Residual anterior pituitary function following transsphenoidal resection of pituitary macroadenomas

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A series of 84 patients with pituitary adenomas greater than 1 cm in diameter is presented. Full preoperative and postoperative endocrine evaluations were carried out, and the effects of transsphenoidal surgery on remaining anterior pituitary function were analyzed. Of the patients who had normal anterior pituitary function before surgery, 78% retained normal function after surgery. Thirty-three percent of those patients with pituitary deficits who did not have panhypopituitarism before surgery had improved function after surgery; 33% had worsened function after surgery. None of the patients with panhypopituitarism before surgery regained function after surgery. Transsphenoidal surgery carries an acceptable risk for sacrificing anterior pituitary function, but the risk is greater in patients with larger tumors and preoperatively compromised pituitary function.

KEY WORDS • transsphenoidal surgery • pituitary tumor • macroadenoma • prolactin • human growth hormone • endocrine testing

TRANSSPHENOIDAL microsurgery has been determined to be a safe and effective method for treating tumors of the pituitary gland. This method has afforded excellent results in treating hormone-secreting microadenomas, and has been effective in treating tumors of sufficient size to cause visual impairment secondary to mass effect.1,4,5,7,11-13 The purpose of this study was to examine the effects of transsphenoidal surgery on remaining anterior pituitary function following removal of tumors greater than 1 cm in size.

Clinical Material and Methods

Patient Population

Between April, 1972, and September, 1982, 84 patients, ranging in age from 19 to 78 years (mean age 44 years), underwent a total of 88 transsphenoidal procedures at the Medical College of Virginia for pituitary tumors greater than 1 cm in diameter. This group included 38 men and 46 women. Of this group, 36 had prolactin-secreting tumors, 15 had growth hormone (GH)-secreting tumors, and 33 had tumors without evidence of known endocrine activity (Table 1). All tumors were classified according to the grading system of Hardy:6 Grade I tumors being less than 10 mm in diameter and confined to the sella; Grade II tumors being greater than 10 mm in diameter but confined to the sella; Grade III tumors having focal sellar erosion; and Grade IV tumors having generalized sellar erosion. Seven patients had Grade II tumors, 14 had Grade III tumors, and 63 had Grade IV tumors. Suprasellar extension was evident in 84% of these patients. Four patients underwent repeat transsphenoidal surgery for residual tumor; the endocrine outcome of these patients was evaluated following the second operation only. Seven patients had been treated elsewhere by craniotomy, irradiation, or both.

Preoperative Studies

All patients underwent a complete endocrinological work-up prior to surgery. This included baseline thyroxine, triiodothyronine resin uptake, and thyroid-stimulating hormone (TSH) levels. The TSH reserve was measured (after 1977) using thyrotropin-releasing hormone stimulation. Adrenocortical function was determined by measuring baseline morning and afternoon serum cortisol levels and 24-hour urinary 17-hydroxycorticosteroid excretion. Adrenocorticotropic hormone (ACTH) reserve was measured by the metyrapone suppression test and insulin tolerance test. Prolactin function was determined (after 1974) by measuring morning
baseline levels along with chlorpromazine stimulation and L-dopa suppression testing. Baseline GH levels were measured, and stimulation during insulin tolerance testing and suppression following glucose loading were carried out. Gonadotropin function was tested by measuring baseline testosterone or estradiol levels and luteinizing hormone and follicle-stimulating hormone levels.

All patients underwent complete neurological, neuroophthalmological, and neuroradiological evaluation preoperatively. Neuroradiological testing included skull films, polytomograms of the sella turcica, angiography, and (before 1975) pneumoencephalography. After 1975, computerized tomography was performed on all patients.

**Surgical Procedure**

All patients were operated on by the transsphenoidal approach described by Hardy, using the operating microscope and intraoperative televised fluoroscopy. A wide bone exposure was carried out in all cases, and as radical a tumor removal as possible was accomplished. Delivery of suprasellar and parasellar extension of the tumor was facilitated by the Valsalva maneuver, with elevation of the intrathoracic pressure to 40 to 50 cm H$_2$O by the anesthesiologist.

Intraoperative tissue biopsies were used when necessary to help distinguish between tumor and normal gland. If the tumor appeared to be invasive, biopsies of the contiguous dura were made to identify normal pituitary tissue. A complete inspection of all surfaces and recesses of the tumor pseudocapsule was made before closure. We elected not to irrigate the tumor cavity with absolute alcohol, as recommended by others, but used moderately vigorous curettage for tumor removal. If no cerebrospinal fluid (CSF) leak was obvious, the operative site was packed with only Surgicel. If there was leakage of CSF, then the sella was packed with fascia lata, muscle, and Surgicel.

