Transsphenoidal microsurgical removal of 250 pituitary adenomas

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In a series of 250 pituitary adenomas, 72 (28.8%) were nonsecreting and 178 (71.2%) produced a hypersecretion syndrome: human growth hormone (83), prolactin (59), and adrenocorticotropic hormone (ACTH) (36). One-fifth had received prior treatment and one-fourth had visual impairment. The technical aspects of the transsphenoidal procedure are given with separate consideration of microadenomas and larger tumors. The results are provided in summary form with emphasis on the favorable outcome following removal of microadenomas. There was one postoperative death, and the complications observed after operation are presented.

KEY WORDS • pituitary tumor • pituitary microadenoma • acromegaly • Cushing’s disease • Nelson’s syndrome • Forbes-Albright syndrome • growth hormone • ACTH • prolactin

The transsphenoidal approach to pituitary tumors, introduced by Schloffer in 1907, was adopted by Cushing, who went on to develop the procedure within the limitations imposed by the era in which he worked. Despite the difficulty of operating in an unmagnified field under conditions of inadequate illumination, pituitary tumors could be removed easily by the transsphenoidal route, and initially the complications associated with the operation were considered acceptable, in view of the available alternatives. Interest in the transsphenoidal approach waned, however, as the transfrontal approach gained a wider acceptance because of its favorable results in relieving visual loss and the diminished risk of serious complications. To Guiot belongs the credit for reviving interest in transsphenoidal surgery. With the refinements in technique added by Hardy, the microsurgical transsphenoidal approach to pituitary tumors has now achieved widespread popularity.

The experience of one of us (C.B.W.), gained during the transsphenoidal removal of 250 pituitary adenomas (from July, 1970, to September, 1976), forms the background for this communication. This series of tumors will be reviewed with the following objectives: 1) to report the results obtained and the risks associated with the procedure; 2) to describe specific technical maneuvers adopted during the course of this experience; and 3) to indicate the emerging role of pituitary microsurgery in the management of secreting adenomas.

Clinical Material

Between June, 1970, and August, 1976, 250 patients underwent transsphenoidal operation for a pituitary adenoma; one-half of them were treated during the final 18 months. This review does not include transsphenoidal operations for Rathke’s pouch cyst, chor-
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doma, carcinoma of non-pituitary origin, craniopharyngioma, teratoma, abscess, and pituitary adenoma accompanied by abscess. During this period, six of these patients underwent transfrontal craniotomy for pituitary adenomas; in three of six patients, craniotomy was a secondary procedure. Fifty-four patients (21.8%) had received prior therapy. Most had received some form of irradiation alone (7.8%) or had undergone craniotomy followed by radiotherapy (7.8%). The remainder had undergone cryohypophysectomy alone (5.2%) or cryohypophysectomy and radiotherapy (1%), and one patient had been treated by all three methods.

Classification of Tumors

The classification of pituitary adenomas according to conventional histopathology using pituitary stains and light microscopy conveys limited and somewhat misleading information. Tumors composed of cells devoid of visible granules (chromophobe) can produce acromegaly, Cushing's disease, or the Forbes-Albright syndrome, although the term "chromophobe adenoma" has been used in the past to denote a nonsecreting (non-functioning) tumor. The inadequacy of light microscopy becomes evident when agranular tumor cells are studied by electron microscopy and specific immunohistochemical techniques. For example, the tumor removed from an acromegalic patient may be agranular by light microscopy, yet electron microscopy will demonstrate cytoplasmic granules of appropriate size, and immunohistochemistry will reveal growth hormone secretory granules. Conversely, the demonstration of hormone-specific secretory granules in a few, or even a majority, of tumor cells in any single tumor may not correlate with clinical hypersecretion of the hormone. The best example concerns prolactin. In many well documented instances, the presence of prolactin secretory granules and hyperprolactinemia are not accompanied by any recognizable clinical manifestations. This discrepancy between hypersecretion and overt clinical reflection of the hypersecretory state has several explanations, among which the requirement of certain endocrine preconditions and the production of a biologically imperfect (or incomplete) hormone are two likely possibilities.

To avoid confusion, as well as controversy, the tumors in our series are classified on the basis of clinical, as opposed to morphological, criteria. Tumors unaccompanied by any clinical manifestation of pituitary hypersecretion are designated nonsecreting. Secreting tumors, the other category, are classified according to the hypersecreted hormone and related syndromes as follows: growth hormone (HGH), producing acromegaly and gigantism; prolactin (PRL), producing amenorrhea and galactorrhea in females, and loss of libido, gynecomastia, and galactorrhea in males; and adrenocorticotropic hormone (ACTH), producing Cushing's disease and Nelson's (post-adrenalectomy) syndrome. In this series we encountered no example of adenomas secreting either thyrotropic (TSH) hormone or the gonadotropic hormones (GTH). By this system of classification, 72 (28.8%) were nonsecreting adenomas and, of the secreting adenomas, 83 (33.2%) were HGH-producing, 59 (23.6%) PRL-producing, and 36 (14.4%) ACTH-producing.

