Endoscopic Transcranial and Intracranial Resection: Case Series and Design of a Perioperative Management Protocol

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ABSTRACT

Purely endoscopic resections of transcranial/intracranial pathology represent an exciting minimally invasive option for some patients. There is an abundance of literature on surgical techniques, though very little deals with perioperative management, which is critical for good outcomes. We present a detailed case review and a perioperative management protocol with specific reference to skull base and neuroanatomy. We performed a retrospective chart review and analysis of outcomes and complications by approach and design and prospective employment of a perioperative management protocol in a major tertiary care referral hospital. We included patients undergoing endoscopic skull base approaches by the two senior surgeons from September 2005 to April 2009, selecting of transcranial/intracranial cases for detailed review. Our main outcome measures included perioperative morbidity, mortality, and complications; degree of resection; recurrence rate; and survival. Fifteen patients met study criteria. No perioperative mortality occurred. There were two major and four minor complications. Mean follow-up was 15 months; 11/13 patients with malignancies had no evidence of disease. A perioperative management protocol was designed from these data and has resulted in decreased lumbar drainage and increased fluid/electrolyte monitoring. Endoscopic transcranial/intracranial anterior skull base surgery is both safe and effective when a complete understanding of the surgery and perioperative management is achieved.

KEYWORDS: Extended endonasal approach, endoscopic, anterior skull base, skull base neoplasm

Minimally invasive surgery has become a significant trend across specialties, with the goal of reducing patient morbidity while maintaining effective oncological treatment. Efforts to reduce perioperative morbidity and mortality have been applied with increasing sophistication in the most complex anatomic regions of the

human body, including the anterior skull base and intracranial space.

The routine employment of endoscopic sinus surgery in the management of chronic infectious and inflammatory sinus disease has led to significant improvements in both endoscopic skills and surgical

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technology. Application of endoscopic surgery to the treatment of sinonasal tumors, such as inverted papilloma, has followed naturally.¹⁻⁴ In recent years, endoscopic indications have expanded further to include many sinonasal malignancies and anterior skull base neoplasms.⁵⁻⁸ Purely endoscopic oncological resections are now possible, with the benefit of decreased perioperative morbidity and improved cosmesis compared with open approaches.⁸

The literature in this field is still developing. Lack of specific perioperative management protocols for complex patients has the potential to significantly inhibit the routine and safe application of endoscopic techniques to the anterior skull base. In particular, cases where intracranial extent is present—obligating entry of the anterior cranial fossa and skull base reconstruction—demand a complete understanding of the myriad potential complications.

METHODS

Retrospective review of medical records of patients treated for anterior skull base neoplasms between September 2005 to April 2009 by the two senior authors was performed. All surgical procedures and postoperative care took place at the University of Pennsylvania. This study was approved by the Institutional Review Board.

Inclusion and Exclusion Criteria

Patients undergoing purely endoscopic skull base surgery were selected. Cases where intracranial work was required were subsequently identified by detailed review of operative and billing records. To qualify for further review, cases must have been performed with the goal of definitive resection. Revision surgeries following open procedures, surgeries for tumor recurrence, and transsphenoidal approaches were excluded.

Data Collection and Analysis

All clinical charts, pathology, and imaging reports were reviewed. Demographic information, diagnosis, and tumor stage were recorded. Operative records were used to determine specific aspects of the approach and extent of resection, as well as the materials and methods used for skull base reconstruction. Tumors were staged according to the American Joint Committee on Cancer (AJCC) or Kadish criteria.^{9,10}

Clinical course, including hospital and intensive care unit length of stay, lumbar drainage, and postoperative complications, was recorded. Postoperative disease state was determined by review of surveillance imaging and endoscopy at the most recent encounter and was defined as no evidence of disease (NED), alive with disease, or died of disease. Length of follow-up was

measured at the most recent office visit or surveillance imaging.

Where appropriate, data are presented as mean $\pm$ standard deviation. Comparison of complication rates was performed using a Fisher exact test.

