Transsphenoidal microsurgical management of Cushing's disease

Report of 100 cases

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The development of transsphenoidal microsurgery and the refinement of endocrinological and radiological diagnostic procedures have afforded therapeutic options appropriate to the individual case in patients with hypercortisolism. The present series of 100 cases is derived from 104 patients with the diagnosis of Cushing's disease who underwent transsphenoidal pituitary exploration between 1974 and 1981. Excluding four patients in whom the pituitary gland was not exposed because of intraoperative technical difficulties, an overall cure rate of 78% was achieved. Among 71 patients with tumors confined to the sella turcica, 87% had correction of their hypercortisolism, 11% represented therapeutic failures, and one patient had tumor recurrence. In contrast, among 25 patients with extrasellar extension, correction of hypercortisolism was achieved in only 48%, 40% failed to respond, and 12% of the patients had recurrence. Four patients who failed to respond to total hypophysectomy have ectopic sources of adrenocorticotropic hormone.

The results indicate that transsphenoidal microsurgical exploration for a basophilic adenoma is the procedure of choice in adults and children with Cushing's disease. The diagnostic and surgical approach to these tumors, as well as pitfalls in the transsphenoidal treatment of Cushing's disease, are discussed.

KEY WORDS • Cushing's disease • hypercortisolism • pituitary tumor • transsphenoidal microsurgery • basophilic adenoma

Cushing's disease is a serious endocrinopathy characterized by hypersecretion of adrenocorticotropic hormone (ACTH) by the pituitary, together with the resulting bilateral adrenocortical hyperplasia and chronic hypercortisolism. Although the etiology of Cushing's disease is still debated, pituitary tumors are estimated to be present in at least 60% of patients with this disorder. In our experience, the frequency of pituitary adenomas is even higher. We report the results of management by transsphenoidal microsurgery in a series of 100 patients with the diagnosis of Cushing's disease.

Clinical Material and Methods

Patient Population

Between February, 1974, and October, 1981, 104 patients who were diagnosed as having Cushing's disease underwent transsphenoidal microsurgical exploration of the sella turcica at the University of California, San Francisco. Of these, 86 patients were females and 18 were males. The clinical features of these patients are summarized in Table 1.

The average age of patients at the time of surgery was 35 years. Nineteen patients had the onset of disease during childhood or adolescence, and 13 of these patients had surgery before the age of 20 years. Nine patients had undergone unsuccessful pituitary irradiation, and three had recurrent Cushing's disease after presumed bilateral total adrenalectomy. The average duration of disease at the time of surgery was 5 years (range 4 months to 28 years).

Four patients have been excluded from this case analysis for reasons explained later. For the remaining 100 patients, the average length of follow-up review has been 4.6 years; the range is from 20 months to 9.2 years. Over 90% of the patients have been followed for more than 2.5 years.
TABLE 1
Clinical features of 100 patients with Cushing's disease*

<table>
<thead>
<tr>
<th>Feature</th>
<th>Percent</th>
<th>Feature</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>obesity</td>
<td>91</td>
<td>headache</td>
<td>21</td>
</tr>
<tr>
<td>hypertension</td>
<td>63</td>
<td>pigmentation</td>
<td>18</td>
</tr>
<tr>
<td>hirsutism</td>
<td>59</td>
<td>edema</td>
<td>15</td>
</tr>
<tr>
<td>bruising</td>
<td>54</td>
<td>growth arrest</td>
<td>10</td>
</tr>
<tr>
<td>mental disturbance</td>
<td>47</td>
<td>kidney stones</td>
<td>10</td>
</tr>
<tr>
<td>menstrual/libido</td>
<td>46</td>
<td>infections</td>
<td>9</td>
</tr>
<tr>
<td>stria</td>
<td>46</td>
<td>hypokalemia</td>
<td>8</td>
</tr>
<tr>
<td>myopathy</td>
<td>34</td>
<td>insomnia</td>
<td>7+</td>
</tr>
<tr>
<td>diabetes mellitus</td>
<td>32</td>
<td>alopecia</td>
<td>6+</td>
</tr>
<tr>
<td>acne</td>
<td>32</td>
<td>galactorrhea</td>
<td>5</td>
</tr>
<tr>
<td>plethora</td>
<td>31</td>
<td>ketoacidosis</td>
<td>2</td>
</tr>
<tr>
<td>osteoporosis</td>
<td>29</td>
<td>neuropathy</td>
<td>2</td>
</tr>
<tr>
<td>fatigue</td>
<td>25</td>
<td>heart failure/cardiac</td>
<td>2</td>
</tr>
</tbody>
</table>

* Ulcer, renal cyst, syncope, hypokalemia, galactorrhea, visual symptoms, heat intolerance, diarrhea, and sweating were each a clinical feature in 1% of cases.