Radiographic Evaluation and Tumor Size

At the time of referral, the diagnosis of pituitary tumor had been established by one or more of the following findings: radiographic evidence of an abnormal sella turcica, endocrine evidence of pituitary hypersecretion, and diagnostic clinical manifestations of a hypersecretory state. As the initial procedure, biplane hypocycloidal polytomograms of the sella turcica were obtained to determine the location of focal changes produced by small tumors, to detect any extension of the tumor into the sphenoid bone and sphenoid sinus, and to define the anatomy of the sphenoid sinus. With the occasional exceptions noted later, all patients also underwent bilateral carotid angiography and pneumoencephalography. A few patients were referred with a current pneumoencephalogram in hand; some studies were of acceptable quality, others were repeated. Precise delineation of a tumor's superior surface is essential in virtually every case. Of comparable importance is the pattern of intrasellar air when a tumor is associated with a partially empty sella turcica; this is often, but not always, seen after prior treatment. The preceding requirements are satisfied by multi-

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...ple biplane polytomographic cuts at 2-mm intervals.

Bilateral carotid angiograms provide limited but invaluable information. Preoperative knowledge of unsuspected disease and anomalies in the cavernous course of the carotid arteries justifies the small risk of the procedure in competent hands. The basal view detects lateral extension of the tumor. Cavernous sinus phlebography, an alternative method for defining the lateral surface of an intrasellar mass, has been used rarely except in the following three situations: failure to opacify a carotid artery, proptosis, and clinical involvement of the cavernous sinus.

The relatively small size of the adenomas in this series, as compared with others, reflects the high proportion (71.2%) of secreting adenomas. Discounting slight superior bulging of the sellar diaphragm, almost one-half (48.4%) of these tumors were confined to the sella; within this group, 86% had a diameter of 1 cm or less. Significant suprasellar extension was observed in 34.8%, sphenoidal (infrasellar) extension in 17.6%, and both suprasellar and infrasellar extension in 6.8%.

Exceptions to the preceding sequence of diagnostic studies were made in three patients who had the following features in common: advanced and progressing loss of vision in both eyes, an enlarged sella turcica, a computerized tomography (CT) scan demonstrating a large, contrast-enhancing suprasellar mass, and an age of over 80 years. For these patients, we reasoned that the potential morbidity from angiography and pneumoencephalography was comparable to that from transsphenoidal exploration, and operation was undertaken with this understanding. In all three cases, the tumor proved to be a pituitary adenoma. Satisfactory removal was accomplished in each instance. The diagnostic accuracy of current CT scanning justifies an occasional deviation from the usual preoperative evaluation under special circumstances. These exceptional cases are rare (three of 250 cases) and, given this situation, the operation should be undertaken only by a surgeon who has had considerable experience.

Additional Preoperative Evaluation

In the present series, detailed preoperative endocrine studies were performed in patients with secreting tumors and in many patients with nonsecreting tumors. For the patient without clinical manifestations of pituitary hypersecretion, the preoperative endocrine evaluation can be restricted to the testing of target organ function for purposes of replacement therapy. The endocrine assessment of patients harboring secreting tumors should be detailed. Particularly in the case of Cushing's disease and the Forbes-Albright syndrome, expert endocrinological evaluation is required to identify conditions that mimic secreting pituitary adenomas. On the basis of diagnostic endocrine profiles, microadenomas have been removed from perfectly normal sellae in a small number of patients with Cushing's disease and the Forbes-Albright syndrome, and we anticipate wider acceptance of this practice. A full account of the preoperative and postoperative endocrine findings will be provided in subsequent papers dealing with individual hypersecretory states.

Neuro-ophthalmological testing revealed visual field deficits in 60 patients (24%), only 28 (11.2%) of whom had visual symptoms. Impairment of extraocular muscle function was detected in 12 patients (4.8%), all of whom were symptomatic. The details related to the visual system have been reported separately.

