The Role of the Le Fort I Maxillotomy in the Management of Incompletely Resected Pituitary Macroadenomas

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ABSTRACT

Objective: The options available for the treatment of a nonsecreting pituitary macroadenoma that has been incompletely resected include reoperation, fractionated radiation therapy, and radiosurgery. Reoperation in this setting may be hindered by the same obstacles that prevented a complete resection during the initial surgical procedure, and should prompt consideration of an alternate approach or exposure. **Methods:** Between January 1998 and December 2003, 10 consecutive patients were referred to the Department of Neurosurgery at the University of Texas Southwestern Medical Center for the evaluation of a nonsecreting pituitary macroadenoma that measured 3 cm or greater in diameter despite having undergone an attempt at a complete resection elsewhere. Each of these patients was reoperated using a Le Fort I maxillotomy to enhance the exposure provided by a traditional transsphenoidal approach. **Results:** A total or near total (> 95%) resection was achieved in each case. One patient required reoperation for the repositioning of a fat graft to treat a cerebrospinal fluid fistula and one patient experienced a worsening of anterior pituitary function postoperatively. Five patients noted improved vision and no patient experienced further visual loss. Three patients have required subsequent treatment of small foci of recurrent or progressing tumor with stereotactic radiation therapy. No patient has received fractionated radiation therapy. **Conclusion:** The added exposure provided by a Le Fort I maxillotomy facilitates the resection of pituitary macroadenomas that have been incompletely resected by a traditional transnasal, trans-sphenoidal approach.

KEYWORDS: Le Fort I maxillotomy, macroadenoma, pituitary adenoma, trans-sphenoidal surgery

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The majority of nonfunctioning pituitary adenomas may be safely and effectively removed by means of a transnasal, trans-sphenoidal approach, using either the operating microscope or endoscopic techniques. Large tumors, those of fibrous consistency, and those with an invasive growth pattern are difficult to completely remove via this route, however, and a subtotal resection may leave the patient with persistent symptoms or at risk for a symptomatic recurrence of the tumor.

There are three options available for the treatment of a nonsecreting pituitary macroadenoma that has been incompletely resected: reoperation, fractionated radiation therapy, and radiosurgery. Although fractionated radiation therapy is generally believed to halt or delay the progression of residual pituitary tumors, it does not typically produce a decrease in tumor volume, and is therefore of limited value in relieving ongoing compression of the optic nerves or chiasm. Radiosurgery has been shown to produce a decrease in the size of residual nonsecreting tumors, but its use is limited when the tumor is in close proximity to the optic nerves or chiasm.^{1,2} These considerations suggest that a pituitary tumor should be resected as completely as possible prior to considering treatment with either fractionated radiation therapy or radiosurgery.

Several surgical strategies have been proposed in an effort to improve the safety and completeness of resection of large pituitary adenomas, including staged or simultaneous trans-sphenoidal and transcranial exposures,³⁻⁶ staged trans-sphenoidal procedures,⁷ and various modifications of the trans-sphenoidal approach,^{8,9} including the addition of a Le Fort I maxillotomy to the procedure.^{10,11} A Le Fort I maxillotomy has been used to enhance the exposure and resection of large and giant pituitary adenomas at the University of Texas Southwestern Medical Center (UTSWMC) since 1995. On the basis of total or near-total resections of those tumors that do not invade the cavernous sinus with this approach, it was elected to explore its use in the setting of large residual or recurrent tumors. This article describes the integration of

a Le Fort I maxillotomy into a sublabial, trans-septal exposure of the sphenoid sinus, and the use of this exposure for the treatment of nonsecreting pituitary macroadenomas that have been incompletely resected using a conventional trans-sphenoidal approach.

MATERIALS AND METHODS

Between January 1998 and December 2003, 10 consecutive patients were referred to the Department of Neurosurgery at UTSWMC, despite having undergone trans-sphenoidal surgery elsewhere, for the evaluation and treatment of a nonsecreting pituitary macroadenoma that measured 3 cm or greater in at least one diameter. None of the patients had been treated with radiation therapy or radiosurgery. At the time of referral to UTSWMC the maximum diameters of the 10 tumors ranged from 3.0 to 4.3 cm. Despite the large sizes of these residual tumors, only one of them had penetrated the medial wall of the cavernous sinus. These 10 patients had undergone previous surgery by eight different neurosurgeons, all within the state of Texas. Eight patients had undergone a single trans-sphenoidal procedure; two had undergone both trans-sphenoidal and transcranial operations. Endoscopic techniques had not been used in any case. The 10 patients ranged in age from 37 to 69 years and included 3 women and 7 men. Each of the patients was reoperated at UTSWMC using a Le Fort I maxillotomy to enhance the exposure provided by a traditional trans-sphenoidal approach. The time intervals between the most recent prior operation and the Le Fort I maxillotomy ranged from 16 to 69 months, with a median of 24.5 months.