Endocrinological Procedures and Findings

Preoperatively, the evaluation of patients suspected to have Cushing's disease began with verification of sustained hypercortisolism. When possible, determinations of the morning and evening levels of cortisol in plasma and the 24-hour free-cortisol level in urine were obtained when the patient was admitted to the hospital. The diagnosis was routinely established by: 1) the demonstration of non-suppressibility of steroids in plasma and/or urine by the administration of low-dose dexamethasone, but at least 50% suppressibility with high-dose dexamethasone; and 2) the finding, in the presence of hypercortisolism, of measurable (usually normal or slightly elevated) levels of ACTH in plasma, as determined by immunoassay techniques.

In most cases, 24-hour levels of keto- and 17-hydroxycorticosteroids in urine were measured to obtain baseline levels and to monitor the response to suppression tests. Late in the series of patients, if the etiology of the hypercortisolism was in question, selective venous sampling of plasma ACTH was performed.

All patients were given exogenous steroids on the day of surgery; the dosage was tapered to maintenance levels within 10 days after surgery. In the early postoperative period, a maintenance dosage of dexamethasone was substituted for hydrocortisone for 24 hours, so that baseline morning and evening levels of cortisol in plasma could be assessed. At 6 weeks after their transphenoidal operation, patients had their first routine follow-up visit. Fifty-three of the patients were followed endocrinologically in our General Clinical Research Center (GCRC); the rest were followed by their referring physicians.

Endocrinological remission was defined as: 1) the resolution of symptoms and signs of hypercortisolism; 2) the return of plasma ACTH and cortisol levels to normal; and 3) the return of normal cortisol suppression after the administration of low-dose dexamethasone. In all but one of the patients who were believed to be in remission and who were tested in our GCRC, return of the normal diurnal variation in ACTH and cortisol secretion was observed. As described elsewhere, prolonged suppression of the pituitary-adrenal axis was routinely noted in the patients who were in remission.

Radiological Procedures and Findings

The preoperative radiological evaluation included polytomography of the sella turcica and thin-section computerized tomography (CT), with sagittal and coronal reformations, of the sellar region. The latter was the primary preoperative radiological study. Metrizamide cisternography with CT was used, when indicated, to evaluate unusual suprasellar and parasellar extension and to help differentiate a low-density adenoma from a partially empty sella.

Carotid angiography proved to be generally uninformative and was deleted from the preoperative evaluation, as was pneumoencephalography when high-resolution CT scanning became available. Abdominal ultrasonography, iodocholesterol scanning, CT of the adrenal glands, and adrenal arteriography were used selectively.

In 30% of patients, preoperative radiological studies revealed no abnormality; and in 25% of cases, at least one radiological study was believed to be misleading. In some cases, incidental abnormalities of bone that were demonstrated on polytomography could not be explained by the intraoperative findings; the same was often true of variations in pituitary gland attenuation that were visualized on CT. Pars intermedia cysts that were thought preoperatively to represent adenomas but, at the time of surgery, appeared unrelated to a coexisting pituitary adenoma were demonstrated in the CT evaluation of four patients. In a fifth patient, now believed to have an ectopic source of ACTH secretion, a pars intermedia cyst that was thought preoperatively to be an adenoma was visualized on the preoperative CT scan. Overall, however, CT scanning provided the most reliable information on the sella turcica and its contents. The most frequent finding was a focal area of decreased attenuation.

When indicated, percutaneous transfemoral selective venous sampling for ACTH was performed. Sites from which ACTH samples were obtained to compare to a peripheral venous sample were the inferior petrosal sinus, jugular bulb, thyroidal veins, and the superior and inferior vena cava.

Surgical Pathology and Results

The operative procedure described previously was performed by one surgeon (C.B.W.). In consenting adults, a total hypophysectomy was performed if no abnormal tissue was identified during the transphenoidal exploration. For children and young adults in whom no tumor was found, postoperative irradiation or medical therapy was recommended instead of hypophysectomy.
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Five patients, who were operated on early in the series, represented technical therapeutic failures because dural venous sinus bleeding prevented exposure of the pituitary gland. Four of these patients have been excluded from this case analysis, although one was subsequently cured by cryohypophysectomy. The fifth patient, who is included in this analysis, underwent a second transsphenoidal exploration after undergoing an unsuccessful course of pituitary irradiation.