RESULTS

Cohort Characteristics

Fifteen patients, 10 men (67%) and 5 women (33%), met study criteria. Mean age was 58 years (range 44 to 76). Demographics, tumor types, extent of resection, adjuvant therapies, and current status are listed in Table 1. Overall, 13 of 15 tumors were malignant. The type and extent of sinonasal work, skull base approach, and details of the transcranial or intracranial component are presented in Table 2. Lumbar drains were placed preoperatively in eight patients (53%). When a lumbar drain was placed, intrathecal fluorescein was used for visualization of dural tears and confirmation of successful cerebrospinal fluid (CSF) leak repair.

The transcribriform approach was used in 12 cases (80%), transplanum-transtuberculum in two cases (13%), transclival in one case (7%). Where appropriate, the “two nostrils four hands” technique was employed.¹¹ Two patients (13%) with tumors along the anteriormost ethmoid roof in the area of the frontal sinus ostia underwent a Draf 3 (modified Lothrop) procedure to provide functional frontal sinus drainage. One patient (with chondrosarcoma) underwent removal of the lamina papyracea owing to tumor abutment and a small area of potential invasion. One patient (7%) with esthesioneuroblastoma required a minimal gyrus rectus corticectomy owing to frank tumor invasion of the pia mater.

Skull Base Reconstruction

Anterior skull base defects were reconstructed with multiple materials, often in combination. For small defects, free fat and fascia grafts were preferred, particularly in the cribriform area. For larger defects, allograft materials and local flaps were employed. Allograft materials included acellular dermis (AlloDerm, Lifecell, Branchburg, NJ) and lipophilized dura (DuraGen, Integra NeuroSciences, Plainsboro, NJ) and were used in six cases (40%). The Hadad-Bassagasteguy (nasal septal rotation) flap was used 47% of the time—alone in three cases (20%) and with lipophilized dura in four cases (27%).¹²

Complications

No perioperative mortalities, vision loss, orbital hematoma, extraocular muscle injury, or tension pneumocephalus occurred. One patient (7%) developed a

Table 1 Clinical Data for the Study Cohort

	Patient Age (y)	Tumor Histology	Tumor Stage	Skull Base Approach	Adjuvant Therapy	Extent of Resection	Current Status
1	71	Adenoid cystic	Stage 4	Transcribriiform	Radiation	Complete	NED
2	53	Adenocarcinoma	Stage 4	Transcribriiform	Radiation	Complete	NED
3	55	Esthesioneuroblastoma	Kadish C	Transcribriiform	Radiation	Complete	NED
4	71	Adenocarcinoma	Stage 4	Transcribriiform	Radiation	Complete	NED
5	62	Mucosal melanoma	Stage 1*	Transcribriiform	Radiation	Complete	NED
6	76	Adenocarcinoma	Stage 4	Transcribriiform	Chemotherapy, radiation	Complete	NED
7	42	Teratocarcinosarcoma	Stage 3	Transcribriiform	Chemotherapy, radiation	Complete	NED
8	54	SNUC	Kadish C	Transcribriiform	Radiation	Complete	DOD
9	54	Chordoma	Kadish C	Transclival	None	>90%	AWD
10	56	Schwannoma	NA	Transcribriiform	None	Complete	NED
11	44	Esthesioneuroblastoma	Kadish C	Transcribriiform	Radiation	Complete	NED
12	53	Esthesioneuroblastoma	Kadish C	Transcribriiform	Radiation	Complete	NED
13	50	Chondrosarcoma	Stage 4	Transplanum-transtuberculum	None	Complete	NED
14	53	Meningioma	NA	Transplanum-transtuberculum	None	Complete	NED
15	75	Esthesioneuroblastoma	Kadish B	Transcribriiform	Radiation	Complete	NED

*Staging for sinonasal mucosal melanoma is not well defined; this lesion was <2 cm in diameter, but occurred on the superior septum and ethmoid roof.

