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Original Article

The complications of endoscopic transsphenoidal surgery for pituitary neoplasms

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Abstract: Objective: This study aims to analyze the complications of endoscopic transsphenoidal surgery for pituitary neoplasms. Methods: 326 patients who underwent neuroendoscopic endonasal transsphenoidal surgery at the neurosurgery department of the First Affiliated Hospital of Chongqing Medical University from July 2012 to July 2015 were enrolled in this retrospective analysis. Results: Among the 326 patients, the cases of postoperative hyponatremia, diabetes insipidus, hypopituitarism, postoperative cerebrospinal fluid leak, meningitis, cranial nerves palsy, epistaxis, sphenoid sinusitis, internal carotid artery injury and residual tumor bleeding respectively are 32 (9.8%), 12 (3.7%), 23 (7.1%), 13 (4.0%), 1 (0.3%), 3 (0.9%), 5 (1.5%), 3 (0.9%), 1 (0.3%) and 1 (0.3%). Conclusion: Endoscopic endonasal transsphenoidal surgery has the considerable total resection rates for pituitary adenomas and preventable postoperative complications.

Keywords: Neuroendoscopy, pituitary neoplasms, complication

Introduction

Pituitary neoplasms are benign tumors and mainly originate from adenohypophysis, classified differently according to their size or endocrine function. Pituitary microadenomas are defined as a group tumors of less than one centimeter in diameter, correspondingly all the others greater than acentimeter in diameter are called as pituitary macroadenomas. On the basis of another classification method, they be divided into functional or non-functional adenomas, and functional adenomas are named after the hormone they secrete. Nowadays, the main treatment of pituitary neoplasms is surgery combined with other comprehensive therapy. Endoscopic transsphenoidal surgery achieves recognition for small trauma, clear panoramic views and removing the parasellar extensions not visualized by the microscope in nearly 25 years. The retrospective study collects and analyzes the clinical material, especially postoperative short-term complications, in the pituitary tumor patients treated with neuroendoscopic therapy.

Materials and methods

Patient population

This retrospective study consists of 326 patients (142 males and 184 females; age range 12-79 years, mean age 47.2 years) underwent endoscopic endonasal transsphenoidal surgery for pituitary neoplasms at the neurosurgery department of the First Affiliated Hospital of Chongqing Medical University from July 2012 to July 2015. The dominant clinical presentations were headache, visual impairment, pituitary insufficiency, cranial-nerve palsy, amenorrhea, acromegaly and Cushing's syndrome (**Table 1**). 13 patients without obvious clinical symptoms had been incidentally found on imaging study (**Table 1**). The patients were followed up for 3 to 39 months after surgery.

Auxiliary examinations

All patients were evaluated by magnetic resonance (MR), computed tomography (CT) and CT angiography (CTA) before neuroendosco-

Table 1. The Dominant Clinical Presentations of 326 Patients with Pituitary Neoplasms

Clinical symptoms	Number	Percentage (%)
Total no. patients	326	100
Headache	257	78.8
visual impairment	149	45.7
Amenorrhea	77	23.6
Acromegaly	87	26.7
Cushing's syndrome	10	3.1
pituitary insufficiency	74	22.7
cranial-nerve palsy	11	3.4

Table 2. The Number of All Kind of Pituitary Neoplasms

Tumor type	Total (%)	Micro- (%)	Macro- (%)
Non-functional	151 (46.3)	17 (11.3)	134 (88.7)
PRL	75 (23)	21 (28)	54 (72)
GH	87 (26.7)	15 (17.2)	72 (82.8)
ACTH	9 (2.8)	7 (77.8)	2 (22.2)
TSH	2 (0.6)	1 (50)	1 (50)
Mixed	2 (0.6)	1 (50)	1 (50)
Total	326 (100)	62 (19)	264 (81)

Total, total pituitary neoplasms; Micro-, pituitary microadenomas; Macro-, pituitary macroadenomas; Non-, *functional* non-functional adenomas; PRL, PRL-secreting adenomas; GH, GH-secreting adenomas; ACTH, ACTH-secreting adenomas; TSH, TSH-secreting adenomas; Mixed, mixed pituitary adenomas.