During the first transsphenoidal exploration of the 100 patients included in this analysis, 85 selective adenomectomies and 12 total hypophysectomies were performed (Table 2). Three patients in whom no abnormality was demonstrated intraoperatively underwent exploration only. One of these three was a child, and the other two were young adults who declined total hypophysectomy. Cushing’s disease has persisted in all three of these patients.

Nine patients underwent a second transsphenoidal procedure. In two of these cases, the procedure was for the repair of postoperative cerebrospinal fluid (CSF) leaks. In three patients who had a second exploration after they failed to respond to interim irradiation, severe scarring prevented adequate exploration of the sella turcica contents and total hypophysectomy. One patient had a second exploration because the disease recurred after a 4-year remission following selective adenomectomy. The remaining three patients had had a good clinical response to selective adenomectomy; however, they still had laboratory evidence of persisting disease. During their second exploration, two of these patients underwent a total hypophysectomy, and the third a hemihypophysectomy. All three have enjoyed long-term remission of disease.

Histological verification of a pituitary adenoma was not obtained in 18 cases. In the 82 patients with histologically confirmed tumors, 60 harbored microadenomas and 22 had macroadenomas. In 66 patients, the tumor could be localized to a primarily right- or left-sided location. Eleven patients had a midline tumor: two of these were confined to the neurohypophysis and intermediate lobe. In 23 patients, there was either bilateral tumor or no tumor, or the location of origin was undetermined. Four patients had pars intermedia cysts in addition to their adenomas. The average diameter of all tumors was 5 mm. Routine histological examination showed that the majority were chromophobe adenomas. Tumors that were evaluated by immunofluorescence or ultrastructural techniques revealed cells with characteristics of corticotrophs. No cases of diffuse hyperplasia were demonstrated.

Overall, 78 patients responded to surgery: 71 to selective microsurgery and seven to total hypophysectomy (Table 2). Of those who responded initially, four patients (all of whom had a selective adenomectomy) had a recurrence of disease. Four of the 22 patients who failed to respond to surgery are believed now to have an ectopic source of ACTH.

Table 3 summarizes the results in relation to the size and extent of the tumor. Of 60 patients with a histologically confirmed microadenoma, 55 (92%) have had long-term remission, and one patient (2%) has had a recurrence. Three of the four patients with microadenoma whose disease persisted had lateral extrasellar extension of their tumor that prevented adequate surgical resection. In contrast, only 10 (45%) of the 22

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Results of pituitary microsurgery in 100 cases of Cushing’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedures &amp; Results</td>
<td>No. of Cases</td>
</tr>
<tr>
<td>selective microsurgery</td>
<td>67</td>
</tr>
<tr>
<td>correction of hypercortisolism</td>
<td>4</td>
</tr>
<tr>
<td>persistence of disease</td>
<td>14</td>
</tr>
<tr>
<td>recurrence of disease</td>
<td>3</td>
</tr>
<tr>
<td>exploration only</td>
<td>4</td>
</tr>
<tr>
<td>total hypophysectomy</td>
<td>100</td>
</tr>
<tr>
<td>correction of hypercortisolism</td>
<td>7</td>
</tr>
<tr>
<td>persistence of disease</td>
<td>1*</td>
</tr>
<tr>
<td>ectopic source of ACTH</td>
<td>4</td>
</tr>
</tbody>
</table>

