Transsphenoidal surgery in patients with acromegaly: operative strategies for overcoming technically challenging anatomical variations

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Object. In addition to difficulties with anesthetic and medical management, transsphenoidal operations in patients with longstanding acromegaly are associated with inherent intraoperative challenges because of anatomical variations that occur frequently in these patients. The object of this study was to review the overall safety profile and anatomical/technical challenges associated with transsphenoidal surgery in patients with acromegaly.

Methods. The authors performed a retrospective analysis of 169 patients who underwent endoscopic transsphenoidal operations for growth hormone–secreting adenomas to assess the incidence of surgical complications. A review of frequently occurring anatomical challenges and operative strategies employed during each phase of the operation to address these particular issues was performed.

Results. Of 169 cases reviewed, there was no perioperative mortality. Internal carotid artery injury occurred in 1 patient (0.6%) with complex sinus anatomy, who remained neurologically intact following endovascular unilateral carotid artery occlusion. Other complications included: significant postoperative epistaxis (5 patients [3%]), transient diabetes insipidus (5 patients [3%]), delayed symptomatic hyponatremia (4 patients [2%]), CSF leak (2 patients [1%]), and pancreatitis (1 patient [0.6%]). Preoperative considerations in patients with acromegaly should include a cardiopulmonary evaluation and planning regarding intubation and other aspects of the anesthetic technique. During the nasal phase of the transsphenoidal operation, primary challenges include maintaining adequate visualization and hemostasis, which is frequently compromised by redundant, edematous nasal mucosa and bony hypertrophy of the septum and the nasal turbinates. During the sphenoid phase, adequate bony removal, optimization of working space, and correlation of imaging studies to intraoperative anatomy are major priorities. The sellar phase is frequently challenged by increased sellar floor thickness, distinct patterns of tumor extension and bony invasion, and anatomical variations in the caliber and course of the internal carotid artery. Specific operative techniques for addressing each of these intraoperative challenges are discussed.

Conclusions. Transsphenoidal surgery in patients with longstanding acromegaly frequently poses greater challenges than operations for other types of sellar lesions, yet these challenges may be safely and effectively overcome with the anticipation of specific issues and implementation of various intraoperative techniques.

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Key Words • sella turcica • transsphenoidal surgery • pituitary adenoma • acromegaly • growth hormone • endoscopy

Acronegaly is a life-threatening systemic condition caused by excess production of GH, almost always from a functional pituitary adenoma, and it is associated with increased patient mortality if left untreated.2,12,19 Transsphenoidal surgical intervention in patients with acromegaly has several inherent challenges, as it is a minimally invasive approach in patients with structural features that are generally enlarged. As a result of the chronic systemic disease, potential hurdles are frequently encountered in the anesthetic, surgical, and perioperative medical management in these cases.5,9,16,18–20,26
From an anatomical perspective, numerous pathological changes involving soft-tissue edema, nasal polyps, and bony remodeling often contribute to the complexity of the operation, as natural working corridors are typically more restricted and deeper than in other patients. Because transsphenoidal surgery relies on the ability to visualize and identify key anatomical landmarks during each phase of the operation, we aimed to characterize the particular anatomical characteristics and technical surgical considerations that arise frequently in patients with longstanding acromegaly. Particular pitfalls that may be prevented or avoided if awareness of these issues is maintained, and specific operative techniques that can be employed to overcome many of these challenges, are discussed.

Methods

The intraoperative observations and techniques reported in this review were derived from a retrospective analysis of 169 cases involving patients with GH-secreting pituitary adenomas treated in a combined series of 743 endoscopic transsphenoidal operations for pituitary adenomas at the Università degli Studi di Napoli Federico II and Brigham and Women’s Hospital since January 2000.

The intention of this particular study is not to report the surgical or endocrinological outcomes associated with acromegaly. Rather, we aimed to assess the safety and complication rate associated with the endoscopic technique in patients with GH-secreting adenomas, and to identify some of the most pronounced anatomical features that are frequently encountered in patients with longstanding acromegaly that can make the operation more challenging than in patients with other types of pituitary adenomas. The aspects identified in this report were derived from the retrospective review of imaging data (CT and MR imaging), preoperative clinical assessments, operative reports, intraoperative observations, and video recordings in the 169 patients undergoing endoscopic transsphenoidal operations for GH-secreting adenomas.

