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SUBOPTIMAL SPHENOID AND SELLAR EXPOSURE: A CONSISTENT FINDING IN PATIENTS TREATED WITH REPEAT TRANSSPHENOIDAL SURGERY FOR RESIDUAL ENDOCRINE-INACTIVE MACROADENOMAS

OBJECTIVE: In a series of patients with residual endocrine-inactive macroadenomas who underwent repeat surgery, we assess possible reasons for prior subtotal removal, reoperative success, complication rates, and patient impressions.

METHODS: All patients were identified who had a prior subtotal removal of an endocrine-inactive macroadenoma and were reoperated on for residual sellar tumor via an endonasal approach.

RESULTS: Over 6 years, of 188 consecutive patients with endocrine-inactive adenomas, 30 (16%) had repeat surgery (age, 15–77 yr; median interval between surgeries, 25 mo; median follow-up, 20 mo). Maximal tumor diameter averaged 2.4 ± 0.9 cm. At reoperation, a suboptimal bony exposure was seen in all 30 patients: at the sphenoid keel, the sella, or both in 97, 93, and 90% of patients, respectively. Cavernous sinus invasion was seen in 16 (53%) patients and a fibrous/rubbery consistency in 12 (40%). Gross total tumor removal was achieved in 17 (57%) patients, including 12 of 14 (86%) with noninvasive tumors and 5 of 16 (31%) with invasive tumors, ($P < 0.01$). All six fibrous/rubbery but noninvasive tumors were totally removed. Of 16 patients with preoperative visual loss, 15 (94%) improved. Complications included one each of cerebrospinal fluid leak, delayed sinusitis, and new hypothyroidism. In 17 patients with prior sublabial surgery who completed questionnaires, the second (endonasal) surgery was associated with an easier recovery, less pain, and better nasal airflow in 82, 88, and 93%, respectively ($P < 0.0001$).

CONCLUSION: In patients with residual sellar endocrine-inactive adenomas, a suboptimal opening at the sphenoid keel or sella at the first surgery and a high proportion of fibrous/rubbery tumors likely contributed to prior subtotal removal of otherwise accessible tumor. With a wider exposure, most noninvasive tumors can be totally removed, whereas invasive tumors can be effectively debulked. An endonasal reoperation is well tolerated with a low complication rate.

KEY WORDS: Direct endonasal approach, Endocrine-inactive pituitary macroadenoma, Reoperation, Residual tumor, Surgical exposure

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Endocrine-inactive pituitary adenomas are the most common surgically treated pituitary tumor. Because they are not associated with hormonal hypersecretion, with the occasional exception of hyperprolactinemia secondary to "stalk effect," these tumors are typically diagnosed as macroadenomas causing visual loss, hypopituitarism, or headaches (10, 21). Given that no effective pharmacotherapy exists for these tumors, transsphenoidal removal is considered the optimal treatment. However, complete removal was reported in only 35 to 70% of patients in recent series (25, 26), although a higher total removal rate is seen in patients without cavernous sinus invasion (25, 26, 33). Tumor recurrence after gross total and subtotal resection has been reported in 6 and 38% of patients, respectively, if postoperative radiotherapy is not performed (10, 23, 31).

Several earlier papers have reported on the efficacy of repeat transsphenoidal surgery, with both microscopic and endoscopic techniques, for both endocrine-active and endocrine-inactive tumors (2, 3, 20, 21, 24, 28, 29). However, these reports typically included recurrent as well as residual tumors, and none provided a systematic assessment of why a prior subtotal removal was achieved. Given that subtotal removal of endocrine-inactive adenomas is relatively common, often necessitating repeat surgery or radiotherapy, we sought to determine possible reasons for prior incomplete removal in our own series of reoperated patients while also defining the efficacy and complications. Because the first operation in almost 80% of the patients in this series was through a sublabial approach, which theoretically provides a wider anatomic exposure than the direct or transseptal endonasal approaches (9), we also attempted to determine whether suboptimal use of this greater sublabial exposure was a factor in achieving a subtotal removal. All patients in this series were reoperated upon using a direct endonasal microscopic approach, as described by Griffith and Veerapan (13) and others, including our own group (2, 7, 33).