* Posterolateral extrasellar extension precluded adequate resection of tumor.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Surgical outcome in relation to size, extension, and histological confirmation in 100 patients with Cushing’s disease*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size &amp; Confirmation</td>
<td>Tumor Grade</td>
</tr>
<tr>
<td>microadenomas</td>
<td></td>
</tr>
<tr>
<td>positive histology</td>
<td>I-O</td>
</tr>
<tr>
<td>I-A</td>
<td>3</td>
</tr>
<tr>
<td>I-E</td>
<td>1</td>
</tr>
<tr>
<td>III-O</td>
<td>2</td>
</tr>
<tr>
<td>subtotal</td>
<td>55</td>
</tr>
<tr>
<td>negative histology</td>
<td>I-O</td>
</tr>
<tr>
<td>I-A</td>
<td>2</td>
</tr>
<tr>
<td>EO</td>
<td>0</td>
</tr>
<tr>
<td>subtotal</td>
<td>8</td>
</tr>
<tr>
<td>total microadenomas</td>
<td>63</td>
</tr>
<tr>
<td>(86)</td>
<td>(13)</td>
</tr>
<tr>
<td>macroadenomas</td>
<td></td>
</tr>
<tr>
<td>positive histology</td>
<td>II-O</td>
</tr>
<tr>
<td>II-A to E</td>
<td>1</td>
</tr>
<tr>
<td>III &amp; IV</td>
<td>2</td>
</tr>
<tr>
<td>subtotal</td>
<td>10</td>
</tr>
<tr>
<td>negative histology</td>
<td>II-A</td>
</tr>
<tr>
<td>total macroadenomas</td>
<td>11</td>
</tr>
<tr>
<td>(48)</td>
<td>(39)</td>
</tr>
<tr>
<td>ectopic source of ACTH</td>
<td>0</td>
</tr>
<tr>
<td>series total</td>
<td>74</td>
</tr>
<tr>
<td>(74)</td>
<td>(22)</td>
</tr>
</tbody>
</table>

* Numbers in parentheses are percentages. Tumor grading according to Wilson, et al.22 EQ = explored only; ACTH = adrenocorticotropic hormone.

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patients with a confirmed macroadenoma had remis-

sion following surgery; in three patients, the disease
recurred. Like the three patients with microadenoma
whose disease persisted, all of the nine (41%) patients
with a confirmed macroadenoma who failed to respond
to surgery had extrasellar extension of their tumor.

In 71 of the 96 patients considered to have a pituitary
adenoma (82 confirmed; 14 not confirmed), it was
believed, based on observations made at surgery, that
the tumor was confined to the sella turcica (Table 4).
As noted earlier, four of the 100 patients probably had
an ectopic source of ACTH. The other

patient, who did not suppress endogenous steroids after the
administration of high-dose dexamethasone. In three of
these, the decision to explore the pituitary was based
on the presence of what was thought to be significant
sellar radiological abnormalities, however, pituitary exploration was under-
taken. Two of the three had selective removal of their
microadenomas. The other patient responded to total
hypophysectomy, although a tumor was not demon-
strated histologically. All three patients have had remis-
sion of disease.

Unusual Patient Subgroups

Three patients failed to meet the endocrinological
criteria for exploration, as they demonstrated suppress-
sibility of steroids in response to the administration of
low-dose dexamethasone. Because of the severity of
their symptoms and the presence of radiological abnor-
malities, however, pituitary exploration was under-
taken. Two of the three had selective removal of their
microadenomas. The other patient responded to total
hypophysectomy, although a tumor was not demonstrated histologically. All three patients have had remis-
sion of disease.

Pituitary exploration was undertaken in six patients
who did not suppress endogenous steroids after the
administration of high-dose dexamethasone. In three of
these, the decision to explore the pituitary was based
on the presence of what was thought to be significant
sellar radiological abnormalities. However, all three
failed to respond to total hypophysectomy and are now
believed to have an ectopic source of ACTH. The other
three, evaluated later in the series, underwent selective

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TABLE 4
Results of transsphenoidal microsurgery in patients with
intrasellar tumors and with extrasellar extension

<table>
<thead>
<tr>
<th>Factor</th>
<th>Intrasellar Tumors</th>
<th>Extrasellar Extension</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>Percent</td>
<td>No.</td>
</tr>
<tr>
<td>no. of patients</td>
<td>71  100</td>
<td>25  100</td>
</tr>
<tr>
<td>correction of hyper-cortisol</td>
<td>62  87</td>
<td>12  48</td>
</tr>
<tr>
<td>selective adenomectomy</td>
<td>55  77</td>
<td>12  48</td>
</tr>
<tr>
<td>total hypophysectomy</td>
<td>7   10</td>
<td>0</td>
</tr>
<tr>
<td>failures</td>
<td>8   11</td>
<td>10* 40</td>
</tr>
<tr>
<td>selective adenomectomy</td>
<td>8†  11</td>
<td>9  36</td>
</tr>
<tr>
<td>total hypophysectomy</td>
<td>0   0</td>
<td>1‡  4</td>
</tr>
<tr>
<td>recurrence</td>
<td>1§  1</td>
<td>3  12</td>
</tr>
<tr>
<td>selective adenomectomy</td>
<td>1   1</td>
<td>3¶  12</td>
</tr>
<tr>
<td>total hypophysectomy</td>
<td>0   0</td>
<td>0</td>
</tr>
</tbody>
</table>

* Includes three patients who underwent debulking procedures only.
† Selective adenomectomy or exploration only.
‡ Incomplete because of posterolateral extrasellar extension.
§ Patient had remission after a second surgical procedure.
¶ All patients with childhood onset.


t Selective adenomectomy or exploration only.