pic therapy; classified into two types: pituitary microadenomas and pituitary macroadenomas. In addition, they all accepted ophthalmologic examinations. All the endocrine measurement also was applied during their hospitalization, including plasma growth hormone (GH), insulin-like growth factor 1 (IGF-1), prolactin, adrenocorticotrophic hormone (ACTH), cortisol, thyroid-stimulating hormone (TSH), free thyroxine, luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone and estradiol levels (**Table 2**). The endocrine status and neuroimaging also are two important parts of the follow-ups. In this report, MR and CT evaluated the effect of surgery in 24 hours after operation and the endocrine measurement was performed at the first and seventh day postoperatively. The routine follow-ups include the endocrine measurement at the third, sixth postoperative months and annually and neuroimaging in necessity.

Endoscopic transsphenoidal surgery procedure

To put it simply, the patient stays the supine position and the head back fifteen degrees after general anesthesia and tracheal intubation. Following the disinfected face and nasal cavities, put 0.01% epinephrine solution cotton patch into the nasal cavity chosen according to the CT and MR images to gradually expand the space. Find the sphenoid ostium under an endoscope and make an arc-shaped incision approximately 1.0-2.0 cm above it on the nasal septum mucosa to reveal the septum backend and sphenoid sinus anterior wall. Carefully drill and ground the anterior wall of the sphenoid sinus and the sphenoid sinus septa to show the sellar floor. According to preoperative neuroimaging, decide the range of opened sellar floor and incise the dura. Remove the tumor with a curet or a suction apparatus on the premise of identifying the adenoma clearly. Then reconstruct the sellar floor by using artificial dura and pedicled nasal mucosa if the sellar floor has a big coloboma. Finally the nasal cavity is packed by Vaseline gauze strip.

Results

Outcomes of surgery

The study reports 151 cases of non-functional adenomas with a rate of total resection of 81.5% and the rates of microadenomas and macroadenomas are respectively 100% (17 cases) and 79.1% (106 cases). Among the 75 with PRL-secreting adenomas, 62 cases (82.7%) decreased to normal blood PRL levels after the operation including 20 microadenomas and 42 macroadenomas. There are 61 (70.1%) patients with GH-secreting adenomas who achieved normal GH levels; of them, microadenomas are13 (86.7%) and macroadenomas are 48 (66.7%). Of the 9 Cushing's disease patients, a total of 8 (88.9 %) had normal ACTH levels; 1 of 2 macroadenomas and all of microadenomas recovered. 2 patients suffered from TSH-secreting adenomas and the blood TSH level of all cases reached the normal level. Two patients with mixed pituitary adenomas had normalized hormone levels postoperatively (**Table 3**).

Table 3. The Remission rates of Endoscopic transsphenoidal surgery in the Pituitary Neoplasms*

Tumor type	N	Total (%)	Micro- (%)	Macro- (%)
Non- functional	151	123 (81.5)	17 (100)	106 (79.1)
PRL	75	62 (82.7)	20 (95.2)	42 (77.8)
GH	87	61 (70.1)	13 (86.7)	48 (66.7)
ACTH	9	8 (88.9)	7 (100)	1 (50)
TSH	2	2 (100)	1 (100)	1 (100)
Mixed	2	2 (100)	1 (100)	1 (100)
Total	326	258 (79.1)	59 (95.2)	199 (75.4)

Remission criteria*: non-functional adenomas are resected totally which judged by the surgeon and neuroimaging and functional adenomas achieve normalized hormone levels.