The Transsphenoidal Approach

Indications and Contraindications

In our view, the transsphenoidal approach to pituitary adenomas is the procedure of choice in the operative treatment of adenomas confined to the sella turcica, tumors associated with cerebrospinal rhinorrhea, pituitary apoplexy, and tumors with sphenoidal extension. Transsphenoidal removal is favored for tumors accompanied by paracentral scotoma because this field deficit usually indicates retrochiasmal extension, a pre-fixed optic chiasm, and a tumor that is difficult to remove by means of the standard subfrontal approach. It provides an attractive alternative to craniotomy for patients in suboptimal general health due to advanced age and concurrent serious medical conditions. In the treatment of adenomas with moderate suprasellar extension, transsphenoidal removal is an alternative to the transfrontal approach and, in our experience,
involves fewer major and minor complications than craniotomy. Unless a contraindication exists, we have selected a transsphenoidal approach when any earlier therapeutic effort has failed.

Contraindications to the transsphenoidal approach are as follows:

1. Dumbbell-shaped adenomas constricted at the diaphragma sellae contraindicate the transsphenoidal approach because visualization and safe sphenoidal delivery of a suprasellar mass require a wide sellar aperture.
2. Lateral suprasellar extensions, although uncommon, cannot be visualized through a midline operative field and should be approached by craniotomy.
3. A massive suprasellar tumor cannot be handled adequately with the limited exposure afforded through the sphenoidal sinus. The usual suprasellar mass causing chiasmal compression presents no problem because normal intracranial pressure, aided by the pulsation of surrounding cerebrospinal fluid (CSF), forces the suprasellar component downward into the expanded sella.
4. Finally, an incompletely pneumatized sphenoid is a relative contraindication to the transsphenoidal approach.

Preoperative Preparation

For 48 to 72 hours before the day of operation, the patient receives Neo-synephrine (1/4%) and bacitracin (1000 units/cc) nose drops. Hydrocortisone (100 mg) is given by mouth on the evening before operation and 100 mg is injected intravenously at the same time as a general anesthetic is administered. We no longer administer antibiotics preoperatively for two reasons: first, almost all cultures of sphenoid mucosa removed and submitted routinely at operation are either sterile or grow normal respiratory flora and non-pathogenic bacteria; second, only one of the patients undergoing transsphenoidal operation as a primary procedure developed meningitis, and she had received ampicillin pre- and postoperatively.

Operative Procedure

The procedure is carried out in the manner described by Hardy. If the tumor extends above the sella, then the third ventricle and suprasellar cisterns are filled with air introduced through an indwelling lumbar subarachnoid catheter. Fluoroscopic monitoring and direct visualization with the operating microscope (300 mm objective, × 12.5 magnification eyepieces) guide all maneuvers performed after the sphenoid sinus has been entered.

The anterior wall of the sella is perforated with an air drill; then, using small punches, bone is removed from the tuberculum sellae superiorly to the floor inferiorly, and laterally to each medial edge of the cavernous sinus. With bipolar forceps, the exposed dura is coagulated around its periphery and excised to permit maximum exposure of the sellar contents.

Intrasellar Adenomas

Tumors having a diameter of 5 mm or less are seldom visible at the exposed surface. Most small tumors occupy a lateral lobe, and polytomograms usually indicate the tumor's position (left or right, anterior or posterior). Further, the sella may exhibit focal bulging and thinning as a guide to the neighboring adenoma. If the tumor's location is not apparent, the initial maneuver is a horizontal incision carried to the pars intermedia and dividing the anterior pituitary into upper and lower halves.

The small adenoma of Cushing's disease may occupy the posterior lobe, as has been seen in one of our cases and in one of Cushing's original cases. For HGH- and PRL-secreting adenomas, the second maneuver is a vertical incision into each lateral lobe carried to the pars intermedia; for ACTH-secreting tumors, a midline vertical incision has a higher probability of disclosing the adenoma. Finally, the remaining vertical incisions are made to complete the total of one horizontal and three vertical incisions.

Adenomas are discrete and, while consistency and color may vary, ordinarily the distinction from normal anterior pituitary tissue is unequivocal. Although distinction from the posterior lobe may be difficult, confirmation by frozen section will be decisive. Multiple incisions into the anterior pituitary have not produced detectable impairment of function.

Larger intrasellar tumors present little problem in exposure, except for certain PRL-secreting adenomas that occupy the lateral angle at the base of the dorsum sellae and frequently burrow into the body of the
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Sphenoid bone. Adequate exposure of these tumors requires removal of the ipsilateral sellar floor and subjacent cancellous sphenoid bone.

All gross tumor is removed under X 16 or X 25 magnification. Since the boundary between tumor and normal gland is distinct, we do not obtain frozen sections of grossly normal tissues. When the tumor is confined to the sella, and if the cavity does not communicate with the subarachnoid space, Gelfoam soaked in absolute alcohol is packed into the cavity to destroy any remaining microscopic nests of tumor cells. This is repeated for a total exposure to alcohol of 6 to 10 minutes. Although alcohol penetrates the exposed surface of the normal gland, the depth of penetration must be slight because we have observed no detrimental effect on pituitary function.

