal approach, transcallosal approach, and transcortial-transventricular approach [6]. The principal for the selection of different approaches is based on the location and adhesion of the main tumor.

The selections of surgical approach in different treatment groups are related to the preference and experience of the surgeons. The proportional use of the transsphenoidal approach in craniopharyngioma ranges 10%–75% [6]. Transsphenoidal surgery was initially considered to remove intrasellar craniopharyngioma due to the development of tumors from the intrasellar area to the sphenoid sinus. Surgeons could not remove them under visual control by choosing the transcranial approach; therefore, transsphenoidal approach was the absolute operation indication. When a craniopharyngioma in the sellar region was within an enlarged sella turcica, the suprasellar lesion was located under the diaphragma sellae, which acted as an anatomic barrier preventing invasion of or adherence to vital structures. Since a part of suprasellar lesions could be removed by transsphenoidal surgery, the surgical indication was expanded to include infradiaphragmatic craniopharyngioma [7]. Owing to developments in the extended transsphenoidal approach and use of endoscopy, reports of treating craniopharyngiomas located in the suprasellar area, parasellar region, and in the third ventricle using transsphenoidal surgery have increased.

The use of transsphenoidal surgery is convincing. Craniopharyngiomas involving the sella turcica are often cystic or friable [8–9] making intracapsular resection relatively easy. Infradiaphragmatic craniopharyngioma usually does not infiltrate surrounding structures. Therefore, excision of the capsule from the optic chiasm, hypothalamus, and pituitary stalk can be carefully performed [10]. Transsphenoidal surgery involves less severe trauma, better exposure of sellar lesions, and more efficient decompression of the chiasm and optic nerves with reduced risk of vision worsening [11] compared with transcranial approaches. The total resection rate of transsphenoidal microsurgical treatment of infradiaphragmatic craniopharyngioma as reported in the literature ranges from 27.7% to 89.7%; in our study, total resection was achieved in 25 patients (83.3%). The patients who undergo subtotal resection should receive stereotactic or general radiotherapy. During the follow-up period, one patient exhibited recurrence 2 years after surgery, and underwent further transsphenoidal surgery. No recurrence occurred in any other patients. Compared with the 8% reported in a Meta-analysis, the rate of the postoperative recurrence of craniopharyngioma ranges 0–17.6% [6]. In our study, the recurrence rate was 3.6%.

Table 2 Comparison of the results pre-and post operation

Variable	Preoperative cases		Postoperative cases	
	n	%	*n*	%
Diabetes insipidus	4	13.4	12	40
Adrenal function deficit	10	33.3	11	36.7
Thyroid function deficit	2	6.7	6	20
Hyperprolactinemia	8	26.7	0	0
Visual deficit	16	53.3	3	10

The postoperative recovery rate of patients with vision or visual field defects ranges from 70% to 90% in transsphenoidal surgery, a higher recovery rate than transcranial surgery in general [4]. In our study, the recovery rate was 81.3%, similar to results reported in the literature. The patients with preoperative endocrinological diseases did not improve after surgery. Two patients with preoperative diabetes insipidus are receiving long-term pharmacological treatment to control urine volume, and 2 patients with preoperative hypothyroidism also needed to take long-term medication after the operation. Postoperative normalization of excessive prolactin secretion was detected in 8 patients, and the clinical symptoms dissipated. Similar cases were also reported by other groups that preoperative hypopituitarism is rarely cured after surgery, and most patients with high level of prolactin recover after their operation [12]. The results regarding visual deficits and endocrinological function pre-and postoperatively are shown in Table 2.

Complications

Diabetes insipidus is the most frequent endocrinopathy following both transsphenoidal surgery and transcranial surgery for craniopharyngioma [8]. The ratio of patients with postoperative diabetes insipidus reported by

treatment groups differ. One group reported that 60% of patients were diagnosed with diabetes insipidus [8]. The histological type of tumor and frequent disturbance of the pituitary stalk in transcranial surgery are probably the reasons that the ratio of patients with postoperative diabetes insipidus (54.8%) after transcranial surgery is higher than the 31.7% after transsphenoidal surgery. In our group, 8 (26.7%) patients were newly diagnosed with diabetes insipidus after surgery, and they were cured in 3 months. Electrolyte disturbance appeared in 2 patients and resolved after appropriate drug treatment. The most common technical complication of transsphenoidal surgery is CSF leakage. Materials for repairing the sellar floor are varied, including titanium mesh, silicon resin, and nasal bone fragments glued using fibrin glue. Fat, fascia, and fibrin glue were used by Buchfelder M *et al* to reconstruct the sellar floor [1]. As a study in the literature has reported, the incidence of CSF leakage ranges from 2% to 33% [13]. In our cases, all sellar floors were patched with autogenous broad fascia and fat. Postoperative CSF leakage occurred in 6 (20%) patients and was successfully treated through continuous lumbar drainage or repair of the sellar floor. None of the patients with CSF leakage experienced meningitis. Six patients were newly diagnosed with pituitary dysfunction, and the disturbed function normalized after 3 months. Since the 1980s, the perioperative mortality of craniopharyngioma decreased from 9% to 0% with progress in microtechniques and improvement of surgical skills. There were no cases of perioperative death in our group, although in one patient, the condition worsened because of impaired hypothalamus function over the 6-month follow-up period.

Conclusions

Transsphenoidal surgery is an ideal choice in treating infradiaphragmatic craniopharyngioma. The patients whose tumors were not totally resected should receive stereotactic or general radiotherapy to reduce the risks of recurrence. Routine repair of diaphragma sellae is needed during the operation, and postoperative CSF leakage can be mostly cured. The transsphenoidal approach, which preserves pituitary function and avoids damages to the hypothalamic structures and optic nerve, is associated with fewer complications and a lower mortality rate compared with the transcranial approach. For tumors that could not be or were not totally resected in the first operation, total resection would be more difficult or impossible during a secondary operation.

Conflicts of interest

The authors indicated no potential conflicts of interest.

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