Patient Characteristics and Complications

The patient characteristics and the complications are presented in Table 1. The mean patient age was 44 years (range 16–75 years). There was a slight male preponderance, with 54% of patients being male and 46% female. Reoperation for recurrent tumor was performed in 7% of the cases, with the endoscopic transsphenoidal procedures in the other 93% being primary operations. Macroadenomas were present in 61% of patients, and 39% had microadenomas.

There were no cases of operative mortality. Internal carotid artery injury occurred in 1 patient (0.6%), a 31-year-old man with a GH-secreting microadenoma and complex sphenoid sinus anatomy. Immediately following the injury, the area of hemorrhage was packed and the patient was immediately transported to the endovascular suite for balloon test occlusion and successful coil embolization of the left ICA. The patient had excellent collateral circulation and developed no neurological sequelae as a result of this injury. He was taken back to the operating room the same day for gross-total resection of the tumor.

TABLE 1: Characteristics and surgical complications in 169 patients undergoing endoscopic endonasal transsphenoidal surgery for GH-secreting adenomas

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean age in yrs (range)</td>
<td>44 (16–75)</td>
</tr>
<tr>
<td>sex</td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>91 (54)</td>
</tr>
<tr>
<td>female</td>
<td>78 (46)</td>
</tr>
<tr>
<td>tumor size</td>
<td></td>
</tr>
<tr>
<td>microadenoma</td>
<td>66 (39)</td>
</tr>
<tr>
<td>macroadenoma</td>
<td>103 (61)</td>
</tr>
<tr>
<td>recurrence/reop</td>
<td>11 (7)</td>
</tr>
<tr>
<td>complications</td>
<td></td>
</tr>
<tr>
<td>death</td>
<td>0 (0)</td>
</tr>
<tr>
<td>ICA injury</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>severe epistaxis</td>
<td>5 (3)</td>
</tr>
<tr>
<td>transient DI</td>
<td>5 (3)</td>
</tr>
<tr>
<td>symptomatic hyponatremia</td>
<td>4 (2)</td>
</tr>
<tr>
<td>pancreatitis</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>CSF leak</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>

*Values represent numbers of patients (%) except as otherwise indicated.

No patient developed postoperative visual loss. Postoperative delayed epistaxis (arterial bleeding) developed in 5 patients (3%). Of these patients, 3 were treated successfully with nasal packing alone. The other 2 had refractory bleeding requiring endovascular occlusion. Transient DI developed in 5 patients (3%), with no cases of permanent DI. Four patients (2%) developed symptomatic delayed hyponatremia due to the syndrome of inappropriate antidiuretic hormone hypersecretion (SIADH), which resolved with fluid restriction and no neurological sequelae in all cases. One patient (0.6%) developed transient pancreatitis thought to be secondary to medication administration. Two patients (1%) developed postoperative CSF leaks. One of these patients required reoperation for abdominal fat graft placement; in the other patient, the leak was successfully managed with temporary lumbar drainage. Two patients (1%) with acromegaly and atypical nasal anatomy underwent intraoperative conversion to a microscopic approach.

Operative Strategies for Endoscopic Transsphenoidal Surgery in Patients With Acromegaly

Based on our review of these cases, several challenges were identified at each particular phase of the operation that were highlighted as being more pronounced in patients with acromegaly (Table 2). These intraoperative observations and recommended intraoperative technical strategies to address them are discussed below.

Preoperative Considerations. As with all neurosurgical patients undergoing transsphenoidal pituitary surgery, a detailed preoperative assessment is a priority in patients with acromegaly. Because anesthesia-related complica-
Transsphenoidal surgery in patients with acromegaly

TABLE 2: Clinical and anatomical features in acromegaly posing various challenges for endoscopic transsphenoidal operations