After obtaining permission from the Institutional Review Board, a retrospective review was performed of these patients' medical records to determine outcome from the standpoint of the completeness of tumor resection, visual and endocrine function, and long-term tumor control.

OPERATIVE APPROACH

The operative approach was similar to one devised jointly by the two senior authors for the resection of newly diagnosed pituitary macroadenomas believed to be too large to be completely resected using a conventional trans-sphenoidal approach. The patient was positioned supine with the neck flexed 15 degrees toward the left shoulder and fixed in a Mayfield head-holder. Hyperventilation and diuresis were not used so that the pressure of the intracranial contents helped deliver the superior portion of the tumor into the sella. (Intralumbar injection of air or saline was therefore not necessary.) A topical vasoconstrictor was used to diminish bleeding from the nasal mucosa, and lidocaine with 1:100,000 epinephrine was injected into the maxillary vestibule for the same purpose. An armored oral endotracheal tube was brought out posterior to the last molar and wired to a posterior mandibular tooth to prevent dislodgment. Lateral fluoroscopy was used to confirm the position of the tuberculum sellae, and in those cases in which it was still mineralized, the top of the dorsum sellae.

Using a sublabial incision, the anterior face of the maxilla and the pyriform aperture were subperiosteally exposed. The nasal mucosa was dissected from the pyriform apertures and the floor and lateral wall of the nasal cavity. Small miniplates were adapted just lateral to the pyriform aperture and the zygomaticomaxillary buttress bilaterally and holes were drilled in the maxilla for the later securing of mini-plates across the Le Fort I level to hold the maxilla back into its proper position. A Le Fort I maxillotomy was performed, and the maxilla was mobilized and retracted inferiorly. A wire attached to two bone screws placed in the anterior maxilla was tied to a long strip of gauze anchored to the foot of the bed to maintain the inferior position of the maxilla for the remainder of the surgery. The nasal mucosa was then dissected from both sides of the bony nasal septum (ethmoid and vomer). The cartilaginous nasal septum was disarticulated from the bony septum and displaced to the left side. The submucosal dissection was

carried posteriorly on either side of the bony septum until the anterior face of the sphenoid sinus had been completely exposed. Septal scissors were used to remove the bony septum from the base of the skull for later use during closure. A Hardy-Cushing retractor was inserted into the opening created by the inferiorly positioned maxilla at the pyriform aperture, taking care not to enter the sphenoid sinus, and opened to an internal diameter of ~25 mm (Fig. 1). If necessary, the retractor could be angled to the left or right during tumor resection to further enhance the lateral exposure provided.

The remainder of the anterior wall of the sphenoid sinus was removed piecemeal as far laterally as necessary to provide access to the lateral aspects of the tumor. The inferior pole of the tumor was usually apparent within the sphenoid sinus. The inferior portion of the tumor was removed beginning posteriorly and working laterally and anteriorly, and this sequence was repeated until the superior pole of the tumor, covered by a capsule of dura posteriorly and thickened arachnoid anteriorly, descended into the sella. Tumor remnants could usually be gently suctioned from this capsule without tearing it, so that it was eventually all brought into view within the sella by the pressure of the intracranial contents. If the tumor capsule was intact at the end of the

Figure 1 Schematic diagram of the transverse exposure provided by a Le Fort I maxillotomy with a trans-sphenoidal retractor in place.

resection, a thin layer of autologous fat harvested from the abdominal wall was placed in the sphenoid sinus and its anterior and inferior walls were reconstructed with the bone harvested from the nasal septum. Because patients had had previous surgery via the transnasal route, occasionally there was inadequate bone available from the resected nasal septum and allogeneic bone was used for this purpose. If the capsule was torn, the enlarged sella and the sphenoid sinus were filled with fat and a lumbar subarachnoid drain was placed postoperatively.

