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Perioperative Complications of Transseptosphenoidal Excision for Pituitary Adenomas

ABSTRACT—Although complications of transseptosphenoidal (TSS) pituitary surgery have been discussed in the literature, there has not been an analysis of complication rates related to clinical features and the nature of the tumor. A retrospective review of 366 TSS procedures (354 patients) for excision of pituitary adenomas evaluated the incidence and management of perioperative complications. The mortality rate was 0.82%. The most frequently encountered complications were transient diabetes insipidus (8.74%) and cerebrospinal fluid (CSF) rhinorrhea (4.10%). Other complications included exacerbation of visual acuity and visual field defects, hemorrhage, hydrocephalus, and meningitis. The factors evaluated were gender, age, tumor size, hormone secretory status, and any history of prior pituitary surgery.

There was a significantly higher incidence of transient diabetes insipidus in patients with hormone-secreting tumors. Minor and total complication rates were significantly increased in microadenomas, hormone-secreting tumors, in female patients, and in patients less than 60 years of age, reflecting the increased incidence of transient diabetes insipidus in young female patients with hormone-secreting tumors. Observed intraoperative CSF leaks predisposed to postoperative CSF rhinorrhea. There were no identifiable risk factors for major complications. (*Skull Base Surgery, 6(4):231–235, 1996*)

The transseptosphenoidal (TSS) approach for resection of pituitary adenomas offers a direct midline approach to the sphenoid sinus and the sella turcica with excellent tumor exposure. It avoids retraction of the brain or optic nerves and presents minimal risk of injury to the brain or vascular structures.[1] Although the complications of TSS surgery for the treatment of pituitary adenomas have been discussed in the literature,[2–8] no series has analyzed complication rates to identify the factors that predispose to specific complications. In this report, we studied complication rates related to gender, age, tumor size, hormone secretory status, and history of prior pituitary surgery.

MATERIALS AND METHODS

We retrospectively reviewed the records of 354 patients (366 procedures) who underwent TSS excision of pituitary adenomas at New York University Medical Center between January 1978 and May 1994. Indications for operation included optic nerve or chiasm compression by tumor and hormonally active tumors producing endocrinopathy. Patients who underwent TSS surgery for conditions other than pituitary adenoma are not included in this review. Postoperative complications were defined as those which occurred within 30 days of surgery. Patients

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with diabetes insipidus were followed for a period of 1 year to distinguish transient from permanent forms. Differences in complication rates were determined using the chi-square test of homogeneity and the Fisher Exact test in cases of small occurrence rates. A two-sided alpha level of less than 0.05 was considered statistically significant. No adjustments were made for multiple comparisons.

TSS pituitary adenoma surgery was performed as a combined otolaryngologic-neurosurgical procedure in all cases. The surgical technique for the TSS approach for pituitary tumor resection has been previously described.[9] The operating microscope was always utilized. Fluoroscopic monitoring was always used for suprasellar adenomas and secondary approaches to the pituitary. The sella turcica and sphenoid sinus were packed with an abdominal fat graft if a CSF leak was observed at operation or extensive arachnoidal exposure was present. The fat graft was secured by sphenoid sinus packing, which was removed after 5 to 7 days. Postoperatively, broad spectrum antibiotics were administered to all patients and endocrine replacement was administered as appropriate.

RESULTS

The mean age of the 354 operated patients was 49.5 years, with a range of 11 to 86 years. There were 201 female (57%) and 153 male (43%) patients. In the 354 patients, there were 72 (20%) microadenomas (tumors smaller than 1 cm in size) and 282 (80%) macroadenomas. Hormonally active adenomas were present in 151 (43%), and nonsecreting adenomas were present in 203 (57%) patients (Table 1). Preoperative CSF rhinorrhea was present in three patients. Twenty-six patients (7%) had one or more antecedent pituitary surgeries, either TSS or the transcranial approach. The postoperative complications of TSS surgery for pituitary adenomas are presented in Table 2. Major complications occurred in 31 patients (8.5%), and minor complications occurred in 42 patients (11.5%), as delineated in Table 2. The overall complication rate was 18%.

