Staged surgery for irregular giant pituitary adenomas: A report of two cases

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Abstract. The resection of giant pituitary adenomas is one of the most challenging brain surgeries, especially when the giant pituitary adenomas have an irregular shape or irregular growth position. The purpose of the present study is to propose staged surgery for irregular giant pituitary adenomas through a retrospective analysis of two cases. The cases of two patients with irregular giant pituitary adenomas who underwent staged surgery are retrospectively analyzed. In one case, a 51-year-old male was hospitalized after 2 months of memory loss. Brain MRI showed that the pituitary adenoma was paginated and located in the sellar and right suprasellar regions, with a size of ~6.15x6.11x5.69 cm. In the second case, a 60-year-old male had a history of intermittent vertigo for 10 years and paroxysmal amaurosis for 1 year. Brain MRI showed that the pituitary adenoma grew laterally and eccentrically, and was located in the sellar region, with a size of ~4.35x3.96x3.07 cm. Both patients underwent staged surgery; more specifically, the tumors were totally removed through two-stage surgery. In the first-stage operation, most of the tumor was removed by the microscopic transcranial approach, while in the second-stage operation, the residual tumor was removed by the endoscopic transsphenoidal approach. Both patients recovered well without obvious postoperative complications after staged surgery. There was no recurrence during the follow-up. Staged surgery is characterized by only treating tumors in the visual field and achieving a total tumor resection, which has the advantages of a high tumor resection rate, high safety and fewer postoperative complications. Staged surgery is especially suitable for irregular giant pituitary adenomas with an irregular shape or irregular growth position.

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Introduction

A pituitary adenoma is a benign neuroendocrine tumor that originates from the adenohypophysis and accounts for 10-20% of all primary intracranial tumors (1,2). According to the diameter of the tumor, pituitary adenomas are divided into micro-adenoma, macro-adenoma and giant adenoma (3). Among them, giant pituitary adenoma refers to a pituitary adenoma with a diameter >4 cm, accounting for 6-10% of all pituitary adenomas (4). Due to its large size, the giant pituitary adenoma can confer a series of clinical symptoms on patients, such as headaches, dizziness, amaurosis, vision loss and endocrine abnormalities, among others (5). In addition, giant pituitary adenomas can be divided into functional adenomas and non-functional adenomas (6,7). For some functional giant pituitary adenomas, such as prolactinomas and growth hormone adenomas, symptomatic treatment to reduce prolactin and growth hormone levels can be adopted (8). However, once drug treatment is not effective, surgical treatment should be considered. For other types of functional giant pituitary adenomas and non-functional giant pituitary adenomas, surgical treatment is considered as the first-line treatment (9,10). Giant pituitary adenomas tend to extend to multiple anatomical compartments, often enclose neurovascular structures and show high invasiveness (11). Due to the characteristics of a huge volume and extracellular extension, surgical resection of giant pituitary adenomas is still a challenge (12). Generally, the surgical strategy can be divided into single surgery and staged surgery. It has been reported that radical resection of giant pituitary adenomas through a single surgery is achieved in less than one-third of cases (13). Staged surgery can greatly improve the tumor resection rate, even up to 100% (14). Furthermore, irregular giant pituitary adenomas have unique shapes and locations, which further increases the difficulty of surgery and the risk of postoperative complications. Therefore, for irregular giant pituitary adenomas, it is necessary to customize personalized staged surgery. The present study reports two cases of giant pituitary adenomas with an irregular growth shape and position, respectively. To achieve the radical resection of the tumor, the staged surgery was customized according to the location and shape of the tumor, specifically, resection of most of the tumor by first-stage surgery using the microscopic transcranial approach, followed by the total resection of the residual tumor by second-stage surgery using the endoscopic transsphenoidal approach.

Case report

Case 1. A 51-year-old man was admitted to the Department of Neurosurgery of Chongqing General Hospital (Chongqing, China) in August 2015 due to memory loss for 2 months. No obvious abnormalities were found in terms of other clinical symptoms or on physical examination. Brian MRI revealed a large space-occupying lesion in the sellar region, and the tumor grew from the sellar region to the right lateral ventricle. Fig. 1A-C shows the axial, coronal and sagittal MRI, indicating that the size of the tumor was 6.15x6.11x5.69 cm and the shape of the tumor was paginated. The tumor had the characteristics of a huge volume, a high probability of adhesion with surrounding tissues (such as arteries, optic nerves and optic chiasma) and an irregular shape, leading to large blind areas of the visual field, all of which would make it difficult to achieve a total tumor resection through a single operation and greatly increase the incidence of postoperative complications. Therefore, two-stage surgery was planned to totally remove the irregular giant pituitary adenoma. In the first-stage operation, most of the tumor was removed by the microscopic transcranial approach, while in the second-stage operation, the residual tumor was removed by the endoscopic transsphenoidal approach.