AWD, alive with disease; DOD, died of disease; NA, not applicable; NED, no evidence of disease; SNUC, sinonasal undifferentiated carcinoma.

postoperative CSF leak and two patients (13%) developed mild to moderate pneumocephalus; one required repeat head computed tomography (CT) but no intervention, and the other occurred with the CSF leak. There were two infectious complications: one acute bacterial sinusitis and one pneumonia. Each case occurred after hospital discharge, and outpatient oral antibiotics was sufficient treatment. No cases of meningitis or other intracranial infection occurred.

One patient (7%) developed the syndrome of inappropriate antidiuretic hormone secretion (SIADH) after hospital discharge. This required readmission to

the intensive care unit (ICU). There were no cases of transient or permanent diabetes insipidus (DI) or cerebral salt wasting (CSW). There were no carotid injuries, intracranial hemorrhages, ischemic strokes, or perioperative cardiovascular events. No deep venous thromboses (DVT) or pulmonary emboli occurred.

Overall, two major and four minor complications were noted in our series. Both major complications (SIADH, CSF leak) occurred in the transplanum-transtuberculum approach.

Outcomes

In 14 patients (93%), complete resection was possible; one patient with a chordoma was left with minimal residual tumor (Table 1). Survival among malignant tumors was 92% (12/13) at a mean follow-up of 15 months (range 2 to 44). One death occurred at 12 months postoperatively in the patient with sinonasal undifferentiated carcinoma (SNUC), which also represents the only recurrence. This patient underwent revision surgery via an open craniofacial approach with frontal sinus cranialization secondary to extensive tumor involvement of the posterior wall of the frontal sinus and ethmoid roof. Mean hospital length of stay was 3.9 ± 1.7 days, and mean length of ICU stay was 1.4 ± 1.1 days.

Nine patients (60%) were treated with adjuvant radiation therapy in an effort to increase locoregional control. Two patients (14%) with diagnoses of adenocarcinoma and teratocarcinosarcoma also received chemotherapy. No patients had cervical lymph node

Table 2 Details of the Approach and Resection for the Study Cohort

Category	Procedure	Number (%)
Endonasal approach	Sphenoethmoidectomy	15 (100%)
	Middle turbinate resection	12 (80%)
	Frontal sinusotomy	11 (73%)
	Draf 3 (modified Lothrop)	2 (13%)
	Orbitotomy	1 (7%)
	Endoscopic medial maxillectomy	2 (13%)
	Intraoperative CSF leak	14 (93%)
Intracranial approach	Durotomy	14 (93%)
	Dural resection	9 (60%)
	Parenchymal resection	1 (7%)
	Intraoperative CSF leak	14 (93%)

CSF, cerebrospinal fluid.

Figure 1 Preoperative MRI, midsagittal cut, T1 post-gadolinium demonstrating tuberculum sellae meningioma with dural tail and optic chiasm compression.

metastasis during the study period, therefore no neck dissections were performed.

Review of postoperative sinonasal function was performed with the sinonasal outcomes test (SNOT-22). Results varied widely (range 0 to 31), with a mean of 16 ± 11 . The most frequent area of dissatisfaction was olfactory function, with 12 patients (80%) noting moderate or significant hyposmia.

ILLUSTRATIVE CASE

A 54-year-old man with a past medical history of previous tobacco use, lower back pain, and mild sinusitis presented to an outside physician with complaints of headache and vision changes. Magnetic resonance imaging (MRI) revealed a tuberculum sellae lesion, measuring $\sim 1.5 \times 2 \times 1$ cm, consistent with meningioma (Fig. 1).

Endoscopic transplanum-transtuberculum resection proceeded smoothly (Fig. 2A and B). After placement of lipophilized dura, a Hadad-Bassagasteguy flap was used to line the defect in the sphenoid sinus and the midline skull base. This was sealed with fibrin glue (Tisseel, Baxter Inc., Deerfield, IL), and the sphenoid sinus and superior nasal cavity were then packed with Gelfoam (Pharmacia & Upjohn, New York, NY). Soft nasopharyngeal airways were placed bilaterally to support the reconstruction. No leak was observed. Postoperative imaging confirmed a Simpson Grade I resection. The patient's hospital course was uneventful, and he was discharged on postoperative day 3.