METHODS

Patient Population

This study was approved by the investigational review boards of the University of California, Los Angeles and Harbor-University of California Los Angeles Medical Centers. The pituitary tumor database of the University of California at Los Angeles and the Harbor-University of California Los Angeles Medical Centers was retrospectively reviewed. Between 1998 and 2004, 188 consecutive patients with clinically endocrine-inactive pituitary macroadenomas were operated upon, of whom 32 (17%) had transsphenoidal microscopic surgery for residual adenoma. Two patients were excluded, one because of inadequate follow-up and another because repeat surgery was performed only for residual tumor within the medial cavernous sinus, leaving 30 patients for evaluation, all of whom were reoperated upon for significant residual sellar tumor (>1 cm diameter) with or without suprasellar or cavernous sinus invasion. Patients who had surgeries performed for tumor recurrence after a previous gross total removal, those with two-stage operations, or reoperations for complications such as hematoma or cerebrospinal fluid (CSF) leak repair were excluded. The patients' medical records were reviewed to identify the route of prior surgery, pre- and postoperative magnetic resonance imaging (MRI) to determine tumor size and presence or absence of cavernous sinus invasion, pituitary hormonal axis gains and losses, visual status, tumor pathology, complications, and treatment with radiotherapy.

Surgical Technique

All patients were operated via a direct endonasal transsphenoidal approach with the operating microscope, as previously described (33). Fluoroscopy for trajectory guidance was used in all cases. Because anatomic landmarks were often less distinct in such reoperative cases, the first step of the procedure was to identify the residual midline sphenoid keel either inferiorly or superiorly. In the majority of cases, a relatively small opening through the keel was identified, prompting additional bone removal with pituitary and Kerrison rongeurs. Within the sphenoid sinus, mucosa and scar tissue over the sella was removed and the bony defect from the prior surgery delineated. In a minority of cases, in which autologous bone or cartilage seemed to have been placed over the sellar opening, this was separated away from the surrounding bone with dissectors. In the majority of cases, additional sellar bone was then removed with a Kerrison rongeur beyond the prior bony opening to the edges of the cavernous sinus bilaterally and to the cephalad extent of the sella. The extent of the prior opening was readily identified by encountering "virgin" dura without evidence of hemosiderin staining or scar tissue. The dural opening and tumor removal then proceeded in standard fashion using ring curettes and suction. In instances of fibrous or rubbery tumors, sharp dissection with microscissors was often required. Debulking of cavernous sinus tumor was typically performed through existing defects in the medial cavernous sinus wall. No attempt was made to remove tumor lateral to the cavernous carotid arteries. Intraoperative CSF leaks were repaired with either collagen sponge and titanium mesh or with the addition of an abdominal fat graft for larger diaphragmatic defects; tissue glue (Tisseal [Baxter Healthcare Corp., Deerfield, IL] or Bioglue [Cryolife, Inc., Kennesaw, GA]) was used in a minority of cases (11, 17). Nasal packing was not used in the last 20 of 30 cases. All surgeries were performed by the senior author (DFK).

Adequacy of Prior Exposure, Additional Bone Removal, and Tumor Characteristics

Operative notes were reviewed to determine the adequacy of the prior bony openings through the sphenoid keel and sella and whether additional bone was removed at either or both of these sites. In all cases in which an inadequate sphenoid or sellar opening was noted, the amount of additional bone removal was quantified as large, small, or indeterminate. Large additional openings were those in which it was noted that a "large" amount of additional bone was removed in two or more directions (e.g., laterally and superiorly) and in which the prior opening was specifically characterized as "small." Large openings included cases in which the midline keel was found to be intact and the prior sphenoidotomy was only performed unilaterally through one side of the keel. Small additional openings were those in which the bone removal was only in one direction (e.g., laterally or superiorly only), and the term "small" was not used to characterize the prior opening. The amount of bone removal performed at reoperation was considered indeterminate when the extent of bony removal was not well quantified in the operative dictation. Note was also made of whether cavernous sinus invasion was

seen intraoperatively and whether the tumor texture was predominantly fibrous or rubbery.

Follow-up

Gadolinium-enhanced sellar MRI scans were typically obtained within 48 hours of surgery and then at 3 months and 6 to 12 months after surgery. After the first postoperative year, MRI scans were obtained at least annually, depending upon the clinical scenario. On the basis of 3 months or later postoperative MRI, tumor removal was defined as gross total, near gross total (> 90% removal), or subtotal (< 90% removal). The degree of sellar and suprasellar tumor removal was also quantified in this manner for patients with cavernous sinus invasion. Patients with growth of residual tumor were offered stereotactic radiotherapy or radiosurgery with the linear accelerator (Novalis shaped beam) according to tumor volume and distance from the optic apparatus (30).

Questionnaires

As a postoperative routine, letters were mailed or given to patients during follow-up visits requesting consent for study participation (33). Consenting patients were given a questionnaire to be completed at home or, in some cases, over the phone by office staff. Patients were asked to rate their postoperative rhinological discomfort at 2 weeks and 3 months or more after surgery. An additional section was completed by patients who had a previous sublabial surgery to compare recovery after endonasal versus sublabial surgery. Because some of this data have been previously reported (33), only 3-month data and data relating to patients who had a previous sublabial approach are included here.