In the first stage of the operation, the right frontal dura was radially cut, the right frontal lobe was decompressed and the tumor was exposed. It was observed that the tumor adhered to the right optic nerve and the tumor base was located within the sellar septum. After the tumor parenchyma had been exposed to the surgical vision and was removed, part of the tumor capsule remained and this was repeatedly burned by electrocoagulation. A tumor cavity measuring 5.00x4.00x5.00 cm was formed. After the bleeding had completely stopped, the tumor cavity was filled with absorbable hemostatic yarn, the dura was repaired using artificial dura mater, the titanium mesh was cut and used to repair bone holes, the bone flap was reset and fixed, and the muscles, cap aponeurosis and scalp were repaired. Fig. 1D-F shows the sagittal, coronal and transverse cranial MRI after the first stage of surgery, from which it can be seen that most of the tumors have been removed. However, some residual tumor was left in the sellar region, as forcibly removing it would cause postoperative complications, such as cerebrospinal fluid rhinorrhea. The patient developed transient diabetes insipidus and hyponatremia on the 6th day after the operation. After symptomatic treatment, urine output and electrolyte levels returned to normal. After the first stage of the operation, the patient's memory improved slightly. There were no other symptoms or discomfort between the first-stage operation and the second-stage operation.

After 1 year, the patient came to the hospital again for the second-stage operation. The residual tumor was completely removed through the endoscopic transsphenoidal approach. After the dura mater at the sellar base was cut, the tumor was exposed, and the residual tumor tissue was separated and removed along the normal pituitary interface. During the operation, the tumor was found to be slightly firm with some chylous necrosis. Fig. 1G-I shows the brain MRI after the second-stage operation, indicating that the residual tumor was totally removed. Postoperative complications, such as diabetes insipidus, electrolyte imbalance and pituitary dysfunction, did not occur. During the follow-up of 4 years, there was no recurrence. In addition, a telephone follow-up was conducted 6 years after the second-stage operation, and the patient stated that their memory had improved further.

Case 2. A 60-year-old man who had suffered from intermittent dizziness for 10 years and paroxysmal amaurosis for 1 year was admitted to the Department of Neurosurgery of Chongqing General Hospital in February 2019. The intermittent dizziness occurred mainly in the afternoon without obvious triggers, while the bilateral paroxysmal amaurosis occurred 1-2 times per month and lasted for only seconds. The patient received a brain MRI examination, which revealed a 4.35x3.96x3.07-cm lesion in the sellar region, as shown in Fig. 2A-C. The lesion was deep and broke through the sellar septum. Furthermore, the tumor showed lateral eccentric growth. Due to the special location and huge size of the tumor, there was a blind area in the surgical visual field, which would make it difficult to totally remove the tumor in a single operation. Therefore, for this giant pituitary adenoma with lateral eccentric growth, staged surgery was planned to achieve a complete resection of the tumor. Specifically, the first-stage operation was microscopic, to achieve a total resection of the suprasellar tumor, and the second-stage operation was endoscopic transsphenoidal surgery to achieve a total resection of the residual tumor.

In the first stage of surgery, the dura mater was radially opened and suspended to release the cerebrospinal fluid. After the intracranial pressure decreased to a certain extent, the frontal lobes were raised to expose the tumor. The tumor's surface was gray and slightly adhered to the surrounding tissues. As the tumor was lifted, it was observed that the tumor grew from the sellar region to the intracranial region through between the optic nerve and the internal carotid artery on the left. The capsule was cut, and the tumor parenchyma had a tough texture. During the operation, it was observed that the tumor compressed the left optic nerve and internal carotid artery, and adhered to the branches of the basilar artery, failing to totally separate the tumor from the surrounding normal tissues. The intracranial tumor was nearly totally removed, with only a little residual tumor capsule. It is worth noting that to reduce brain tissue traction, the residual intrasellar tumor was left for the second stage of surgery. The brain MRI after the first stage of surgery showed that the intracranial tumor had been nearly totally removed, with residual intrasellar tumor tissue, as shown in Fig. 2D-F. On the 4th day after the operation, the patient developed transient diabetes insipidus and recovered after symptomatic treatment. After the first stage of the operation, the patient reported that the paroxysmal amaurosis had been relieved but that slight intermittent dizziness still existed.