At follow-up on postoperative day 5, the residual packing was removed and the cavity gently debrided.

The nasal septal flap was pink and healthy, and no CSF leak was seen. The patient had noted complete recovery of his vision. Unfortunately, he returned to the emergency department 3 days later with a severe headache and clear rhinorrhea. Head CT revealed mild to moderate pneumocephalus. The patient was taken to the operating room for repair of a presumed CSF leak. Intraoperative endoscopy revealed a dehiscence at one corner of the rotation flap. This was repaired with abdominal fat and fibrin glue, and the nasal cavity was repacked.

The patient was admitted initially to the ward, but postoperative serum electrolytes revealed hyponatremia requiring transfer to the ICU. Fluid replacement and correction of the hyponatremia began slowly, initially with intravenous 3% sodium chloride and later normal saline, oral salt tabs, and fluid restriction. Sodium nadir occurred at 109 mEq before slowly recovering to normal. Sodium at discharge was 139 mEq. At 4-month follow-up, he had made a complete recovery. Three-month postoperative MRI is shown in Fig. 2C.

DESIGN AND IMPLEMENTATION OF A PERIOPERATIVE MANAGEMENT PROTOCOL

Complications Differ between Approaches

Both major complications and four of six total complications occurred in the transplanum-transtuberculum approach. Major complications included SIADH and postoperative CSF leak. Considering the surgical anatomy, this is logical. Bony resection and dural opening at the midline skull base during a transplanum-transtuberculum approach result in a large opening under the chiasmatic cistern. The chiasmatic cistern holds a relatively large volume CSF. In addition, there is a relative lack of downward force from tissues overlying this area. Whereas watertight closure at the cribriform plate may be assisted by the weight of the frontal lobes, no such force exists within the sphenoid sinus or sella. Repair in this approach is thus prone to failure. This is evidenced by the significant postoperative CSF leak rate encountered using this approach, including 62% in the meningioma series by Gardner et al and 33% in the series by de Divitiis et al.^{13,14} Other suprasellar studies have reported postoperative leak rates of 10 to 30%.¹⁵⁻¹⁷

Manipulation of tissues in the sella and chiasmatic cistern may also cause significant pituitary dysfunction and neuroendocrine derangement. Panhypopituitarism may occur in even minimally invasive surgery.^{13,14} Neurohypophyseal dysfunction is more common, however, and leads to either DI or SIADH. DI may be transient or permanent and is the result of deficient antidiuretic hormone (vasopressin). This

Figure 2 Intraoperative endoscopic view of the tuberculum sellae meningioma during resection (A) and the optic chiasm after tumor removal (B). CSF appears yellow as a result of intrathecal fluorescein. (C) Three-month postoperative sagittal MRI demonstrating Simpson grade I resection and healing of the skull base reconstruction.

manifests as an increase in dilute urine and hypovolemia. Loss of free water increases the serum sodium concentration, which may lead to mental status change and significant decline. Studies of endoscopic resection of craniopharyngiomas have shown high rates of hypopituitarism and DI.^{16,17}

SIADH following surgery for pituitary adenoma in the sella or suprasellar compartments has been described but is very rare.¹⁸ Indeed, we present, to our knowledge, the first case of postoperative SIADH following purely endoscopic resection of a cranial base meningioma. SIADH results from continued secretion of ADH despite decreasing serum sodium level, which is normally detected by the hypothalamus. Renal sodium excretion is maintained, however, and the urine is concentrated. Diffuse edema does not occur and the patient is euvoletic. Sodium levels less than 120 mEq/L are attended by nausea, vomiting, headache, and stupor. As sodium concentration declines further, generalized seiz-

ures may occur. Finally, SIADH must be distinguished from CSW, in which hyponatremia results from increased renal excretion of sodium rather than free water retention.¹⁸ This leads to hypovolemia with increased urine output and therefore must not be managed with fluid restriction.