<table>
<thead>
<tr>
<th>Op Phase</th>
<th>Intraop Challenges</th>
<th>Potential Recommendation/Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>preop</td>
<td>airway/laryngeal edema</td>
<td>preop anesthesia evaluation</td>
</tr>
<tr>
<td></td>
<td>cardiopulmonary dysfunction</td>
<td>plan for intubation (awake/fiberoptic)</td>
</tr>
<tr>
<td></td>
<td>venous congestion</td>
<td>elevate thorax, head of bed to at least 15° to improve venous drainage</td>
</tr>
<tr>
<td>nasal</td>
<td>mucosal edema/redundant tissue</td>
<td>use of cottonoids soaked in vasoconstricting agent</td>
</tr>
<tr>
<td></td>
<td>hypertrophic nasal turbinates</td>
<td>resection of nasal turbinates if necessary</td>
</tr>
<tr>
<td></td>
<td>thick sphenoid rostrum, vomer</td>
<td>use of high-speed drill, chisel, or Jansen-Middleton rongeur</td>
</tr>
<tr>
<td>sphenoid</td>
<td>thickened sphenoid septa &amp; mucosa</td>
<td>wide anterior sphenoidotomy</td>
</tr>
<tr>
<td></td>
<td>restricted workspace, collision of instruments</td>
<td>generous posterior nasal septectomy</td>
</tr>
<tr>
<td>sellar</td>
<td>abnormal skull base bony anatomy</td>
<td>imaging–intraoperative anatomical correlation</td>
</tr>
<tr>
<td></td>
<td>atypical caliber &amp; tortuosity of ICAs</td>
<td>intraoperative neuronavigation</td>
</tr>
<tr>
<td></td>
<td>microvascular changes in ICA &amp; cavernous sinus dura</td>
<td>Doppler ultrasound, blunt ring curettes</td>
</tr>
</tbody>
</table>

tions are known to arise more commonly in patients with longstanding acromegaly, preoperative anesthesia, cardiac, and/or pulmonary evaluations are frequently warranted prior to any operation. A cogent plan for intubation based on preoperative airway assessment should be discussed with the anesthesia team. Plans for administration of antibiotics, hormone replacement, pretreatment with somatostatin analogs, or any additional perioperative medications should also be addressed in advance. It is imperative that the correct neuroimaging modalities are used and that the studies are carefully and systematically reviewed preoperatively. Patients with acromegaly often have atypical vascular and bony anatomy that may warrant further imaging, such as CT or CT angiogram studies, in addition to standard MR imaging. In patients with tumor recurrence, or complex vascular, sphenoid sinus, or sellar anatomy, plans for intraoperative neuronavigation should be made and images registered prior to the operation. Patient positioning for the operation may proceed as usual, however, elevation of the patient’s thorax is recommended to facilitate optimal venous outflow from the cranial compartment.

The Nasal Phase: Maintenance of Visualization and Hemostasis. Several technical issues deserve particular consideration during the nasal phase of a transsphenoidal operation in patients with acromegaly, as the early exposure is critical in these patients and often lays the groundwork for a successful operation. The primary challenges during this stage are typically related to the edematous and/or redundant soft tissue of the nasopharynx, and enlarged, hypertrophic bony nasal turbinates, both of which may compromise endoscopic visualization and working space (Fig. 1). Furthermore, nasal polyps are a common finding in patients with acromegaly, and can generally be coagulated and removed with a nasal debrider or scissors at their pedicles early in the operation to improve visualization. The size and rigidity of the nasal turbinates in patients with acromegaly often mandates more forceful lateral displacement using larger instruments than is typically required in other patients, which may result in increased bleeding if the integrity of the mucosa is compromised early in the operation. Maintaining hemostasis at this stage in the procedure is critical, and can be facilitated by routine placement of multiple cottonoids soaked in a vasoconstricting agent (such as lidocaine with epinephrine) medial to the middle turbinate, along the nasal septum. Lateral displacement of the middle turbinate by compression on the cottonoids, instead of the nasal mucosa itself, often minimizes mucosal injury and bleeding, and temporary packing with cottonoids helps maintain the lateral position of the turbinates once they are displaced. Although not routinely performed, resection of the middle turbinate is a viable option for improving visualization in cases where obscuration becomes a persistent issue. Identification of the sphenoid ostium, a key anatomical landmark during this phase that is typically located approximately 1.5 cm above the superior aspect of the posterior choanae, may be more challenging in patients with acromegaly, as the sphenoid ostia are often concealed by redundant nasal mucosa, polyps, bony overgrowth, or thickened mucosa from within the sphenoid sinus. Variations in posterior nasal and sphenoidal bony anatomy, including sinus morphology and bone thickness, require additional consideration for achieving correlation of imaging with intraoperative findings (Fig. 2). Finally, the use of a high-speed drill or chisel may be more likely to aid in the anterior sphenoidotomy in these patients because of the increased bone thickness.