After 6 months, the patient was admitted to the hospital for the second stage of surgery. In the second stage of the operation, the endoscope was placed into the right nasal cavity, the opening of the sphenoid sinus was found under the endoscope, the sphenoid sinus and sellar bone were ground open, the dura was exposed and the dura was cut with a sharp knife. After opening the dura, the residual tumor was observed to be dark yellow-white and hard, as shown in Fig. 3A. The intrasellar tumor was separated along the normal structure of the left cavernous sinus. After scraping off part of the tumor, scar

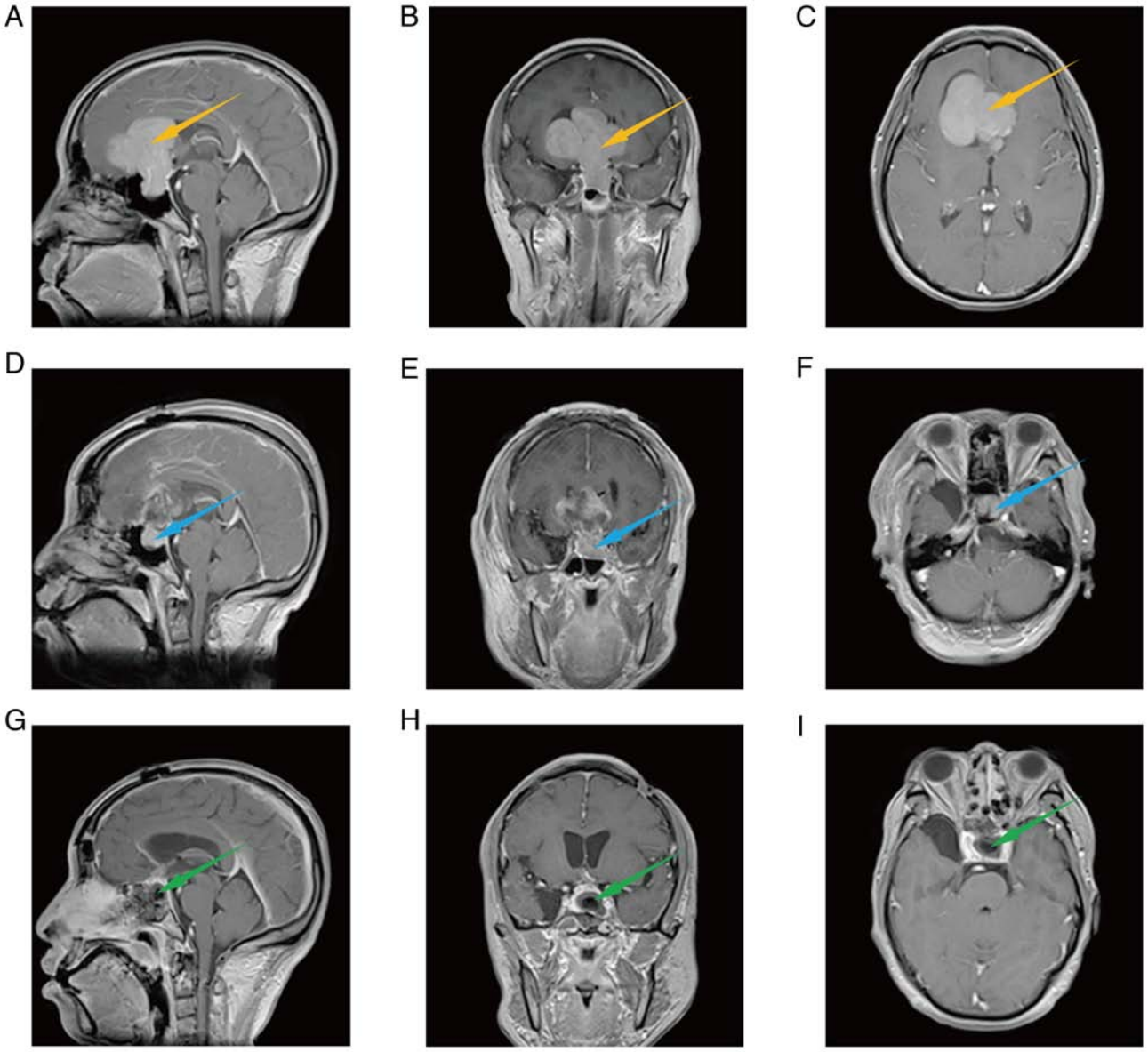

Figure 1. Preoperative and postoperative gadolinium-enhanced T1-weighted cranial MRI of case 1. The (A) sagittal, (B) coronal and (C) transverse views of the preoperative MRI. The (D) sagittal, (E) coronal (F) and transverse views of the MRI after the first-stage operation. The (G) sagittal, (H) coronal and (I) transverse views of the MRI after the second-stage operation. The yellow, blue and green arrows indicate a preoperative tumor, residual tumor and tumor cavity, respectively.

hyperplasia was observed at the sellar septum, as shown in Fig. 3B. Then, the tumor on the scar was removed to achieve gross total resection (GTR) of the tumor. Fig. 3C and D shows the tumor at the stump scar and tumor cavity. Video S1, Video S2, Video S3 and Video S4 are representative surgical videos, which correspond to the surgical procedures shown in Fig. 3A, B, C and D, respectively. The brain MRI after the second stage of surgery indicated that the intrasellar tumor had also been totally removed, as shown in Fig. 2G-I. The patient developed transient diabetes insipidus on the second day after the operation and recovered after symptomatic treatment. Overall, through the staged surgery, the giant irregular pituitary adenoma, including the intracranial and intrasellar regions, had successfully undergone GTR without serious postoperative complications. During the follow-up period of 10 months, there was no recurrence. Moreover, a telephone follow-up that was conducted 3 years after the second-stage operation revealed that the patient's dizziness and amaurosis had disappeared.

Both patients had a good prognosis during long-term follow-up.

Discussion

Due to its large size and irregular growth, a giant pituitary adenoma can cause obvious clinical symptoms such as visual field defects, headaches, dizziness and abnormal hormone levels, with the most common clinical symptoms caused by non-secretory giant pituitary adenomas being visual impairment and visual field defects, followed by headaches (15). Although very rare, giant pituitary adenomas may also sometimes compress the third ventricle, which may lead to the accumulation of cerebrospinal fluid in the lateral ventricle, hydrocephalus and increased intracranial pressure, resulting