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TABLE 5
Complications of pituitary microsurgery in 100 cases of
Cushing's disease

<table>
<thead>
<tr>
<th>Complications</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>myocardial infarction</td>
<td>2</td>
</tr>
<tr>
<td>CSF leak with meningitis</td>
<td>2*</td>
</tr>
<tr>
<td>sinusitis</td>
<td>2</td>
</tr>
<tr>
<td>diabetes insipidus</td>
<td>1</td>
</tr>
<tr>
<td>angiographic complication</td>
<td>1</td>
</tr>
<tr>
<td>postoperative visual disturbance</td>
<td>3</td>
</tr>
</tbody>
</table>

* Both patients had been irradiated preoperatively. CSF = cerebrospinal fluid.

Complications

Morbidity has been minimal in this series of patients,
many of whom were quite ill before treatment (Table 5). Two patients, however, died postoperatively (at 1
week and at 6 months, respectively) of myocardial
infarction. One patient whose tumor invaded the pitui-
tary stalk developed permanent diabetes insipidus, and
the patients who underwent total hypophysectomy had
panhypopituitarism. Two patients who had been irra-
 diated preoperatively developed postoperatively a CSF
leak that required reoperation for repair. One of the
patients with a CSF leak developed meningitis, a mycotic
carotid pseudoaneurysm, and optic nerve damage.
Postoperative visual symptoms developed in two other
patients. One, an interesting patient reported else-
where,10 developed pseudotumor cerebri with signifi-
cant visual signs 2 months after a successful pituitary
operation; the problem resolved when the steroid dos-
age was increased. The other patient, who had had
preoperative irradiation, developed signs of optic nerve
damage consistent with radiation injury several months
after surgery.

Unusual Patient Subgroups

Three patients failed to meet the endocrinological
criteria for exploration, as they demonstrated suppress-
sibility of steroids in response to the administration of
low-dose dexamethasone. Because of the severity of
their symptoms and the presence of radiological abnor-
malities, however, pituitary exploration was under-
taken. Two of the three had selective removal of their
microadenomas. The other patient responded to total
hypophysectomy, although a tumor was not demon-
strated histologically. All three patients have had remis-
sion of disease.

Pituitary exploration was undertaken in six patients
who did not suppress endogenous steroids after the
administration of high-dose dexamethasone. In three of
these, the decision to explore the pituitary was based
on the presence of what was thought to be significant
sellar radiological abnormalities. However, all three
failed to respond to total hypophysectomy and are now
believed to have an ectopic source of ACTH. The other
three, evaluated later in the series, underwent selective
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venous sampling preoperatively: the results of this procedure suggested a pituitary source of increased ACTH. One of these three was found to have both a pituitary and an adrenal adenoma; the other two had selective removal of their pituitary microadenoma. All three patients are in remission.

A total of four adults, all of whom failed to respond to total hypophysectomy, probably have an ectopic source of ACTH. All of these four had ACTH levels greater than 120 pg/ml and, surprisingly, one showed suppression in response to high-dose dexamethasone. In none of the four was abnormal tissue identified at the time of surgery or on histological examination of the excised pituitary gland. A presumed ectopic source of ACTH subsequently has been identified on CT body scanning in two patients: an enlarging lung nodule in one and a retroperitoneal mass near the head of the pancreas in the other. In the third patient, selective venous sampling has shown high levels of ACTH in the superior thyroidal veins. However, no mass was identified in either this or the fourth patient.

In addition to the four patients just described, pituitary tumor was not identified histologically in 14 others. Of these, four patients who had had a total hypophysectomy had remission of disease, as did four of seven who had a selective adenomectomy. The latter four patients had tiny soft tumors that provided insufficient material for pathological examination. The remaining three patients underwent surgical exploration only.

Thirteen of 19 patients with an early onset of disease (during childhood or adolescence) underwent surgery before the age of 20 years, and four of these had a recurrence an average of approximately 2 years after their operation. The average age at the time of recurrence was 22 years.