Because the intranasal working space is often narrow and restricted in a patient with acromegaly, the mobility and range of instruments may be limited, resulting in collision of instruments with the endoscope. A 2-nostril technique with a wide anterior sphenoidotomy and a more extensive posterior septectomy usually alleviates this particular issue, and docking of the endoscope in the superior aspect of the nasal cavity and sphenoid sinus is of paramount importance during the remainder of the operation.
to facilitate 2-handed microsurgical dissection via both nostrils. Realignment of a deviated nasal septum or resection of a septal bone spur may be required in a minority of cases to improve visualization and working room. Although rarely required, conversion to a microscopic or endoscope-assisted operation has been reported to provide some benefits of retraction and hemostasis of soft-tissue structures that may compromise the visualization necessary to complete the operation safely and accurately, especially in patients with acromegaly. Bleeding from the sphenopalatine artery encountered during endoscopic approaches is preferably treated with bipolar cauterization.

The Sphenoid Phase: Maximizing Exposure and Workspace. During the sphenoid phase of the operation, the primary surgical challenges include atypical bony anatomy, achieving adequate exposure and working space within the sinus, and maintenance of hemostasis. Achieving correlation of imaging to intraoperative findings, such as the sphenoid septae, is critical during this phase, as the paranasal sinuses are frequently enlarged in patients with acromegaly, thus potentially giving the surgeon the impression that the sphenoid sinus and sellar face have been adequately exposed when in fact they have not. The use of more powerful rongeurs, such as the Jansen-Middleton rongeur, and/or a high-speed drill is often required to achieve adequate removal of the sphenoid rostrum and thickened sphenoid septa. The chisel can also be a useful instrument for detaching and removing a thick sphenoid rostrum, especially at its inferiormost aspect at the base of the vomer. Thickened sphenoid sinus mucosa and sinusitis are frequently encountered in patients with acromegaly, and once stripped may cause venous bleeding from the sinus walls. This bleeding can usually be readily controlled with saline irrigation, Gelfoam, Surgifoam, and/or compression with cottonoids. The anatomy of the sellar floor and clivus is often atypical in patients with longstanding acromegaly due to chronic bony remodeling, and opening of the sellar floor may also require the use of a chisel or drill. Tumors that secrete GH, however, are also known to have a proclivity for infrasellar extension through the sellar floor and into the sphenoid sinus and clivus, and tumor extension may often be noted early in the sphenoid phase of the approach.

The Sellar Phase: Identification of Key Vascular Structures and Safe Tumor Resection. Patients with longstanding acromegaly have been reported to develop anatomical changes in the caliber and tortuosity of the ICA that may come into play during the sphenoid and sellar phases of the operation (Fig. 3). Because of these variations, it is critical to assess the course of the ICA within the parasellar nasal and cavernous sinuses prior to the operation, as extension of the ICA into the sphenoid sinus (Fig. 4) and a narrow intercarotid distance (Fig. 5)
are observed relatively frequently.\textsuperscript{15,16,24} A small proportion of patients with acromegaly may have “kissing” carotid arteries, in which the surgical approach or plan may require reconsideration for safe tumor removal.\textsuperscript{22} In addition, atypical anatomy of the ICA may be further complicated by complex bony sellar floor and sphenoid sinus anatomy, resulting in a higher likelihood of ICA injury (as occurred in the patient with ICA injury described in Patient Characteristics and Complications, above).

In addition to the macroscopic anatomical changes in parasellar vasculature that may be observed in patients with acromegaly, microvascular changes associated with chronic local and systemic GH excess may cause alterations in the structural integrity of surrounding structures, including the cavernous sinus dura and ICAs, that may contribute substantially to the risk associated with tumor resection.\textsuperscript{16} Growth hormone–secreting adenomas have been implicated as causing local vascular changes that may be associated with deterioration of vessel endothelium and parasellar or intrasellar ICA aneurysm formation.\textsuperscript{1,3,11,25,28} It should be remembered that ICA injury may be more likely to occur in patients with GH-secreting adenomas than in those with any other kind of pituitary adenoma as a result of the anatomical and microvascular changes mentioned. For this reason, use of the Doppler microprobe and intraoperative neuronavigation are useful intraoperative adjuncts for improving the safety profile associated with dural opening and tumor resection in some patients with acromegaly undergoing transsphenoidal surgery.\textsuperscript{14,17}