Table 4. The Postoperative Complications of Endoscopic transsphenoidal surgery in the Pituitary Neoplasms

Complication type	Number	Percentage (%)
Hyponatremia	32	9.8
Hypopituitarism	23	7.1
Postoperative cerebrospinal fluid leak	13	4.0
Transient diabetes insipidus	10	3.1
Permanent diabetes insipidus	2	0.6
Epistaxis	5	1.5
Sphenoid sinusitis	3	0.9
Cranial nerves palsy	3	0.9
Internal carotid artery injury (death)	1	0.3
Meningitis	1	0.3
Residual tumor bleeding (death)	1	0.3

Postoperative complications

According to the report, New-Onset hyponatremia is the most common postoperative complication; 32 (9.8%) patients suffered from hyponatremia after surgery and were cured before discharge. 12 (3.7%) patients had newly diagnosed diabetes insipidus, including 2 patients with permanent diabetes insipidus and 10 patients with transient diabetes insipidus. 23 (7.1%) cases of these patients are found hypopituitarism and treated with the hormone replacement therapy. 13 (4.0%) cases of postoperative cerebrospinal fluid leak are recorded and all of them recovered through lying in bed or lumbar cisterna drainage. One meningitis caused by postoperative cerebrospinal fluid leak occurred. Three (0.9%) patients newly had cranial nerves palsy after the endoscopic endonasal transsphenoidal surgery. In addition to the above, 5 (1.5%) epistaxis, 3 (0.9%) sphenoid sinusitis, one internal carotid artery injury and one residual tumor bleeding are reported. Among them, the patient with internal carotid artery injury was diagnosed traumatic pseudoaneurysm because of the surgery and died of aneurysm rupture. Another death case is the patient with residual tumor bleeding and her family members refused any rescue measures when she was suffering hemorrhage (**Table 4**).

Discussion

Since the first pure endoscopic endonasal transsphenoidal surgery was reported by Jankowski and colleagues from the Department of Otorhinolaryngology-Head and Neck Surgery in 1992 [1], endoscopic transsphenoidal surgery was recognized and applied gradually on the field of neurosurgery, especially pituitary neoplasms and other brain tumors in midline, and the increasingly mature technology of endoscopic transsphenoidal pituitary surgery has been widely applied and more and more new technologies are used to improve the surgery safety and effectiveness in last decade [2-5]. Mami Ishikawa and colleagues reported the use of endonasal ultrasonography in the neuroendoscopic transsphenoidal surgery and proved it is useful to the surgery which can provide real-time dynamic images [2]. Takuichiro Hide and colleagues reported 26 patients who suffered from pituitary adenomas were applied the indocyanine green endoscope, which means the patients were injected 12.5 mg of indocyanine green into a peripheral vein as a bolus and observed the internal carotid arteries, cavernous sinus, intercavernous sinus and pituitary in the endoscopic endonasal transsphenoidal surgery, and they thought that the real-time observation of the blood supply to the optic nerves and pituitary helps to predict the preservation of their function [3]. Besides, the three-dimensional endoscopy and image guidance were reported in the endoscopic endonasal transsphenoidal surgery [4, 5]. In this study, the pure endoscopic endonasal transsphenoidal surgery is the only operative method.

Outcomes of surgery

Before talking about complications of any treatment, it is important and necessary for the therapy to ensure the curative effect. The non-functional adenomas and functional adenomas have different surgical targets. The treatment of non-functional adenomas mainly improved the symptoms attributed to the mass effect; however the aim of the treatment of functional adenomas is removing the tumor totally and achieved normal hormone levels besides the above. This report shows moderateremission rates (as describe in previous section) of endoscopic transsphenoidal surgery in the pituitary neoplasms compared with other reports [6-14]. The rate of complete resection of non-functional ad-enomas varies from 56% to 97% in some published reports [6-9]. It was reported that 50.9%-94% of PRL-secreting adenomas achieved normal hormone levels [6, 8, 10-12]. 46%-89% of GH-secreting adenomas decreased to normal blood GH levels after the operation according to some former reports [6, 10, 11, 13]. The remission rate about Cushing's disease ranged from 61.1% to 95% in other literatures [6, 10, 11, 14]. The quantity of TSH-secreting adenomas and mixed adenomas is rare compared with the other kind of pituitary adenomas according to the study and their remission rates offer scant guidance.

