Clinical Predictors of Diabetes Insipidus After Transcranial Surgery for Pituitary Adenoma

Songquan Wang[1-3], Deling Li[1-3], Ming Ni[1-3], Wang Jia[1,2], Qing Zhang[1-3], Jue He[1-3], Guijun Jia[1-3]

■ OBJECTIVE: **Diabetes insipidus (DI) is a well-known complication of transsphenoidal pituitary adenoma surgery. However, the risk factors for DI after transcranial surgery have not been clarified. In this study, the clinical parameters for predicting DI after transcranial surgery were investigated.**

■ METHODS: **The perioperative records of 90 patients who underwent transcranial (TC) surgery at the authors' institution between November 2011 and March 2013 were chosen from 1657 patients with pituitary adenoma and retrospectively analyzed. The degree of deformation of the third ventricle and hypothalamus were assessed by preoperative magnetic resonance imaging.**

■ RESULTS: **Immediate postoperative DI was found in 30 patients (33.3%). Persistent DI was noted in 11 patients (12.6%). Compared with patients in the nonpostoperative DI group, those with postoperative DI had a higher degree of deformation of the third ventricle and hypothalamus ($P < 0.001$). In a binary logistic regression analysis, the degree of deformation of the third ventricle and hypothalamus (odds ratio [OR], 3.079; 95% confidence interval [CI], 1.600–5.925; $P = 0.001$) had a significant positive correlation with immediate postoperative DI, as well as postoperative hemorrhage (OR, 6.235, 95% CI, 1.457–26.689; $P = 0.014$). Postoperative hemorrhage (OR, 4.363; 95% CI, 1.021–18.647; $P = 0.047$) showed a positive correlation with permanent DI, as well as the degree of deformation of the third ventricle and hypothalamus (OR, 2.336; 95% CI, 1.005–5.427; $P = 0.049$).**

■ CONCLUSIONS: **The degree of deformation of the third ventricle and hypothalamus assessed by preoperative magnetic resonance imaging may help to predict postoperative DI. Postoperative hemorrhage might increase the incidence of postoperative DI, whether it is immediate postoperative DI or permanent DI.**

INTRODUCTION

Diabetes insipidus (DI) is a common complication after pituitary adenoma resection. Surgical manipulation in the areas of the posterior pituitary, pituitary stalk, hypothalamus, and infundibulum may cause disturbances in arginine vasopressin (AVP) secretion,[1,2] which could lead to transient or permanent DI. Polyuria and uncontrolled excretion of dilute urine are 2 hallmarks of the clinical manifestations, which, if not treated, increase patients' serum sodium and serum osmolality levels. These conditions potentially develop into dehydration, lethargy, irritability, and, in the case of severe hypernatremia, seizures.[1,3]

Pituitary adenoma treatments include medicine and surgery. Prolactin adenomas can be treated mainly by dopamine agonists[4,5]; the other adenomas must be removed by surgery. There are 3 main surgical approaches to resect pituitary adenomas: the microscopic transsphenoidal (TS) approach, endoscopic TS approach, and transcranial approach. Because most pituitary

Key words
- Diabetes insipidus
- Pituitary adenoma
- Postoperative hemorrhage
- Transcranial surgery

Abbreviations and Acronyms
AVP: Arginine vasopressin
CI: Confidence interval
CT: Computed tomography
DI: Diabetes insipidus
GH: Growth hormone
GTR: Gross total resection
MRI: Magnetic resonance imaging
OR: Odds ratio
TS: Transsphenoidal
TSS: Transsphenoidal surgery

From the [1]Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing; [2]China National Clinical Research Center for Neurological Diseases (NCRC-ND), Beijing; and [3]Beijing Key Laboratory of Brain Tumor, Beijing, China

To whom correspondence should be addressed: Guijun Jia, M.D., Ph.D. [E-mail: jiaguijun2013@163.com]

Songquan Wang and Deling Li contributed equally to this work.

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adenomas can be removed through the TS approach, whether using the microscopic or endoscopic TS approach, the particular nature of DI after TSS and detailed information regarding patients and surgery-specific risk factors have been elucidated. Postoperative DI in these patients is mostly transient and benign; permanent DI, reportedly resulting from more proximal damage to the pituitary stalk and cell bodies in the hypothalamic nuclei, occurs in about 0%–8.8% of patients.[6,7] However, the transcranial approach still plays a role in about 1%–10% of giant adenomas.[8-10] These giant pituitary adenomas, which must be resected through a transcranial approach, often damage the pituitary stalk and hypothalamus. Reports of patients with postoperative DI after the transcranial approach are rare. Thus, we chose to review these patients in our hospital to understand the real risk factors for postoperative DI. This retrospective cohort encompasses data from 90 patients who underwent transcranial surgery, thus representing the largest cohort in recent studies.