Discussion

Fifty years ago, Cushing reported 12 patients who had clinical manifestations of hypercortisolism. His postmortem demonstration of basophilic adenomas in six of eight patients studied implicated a pituitary etiology in the disease named in recognition of his initial description of this entity.

In our series of 100 patients, pituitary tumors were demonstrated histologically in 82% of cases. Moreover, the remission of disease in the patients who had a selective adenomectomy but no histological verification of tumor strongly suggests that, in these patients, adenomas were present but were lost in the process of exploration and removal. The presence of Crooke's hyaline changes in corticotrophs of excised normal anterior pituitary glands, the failure to demonstrate diffuse hyperplasia in cases of total hypophysectomy, and the high incidence of long-term remission (together with a low recurrence rate in patients entering remission after selective adenomectomy) further support a primary pituitary etiology in Cushing's disease. The exceptional report of Cushing's disease in association with an ectopic pituitary adenoma also supports the likelihood of the responsible defect being at the glandular level.11

As was observed in studies evaluating pituitary irradiation for the treatment of Cushing's disease,10,16 differences between adults and children in their response to therapy are noted after surgery, also. Whereas children appear to respond more favorably than adults to pituitary irradiation, three of the four recurrences in this series were in patients who had onset of disease before 20 years of age. The average age of these three patients at recurrence was 22 years. In addition, the only patient in remission known to lack the normal diurnal variation in plasma cortisol belongs to this group,* as does one of the patients who had surgical exploration only and a patient whose 2-mm adenoma was confined to the neurohypophysis. The excellent response to surgery of the other patients under 20 years old, however, seems to limit speculation about the significance of the differences between the response of adults and children to surgical intervention.

Concerning prognosis, Lamberts, et al. recently proposed that there are two types of ACTH-secreting pituitary adenomas: 1) those that originate within the anterior lobe of the pituitary, and 2) those that originate from the intermediate lobe. These authors demonstrated the presence of neural tissue within the adenomas from six patients whose preoperative evaluation revealed good suppression of ACTH secretion by bromocriptine, but a decreased sensitivity to dexamethasone. They believed that these tumors originated from the intermediate lobe and were preceded by a hypothalamic-dependent hyperplastic lesion. Only one of the six patients responded to microsurgery. In light of these observations, we are reviewing our cases for the presence of neural tissue within adenoma specimens. It is possible that the young patients whose disease recurred and those patients who only underwent surgical exploration may have "intermediate lobe" lesions.

In this series, no correlation was noted between the histological characteristics, the size or location of the tumor, or the duration of severity of symptoms. There was also no relationship between these factors and prognosis unless lateral extension was also present. In fact, the primary predictor of adverse outcome to surgical management was lateral extrasellar extension of tumor. Prior pituitary irradiation was associated with increased scarring that, in some cases, interfered with surgical exploration or total hypophysectomy; prior irradiation also increased the likelihood of postoperative complications.

Despite the many pitfalls to accurate diagnosis, the decision to explore the pituitary gland should be based solely on endocrinological criteria. Selective venous sampling should be carried out, along with CT body scanning, whenever there is a doubt about the accuracy

* This patient since has undergone selective removal of a recurrent adenoma and is again in remission.

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of the diagnosis. The radiological findings should serve only to provide anatomical information once the diagnosis has been established. False-positive or false-negative findings and poor correlation with the surgical findings undermine the value of radiological procedures for diagnosis. Our current experience suggests that high-resolution CT scanning provides the most reliable anatomical information. We look for a discrete area of altered attenuation, upward convexity of the superior surface of the gland, and deviation of the pituitary stalk away from the side of the tumor.

Because the adenoma may occupy the posterior lobe, total hypophysectomy for Cushing's disease requires exenteration of the sella. The varied locations, the small average size, the occasionally semiliquid consistency of Cushing's adenomas, and their frequent resemblance to the neurohypophysis emphasize the need for a meticulous surgical exploration. If no pathological tissue is identified intraoperatively in an adult patient, the virtual certainty of cure and the low morbidity associated with the procedure, when compared with the serious consequences of persistent hypercortisolism, provide a compelling argument for total hypophysectomy.

Our results indicate that, if one excludes individuals in whom total hypophysectomy was not an option and those whose diagnosis did not meet strict endocrinological criteria, over 90% of patients with Cushing's disease will have a lasting remission following transsphenoidal microsurgery. We believe that transsphenoidal microsurgical exploration of the pituitary gland should be the primary treatment of all patients with Cushing's disease.

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References


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