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Clinical Article

Preliminary Surgical Results of Open Sella Method with Intentionally Staged Transsphenoidal Approach for Patients with Giant Pituitary Adenomas

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Objective : This study is designed to evaluate the clinical outcome, the safety and the effectiveness of the open sella methods(OSM) with intentionally staged transsphenoidal approach(TSA) for giant pituitary adenomas(GPA).

Methods : Eight patients with GPA were managed by the OSM with intentionally staged TSA. There were 5 nonfunctioning adenomas, 2 prolactin- secreting adenomas, and 1 growth hormone-secreting adenoma. Among them, 6 patients underwent two times of TSA, one patient underwent three times of TSA, and the other patient underwent two times of TSA followed by radiation therapy. The mean time interval between staged operations was 3.9 months except for one case.

Results : Seven out of the eight patients with GPA treated with the OSM with intentionally staged TSA showed that the tumors were completely removed on magnetic resonance imaging and that they were free from headache and visual problem suffered previously. Only one patient experienced severe complications including panhypopituitarism, cerebrospinal fluid rhinorrhea and permanent diabetes insipidus.

Conclusion : With the surgical treatment for 8 cases of GPA, which extended to the suprasellar and parasellar area, we suggest that the OSM with intentionally staged TSA is a safe and effective method in management for GPA.

KEY WORDS : Giant pituitary adenomas · Intentionally staged operation · Open sella method.

Introduction

Pituitary tumors account for approximately 7~17% of all the brain tumors[15]. A majority of pituitary tumors are benign, but sometimes they rapidly extend to suprasellar region and cause significant neurological complications like other invasive brain tumors do[6,7,13,20,25]. Some authors have referred to these giant pituitary adenomas as adenohypophyseal carcinoma to distinguish them from ordinary pituitary tumors in that these giant tumors are invasive and cause neurological complications and that they don't respond well to surgical procedures and radiotherapy(RT)[4,6,7,30]. There are still controversies over the feasibility of surgical treatment for giant pituitary adenomas. The purpose of this study is to assess the clinical outcome, the safety and effica cy of the open sella method(OSM) with intentionally staged transsphenoidal approach(TSA) for giant pituitory adenomas(GPA).

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Materials and Methods

Among 103 patients who were treated for pituitary tumors in the neurosurgical department of our institute from September 1999 through October 2003, 15 patients with GPA were treated with TSA. Five patients among them were treated with single TSA without the staged operation and the additional surgery was not required. And two patients who had been conducted with OSM via transsphenoidal route did not undergo the staged TSA but underwent RT or radiosurgery. So those seven patients were excluded from this study, and eight patients with GPA were selected for this study. These eight patients underwent surgery for pituitary adenomas via transsphenoidal route with intentionally staged operation. Of these 8 patients, 6 were males and 2 were females with an average age of 43.5 years. Their pituitary adenomas were as large as 40mm or above. Tumors were graded by the Hardy's classification in terms of the extension into sellar turcica and suprasellar extension, resulting in 2 grade C's and 6 grade D's. The average diameter of tumors was around 5.2cm (4.0~6.5cm). There were 5 nonfunctional adenomas, 2 prolactin-secreting adenomas and 1 growth hormone-secreting adenoma. The internal carotid artery was

Table 1. The patient's profiles

No.	Sex	Age(yr)	Characteristics	Size(cm)	CS[a] invasion	Method	Interval(month)
1	M	52	nonfunctioning	4.5	(−)	ISTSA[b] + TSA[c]	3
2	M	55	GH-secreting	6.5	(+)	ISTSA + TSA+ TSA	5+3[f]
3	F	19	PRL-secreting	4.0	(−)	ISTSA + TSA	23[e]
4	M	31	nonfunctioning	5.5	(+)	ISTSA + TSA	3
5	F	67	nonfunctioning	4.5	(−)	ISTSA + TSA	7
6	M	44	nonfunctioning	5.0	(+)	ISTSA + TSA	3
7	M	55	nonfunctioning	6.0	(+)	ISTSA + TSA	3
8	M	25	PRL-secreting	5.5	(+)	ISTSA + TSA + RT[d]	4 + 3[g]

a; CS, cavernous sinus, b; ISTSA, intentional staged transsphenoidal approach, c; TSA, transsphenoidal approach, d; RT, radiation therapy, e; one case dropped during the 23 month follow up period, f; time interval between second TSA and third TSA, g; time interval between second TSA and RT.

encased in 5 cases, which were all nonfunctional adenomas. The TSA was done for all the patients and they were operated using the OSM followed by intentionally staged approach. The time interval between staged operations averaged 3.9 months, excluding a case dropped during the 23 month follow-up period. The OSM with intentionally staged TSA was performed as palliative treatment for all patient followed by additional TSA or RT, designed to remove residual tumors (Table 1).