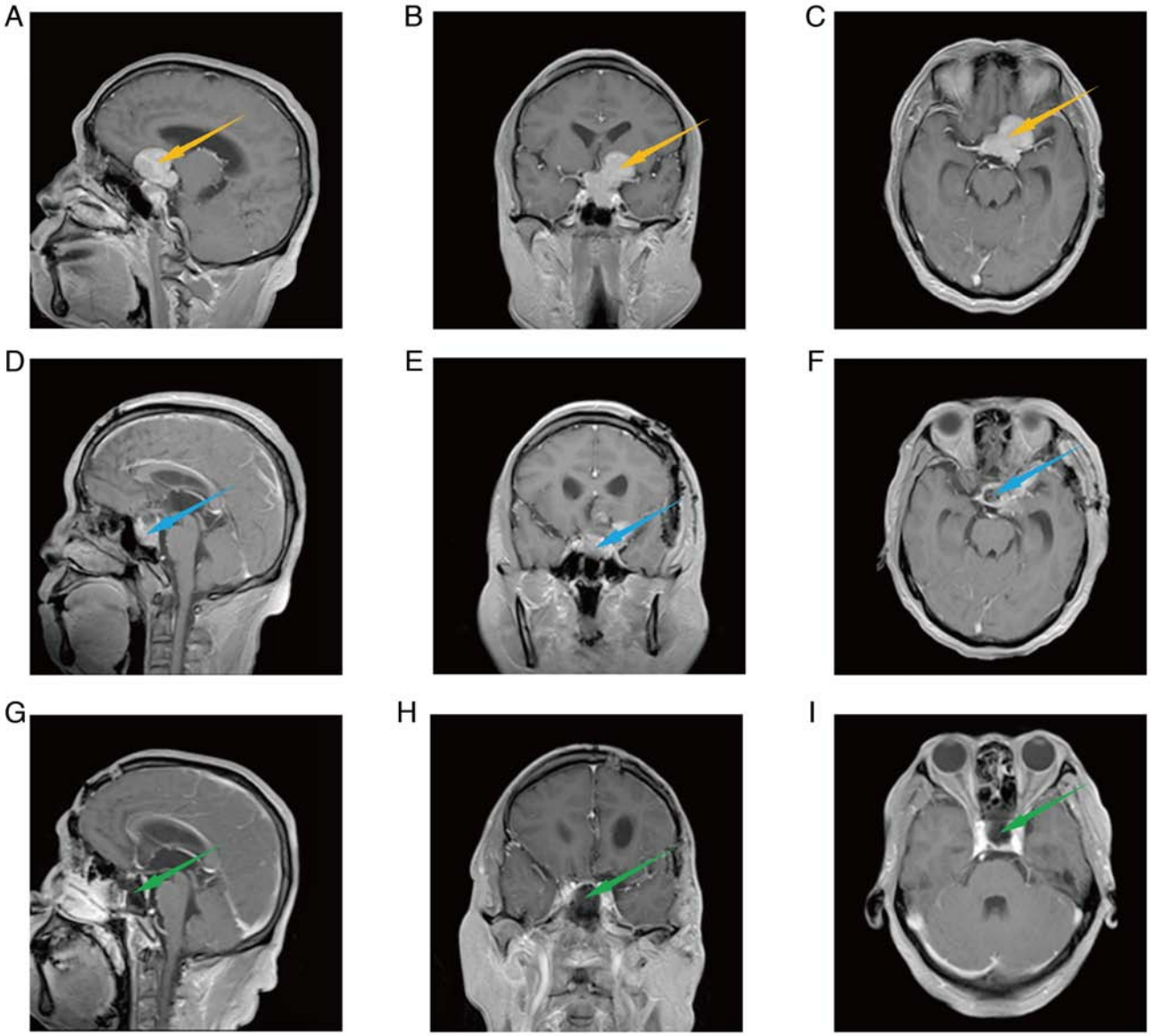

Figure 2. Preoperative and postoperative gadolinium-enhanced T1-weighted cranial MRI of case 2. The (A) sagittal, (B) coronal and (C) transverse views of the preoperative MRI. The (D) sagittal, (E) coronal and (F) transverse views of the MRI after the first-stage operation. The (G) sagittal, (H) coronal and (I) transverse views of the MRI after the second-stage operation. The yellow, blue and green arrows indicate a preoperative tumor, residual tumor and intrasellar tumor cavity, respectively.

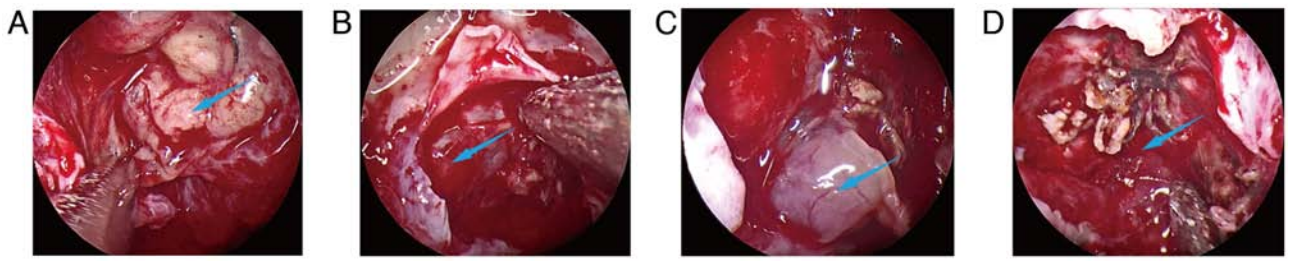

Figure 3. Intraoperative images of case 2 during the second stage of surgery. (A) Separation of the tumor from the left cavernous sinus. (B) Exposure of the sellar septum. (C) Treatment of the tumor in the scar of the stump. (D) Tumor cavity. The arrows indicate the intrasellar tumor, sellar diaphragm, residual scar tumor and tumor cavity, respectively.

in nausea, vomiting and other symptoms (16,17). Therefore, it is necessary to treat giant pituitary adenomas to improve the quality of life of the patients. At present, for giant prolactinomas and giant growth hormone adenomas, drug therapy can be used. For other giant pituitary adenomas, surgery is the first choice.