After the tumor resection, the cartilaginous septum was repositioned in the midline and the maxilla repositioned and stabilized with the previously adapted titanium mini-plates. Prior to closure of the sublabial incision, a suture through the anterior nasal spine and cartilaginous nasal septum was used to maintain the position of the septum. Intranasal silicone splints were then placed to re-adapt the nasal mucosa in the midline and these were secured with a silk suture placed through the membranous nasal septum. The anesthetic was reversed, and the patient was extubated in the operating room.

ANALYSIS

The duration of surgery was recorded from the medical records. Postoperative MR scans obtained 3 months after surgery were used to determine the completeness of tumor removal. Follow-up information on the patients, including further treatment, was gathered from the medical records.

RESULTS

For the 10 surgical procedures, the mean operative time was 276.5 minutes (range, 205 to 340 minutes) and the average length of stay was 5.3 days (range, 4 to 9 days). One patient was returned to the operating room for the repositioning of a fat graft to treat a cerebrospinal fluid fistula. One patient experienced worsening of anterior pituitary function postoperatively, and another patient developed diabetes insipidus postoperatively. Four patients noted improved anterior pituitary function. Five patients

Table 1 Visual and Endocrine Outcome

Patient	Preoperative Visual Fields	Postoperative Visual Fields	Preoperative Endocrine Replacement	Postoperative Endocrine Replacement
1	Incomplete bitemporal hemianopsia	Improved	Hydrocortisone	None
2	Incomplete bitemporal hemianopsia	Improved	None	None
3	Normal	Unchanged	Thyroid	Thyroid
4	Incomplete bitemporal hemianopsia	Improved	Testosterone	None
5	Incomplete bitemporal hemianopsia	Unchanged	Thyroid, testosterone	Total anterior pituitary replacement
6	Normal	Unchanged	Thyroid, testosterone	Thyroid, testosterone
7	Complete bitemporal hemianopsia	Improved	None	DDAVP
8	Incomplete bitemporal hemianopsia	Unchanged	Total anterior pituitary replacement	Total anterior pituitary replacement
9	Complete bitemporal hemianopsia	Improved	Testosterone	None
10	Complete bitemporal hemianopsia	Unchanged	Hydrocortisone, testosterone	None

DDAVP, Desmopressin acetate.

noted improved vision and no patient experienced further visual loss (Table 1).

A total or near-total (> 95%) resection was achieved in each case as documented by an MR scan obtained 3 months postoperatively. After a mean follow-up of 44.7 months for the series as a whole, three patients have required subsequent treatment of small foci of residual or progressing tumor with stereotactic radiosurgery. No patient has received fractionated radiation therapy (Table 2).

DISCUSSION

The options available for the management of an incompletely resected nonfunctioning pituitary adenoma include observation with serial MR scans, fractionated radiation therapy, stereotactic radiosurgery, and reoperation. The best option in a given case will depend on the age and general health of the patient, and the size and location of the residual tumor.

Both proliferation indices and clinical experience suggest that the growth rate of most pituitary adenomas is slow,^{12,13} and in follow-up periods of

less than 5 years many residual tumor fragments do not enlarge enough to produce clinical symptoms.¹² Recent series report radiographic recurrence or progression rates of 6 to 20% at 5 years for nonfunctioning adenomas treated with trans-sphenoidal surgery alone.¹⁴⁻¹⁶ This experience suggests that older or infirm patients with nonfunctioning adenomas who have small residual tumor fragments distant from the optic chiasm are unlikely to experience recurrent symptoms and may be safely observed. Additional treatment with some form of radiation or reoperation should be considered in younger patients or in those older patients with a significant volume of residual tumor.

Fractionated radiation therapy, which was once routinely administered following pituitary adenoma surgery, rarely produces a measurable decrease in the volume of a residual tumor, and is therefore of limited value in relieving visual loss produced by compression or distortion of the optic chiasm. Although retrospective data suggest that fractionated radiation may prevent or delay the regrowth of a pituitary adenoma following its complete or nearly complete removal,^{14,16} its role in preventing the progression of a large volume of residual tumor is less clear.^{17,18} This form of

Table 2 Extent of Resection and Outcome

Patient	Volume of Residual Tumor at Referral* (cm ³)	Extent of Resection with Le Fort I Maxillotomy†	Duration of Follow-up (mo)	Outcome
1	30	Near Total	24	No progression of residual tumor
2	16	Total	20	No progression of postoperative changes
3	8	Near Total	54	No progression of residual tumor
4	10	Total	49	No progression of postoperative changes
5	9.5	Near Total	66	Progression at 66 months treated with gamma knife radiosurgery
6	12	Total	53	No progression of postoperative changes
7	15	Total	5	No progression of postoperative changes
8	14	Total	42	No progression of postoperative changes
9	12	Near Total	74	Progression at 45 months treated with gamma knife radiosurgery
10	13	Near Total	60	Gamma knife at 3 months for residual tumor

*Volume calculated as $\frac{4}{3}\pi r_1 r_2 r_3$.