Before the surgery, we had planned the OSM with intentionally staged operation for 15 patients with GPA, such as Hardy's classification C and D. However, in 5 patients, the tumor was totally removed via single transsphenoidal operation. These tumors were easily brought into the line of vision after the internal debulking of the tumor and other techniques, which include the Valsalva maneuver and infusion of air or lactated Ringer's solution (10~30ml) through a lumbar puncture. And in two patients who had undergone the OSM, the follow-up MRI at 3 months after the first surgery showed no remnant tumors in the sellar and suprasellar area but some remaining tumors encasing cavernous sinus. So these two patie-nts were managed with RT or radiosurgery followed after first TSA instead of intentionally staged TSA. As a result, the OSM with intentionally staged TSA was employed in the remaining 8 patients.

The prevention against cerebrospinal fluid(CSF) leakage from arachnoid rupture and the strict homeostasis are mandatory in the OSM with intentionally staged TSA. For that purpose, during performing internal debulking, outer capsules covering dome and lateral wall of the tumor should be preserved intact and after vigorous hemostasis, any intrasellar drainage tube or catheter was not indwelt in order not to provoke CSF leakage. And the hemostasis should be ensured by using the Surgicel® (Ethicon Co.), the Valsalva maneuver and raising blood pressure. The floor of sella turcica was not remodeled with bone graft or fat and sphenoid sinus was left open without fat graft. The nasal cavity was packed with Merocel® (M-pact Co.). All the patients after OSM were kept in absolute bed rest for 7 days or more.

The intentionally staged second TSA was done in three to four months after the first TSA in six cases (Fig. 1). And in one particular case, the TSA was performed three times with the same time interval between operations. In the remaining one case with prolactin-secreting tumor, the second TSA was followed by RT due to remnant in the cavernous sinus (Table 1).

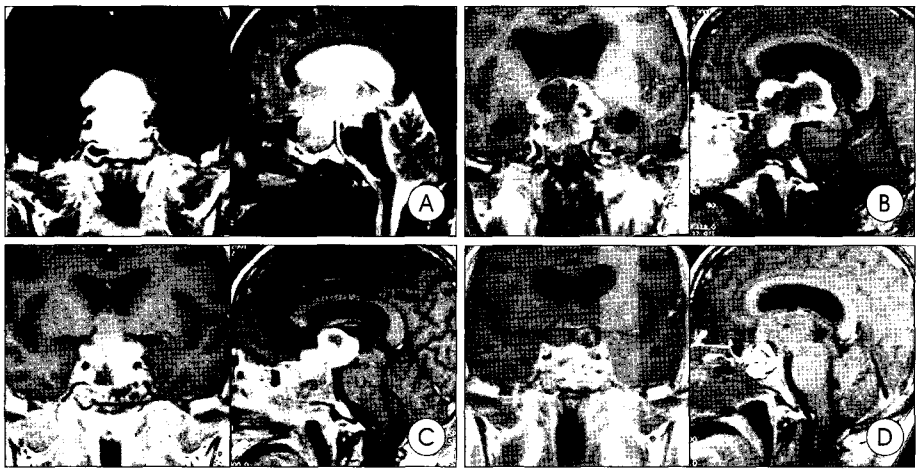

Fig. 1. A : Preoperative coronal T1-weighted magnetic resonance (MR) image with gadolinium enhancement and sagittal T2-weighted MR image, demonstrating a giant pituitary adenoma with supra- and retrosellar extension. B : Postoperative MR image shows subtotal resection of the tumor. C : Coronal and sagittal MR images obtained 3 months after 1st transsphenoidal approach(TSA) using induced pressure and the open sella method. D : Coronal and sagittal T1-weighted MR images after 2nd TSA show total removal of the remained supra- and retrosellar tumor.

Results

In eight cases with the OSM with intentionally staged TSA, the procedure proved the effectiveness in relieving headaches and visual problems caused by the pituitary tumors. Of six pat-

Table 2. Postoperative complications

Complications	ISTSA[a]+TSA[b]	ISTSA+TSA+(TSA or RT[c])
Diabetic Insipidus		
transient	4	1
permanent	0	1
Rhinorrhea	1	1
Cerebral Infarction		
< 2 month	0	0
long term	0	0
Visual acuity impaired	0	0
Intratumoral bleeding	0	0
Panhypopituitarism	0	1
CN II damage	0	0
Wound infection	0	1

a; ISTSA, intentional staged transsphenoidal approach, b; TSA, transsphenoidal approach, c; RT, radiation therapy

ients, diabetes insipidus was complicated after surgery; 5 cases were transient ones and one case was permanent. One patient, who underwent three times of TSA, complicated by CSF leakage, resultant tension pneumocephalus and ventriculitis, and suffered from permanent diabetes insi-pidus and panhypopituitarism.

Three patients with hormone-producing adenomas showed that their hormone secretion went down after surgery, but in one patient still showed higher hormone level than normal. This one patient had a prolactin-secreting tumor and a remnant tumor was found encasing cavernous sinus after intentionally staged TSA, resulting in additional RT and bromocriptine medication. Fortunately, there were no other disastrous complications including cranial nerve damages, intratumoral hemorrhage and cerebral infarctions after the OSM with intentionally staged TSA (Table 2).