RESULTS

Patient Cohort

Thirty patients (9 men, 21 women; mean age, 50 yr; range, 15–77 yr) had repeat transsphenoidal surgery (*Table 1*). The median interval from prior surgery to reoperation was 25 months, (range, 1–169 mo), and median follow-up was 20 months (range, 3–68 mo). The prior surgery was by the sublabial route in 23 (77%), the endonasal route in six (20%), and by lateral rhinotomy in one. Twenty-seven (90%) patients had prior surgery at an outside hospital, and three (10%) had their original surgery 6 to 9 years ago by the senior author (DFK, two by the sublabial route and one by the endonasal route). Seven patients had more than one prior surgery, including two with craniotomies. Two patients had prior radiotherapy.

Clinical Presentation before Reoperation

Patients exhibited new or persistent visual deficits, pituitary failure, or headache in 53, 57, and 50%, respectively (*Table 1*). Serial MRI scans documented residual tumor without interval growth in 17 (57%) patients (median interval from prior surgery to reoperation, 13 mo) and residual tumor with interval growth in 13 (43%) patients, (median interval from prior surgery to reoperation, 33 mo). Maximal tumor diameter before reoperation averaged 2.4 ± 0.9 cm and ranged from 1.1 to 4.4 cm.

TABLE 1. Patient characteristics

No. of patients	30
Follow-up	
Median (mo)	20
Range (mo)	3–68
Age	
Mean (yr)	50
Range (yr)	15–77
Sex, male	9
Sex, female	21
Prior surgical approach (%)	
Sublabial	23 (77)
Endonasal	6 (20)
Lateral rhinotomy	1 (3)
Previous radiation (%)	2 (7)
Interval between prior and re-do surgery	
Median (mo)	25
Range (mo)	1–169
Presentation before second surgery (%)	
Symptoms	
New or persistent visual loss	16 (53)
Pituitary failure	17 (57)
Headaches	15 (50)
3rd nerve palsy	1 (3)
Imaging	
Residual sellar tumor growing	13 (43)
Large sellar residual tumor	17 (57)
Maximum tumor diameter	
Mean (cm)	2.4
Range	1.1–4.4

Factors Contributing to Previous Incomplete Tumor Removal

Tumors exhibited cavernous sinus invasion in 16 (53%) patients, were predominantly fibrous or rubbery in 12 (40%) patients, and in six (20%) patients, tumors had both cavernous sinus invasion and a fibrous/rubbery consistency. At reoperation, all 30 patients were found to have an inadequate bony opening at either the sphenoid keel, sella, or both. Specifically, inadequate exposure was encountered at the sphenoid keel, the sella, or both the sphenoid and sella in 97, 93 , and 90% of patients, respectively (*Table 2*). The amount of additional bone

removed at reoperation at the sphenoid and sella was quantified as large in 45 and 79%, small in 21 and 7%, and indeterminate in 34 and 14%, respectively. In four (13%) patients, the prior opening through the sphenoid keel was only unilateral with the midline keel still intact, as shown in *Figures 1* and *3*. Similarly, the prior sellar opening was typically small, often only using only the lower portion of the sellar floor, necessitating a large amount of additional bone removal, as shown in *Figures 2* and *3*.

Tumor Removal Rates

As shown in *Table 3*, a gross total tumor removal was possible in 17 (57%) patients including 12 of 14 (86%) with noninvasive tumors and 5 of 16 (31%) with tumors invading the cavernous sinus ($P < 0.01$). All six fibrous but noninvasive tumors were totally removed. Of 11 patients with subtotal removal who also had cavernous sinus invasion, the sellar and suprasellar tumor component was removed in gross total fashion in three and in near gross total (>90% removal) in eight. In the remaining two patients with noninvasive tumors (1 with prior radiotherapy), both had subtotal tumor removal of the sellar component. Thus, the extent of sellar and suprasellar tumor removal in all 30 patients was gross total, near gross total, or subtotal in 66.7, 26.7, and 6.7%, respectively.

Visual and Hormonal Recovery

Of 16 patients with preoperative visual field or acuity deficits, 15 (94%) had visual improvement, and one patient had no change (*Table 4*). Gain of a hormonal axis occurred in three (10%) patients, including two with gonadal recovery and one with adrenal axis recovery. One (3%) patient developed postoperative hypothyroidism. One (3%) patient developed long-term diabetes insipidus requiring desmopressin acetate for 4 years, which then resolved. Transient delayed hyponatremia within the first week after surgery occurred in one patient.

TABLE 2. Intraoperative findings in 30 patients

Inadequate bony exposure[a](%)		
Sphenoid keel	29	(97)
Sella	28	(93)
Both sphenoid keel and sella	27	(90)
Either sphenoid keel or sella	30	(100)
Extent of additional bone removal (%)		
Sphenoid keel (n = 29)	**Sella (n = 28)**	
Large: 13 (45)	Large: 22 (79)	
Small: 6 (21)	Small: 2 (7)	
Indeterminate: 10 (34)	Indeterminate: 4 (14)	
Tumor characteristics (%)		
Cavernous sinus invasion	16	(53)
Fibrous or rubbery tumor consistency	12	(40)

[a] There was no difference in the rate of small sphenoid and sellar openings between the sublabial and endonasal approaches.