Postoperative complications

The study reports 326 cases pituitary adenomas after the endoscopic transsphenoidal surgeries. The surgeon of these surgeries had completed more than 200 cases of endoscopic transsphenoidal surgery in pituitary adenomas and his surgical technique has stayed relatively steady. Bokhari and colleagues reported the outcomes would tend to be stable after 30 to 40 cases of the surgery [15]. Except for the experience of the surgeon, multi-department cooperation is another premise of achieving good results in the surgery. Before the surgery, magnetic resonance, computed tomography and CT angiography evaluated the anatomical features of the surgical site, including the location, shape, size and growth of the tumor, the relative position between the tumor and other important structures such as the cavernous sinus, internal carotid artery and the optic chiasma, the location of normal pituitary tissues and the anatomy of nasal cavities and paranasal sinus. This information can help the surgeon to finish the therapy better and achieve fewer complications. In the study, otolaryngologists play a significant role and teach the surgeon how to protect the nasal mucosa and the normal anatomy and function of nose.

In the study, postoperative hyponatremia, diabetes insipidus and hypopituitarism are respectively 32 (9.8%), 12 (3.7%) and 23 (7.1%). They are closely related to the protection of the pituitary stalk, the pituitary gland and hypothalamus. During the operation, impertinent tension, resection and electrocoagulation would cause the above complications. Packing excessively for hemostasis also should be avoided and subtotal removal is a better choice in necessity. The urine volume of patients in the end of operation reminds the surgeon the possibility of diabetes insipidus. In this report, all of postoperative hyponatremia were controlled in hospital through restricting the entrance of water or supplement of sodium. Minirin is used to treat diabetes insipidus and the urine volume of patients should be monitored to adjust the appropriate dose. The patients with hypopituitarism treated with the hormone replacement therapy and most of them recovered in six months.

Postoperative cerebrospinal fluid (CSF) leak was reported in the earlier literatures and the rate varied from 0.9% to 6% [16-18]. 13 (4.0%) cases of postoperative CSF leak are recorded in the series. CSF leak happens when the surgeon treats the tumors or validates the anatomic structure closed to the diaphragm sella during the surgery. After operation, the changes of intracranial pressure could cause the CSF leak. There are two key points which are used to avoid this complication: the mass located 12 o'clock direction is removed in the end and artificial dura, autologous fat, muscle and fascia are used to reconstruct the sellar floor. All of them recovered through lying in bed or lumbar cisterna drainage. One of these patients developed to the meningitis and treated with antibiotics.

Five (1.5%) epistaxis and three (0.9%) sphenoid sinusitis are recorded. The rate of postoperative epistaxis is between 0.6% and 1.6% [16, 17, 19]. The rate of postoperative sphenoid sinusitis is between 0.4% and 2.05% [6, 16, 17]. Epistaxis is caused by the injury of nasal mucosa, the branch of sphenopalatine artery on the nasal septum hemorrhage or capillaries bleeding on Little's Area. Routine nasal endoscopic examination can ensure stuffy noses airway and observe the recovery of nasal mucosa. Washing out the nasal passages is a convenient way to protect noses after the endoscopic endonasal transsphenoidal surgery. The nasal packing is the solution of epistaxis, and antibiotics and intranasal budesonide are used in sphenoid sinusitis.

Internal carotid artery injury and cranial nerves palsy have a very close relationship with the understanding of anatomy. The operation should be done along the middle line according to the anatomy signs and go on after recognizing the important structures. Preoperative CTA is important for the surgeon to recognize the internal carotid artery and the surrounding.

Conclusion

This study reports the general data, outcomes and postoperative complications of 326 patients with pituitary neoplasm who suffered from the pure endoscopic transsphenoidal surgery. According to the analysis, the rates of most postoperative complications are related to the removal degree. The advantages and disadvantages of extremely resection of tumors should be studied in the later research. Besides, we need many large data samples to sum up the experience of the endoscopic transsphenoidal surgery of pituitary neoplasms with the development of Neural endoscopic technology.

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Disclosure of conflict of interest

None.

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