†Total: no residual tumor; near total: < 5% of initial tumor volume remained.

radiation is associated with a significant incidence of diminished anterior pituitary function, believed to be due to the late effects of radiation on the hypothalamus, and with anecdotal reports of cognitive dysfunction, visual impairment, and secondary tumor formation.^{19,20} These considerations argue that fractionated radiation therapy may not be the best treatment for a patient with a long life expectancy and a large volume of residual tumor, especially when the residual tumor distorts the optic chiasm.

In the recent past, stereotactic radiosurgery has been employed as an adjunct to surgery for the treatment of pituitary adenomas in an effort to deliver an ablative dose of radiation to the residual tumor, while avoiding the late effects of fractionated radiation on surrounding structures. Pollock and Carpenter reported that 16 of 33 nonfunctional pituitary adenomas treated with the gamma knife decreased in size at a median follow-up of 43 months.² Losa et al reported that 23 of 54 nonfunctioning adenomas treated with the gamma knife decreased in size by 20% or more.¹ These two authors reported similar tumor control rates, 97% and 88% respectively, at 5 years. Unfortunately, the low radiation tolerance of the optic nerves and chiasm limits the radiosurgical dose that can be safely delivered to large pituitary adenomas, especially those that contact the optic apparatus.

There are few reported series of reoperation for nonfunctioning pituitary adenomas, and in these it is often unclear whether the reoperated tumor was a residual remnant after a recent unsuccessful attempt at a total removal, or a true recurrence. Benveniste and colleagues, utilizing the operating microscope and either a sublabial or an endonasal approach, reported 96 consecutive patients who underwent repeat trans-sphenoidal surgery for recurrent or residual pituitary adenomas. Of the 42 patients who were reoperated for mass effect, a gross total resection was achieved in only 10. Of the remainder, 3 patients required further surgery in the immediate postoperative period for large residual tumor fragments and an additional 6 relapsed at a mean of 31 months postoperatively.¹² Cappabianca

and associates reported their experience using endoscopic endonasal trans-sphenoidal surgery to treat residual or recurrent pituitary adenomas. In the 6 patients with nonfunctioning macroadenomas, they were able to achieve a total removal in 2, a subtotal (> 80%) resection in 1, and a partial resection in 3.²¹ Using an endoscopic technique, Rudnik and colleagues achieved a complete removal in 6 of 9 patients with residual or recurrent nonfunctioning adenomas not involving the cavernous sinus.²² In none of these series were the reasons for the incomplete resections examined.

When evaluating a patient who has undergone the subtotal resection of a pituitary tumor elsewhere, it is tempting to believe that a more experienced or aggressive surgeon might have utilized the same surgical approach and succeeded where the initial surgeon had failed. Although the experience, ability, and intent of the initial surgeon should be considered in this setting, other explanations for the initial failure to completely remove the tumor should be sought. For example, those tumors with an eccentric suprasellar extension or true cavernous sinus invasion may be difficult to expose via the trans-sphenoidal route, and their complete resection may require both transcranial and trans-sphenoidal exposures. Even large and giant tumors do not always invade the cavernous sinus, however, and in a review of 118 nonfunctioning pituitary adenomas measuring over 4 cm in one dimension at initial presentation, Goel et al noted that only half of the tumors invaded the medial wall of the cavernous sinus.²³ For some large tumors, it may be the case that the consistency of the tumor and its absolute size relative to the available exposure hinder its complete removal. The diameter of the pyriform aperture varies among individuals (Fig. 2),²⁴ and in some patients the transverse exposure provided by a traditional trans-sphenoidal approach may be restricted by a narrow pyriform aperture. In this setting, if the tumor is unusually large, or is fibrous in consistency, a limited exposure might impair the extent of the tumor resection.