Discussion

The purpose of any surgical procedures for GPA is not only to remove tumors and to relieve the pressure on the optic apparatus and cranial nerves, such as oculomotor nerve, but also to preserve the secretory function of the pituitary gland and to protect normal brain function. However, it is not easy to fulfill this objectives if the tumor is very large or extends into parasellar areas. To remove GPA with suprasellar extension, various surgical procedures have been introduced. Some authors stressed that the TSA is effective to excise even GPA, but the extension into the cavernous sinus would make it impossible to completely eliminate the tumor because the tumor is not easily accessible[2,9]. Furthermore, the tumors with extension to the frontal, temporal or posterior fossa or that are compressed by the diaphragm sella in the shape of a dumbbell are usually treated with either the transcranial approach or the combined transsphenoidaltranscranial approach.

The TSA was launched as the most effective first-line treatment for pituitary adenomas by Hardy about 30 years ago[11].

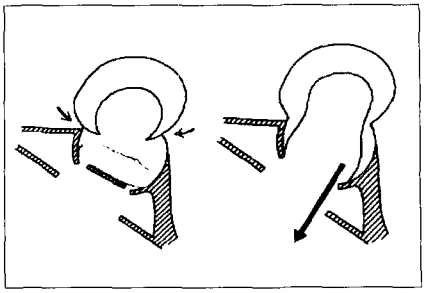

Fig. 2. An illustration of transsphenoidal removal of pituitary adenoma with suprasellar extension. A : traditional fashion of adenomectomy and wound closure. Radical excision may cause cerebrospinal fluid leak from points of arrows. B : The limb of adenoma near and above dorsum sellae and tuberculum sellae is tentatively not excised in the proposed method of intrasellar drainage. The arrow indicates the route of drain. Formerly, a bony bridge was placed at the sella floor for fear of prolapse of diaphragma sella. Now, the sella floor is left open (by Kuwayama A.).

Griffith et al. initiated the use of fluroscopy and microscope while conducting the procedure and strengthened the effectiveness of the TSA as initial treatment for pituitary adenomas[21]. Wilson and Fahlbusch claimed that more than 90% of pituitary adenomas can be removed with the TSA despite the infiltrative growth of the tumors[3,29]. Snow et al. alleged that the TSA should be considered as the initial treatment when MRI showed high signal intensity on the T2 weighted image because it means the tumor may have soft intensity[22]. For the removal of the suprasellar tumor, TSA may be assisted by other techniques, including the Valsalva maneuver, elevation of jugular venous pressure and the infusion of air, normal saline or lactated Ringer's solution through a lumbar catheter. Spaziante and others suggested that the TSA using air-infusion technique could remove suprasellar tumors without causing complications for 63% of patients with large pituitary adenomas[23]. But this technique is not useful when the tumors, especially fibrous ones, are enlarged, and the tumor mass does not come down toward the sellar turcica. For this case, Hardy and others assured that the use of the intentionally staged TSA was more effective[10]. Kuwayama and others also supported the effectiveness and the safety of the OSM with staged TSA and they favored intrasellar drainage technique[12,19](Fig. 2). They added that in spite of using method of elevating intracranial pressure, if remnant tumor exists in suprasellar region after first TSA, the method of leaving sella open enables remaining tumor to descend into sellar turcica in two months after first TSA. Mohr and others claimed that 89% of patients with fibrous or dumbbell-shaped GPA graded B and C by the Hardy's classification were succ-

essfully cured with the intentionally two-staged TSA using the OSM[18]. Even for the tumors extending into the lateral wall of the cavernous sinus, the transmaxillosphenoidal or an revised version of the TSA, were alleged more effective than the transcranial approach to eliminate the tumors[5,14].

Approximately 5~7% of GPA are fibrous, making the use of TSA difficult[16,17]. Nakane and others said that prolactin-secreting adenomas are so fibrous and invasive that the tumor can not extend down, and in the case of being blocked by the diaphragma sella, it is impossible to make the access to the tumor through the transsphenoidal route[19]. Since about 30% of GPA in the size of 3cm or more in diameter invaded the cavernous sinus and 83% of those with a diameter of 4 cm or more extended to at least two directions, the use of single TSA cannot be optimized for tumor removal[1,26,27,29].

Although the residual tumors can be destroyed by radiation, in order to lower the possibility of recurrence, Ohata and others insisted that the transcranial approach should be preferred over the RT for the treatment for the relapse of nonfunctional GPA[8,24,27,28], because of radiation-related complications, including optic nerve atrophy, the necrosis of normal brain tissue, and pituitary gland hypofunction.

Conclusion

There are still controversies over the feasibility of any surgical approach for GPAs, especially with extension to frontal and temporal fossa with or without large vessel encasement. The focus of surgical goal for GPA is aimed at not only preserving the secretory function of the pituitary gland and recovering brain function without complications including cerebral infarction, intracranial hemorrhage and cranial nerve damages etc., but also removing tumors as much as possible and eventually relieving the pressure on the adjacent neurovascular structures. In this preliminary study, the TSA was used as the primary therapeutic modality and was effective and safe in reducing both morbidity and mortality rate of patients with GPA, especially if supported by the OSM with intentionally staged TSA.

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