PATIENTS AND METHODS

Patients and Transcranial Surgery Indications

In the Department of Neurosurgery at Beijing Tiantan Hospital, 1657 patients with pituitary adenoma underwent surgery between November 2011 and March 2013. Among these patients, we chose the perioperative records of 90 patients who achieved tumor resection via transcranial surgery. All patients included in this series underwent transcranial pituitary tumor resection performed by a single team of experienced neurosurgeons in Beijing Tiantan Hospital. The postoperative follow-up was conducted at 3 months, 6 months, and then every 1 year after surgery. The mean follow-up period was about 44 months (range, 36–55 months). The institutional review board of Beijing Tiantan Hospital approved this study.

In 1657 cases, 1567 patients received TSS to resect a pituitary adenoma, including 244 cases through an endoscopic TS approach. However, some patients' tumors had the following features considered to be unfavorable for a TS route: 1) tumor predominantly located in the suprasellar area and/or the sella turcica was too narrow and small, 2) dumbbell-shaped or hourglass-shaped tumors with a constriction at the level of the opening in the diaphragma sellae, 3) asymmetric subfrontal and/or retrosellar tumor extension, 4) middle fossa tumor extension, 5) encasement of subarachnoid arteries, 6) tumor predominantly within the cavernous sinus, 7) brain invasion with cerebral edema, and 8) previous surgery and/or radiation therapy. When patients had 1 or more of these features, we decided to use a transcranial approach.

Radiologic Measurements

Preoperative magnetic resonance imaging (MRI) of the sellar region was acquired through T1-weighted sequences with and without gadolinium enhancement, and through T2-weighted sequences. The largest vertical, transverse, and anteroposterior diameters of the tumor in the coronal and sagittal planes were measured in a subsequent analysis. The degree of deformation of the third ventricle and hypothalamus was modified from a criteria for craniopharyngioma[11] and graded as follows: degree 0, tumors were mainly located in the sellar region and under the hypothalamus, and the structure of the third ventricle and hypothalamus was complete and identifiable; degree 1, tumors expanded into the third ventricle but it was still identifiable, with no hydrocephalus, and the complete structure of the hypothalamus could not be found; degree 2, severe deformation of the third ventricle and hypothalamus, the normal structures could not be identified, and hydrocephalus could be seen on MRI (Figure 1). The postoperative radiologic examination was performed within 1 week. Gross total resection (GTR) was defined as a residual tumor not visible on postoperative MRI scans. Subtotal resection was defined as a residual tumor that was less than 10% of the preoperative volume, and partial removal was defined as >10% of the tumor was left behind.[12] The volume of tumor was estimated approximately by the formula (vertical diameter × transverse diameter × anteroposterior diameter)/2. We also collected the postoperative computed tomography (CT) scans 4 hours after the operation to judge which patients had postoperative hemorrhaging. We did not use any blood products in the sella and we performed careful hemostasis. When postoperative CT scans showed a high-density shadow in the operating area, we considered a postoperative hemorrhage to have occurred. The finding of high-density material in the sellar or parasellar area is usual after any cranial surgery and does not always mean that an important bleed has occurred. However, we believed that blood in the manipulation area might cause vasospasm, which could affect the blood supply in the hypothalamus area, whether the blood was derived from active bleeding or not. Thus, we applied a stricter criterion for postoperative hemorrhaging than we ever had previously.

Clinical Parameters

A database was created for the 90 patients who underwent transcranial surgical resection of a pituitary adenoma. Pertinent information, including demographic data, surgical pathologic findings, surgical blood loss, and complications were entered into the database. For the evaluation of preoperative anterior pituitary function, basal plasma levels of cortisol, growth hormone (GH), thyroid-stimulating hormone, triiodothyronine (T3), thyroxine (T4), luteinizing hormone, follicle-stimulating hormone, prolactin, testosterone, estradiol, and progesterone were measured. Serum electrolyte levels, fluid intake, and urine output and urine specific gravity were recorded daily in the hospital after surgery, and these data were then evaluated at 3 months, 6 months, and every 1 year after surgery. In patients with increased urine output (>300 mL/hour for 3 hours), serum electrolyte levels, urine output, and urine specific gravity were measured more closely (about twice daily). Patients without signs of adrenal insufficiency were given low-dose steroids to mitigate the stress of surgery (80 mg of hydrocortisone orally twice daily for 2 days postoperatively). Patients with signs of adrenal insufficiency preoperatively were given suitable doses of steroids to correct the insufficiency.

DI was defined as daily urine output greater than 5000 mL in the absence of glycosuria and diuretics combined with urine specific gravity less than 1.005.[13,14] Those who were diagnosed with DI were treated with a synthetic analogue of AVP, desmopressin (1-deamino-8-d-AVP; trade names, DDAVP, Stimate, and Minirin), which has a prolonged antidiuretic action and can be administered orally or intravenously.