Table 2. Overall Postoperative Complications in 354 Cases

Complication	*Number*	*Percent*
Major complications		
Postoperative CSF rhinorrhea	15	4.2
Intracranial hemorrhage	9	2.5
Hypopituitarism	6	1.7
Permanent diabetes insipidus	5	1.4
Hydrocephalus	5	1.4
Meningitis	3	0.8
Mortality	3	0.8
Permanent visual acuity degeneration	2	0.6
Minor complications		
Transient diabetes insipidus	32	9.0
Epistaxis	6	1.7
Septal perforation	3	0.8
SIADH	2	0.6
Abdominal wound hematoma	1	0.3
Sublabial wound hematoma	1	0.3
Other medical/surgical complications		
Deep venous thrombosis	2	
Pneumonia	2	
Pulmonary embolism	2	
Urinary tract infection	2	
Conjunctivitis	1	
Corneal abrasion	1	
Diverticular perforation	1	
Hemorrhagic gastritis	1	

Mortality

There were three deaths among the 354 patients, a mortality rate of 0.8%. One fatality, a 60-year-old female, was due to an intraoperative, intracerebral hematoma. The second death occurred in a 78-year-old female patient with a history of cerebrovascular disease, who required transsphenoidal reexploration for a sellar and suprasellar hemorrhage. The third death was a 49-year-old male patient who developed postoperative CSF rhinorrhea and hydrocephalus with herniation of the third ventricle into the sella turcica. He underwent multiple procedures for repair of persistent CSF rhinorrhea and shunting for hydrocephalus. He ultimately died of ventriculitis.

Table 1. Tumor Endocrine Characteristics

	Macroadenomas (282) *Number*	*Microadenomas (72)* *Number*	*Total (354)* *Total*
Hormone secreting			
Prolactin	44	29	73
Growth hormone	28	32	60
ACTH	6	5	11
Growth hormone/prolactin	5	0	5
Thyroid stimulating hormone	2	0	2
Total	85 (30%)	66 (92%)	151
Nonsecreting	197 (70%)	6 (8%)	203

CSF Rhinorrhea, Hydrocephalus, and Meningitis

Arachnoidal tear with a CSF fistula was recognized in 55 patients (15.5%) at the time of surgery. All patients with observed arachnoidal tears or CSF leaks were treated with intrasellar fat grafts and packing of the sphenoid sinus with fat (except one patient with acute sphenoid sinusitis). Of the 55 patients, 10 (18%) developed postoperative CSF rhinorrhea. Overall, there were 15 patients with postoperative CSF rhinorrhea, 10 of whom (67%) had arachnoidal tears and CSF leaks recognized at the time of operation.

Of the 15 patients (4.2%) with postoperative CSF rhinorrhea, 13 had macroadenomas and 2 had microadenomas. Nine of the 15 patients were treated successfully with lumbar drainage alone. Immediate reexploration for placement of fat grafts was performed in two patients. Both lumbar drainage and reexploration with intrasellar placement of a fat graft were required in four patients. Two patients required two or more operations with graft placement for persistent CSF rhinorrhea; both developed hydrocephalus and meningitis. The incidence of postoperative CSF rhinorrhea was highest in macroadenomas, although this was not statistically significant. The incidence of intraoperative CSF leak and postoperative CSF rhinorrhea did not vary significantly when analyzed by age, gender, hormonal activity and history of prior pituitary surgery.

Hydrocephalus occurred in five patients (1.4%), all of whom required the placement of a ventriculoperitoneal shunt. Prior to the development of hydrocephalus, three patients had postoperative CSF rhinorrhea, necessitating reexploration and graft placement, and two of these patients subsequently developed meningitis.

The overall rate of meningitis was 0.82% (three patients). Three patients had postoperative CSF rhinorrhea necessitating a subarachnoid drain prior to the development of meningitis. Two of these patients had multiple reexplorations for graft placement and the ensuing development of hydrocephalus. Macroadenomas were present in all patients with hydrocephalus or meningitis.

Hemorrhage and Visual Deterioration

Hemorrhage within the sella turcica extending into the suprasellar region requiring reexploration occurred in eight patients. All patients had macroadenomas. Deterioration of visual acuity and visual fields were the presenting signs in all eight patients. One patient had an intracerebral hemorrhage due to damage to the anterior cerebral artery. Hemorrhage became clinically apparent within the first 24 hours in four patients, between 24 and 48 hours in two patients, and between 48 and 72 hours in two patients. One patient had two hemorrhages requiring reexploration on postoperative days one and five. She recovered without further complication. Two patients had permanent deterioration of visual acuity despite hematoma evacuation. One patient experienced sudden visual loss several weeks postoperatively due to residual tumor. An external ethmoidectomy with decompression of the optic nerve was performed with subsequent improvement of visual acuity and visual fields. Overall, there were two deaths among these nine patients.