**Postoperative Management**

All patients were monitored neurologically and metabolically in the intensive care unit for 1 to 2 days postoperatively. All patients had repeat endocrinological, neurological, and neuroradiological evaluation 2 to 3 months after surgery, and endocrinological studies were repeated at 6-month to 1-year intervals thereafter. Most patients with residual tumor evident on follow-up radiological or hormonal studies underwent irradiation of the sella. The endocrine results presented in this paper were determined prior to the commencement of radiation therapy.

Management of hormone replacement following surgery was guided by the patient's preoperative endocrine status and by whether normal gland was seen intraoperatively. If patients had normal pituitary function preoperatively and if 20% or more normal-appearing gland was visualized intraoperatively, then steroids were tapered over 3 days unless the patient showed signs of adrenal insufficiency. If patients were receiving steroids before surgery or if the pituitary gland was thought to have been sacrificed during surgery, then an oral daily maintenance dose of 37.5 mg cortisone acetate was prescribed, and the patients were discharged. If they appeared to be doing well and if their thyroid function was intact on follow-up evaluation, then steroids were tapered under careful supervision. Thyroid function was used in this determination because it is usually compromised by mass lesions before adrenal function.

Need for thyroid and gonadal hormone replacement was determined during follow-up studies.

**Results**

**Endocrine Results**

Patients were categorized preoperatively into three groups for this study (Table 1). Group A patients had evidence of normal anterior pituitary function on the basis of intact pituitary-gonadal, pituitary-thyroid, and pituitary-adrenal axes on baseline and provocative testing; prolactin and GH reserve was not included in this definition. This group contained 44 patients. Group B patients had deficits in one or more axes but were not thought to have panhypopituitarism from their baseline and provocation testing results. There were 21 patients in this group. Group C patients were without evidence of anterior pituitary function and required total hormonal replacement. There were 19 patients in this group.
Pituitary function after transsphenoidal surgery

TABLE 3
Postoperative endocrine results in 21 preoperative Group B patients*

<table>
<thead>
<tr>
<th>Preop</th>
<th>Postop</th>
<th>No. of Cases</th>
</tr>
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<tbody>
<tr>
<td>improved</td>
<td>AR</td>
<td>normal</td>
</tr>
<tr>
<td></td>
<td>G</td>
<td>normal</td>
</tr>
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<td></td>
<td>T, G</td>
<td>[G]</td>
</tr>
<tr>
<td></td>
<td>T, G</td>
<td>normal</td>
</tr>
<tr>
<td>made worse</td>
<td>G</td>
<td>PHP</td>
</tr>
<tr>
<td></td>
<td>G</td>
<td>[G, T]</td>
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<tr>
<td></td>
<td>G, T</td>
<td>PHP</td>
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<tr>
<td></td>
<td>G, T, AR</td>
<td>PHP</td>
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<tr>
<td>unchanged</td>
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</tr>
<tr>
<td></td>
<td>G, T</td>
<td></td>
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<tr>
<td></td>
<td>G, AR</td>
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</tbody>
</table>

* [G = decreased pituitary-gonadal function; | T = decreased pituitary-thyroid function; | AR = decreased adrenocorticotropic hormone reserve but not requiring steroid replacement; PHP = panhypopituitary; normal = normal pituitary function.]

Of the 44 preoperative Group A patients, 33 (75%) continued to have normal function on postoperative evaluation. Two additional patients were lost to follow-up review but were believed on clinical grounds to have normal function. The remaining nine patients (21%) were made worse by surgery: six acquired panhypopituitarism; two had isolated gonadal deficiency; and one was hypothyroid and had decreased ACTH reserve, but did not require steroid replacement (Table 2).

Of the 21 patients who were in Group B preoperatively, seven (33%) were improved, seven were unchanged, and seven were made worse endocrinologically by surgery (Table 3). Of the patients improved by surgery, two had deficits in one axis only prior to surgery: one was hypogonadal, and one had decreased ACTH reserve. Both returned to normal after surgery. Three patients were hypogonadal, hypothyroid, and had decreased ACTH reserve (but did not require steroids) before surgery. All three had return of the pituitary-thyroid axis only. Of two patients who were hypothyroid and hypogonadal preoperatively, one had return in thyroid function and the other had return in both axes.