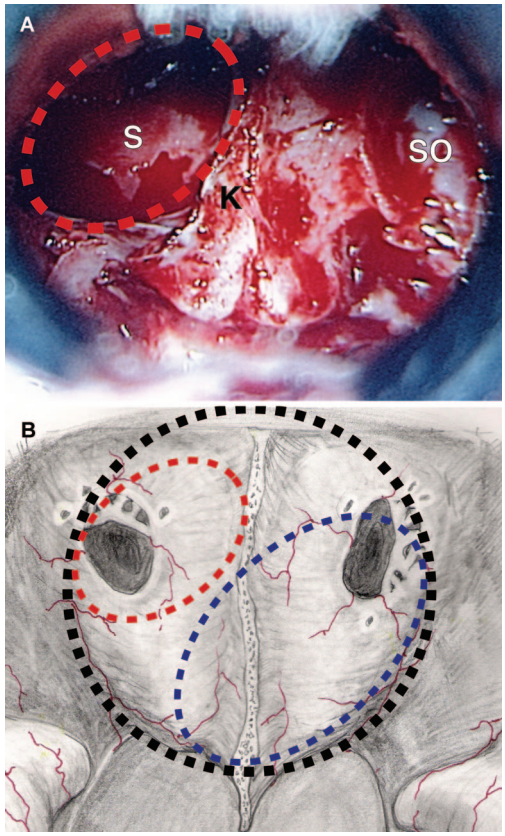

FIGURE 1. A, *intraoperative photograph of sphenoid keel in a patient with prior endonasal surgery showing that at original surgery, only bone to the right of the keel had been removed, whereas the midline keel and the left half of sphenoid bone and sphenoid ostium were left intact.* B, *variations on restricted sphenoid keel openings seen at reoperation* (shaded circles and ovals). *Extent of bone removal in the patient in* A (red oval); *example of other openings seen previously* (blue oval). *Optimal bony removal of the sphenoid keel to provide maximal exposure into the sphenoid sinus* (black circle). S, *prior opening into sphenoid sinus;* K, *sphenoid keel;* SO, *sphenoid ostium.*

Surgical Complications

One (3%) patient with a CSF leak required repeat surgery for repair without sequelae (*Table 4*). One (3%) patient with previous radiation developed sphenoid sinusitis refractory to antibiotics 1 year after reoperation; endoscopic exploration and cultures revealed chronic fungal sinusitis, which resolved with antifungal therapy. There were no vascular injuries, visual worsening, new cranial neuropathies, or mortalities.

Tumor Progression and Radiotherapy

Six of 30 (20%) patients, all with invasive tumors, have had radiotherapy. Two were treated before reoperation. Four were treated after reoperation at 2 to 14 months after surgery with linear accelerator stereotactic radiotherapy because of interval

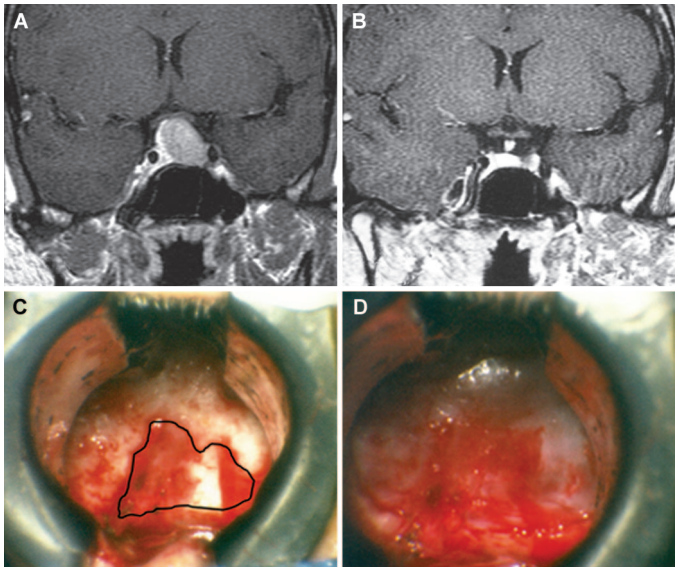

FIGURE 2. A, *preoperative coronal gadolinium-enhanced MRI before reoperation showing noninvasive macroadenoma with compressed normal gland on* right. B, *postoperative MRI 50 months after surgery showing complete tumor removal.* C, *intraoperative photograph of reoperation showing view into sphenoid sinus. Prior bony sellar exposure (*outlined in black*) is small and inferiorly placed.* D, *intraoperative photograph of reoperation after more extensive sellar exposure reaching edge of both cavernous sinuses and tuberculum sellae.*