Perioperative Management Protocol

Details of our perioperative management protocol are presented in Fig. 3. In our current series, lumbar drainage was employed in 53% of patients. However, we have now adopted a practice of lumbar drain placement only in patients undergoing transplanum-transtuberculum approach. No leaks were encountered in transcribriform or transclival cases, and the risk of postoperative CSF leak in these cases, particularly with more recent skull base reconstruction techniques, is perceived as relatively low.^{6,17}

Figure 3 Flowchart of our perioperative management protocol for endoscopic transcranial/intracranial resections. CT, computed tomography; MRI, magnetic resonance imaging; CSF, cerebrospinal fluid; ICU, intensive care unit; OR, operating room; POD, postoperative day.

Skull base reconstruction is undertaken with a pedicled nasoseptal flap whenever possible.¹² This is secured in place with fibrin glue and the cavity is packed with Gelfoam, microfibrillar collagen, or abdominal fat depending on the size of the defect and the length of the flap rotation. Reconstruction is further supported with middle meatal spacers—Meroceel sponges (Med-

tronic-Xomed, Mystic, CT) placed in the finger of a nonlatex glove—and bilateral soft nasopharyngeal airways. Nasopharyngeal airways are removed at hospital discharge, but the remainder of the packing remains in place.

All patients are admitted to the neurosurgical ICU at least overnight. DVT prophylaxis and perioperative antibiotics with blood-brain barrier penetration are standard. Careful attention to the patient's volume status and urine output is critical. Serum electrolytes are assayed postoperatively. Sodium levels less than 135 mEq/L or greater than 145 mEq/L trigger a protocol for frequently repeated measurements. In addition, urine output less than 30 mL per hour or more than 150 mL per hour prompt immediate laboratory draws. Patients experiencing significant hyponatremia are started on seizure prophylaxis.

Postoperative imaging is essential to rule out intracranial bleed or significant pneumocephalus. A routine head CT scan is performed immediately after surgery. Assessment of the extent of surgical resection is also critical and may determine the need for further procedures and adjuvant therapies. MRI with and without gadolinium is performed within 24 hours of tumor resection. Hospital discharge is considered as early as postoperative day 3 for patients who have had a smooth postoperative course, demonstrate no signs of leak or infection, and have been ambulating.

Follow-up is made for 7 to 10 days. At the first postoperative visit, the remainder of the nasal packing is removed but extensive debridement is avoided. Antibiotic therapy is instituted immediately for all postoperative signs/symptoms of acute sinusitis.

Implementation

Our perioperative management protocol has now been employed in two cases. An adenocarcinoma was resected via a transcribriform approach and a chordoma via a transclival approach. No lumbar drains were used. Reconstruction included a Hadad-Bassagasteguy flap in both cases (with lipophilized dura in the transcribriform approach).¹² Each patient was admitted for 2 days and spent 1 night in the ICU. No perioperative complications occurred, and both patients are alive and free of disease at 3-month follow up.

DISCUSSION

In our study, we reviewed 15 patients who underwent endoscopic transcranial/intracranial resections of anterior skull base neoplasms. Though there is a growing body of literature supporting endoscopic approaches, many studies present a combination of endoscopic-assisted resections and a minority of cases involving a true "endoscopic craniotomy."

Our cohort is representative of the breadth of anterior skull base pathology. All cases were advanced stage at the time of surgery, with five AJCC stage IV and five Kadish Stage C lesions in the series.^{9,10} In addition, the single melanoma included is considered stage I only as a result of the poorly defined system for mucosal melanoma—though the poor prognosis of these lesions is clear.¹⁹ Despite the extent of disease, complete resection was possible in 93% of cases. Furthermore, there was only one recurrence over an average follow-up of 15 months. Unfortunately, this patient expired from a recurrent SNUC, though this is characteristic of the disease.²⁰ Eleven of 13 malignancies are currently NED.