Diabetes Insipidus

Diabetes insipidus (DI) was defined as urine output greater than 300 mL/hour for more than 3 hours, with a urine specific gravity of less than 1.002. Transient and permanent DI occurred in 32 patients (9.0%) and five patients (1.4%), respectively. For the most part, these patients were treated with intravenous pitressin and/or DDAVP. Patients with transient DI required an average of 3.5 days of treatment with intravenous pitressin. Three patients were discharged on intranasal DDAVP for 1 month, 6 months, and 1 year, respectively.

Transient DI rates were significantly higher in hormonally active adenomas than nonsecreting adenomas, occurring in 25 of 151 patients (16.6%) with secreting tumors and in 7 of 203 patients (3.4%) with nonsecreting tumors ($p = 0.014$) (Fig. 1).

Although transient DI rates were greater in microadenomas (21%) than macroadenomas (6%), this was not statistically significant ($p = 0.267$). There was no statistical difference in the rate of transient DI when hormonally active microadenomas were compared to nonsecreting microadenomas, and when hormonally active macroadenomas were compared to nonsecreting macroadenomas.

When examining complications by age and gender, transient DI rates were higher in females and patients less than 60 years of age, but this was not statistically significant ($p = 0.074$ and $p = 0.114$, respectively). Similarly, there was no significant increase in transient DI when analyzed by history of prior pituitary surgery ($p = 0.264$). Of the five patients with permanent DI, all had secreting adenomas (three prolactin, two growth hormone).

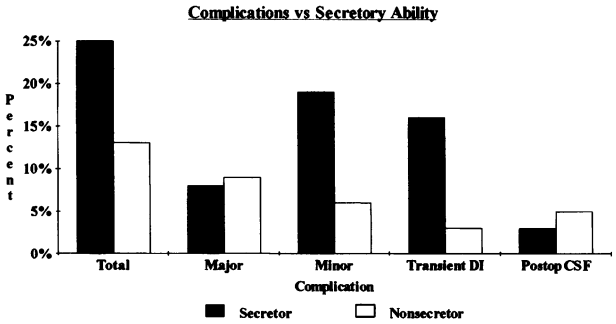

Figure 1. Complications vs. secretory ability.

Other Endocrine Complications

Anterior pituitary dysfunction, including hypopituitarism and syndrome of inappropriate anti-diuretic hormone (SIADH) occurred infrequently in this series. Permanent hypopituitarism resulted in six cases (1.64%). Transient SIADH occurred in two cases (0.55%).

Major, Minor, and Total Complications

Minor and total complication rates were significantly more common in hormonally active adenomas ($p = 0.0001$, $p = 0.0028$), females ($p = 0.022$, $p = 0.012$), and patients less than 60 years of age ($p = 0.002$, $p = 0.011$), reflecting the increased rates of transient DI. Minor complications were significantly higher in microadenomas than macroadenomas ($p = 0.002$), also reflecting higher rates of transient DI in microadenomas. Major complication rates did not vary as a function of age, gender, tumor size, hormonal activity, or history of prior pituitary surgery. There was no significant difference in complication rates when analyzed by history of prior pituitary surgery.

DISCUSSION

This retrospective review confirms the previously reported low morbidity of TSS for removal of pituitary adenomas.[2–8] Mortality was less than 1% and resulted, for the most part, from intracranial hemorrhage and meningitis. Our low rate of complications was due to meticulous attention to detail in the operative and perioperative period.

In other series, carotid artery injury has been the most important cause of mortality and morbidity during the TSS approach to the sella or during adenoma removal.[5,7,10] By maintaining a strictly midline approach to the sella, the carotid artery was never injured in 366 TSS procedures performed in 354 patients in this series. Careful preoperative analysis of the location of the septations of the sphenoid sinus on MRI or CT enabled the operating surgeons to accurately localize the midline and avoid the carotid canal, which is located at the junction of the lateral and posterior wall of the sphenoid sinus. The intersinus septum is usually eccentrically located in relation to the midline; at its posterior extent it may insert on the carotid canal, and if it is grasped with an instrument and twisted the carotid canal may be fractured, exposing or lacerating the carotid artery. Intraoperative fluoroscopy should be available to assist the surgeon during the approach to the sphenoid sinus and sella turcica. In an analogous fashion, the only patient in this series to sustain a vascular injury succumbed when the sphenoid bone at the base of the frontal fossa was fractured and rotated superiorly piercing the dura, lacerating the anterior cerebral artery, and producing an intracerebral hemorrhage.