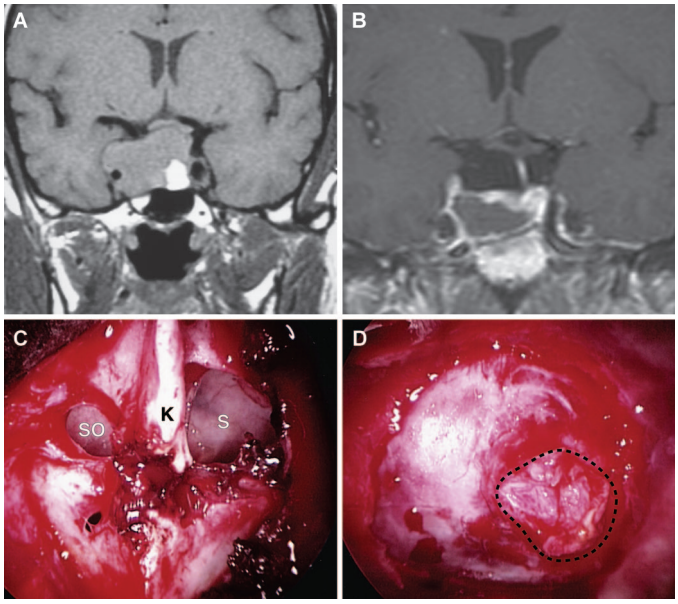

FIGURE 3. *MRI scans and intraoperative images of a patient with a macroadenoma who had a previous sublabial surgery at an outside hospital showing how limited openings of both the sphenoid keel and sella can severely hinder tumor access.* A, *original postoperative T1-weighted noncontrast coronal MRI scan showing left-sided area of tumor debulking and intrasellar fat graft.* B, *gadolinium-enhanced coronal MRI scan after reoperation showing complete intrasellar tumor removal with small residual tumor in right cavernous sinus.* C, *endoscopic photograph at reoperation showing that the prior sphenoidotomy was restricted to the left of the sphenoid keel.* S, *previous sphenoidotomy;* K, *sphenoid keel;* SO, *sphenoid ostium.* D, *endoscopic photograph at reoperation after sphenoidotomy widened, showing a small original left-sided sellar opening and residual fat graft (*dashed circle*) surrounded by newly exposed virgin dura after additional sellar bone removal.*

tumor growth seen before reoperation in three or after reoperation in one. One other patient with imaging evidence of tumor progression during follow-up is awaiting radiotherapy. Thus, overall, 23 of 30 (77%) patients have had no evidence of tumor recurrence or progression with repeat surgery alone, whereas 6 (20%) have had no further tumor progression with radiotherapy, and one additional patient awaits radiotherapy.

Questionnaire Results

Questionnaires were completed by 26 (87%) patients; four were unable to be recontacted. At 3 months or more after surgery, patients quantified their complaints as follows: new headache, none 58%, mild 34%, moderate 8%; facial pain, none 81%, mild 11%, moderate 4%, severe 4%; nasal congestion, none 58%, mild 31%, moderate 11%; decreased nasal airflow, none 80%, mild 16%, moderate 4%; decreased sense of smell, none 72%, mild 28%; upper lip numbness, none 83%, mild 17%. In 17 of 23 (74%) patients with prior sublabial surgery who completed questionnaires, the endonasal approach was less painful (88%), afforded an easier recovery (82%), and resulted in better nasal airflow (93%), ($P < 0.001$).

DISCUSSION

Summary of Findings

In 30 patients who underwent reoperative transsphenoidal surgery for a residual endocrine-inactive macroadenoma, in which the primary goal was to remove accessible sellar and suprasellar tumor, all patients were found to have an inadequate prior bony exposure, including 90% who had suboptimal bony openings of the sphenoid sinus and sella. A gross total resection was achieved in 57% of patients, including 86%

TABLE 3. Gross total tumor removal rates

Overall (%)	17/30 (57)
Cavernous sinus invasion[a] (%)	5/16 (31)
Invasive and fibrous	1/6 (17)
Invasive and nonfibrous	4/10 (40)
No cavernous sinus invasion[a] (%)	12/14 (86)
Noninvasive and fibrous	6/6 (100)
Noninvasive and nonfibrous	6/8 (75)

[a] $P < 0.01$ for comparing tumors with cavernous sinus invasion versus no cavernous sinus invasion.