Growth hormone–secreting adenomas are often noted to have a whiter color than other types of adenomas, which may aid in differentiating them from the anterior pituitary gland (Fig. 6). Growth hormone–secreting microadenomas often arise in a lateral and inferior location in the gland, and larger GH-secreting adenomas have a proclivity for inferior invasion of the bony sellar floor. In tumors invading the clivus and sellar floor, the surgeon should be mindful that the dorsum sella may be eroded. Tumor resection typically proceeds using ring curettes, suction, and tumor forceps, taking care to preserve the normal gland at all times. The use of blunt angled ring curettes in the lateral aspects of the sella and cavernous sinus is typically a safe way of mobilizing tumor medially into the sellar exposure for subsequent removal. Reconstruction of the sellar floor does not differ remarkably from the techniques used in patients with other tumor types although the tortuosity and position of the ICAs

Fig. 3. Axial CT scan obtained preoperatively (A), and intraoperative endoscopic photograph obtained following tumor resection (B) in a patient with acromegaly demonstrating increased caliber and tortuosity of the ICA. In panel B, the right ICA can be visualized immediately behind the sellar dura (white arrows). The location and caliber of the ICA substantially increase the risks associated with dural opening and tumor resection.

Fig. 4. Sagittal (A) and coronal (B) postcontrast MR images obtained in a patient with a GH-secreting macroadenoma and acromegaly. Note the caliber and tortuosity of the ICAs and their extension into the sphenoid sinus in panel B.

Fig. 5. Sagittal (A, C, and E) and coronal (B, D, and F) postcontrast MR images obtained in 3 patients with GH-secreting adenomas. Note the asymmetry of the parasellar ICAs and narrowed inter-ICA distance in all 3 cases.
should be considered at all times if insertion of a rigid buttress for reconstruction is planned.\textsuperscript{10}

**Immediate Postoperative Considerations in Patients With Acromegaly**

Although the majority of patients with acromegaly and preoperative laryngeal edema and/or obstructive sleep apnea will benefit from improved breathing following resection of a GH-secreting adenoma,\textsuperscript{21,23} the surgeon and anesthesia team should maintain vigilance with regard to the patient’s airway immediately after the operation. Although nasal packing is not typically used following endoscopic transsphenoidal procedures, it may be justified in selected cases for the purpose of maintaining hemostasis in patients with acromegaly in whom intraoperative bleeding was a concern. If nasal packing is a consideration, the use of a nasal trumpet on one side (and standard nasal packing on the other) is a useful technique for optimizing airflow and patient comfort following the operation. Finally, continuous positive airway pressure or bilevel positive airway pressure may be required for some patients with chronic or worsened sleep apnea in the early postoperative period. These types of therapy should not be employed, however, if there is any suspicion of a CSF leak.

In the first 24 hours following surgical treatment in patients with GH-secreting adenomas, brisk fluid diuresis is often noted that may mimic DI. In patients with successful treatment of GH-secreting adenomas and normalization of GH levels following surgery, this is often due to diuresis of soft-tissue edema rather than DI, and can be differentiated by obtaining serum sodium and osmolarity levels and urine specific gravity analysis.\textsuperscript{30}

**Conclusions**

In addition to the systemic and cardiopulmonary challenges associated with anesthetic and surgical treatment of patients with GH-secreting adenomas, certain variations in the nasal, bony, and vascular anatomy of patients with acromegaly often pose increased technical challenges during transsphenoidal operations. Excess or redundant soft-tissue edema, abnormal bony anatomy and hypertrophy, and changes in the anatomical course and structural integrity of the ICA may pose remarkable challenges for visualization, exposure, and safe resection of adenomas. Close scrutiny of preoperative imaging studies and implementation of various intraoperative maneuvers may optimize the safety profile associated with these procedures.

**Disclosure**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Zada, Cavallo, Cappabianca, Laws. Acquisition of data: Zada, Esposito, Fernandez-Jimenez, Tasiou, De Angelis. Analysis and interpretation of data: Zada, Cavallo, Esposito, Fernandez-Jimenez, Tasiou, De Angelis, Cappabianca. Drafting the article: Zada, Tasiou. Critically revising the article: Cavallo, Esposito, Fernandez-Jimenez, Tasiou, De Angelis, Cafiero, Cappabianca. Laws. Reviewed final version of the manuscript and approved it for submission: all authors. Statistical analysis: Zada. Administrative/technical/material support: Cavallo, Esposito, Fernandez-Jimenez, Tasiou, De Angelis, Cafiero. Study supervision: Cappabianca, Laws.

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