Carotid artery injury may also occur during tumor resection within the sella turcica and can be avoided by gentle dissection at the lateral extent of the tumor using ring curettes with rounded rather than sharp edges.

Postoperative CSF rhinorrhea has been reported to occur in 1.6% to 9.6% of patients undergoing TSS for resection of pituitary adenomas.[2–8] Our incidence of 4.1% is similar to that reported in the literature. CSF fistulas can result from prolapse of the arachnoid into the sella with subsequent rupture or, as is more commonly the case, from iatrogenic disruption of the arachnoid during tumor resection. When the arachnoid was observed to be torn at the time of operation with leakage of CSF, a fat graft was placed in the sella and sphenoid sinus. Gauze packing was placed in the sphenoid sinus and left in place for 5 to 7 days to hold the fat graft in place. Of the patients with observed intraoperative fistula treated in this fashion, 18% still developed postoperative CSF fistulas. These patients who leaked postoperatively were treated with lumbar subarachnoid drains for periods of up to 5 days.

Interestingly, in one third of the patients who developed postoperative CSF leaks, a tear in the arachnoid or a CSF leak was not detected at the time of surgery and packing of the sella and sphenoid sinus with fat was therefore not carried out. Almost all these patients had macroadenomas and were therefore predisposed to arachnoidal disruption because of increased operative manipulation. Hemorrhage from tumor resection is more likely with larger lesions and may obscure the presence of CSF or a tear in the arachnoid. A Valsalva maneuver at the time of closure might have identified some of the occult arachnoidal tears. In patients with large tumors, consideration should be given to packing the sella with fat regardless of whether CSF is seen.

Meningitis is an infrequent complication of TSS procedures, with a reported incidence of 0.4% to 9%.[2–8] Postoperative meningitis occurred in 0.8% of our patients. Although meningitis was always preceded by CSF rhinorrhea in this series, it may occur in the absence of an observed CSF fistula if the physical integrity of the arachnoid is violated during tumor resection, resulting in passage of pathogenic organisms from the sphenoid sinus into the subarachnoid space.

The incidence of meningitis in the series was minimized by the use of perioperative antibiotics begun at the time of induction of anesthesia and continued until nasal packing was removed, usually at 48 hours. In patients who had sphenoid packing placed for observed intraoperative leaks, intravenous antibiotics were continued until the packing was removed 5 to 7 days postoperatively.

Lumbar spinal drains were utilized only in those patients who developed CSF rhinorrhea postoperatively, whether or not they were packed at the time of surgery. Although lumbar spinal drains are useful adjuncts in the management of postoperative CSF rhinorrhea, they may in themselves predispose the patient to meningitis. Drains were always tunneled subcutaneously away from the site

of lumbar puncture, were maintained with meticulous asepsis, and never kept in place longer than 5 days.

Ophthalmoplegia and postoperative visual deterioration are dreaded complications of TSS surgery and may occur from direct trauma to cranial nerves II, III, IV, or VI, or the optic chiasm or from postoperative hemorrhage. Postoperative hemorrhage, however, is by far the most common cause. Wilson and Dempsey[6] reported exacerbation of visual field defects and ophthalmoplegia in 2.8% and 1.2% of patients, respectively, in their series. In a review of 100 patients, some of whom are included in this report, Cohen et al.[11] reported a 5% incidence of visual deterioration. In this series, nine patients experienced visual deterioration due to postoperative hemorrhage which extended from the sella to the suprasellar cistern with compression of the optic apparatus. All of these patients had reoperation with removal of hematoma; only two of these nine patients had permanent visual deterioration.

Posterior pituitary dysfunction with transient and permanent DI occurred in 8.7% and 1.4% of patients, respectively, and was similar in incidence to that reported in other series.[2–8,12–14] In this series, transient DI was significantly more common in patients with secreting than nonsecreting adenomas. The incidence of transient DI was higher in microadenomas compared to macroadenomas, females, and patients under the age of sixty. However, the difference was not statistically significant. It is likely that the incidence of DI is increased in these patients because patients with secreting adenomas are more likely to be female, below the age of sixty, and to harbor microadenomas. It is likely that the higher incidence of DI in secreting adenomas is due to more vigorous attempts to remove every last bit of tumor. In addition, because these tumors are more likely to be microadenomas, the proximity of a normal pituitary gland may result in increased manipulation of this gland and stalk with transmission of shearing forces to the hypothalamus.