TABLE 4. Visual and hormonal outcomes and complications[a]

Visual improvement	15/16 (93.7%)
Hormonal changes	
Gain of axis	3/30 (10%)
Gonadal	2
Adrenal	1
Loss of axis	1/30 (3.3%)
Thyroid	1
Long-term DI (resolved after 4 years)	1/30 (3.3%)
Delayed hyponatremia	1/30 (3.3%)
Complications	
CSF leak	1 (3.3%)
Visual loss, ICA injury, hematoma, meningitis	0
Sinonasal morbidity: sinusitis	1 (3.3%)
Medical morbidity (pulmonary, cardiac, etc.)	0

[a] DI, diabetes insipidus; CSF, cerebrospinal fluid; ICA, internal carotid artery.

with noninvasive tumors, 31% with cavernous sinus invasion, and in all six patients with fibrous but noninvasive tumors. Repeat surgery achieved a gross total or near gross total removal of residual sellar and suprasellar tumor in 93% of patients. Visual function improved in 94% of effected patients. Surgical complications, new endocrinopathy, and persistent rhinological complaints were uncommon. Although the follow-up period is rather short, 77% of patients achieved tumor control without radiotherapy.

Potential Reasons for Incomplete Removal at Initial Surgery

Prior radiotherapy, a fibrous or rubbery tumor consistency, and inadequate surgical exposure are potential reasons for a subtotal removal of the sellar and suprasellar components of a pituitary adenoma (4, 12, 27). Given that only two patients in the series had prior radiotherapy, this factor was not a major influence in this cohort. In contrast, both tumor consistency and inadequate surgical exposure seem to have been key factors contributing to prior unsuccessful removal. Previous reports indicate that 5 to 13% of pituitary adenomas have a predominantly fibrous or rubbery consistency, whereas in this series, that proportion was increased to 40% (14, 15, 27). Although we assume the fibrous tumors encountered were similarly textured at initial surgery, it is possible that surgery or radiation may have incited fibrous changes in these tumors. Because such tumors are more resistant to removal using standard techniques with ring curettes, their suprasellar components are less likely to descend into the sella as they are debulked and more prone to incomplete removal.

Inadequate Exposure

The other notable finding in this patient cohort was that the prior operation was performed through a relatively restricted sphenoid or sellar bony opening in all patients, prompting additional bone removal at either or both of these key surgical landmarks. Although our attempt to define the extent of additional bony removal was admittedly not rigorously quantitative, the consistency of this finding in 100% of the cohort, and the fact that a large amount of additional bone was removed in 45% of patients at the sphenoid and in almost 80% of patients at the sella, suggests this was an important technical issue. Although the concept of inadequate surgical exposure and its attendant problems is well appreciated in neurosurgery, there are no prevoius reports in the transsphenoidal literature that have documented the extent of prior bony exposure at the sphenoid and sella in patients undergoing reoperation. In fact, this problem seems to be only a point of discussion in previous reports but never quantified (20, 29). For example, in an earlier study, Laws et al. (20) noted unsuccessful surgery could be caused, in part, by inadequate exposure and relative inexperience with the procedure. This experience factor is substantiated by the fact that three patients in this series were operated upon by the senior author 6 to 9 years ago, relatively early in his transsphenoidal experience, and in each case, additional bone removal was performed at reoperation. Although we were unable to quantify the transsphenoidal experience of the original neurosurgeons for the other 27 patients in the cohort, it is likely their experience level was, on average, relatively modest because these patients did not have their initial operation at well-recognized pituitary tumor centers. Other reports of transsphenoidal and transcranial surgery for various pathologies support the idea that a favorable, complication-free outcome is more likely with increasing surgeon experience (6, 8, 22).

Although anatomic and clinical studies have shown the sublabial approach affords a larger exposure to the sphenoid sinus and sella than the direct or transseptal endonasal approaches (1, 9), the findings here suggest that in the majority of cases, the full anatomic potential of both the sublabial and endonasal routes were not fully used by the surgeon. Using cadaveric dissections, Das et al. (9) compared the sublabial, endonasal, and transethmoidal approaches and found the amount of side to side exposure at the sella was similar for all approaches. However, anterior and superior exposure was greatest with the sublabial approach. Badie et al. (1) compared patients who underwent an endoscopic-assisted endonasal approach with the microscope and transseptal approach through either a sublabial or transcolumellar route and concluded the narrower endonasal opening could limit lateral sellar visualization in patients with extensive suprasellar ex-

tension and cavernous sinus invasion. In contrast, Kawamata et al. (16) found similar surgical results with both the endonasal and sublabial routes in 215 patients.