Several surgical strategies have been proposed to improve the exposure of large or invasive pituitary

Figure 2 Anatomic variation in the diameter of the pyriform aperture as reported by Lang.²⁴ (Adapted with permission from Lang J. *Anatomy of the midline*. Acta Neurochir Suppl (Wien) 1985;35:6-22.)

tumors, including a combination of transcranial and trans-sphenoidal approaches, the use of endoscopic techniques, and various modifications of the trans-sphenoidal approach, including the addition of a Le Fort I maxillotomy. The best strategy in a given case will depend on the size and growth pattern of the tumor and on the experience and ability of the surgeon.

The addition of a craniotomy to a trans-sphenoidal approach improves access to the superior aspect of those tumors with an eccentric suprasellar component or extensive invasion and expansion of the cavernous sinus, but does not significantly enhance the exposure of that portion of a tumor lying within a markedly expanded sella or within the central aspect of the suprasellar cistern. For most pituitary tumors that require both transcranial and trans-sphenoidal approaches, it is preferable to stage the procedures, performing the trans-sphenoidal resection first and allowing the opening in the sphenoid sinus and sella to seal before performing a craniotomy,⁵ but simultaneous transcranial and trans-sphenoidal procedures have been reported.^{3,4,6}

Endoscopic techniques now allow neurosurgeons to manage a variety of intracranial and intraspinal disorders with smaller incisions and exposures and shorter operative times than are required for traditional, more invasive approaches. While endo-

scopic techniques allow for the visualization of the margins of large tumors, the access provided is often indirect, and considerable skill and experience are required to completely remove the tumor, achieve hemostasis, and repair the skull base. At the present time, few surgeons have acquired this experience, and in inexperienced hands, especially in the setting of previous trans-sphenoidal surgery, the use of a purely endoscopic approach may limit both the extent of the tumor resection and the repair of the resulting defect in the sellar floor or sphenoid sinus.

The Le Fort I maxillotomy, a procedure commonly used by oral and maxillofacial surgeons to correct bite abnormalities, was first reported for the resection of a pituitary adenoma by Uttley and associates in 1989.¹¹ The procedure itself carries little morbidity, and is commonly performed on an outpatient basis for dental indications.^{25,26} It is readily performed using a sublabial incision, and when combined with a trans-septal exposure of the anterior aspect of the sphenoid sinus, routinely provides a transverse exposure of 20 to 25 mm (E.E. and B.M., unpublished data). This wide transverse exposure, and the ability to vary the angle of approach in the vertical and horizontal planes permitted by the mobile inferior maxillary segment, provide direct access to the anterior, posterior, and lateral margins of large tumors, facilitating both

their resection and the repair of the resulting defect in the skull base (Fig. 3).

Reoperation was recommended for the 10 patients reported here on the basis of the large size of the residual tumor fragment and its prox-

imity to the optic chiasm. Eight of the 10 patients had a residual visual field defect. Although there was residual tumor within the cavernous sinus in 1 case, in every case the majority of the tumor was located both within an enlarged sella and within the

Figure 3 (A) Patient 9, a 46-year-old man, presented with failing vision and was found to have a bitemporal hemianopsia. MR scan prior to initial trans-sphenoidal resection is shown. (B) Patient 9. MR scan was obtained 10 months after a sublabial, trans-sphenoidal approach for what was believed by the initial surgeon to be the complete removal of the tumor. At reoperation using a Le Fort I maxillotomy, this tumor was noted to be fibrous in consistency. (C) Patient 9. MR scan was obtained 10 months after reoperation. Serial MR scans later revealed the progression of a small focus of residual tumor in the patient's right cavernous sinus, which was treated with gamma knife radiosurgery 45 months after the second surgical procedure.

suprasellar cistern. It was assumed that an attempt to resect the residual tumor by a traditional trans-sphenoidal approach would be likely to be impaired by the same obstacles encountered by the initial surgeon, and made even more difficult by post-operative fibrosis within the residual tumor and by reactive changes involving the nasal mucosa and the turbinates. The enhanced exposure provided by the Le Fort I maxillotomy made the resection of the residual tumor technically straightforward in every case, and in no case was there morbidity attributed to the approach itself. In retrospect, some of these tumors were favorable in consistency, and could probably have been removed with a conventional trans-sphenoidal exposure, but it would have been difficult to identify these cases prospectively. The widespread availability of oral and maxillofacial surgeons capable of performing a Le Fort I maxillotomy, the minimal morbidity of the procedure, and the wide exposure of the sphenoid sinus facilitate the resection of pituitary macroadenomas that have been incompletely resected using a traditional transnasal, trans-sphenoidal approach.

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