Injury to the anterior pituitary gland during tumor resection was considerably less common than was posterior pituitary injury. Only 1.6% of patients in this series developed deficiency in one or more pituitary-end organ axes compared with a reported incidence of 0% to 15% in the literature.[2–8,13–15]

Epistaxis and sublabial wound hematomas occurred in 2% of patients and were easily treated without permanent sequelae. Nasal septal perforation as a sequela of dissection of the nasal mucosa[2–8,16] was not seen in this series. Similarly, there were no cases of saddle nose or nasal tip deformities resulting from excessive resection of the anterior nasal spine or septal cartilage.

In summary, our mortality rate of 0.8% in 354 patients is low and consistent with that reported in the literature previously. The major complication rate of 8.5% is also low, and the majority did not result in permanent neurologic sequelae. There were no identifiable risk factors for major complications, and a history of prior pituitary surgery did not increase the rate of postoperative complications.

REFERENCES

1. Hardy J: The transsphenoidal surgical approach to the pituitary. Hosp Practice 14:81–89, 1979
2. Kennedy D: Transsphenoidal approach to the sella: The Johns Hopkins experience. Laryngoscope 94:1066–1073, 1984
3. Black PM: Incidence and management of complications of transsphenoidal operation for pituitary adenomas. Neurosurgery 20: 920–923, 1987
4. Kern EB, Pearson BW, McDonald TJ, Laws ER: The transseptal approach to lesions of the pituitary and parasellar regions. Laryngoscope 89(suppl 15):1–33, 1979
5. Laws ER, Kern EB: Complications of transsphenoidal surgery. In Tindall GT, Collins WF (eds): Clinical Management of Pituitary Disorders. New York: Raven Press, 1979, pp 435–445
6. Wilson CB, Dempsey LC: Transsphenoidal microsurgical removal of 250 pituitary adenomas. J Neurosurg 48:13–22, 1978
7. Laws ER, Kern EB: Complications of transsphenoidal surgery. Clin Neurosurg 23:401–414, 1976
8. Zervas NT: Surgical results for pituitary adenomas: Results of an international survey. In Black PM, Zervas NT, Ridgeway EC, Martin JB (eds): Secretory Tumors of the Pituitary Gland. New York: Raven Press, 1984, pp 377–385
9. Cohen NL: Transseptosphenoidal approach to the sella turcica. In Silver CE (ed): Atlas of Head and Neck Surgery. New York: Churchill Livingstone, 1986, pp 160–165
10. Ahuja A, Guterman LR, Hopkins LN: Carotid cavernous fistula and false aneurysm of the cavernous carotid artery: Complications of transsphenoidal surgery. Neurosurgery 31(4):774–779, 1992
11. Cohen AR, Cooper PR, Kupersmith MJ, et al: Visual recovery after transsphenoidal removal of pituitary adenomas. Neurosurgery 17(3):446–452, 1985,
12. Hans P, Stevenaert A, Albert A: Study of hypotonic polyuria after transsphenoidal pituitary adenomectomy. Intensive Care Med 12:95–99, 1986
13. Newman CB, Kleinberg DL: Preoperative endocrinologic evaluation of the patient with a nonsecreting pituitary tumor. In Cooper PR (ed): Contemporary Diagnosis and Management of Pituitary Adenomas. Park Ridge, IL: American Association of Neurological Surgeons, 1991
14. Tindall GT, Barrow DL, Tindall SC: Prolactinomas: Operative management. In Cooper PR (ed): Contemporary Diagnosis and Management of Pituitary Adenomas. Park Ridge, IL: American Association of Neurological Surgeons, 1991
15. Laws ER, Randall R, Abboud CF: Special problems in the management of acromegaly. In Ludecke DK, Tolis G (eds): Growth Hormone, Growth Factors and Acromegaly. New York: Raven Press, 1987, pp 259–266
16. Gammert C: Rhinosurgical experience with the transseptal-transsphenoidal hypophysectomy: Technique and long-term results. Laryngoscope 100:286–289, 1990