These previous reports and the present study indicate that, regardless of the transsphenoidal approach used, sufficient sphenoid and sellar exposure is critical for achieving adequate sellar and suprasellar access to maximize tumor removal. With a smaller exposure, less illumination from the operating microscope reaches the sella, and the reach of ring curettes and other dissectors is diminished. A limited opening can also preclude clear visualization of the downward herniation of the diaphragma sella as tumor is removed, and, instead, one can mistake a rind of residual suprasellar tumor for the diaphragma sella. Alternatively, one may visualize only a small portion of the diaphragma sella, but presume it has herniated into the sella in its entirety. One is particularly likely to make this error if the tumor is predominantly fibrous or rubbery, as was the case in 40% of patients. The impact of a limited exposure is compounded when both the sphenoid and sellar bony openings are suboptimal, a situation seen in 90% of patients in this series. With two small openings, the tunnel vision of the microscope is even more constricted, and the chance of missing otherwise accessible tumor is further exacerbated.

Maximizing Sphenoid Keel and Sellar Exposure

Several maneuvers are recommended to avoid suboptimal exposure that may limit sellar and suprasellar tumor access. First, intraoperative imaging with fluoroscopy or computerized surgical navigation is recommended for all cases performed with the operating microscope. Second, if performing an endonasal approach, given that the trajectory is typically 10 to 15% degrees across the midline, approaching from the nostril ipsilateral to where the normal gland resides and contralateral to the greatest direction of tumor growth is helpful if not essential. To avoid missing accessible tumor ipsilateral to the nostril of approach, sufficient sphenoid and sellar bone must be removed on this side as well. Third, when exposing the sphenoid keel, the mucosal elevation should reveal the inferior, middle, and superior vertical extensions, including both sphenoid ostia typically seen at the 10 and 2 o'clock locations within the speculum circumference. Sphenoid bone and mucosal removal should extend beyond the lateral edges of the ostia and allow cephalad visualization of the tuberculum sella. Fourth, the sellar opening should extend to the edges of the cavernous sinuses bilaterally and to the tuberculum sella above. The microDoppler probe is useful to localize the cavernous carotid arteries; if the vessels are not audible with the Doppler, more bone should be taken laterally. Finally, an angled endoscope (30 or 45 degrees) is very useful for cephalad and lateral visualization beyond the tunnel vision of the microscope to help identify residual suprasellar or laterally placed tumor (3).

Complications and Rhinological Recovery

Although earlier studies have shown repeat transsphenoidal surgery is associated with a higher complication rate (20, 24), recent reports with the microscope and endoscope have found no difference in CSF leak rate, neurological deficits, or new endocrinopathy (2, 3, 19, 28). The present series confirms reoperative transsphenoidal surgery can be accomplished with a low complication rate, a high rate of visual improvement, and can preclude the need for radiotherapy in many patients. In regard to rhinological recovery, the questionnaire results indicate an endonasal reoperation is well tolerated and typically affords an easier and less painful recovery than the sublabial route. Other studies have also shown the superiority of the endonasal microscopic or endoscopic approaches over the sublabial route in terms of nasal complaints and complications (1, 5, 16, 18, 32). In considering the mucosal scarring along the nasal septum in reoperative transsphenoidal surgery, the direct endonasal approach, which bypasses the great majority of the nasoseptal scar, is ideal for such cases and obviates the need for nasal packing, a major source of acute postoperative discomfort (33).

CONCLUSION

In patients undergoing repeat transsphenoidal surgery for a residual sellar and suprasellar endocrine-inactive macroadenoma, incomplete removal at the prior surgery was likely caused in part by an inadequate sphenoid and sellar exposure. In a large subset of patients, a fibrous or rubbery tumor consistency also likely contributed to incomplete prior removal. An endonasal reoperation provides adequate exposure to remove residual sellar and suprasellar tumor, allows debulking of cavernous sinus tumor medial to the carotid arteries, and can be performed with a low rate of surgical complications, new endocrinopathy, or rhinological complaints.

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COMMENTS

The authors describe a series of patients with residual clinically nonfunctional pituitary adenomas who underwent reoperation. They provide evidence that suboptimal exposure at the sphenoid keel or sella at the first surgery and a high proportion of fibrous/rubbery tumors likely contributed to prior subtotal removal of an otherwise accessible tumor. With a wider exposure, they demonstrate that most noninvasive tumors can be totally removed, whereas invasive tumors can be effectively debulked.

The quality of the data is essentially limited because they were acquired retrospectively. That being said, the authors make an important technical point that suboptimal bony exposure limits the execution of tumor resection. I suspect this is well known to many, but it does not hurt to drive the point home with an analysis from a respected center with an experienced pituitary surgeon.