Two major and four minor complications occurred in our series. One case of mild pneumocephalus resolved with conservative management, and the other occurred in conjunction with the CSF leak. One case each of acute sinusitis and pneumonia were treated with a single course of oral antibiotics. Postoperative CSF leak rate was 7%, which is at the lower end of reported series.^{13–15,17,21} The greatest concern with postoperative CSF leak is ascending infection. Intracranial infection and meningitis have been reported following endoscopic resection, though none occurred in our study.^{15,21}

In addition, we observed a very rare complication of skull base surgery—SIADH. In our illustrative case, a diagnosis of SIADH was made after the patient was readmitted for CSF leak. The exact time course of the neuroendocrine derangement remains unclear, though it seems unlikely that significant hyponatremia was present between hospitalizations. Packing removal and debridement may have led to compromise of the reconstruction, CSF leak, and subsequent hypothalamic-pituitary injury. Though this was transient, it resulted in significant patient discomfort and required additional hospital resources. We advocate waiting 7 to 10 days before packing removal and assessment of the reconstruction.

There were no perioperative mortalities in our study. Though rare in endoscopic approaches, other series have reported some deaths.^{13,14,21} In addition, there were no internal carotid artery injuries and no intracranial hemorrhage. Some series have reported such complications, but vascular injuries remain rare.^{13,14,16} Lastly, the length of stay for our cohort averaged about 4 days. This is commensurate with existing reports and represents an improvement over anterior craniofacial resection (ACFR).²¹

The anterior skull base is extremely complicated, with many critical neurovascular structures in close proximity. Neoplastic lesions may arise from multiple tissue types and extend from either the intracranial space or the paranasal sinuses.²² This area is traditionally approached via ACFR, which pairs a transfacial approach and craniotomy to provide adequate exposure

from above and below.²³ This technique has been used in thousands of cases with good results but poses significant risks.^{24–26} The rate of significant perioperative morbidity is as high as 30 to 50% in modern series, and perioperative mortality is quoted in the range of 5 to 10%.^{24–29} Death or serious loss of function are thus relatively common in this type of resection and may significantly reduce the utility of the operation.

Extended endoscopic approaches were developed to address this concern and have now expanded to include transcranial and entirely intracranial tumors.^{6,8,13,21} A significant body of work exists on the partial or complete endoscopic resection of esthesioneuroblastomas in particular.^{6,30–33} Concerns about the oncological soundness of these approaches for a variety of malignant lesions have also been addressed.^{5–8,33} Further, a recent meta-analysis has shown that outcomes for endoscopically treated esthesioneuroblastomas are equivalent or better than with open approaches.³¹

Given the recent development of purely endoscopic techniques, issues of safety and efficacy are still being addressed. The largest case series comes from an Italian group led by Nicolai and has shown complications rates below those for traditional approaches.²¹ This has been confirmed in smaller series.^{1,6,33} Other series, including those with smaller cohorts, have confirmed the suitability of endoscopic approaches to the sella, suprasellar, and clival regions.^{13,14,16,34–38} These techniques have now been applied to petrous apex pathologies and some vascular lesions.^{39–42}

Minimally invasive surgery is often perceived as minimal risk surgery, which is a serious misconception. Even in the smoothest operation, significant complications are possible—as demonstrated by our illustrative case. We believe that there is significant and growing potential for endoscopic transcranial and intracranial surgery and that rhinologists and head and neck surgeons will play an integral part in its development. Familiarity with the perioperative issues involved in these procedures, however, is essential.

Though a randomized clinical trial in this patient population is precluded for epidemiological and ethical reasons, prospective analysis of treatment paradigms and outcomes will provide a significant amount of information. As more patients are treated and more data analyzed, important questions—from specific oncological failure rates to quality-of-life analyses—will become answerable. This will likely require multi-institutional collaboration across disciplines.

NOTES

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