At present, giant pituitary adenomas are mainly removed by a single surgery via a single surgical approach or a combined

surgical approach. The common surgical approaches are the transsphenoidal and transcranial approaches, both of which have advantages and limitations (18). Generally, the transsphenoidal approach is considered to be the best method for resection of intrasellar pituitary adenomas, but due to the limitations of a deep and narrow working space, the resection of giant pituitary adenomas is still controversial (11). The transcranial approach is usually used to remove the lateral or complex extension of the tumor, which provides more opportunities for a radical resection of the tumor, but also increases the risk of complications and causing higher damage to the surrounding tissue structure (19). Previous studies have shown that single surgery with a single surgical approach (transsphenoidal or transcranial) for giant pituitary adenomas not only has a low GTR rate (44%), but also has very high postoperative complication rate (11%) (20-24). The low GTR rate of single surgery with a single surgical approach may be mainly due to the limited visual field of the microscope and endoscope. To expand the visual field and improve the GTR rate, the combined surgical approaches (transsphenoidal + transcranial or transcranial + transcranial) can be adopted in a single operation (25,26). The main advantage of this is that the tumor can be operated on simultaneously from two approaches, so that the hidden part of the tumor that cannot be seen or touched in the single approach can still be removed (27-29). Compared with that of a single transcranial approach or single transsphenoidal approach, the GTR rate of the combined surgical approaches can be improved to a certain extent (30). However, the cost of improving the GTR rate using a single surgery with combined surgical approaches is an increase in the risk of cerebrospinal fluid leakage. Moreover, this type of surgery requires two surgical teams, two sets of operation equipment and a large operation room, which means that the medical cost and operation difficulty are increased. Therefore, overall, for giant pituitary adenomas, the GTR rates of a single operation via transcranial approach, transsphenoidal approach and combined surgical approaches are still relatively low, but the medical cost and surgical difficulty are increased. Moreover, the GTR of giant tumors may also introduce additional trauma to the patients, including damage to the surrounding normal tissues, massive intraoperative bleeding, an increased possibility of postoperative complications and a longer healing time. To avoid these risk factors, it is not recommended to totally remove the tumor in a single operation, and the staged operation is advocated.

Staged surgery refers to performing a first-stage operation and then a later second-stage operation, in which the specific surgical approach depends on the location of the tumor and the habits of the surgeon. If the transsphenoidal approach is selected for the primary operation, the degree of tumor resection will be small, resulting in an increased probability of complications such as hydrocephalus and cerebrospinal fluid rhinorrhea. Therefore, transcranial surgery is recommended for the first stage of surgery to achieve large-scale resection of the tumor and to reduce the possibility of hydrocephalus, while endoscopic transsphenoidal surgery is recommended for the second stage of surgery to remove the residual tumor. In the present study, 2 patients with giant pituitary adenomas underwent staged surgery, and GTR of the tumor was achieved. The resection of most of the tumor was achieved through the first stage of microscopic transcranial surgery, while GTR was achieved through the second stage of endoscopic transsphenoidal surgery. After the operation, there were no obvious complications except temporary diabetes insipidus. Case 1 was followed up for 4 years without any complications or tumor recurrence. Case 2 was followed up for 10 months without any complications or tumor recurrence. Therefore, for irregular giant pituitary adenomas, staged surgery (first-stage transcranial surgery and second-stage transsphenoidal surgery) can not only improve the GTR rate but also reduce postoperative complications and ensure the quality of life of patients.

In conclusion, the present study retrospectively analyzed two patients with irregular giant pituitary adenoma who underwent staged surgery to achieve total tumor resection without postoperative complications. Furthermore, staged surgery is not limited to the removal of irregular giant pituitary adenomas, but can also be performed for other irregular giant brain tumors.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

CT, JWW, PW, DWZ and NW participated in the conception, design and data acquisition of the paper. CT participated in drafting and revising the manuscript. JWW critically revised the paper. NW ensured that questions related to the integrity of any part of the work were appropriately investigated and resolved. CT, JWW, PW, DWZ and NW confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Chongqing General Hospital (Chongqing, China).

Patient consent for publication

Written informed consent was obtained from the patients for the publication of anonymized data and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

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