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Neurosurgical procedures are generally associated with improved outcomes with a surgeon's greater experience, without exception. Although this statement may seem intuitive, the exact nature through which inexperience negatively impacts the surgical endeavor remains important to define. The definition of these "pearls" is especially important to surgeons in training, but also to experienced surgeons, to achieve consistent results. For example, improved outcomes in aneurysm surgery can result from optimum exposure through cranial base craniotomies, minimization of brain retraction, sequential opening of the cisterns, neurophysiological monitoring, liberal use of temporary clips, sharp microsurgical dissection, careful preservation of perforators, preferential dissection of aneurysm neck rather than the dome, and intraoperative angiography. A list of "must dos" can be generated for each neurosurgical operation. In this article, the authors have provided an analysis of their personal series of reoperated nonfunctional pituitary adenomas to identify similar "pearls" for transsphenoidal pituitary surgery, with focus on the reason why suboptimal results were achieved at the time of first surgery. They have identified suboptimal bony exposure as being an important contributing factor to residual tumor and have attempted to quantify this to some degree. In addition, the authors conclude that surgical inexperience may have led to the suboptimal exposure. I applaud the senior author (DFK) using himself to illustrate the point. I suspect that over the past few years, clinical "pearls" related to dissection and resection of the tumor after optimal bony exposure have also been added to his surgical armamentarium. Nevertheless, the points related to bony exposure made by the authors are important in identifying the reasons for suboptimal resection of nonfunctioning pituitary tumors.

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This is an interesting article that I think makes some very significant points. It demonstrates that one of the major problems in incomplete resection is inadequate exposure. Although some will claim that the problem is from the microscopic approach, rather than an endoscopic approach, I do not think this is true. I agree with the authors that inadequate exposure is more a problem of experience than direct vision. Not opening wide enough is often the number one issue. Understanding the midline and the angle of approach when transnasal is imperative for safety. In a study to be published by Dr. Rhoton, measurements of the range of exposure possible will be demonstrated, and these must be understood at all levels, from the front of the sphenoid sinus to the front of the sella. Experience has a great deal to do with this.

The second point I would like to emphasize is that firm tumors, which make up approximately 5% of adenomas, can be removed totally, but do require a wide exposure and different techniques to bring the tumor into the field of sellar exposure. Curetting alone will not do this. A sharper dissection with delivery of the tumor into the sella followed by piecemeal resection is often necessary.

My third point is that the complication rate for re-exploration need not be any higher than for a primary operation. Our report demonstrated the same incidence of problems as for a primary procedure (1). The take-home message is that repeat surgery can be performed very safely but may never be necessary if the first procedure is performed with adequate exposure for the entire sella.

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For any neurosurgical procedure, extent of resection is related to several interdependent factors. This retrospective analysis by Mattozo et al. describes some of the factors for a cohort (n = 30) of reoperated nonsecretory pituitary adenomas. First and foremost, the surgeon's experience determines extent of resection. Familiarity with three-dimensional anatomy and anatomic variants, ability to deal with bleeding or cerebrospinal fluid leak, optimal positioning of microscope or endoscope, and knowledge of common tumor "hiding places" are all features of successful transsphenoidal tumor removal. In the current report, this is evidenced by the inclusion of three (10%) patients with incomplete resections operated by the senior author (DFK) at an earlier (and presumably less experienced) stage of his career. Second, as this report emphasizes, exposure is a critical factor in determining extent of resection. Inadequate bony removal at the sphenoid rostrum or sella has been nearly uniformly present in patients that I have surgically treated for residual pituitary tumor (both secretory and nonsecretory). When a sublabial approach is used, inadequate bone removal at the anterior sphenoid wall may be related to the fact that this portion of the procedure is often performed by otolaryngologists who are unaware of the exposure requirements for tumor removal. I suspect that inadequate removal of the anterior sella wall occurs because of uncertainty regarding the midline and difficulty controlling venous bleeding from circular and cavernous sinuses at the superior and lateral resection margins, respectively. It should be noted that the sella bone can regenerate, especially when a bone strut has been placed in the bony opening. This may give the false impression of a small surgical opening. Third, tumor consistency and vascularity are important factors in extent of tumor resection. In this case, however, my experience differs from the authors; I have had better success with soft tumors, especially when they invade the cavernous sinus. In general, my experience with reoperation for residual pituitary adenomas has been very similar.

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The University of California at Los Angeles group, led by Daniel F. Kelly, has been playing the role of pace-setter in the evolution of transsphenoidal surgery during the past several years. Everything they do is presented with simple, effective, and original scientific observations, with the offering of innovation within the tradition, i.e., traditional transsphenoidal surgery with the operating microscope with the innovation of the endonasal approach. This article follows in the spirit of the group's previous ones because of the rigor of the statements, simplicity of the analysis, and the evidence of the results, which indicate the repeat surgery is as secure and effective a solution as the other surgeries presented by the authors. Another interesting aspect of this report is its focus on a series of patients with recurrent endocrine-inactive pituitary macroadenomas, which points attention to this specific disease, thus avoiding the frequent "potpourri" of different diseases that could lead to vague, emphatic, and favorable conclusions, which raise doubts as to analysis of the results. Also, the analysis of the "failure" of first surgery and the multiple factors contributing to it is very interesting.

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