Seven Group B patients were made worse by surgery. Three were hypogonadal only before surgery; one of these was also made hypothyroid and two acquired panhypopituitarism. One additional patient was hypogonadal, hypothyroid, and had diminished ACTH reserve before surgery; he also acquired panhypopituitarism. All seven Group B patients who were unchanged following surgery were hypogonadal before surgery. One was also hypothyroid and one had decreased ACTH reserve preoperatively.

Group C contained 19 patients. All of them had panhypopituitarism and showed no evidence of improvement of anterior pituitary function following surgery.

Loss of anterior pituitary function following surgery was examined in relation to tumor grade. All seven patients with Grade II tumors were in Group A, and none lost pituitary function. Twelve of the 14 patients with Grade III tumors were in Group A or B, and two (16%) were made worse by surgery. Thirty-two of the 63 patients with Grade IV tumors were in Group A or B, and 14 (43%) were made worse. Of 11 Group A or B patients who acquired panhypopituitarism, 10 had Grade IV tumors.

Early Surgical Results

Total gross tumor removal was considered to have been achieved if patients lacked evidence of residual tumor on follow-up radiographic or endocrinological studies. Residual tumor was believed to be present in the prolactinoma patients if postoperative prolactin levels were above 25 ng/ml. Residual tumor was thought to be present in acromegalic patients if the postoperative GH was above 5 ng/ml. The non-secreting tumors were considered extirpated if a total removal was believed to have been obtained at surgery and if no tumor was evident clinically or radiographically on follow-up evaluation. Table 4 shows the results of this series.

Four patients underwent repeat transsphenoidal exploration for residual tumor. Two were patients with prolactinomas and two were acromegalic patients. Only one, a patient with acromegaly, improved after the second procedure.

Complications

There were two deaths in this series. One was the result of an internal carotid artery hemorrhage, and one was from congestive heart failure in an acromegalic patient 6 weeks following surgery. There were six cases of temporary CSF leak, one fractured maxilla, and two ocular nerve palsies (one third nerve and one fourth nerve palsy). There were four cases of permanent diabetes insipidus.

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Discussion

Preservation of anterior pituitary function following transsphenoidal surgery for pituitary adenomas can be expected in most cases. Faria and Tindall\(^4\) reported a series of 97 patients with prolactinomas of all sizes who had complete preoperative and postoperative testing. They found that pituitary function was preserved in 77% of patients with normal preoperative function. Of the patients with deficits in one axis or more preoperatively, 37% improved and 6% worsened. McLanahan, \(et \al.\)^\(^9\) reported on 40 patients with tumors of all types and of varying sizes. They found that of the 12 patients with tumors less than 1 cm in size who had normal pituitary function, all retained normal function after surgery. Of the 10 patients with normal pituitary function and tumors between 1 and 2 cm in size, two were made worse. They had only one patient with normal pituitary function before surgery with a tumor greater than 2 cm in size, and function was retained.

Baskin, \(et \al.\),\(^1\) reported a series of acromegalic patients undergoing transsphenoidal surgery. They found that only 9% of patients not previously treated by other modalities had hypopituitarism as a result of the surgery, but that 60% of those treated previously had panhypopituitarism after surgery. Laws, \(et \al.\),\(^7\) reported a series of 82 patients operated on for acromegaly with both small and large tumors. They found worsening of function after surgery in 15 patients.

Our results of anterior pituitary function preservation following surgery on tumors greater than 1 cm in size demonstrate that preoperative pituitary function is the most important criterion for predicting postoperative function. With larger tumors, however, there is a greater likelihood for the worsening of pituitary function following surgery. Our finding that none of the hypopituitary patients regained function is not surprising and agrees with the series of McLanahan, \(et \al.\)^\(^9\). Of interest are recent reports of the significant decrease in size of prolactinomas treated with bromocriptine\(^10\) and a report of significant return in pituitary function in a patient with a large prolactinoma treated with bromocriptine.\(^8\) Bromocriptine may be a useful adjunct to surgery on large tumors and may improve the chance of regaining pituitary function.

Regarding pituitary function, we conclude that transsphenoidal surgery is a safe technique for managing larger pituitary tumors. It carries a risk of sacrificing remaining anterior pituitary function that is not unlike that reported in series describing smaller tumors. The risk of sacrificing function is greater for patients with impaired preoperative function and for patients with larger tumors. Patients with large adenomas should undergo pituitary endocrinological testing preoperatively. Postoperative hormonal replacement therapy should be given only when necessary, and be individualized according to the patient's specific hormonal deficiencies.

References


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