Packing of the remaining cavity varies according to the tumor's superior surface in relation to the sellar diaphragm. If removal of the tumor has exposed the diaphragm or arachnoid, fascia lata is placed over this surface and held in place with fat and Surgicel, the latter serving to maintain the mobile fat in position. Alternatively, fat without fascia is used to fill the cavity. In the event of a frank leakage of CSF, a second piece of fascia lata is placed over the anterior dural opening before closing the sella with a piece of septal cartilage. Removal of muscle causes a painful thigh, and the use of fat has proved equally satisfactory. A piece of cartilage carved to cover the sellar opening is slipped inside the dural edges in the case of larger tumors, or is placed extradurally beneath the bone edges in the case of smaller tumors. After the anesthesiologist briefly elevates intrathoracic pressure to verify adequate exclusion of CSF, the cartilage graft and surrounding bone are covered with a thin layer of biologic adhesive.

Adenomas with Suprasellar Extension

The lumbar spinal subarachnoid catheter, used to inject air at the onset of the operation, is retained by the anesthesiologist to control the position of the suprasellar tumor and its "capsule" (a thin layer of tissue composed of thinned and stretched dura, arachnoid, and compressed pituitary gland). The surgeon must visualize the entire undersurface of the suprasellar capsule. This presents no problem with tumors of modest suprasellar proportions because the capsule is forced into the sella by the slightly increased intracranial pressure associated with general anesthesia. If the suprasellar capsule does not descend as removal of the intrasellar tumor proceeds, as is sometimes the situation after pneumoencephalography, the anesthesiologist can inject small increments of normal saline into the subarachnoid catheter until intracranial pressure forces the suprasellar tumor into the operative field. Less often, the capsule falls to the bottom of the excavated sella, obscuring the tumor's posterior extension above and behind the dorsum sellae. In this instance either hyperventilation or withdrawal of CSF will elevate the capsule to allow visualization of any tumor remaining in a posterosuperior direction. A dental mirror is used for inspecting all surfaces of the cavity remaining after removal of larger tumors and, with practice, one can obtain an excellent view of otherwise inaccessible areas.

Two or more silver clips are attached to the midportion of the suprasellar capsule for two purposes: first, as a guide to avoid excessive packing of the sella; and second, as a marker to follow in the early postoperative period for hematoma, and later on for regrowth of tumor.

Bacitracin solution is used frequently during the procedure to irrigate the operative field. After a final irrigation the speculum is removed, the sublabial incision is closed with catgut sutures, and both nasal cavities are packed gently with Vaseline gauze coated with bacitracin ointment.

Adenomas with Extension into the Sphenoid Sinus

With surprising frequency, small nodules of tumor perforate the dura and bone to lie within the sphenoid sinus, rarely within the body of the sphenoid bone, covered only by mucosa. These small extensions can be removed cleanly and without difficulty. Massive extensions into the sinus are difficult and sometimes impossible to remove completely, and the deficient sellar walls make orientation difficult. When tumors that recur after radiotherapy have extended into the sphenoid sinus, we have used alcohol without any ill effects. Otherwise, the probability of residual tumor in the sphenoid sinus is an indication for appropriately directed postoperative radiotherapy.
Postoperative Management

In uncomplicated cases, the dose of hydrocortisone, initially 100 mg/day, is reduced quickly to full replacement (25 mg/day) and is maintained at that level until normal adrenal function is established, usually at the time of scheduled endocrine evaluation in 6 weeks or at the completion of radiotherapy. Pitressin (aqueous) is administered as required. Most patients take fluids by mouth within 12 hours and may engage in unrestricted activity. Nasal packs are removed in 48 to 72 hours. The mean period of hospitalization has been 7.6 days.

Postoperative Radiotherapy

Postoperative irradiation has been recommended in all cases of nonsecreting tumors, as well as in cases of known residual tumor. Postoperative radiotherapy can be, and usually has been, withheld if removal of the tumor was grossly complete and postoperative values of a secreted hormone are within normal limits. In addition, we are following a small number of patients with grossly removed PRL-secreting adenomas whose postoperative endocrine state is normal, except for slightly elevated PRL values, because we are uncertain as to the significance of this slight residual abnormality. To date, no patient in this group has shown any further elevation of PRL values and, in several instances, serial values indicate a progressive return toward normal.

Summary of Cases

Results will be described without providing detailed data. A full presentation of endocrine studies is beyond the scope of this communication; these details are presented elsewhere.4,20,23,24

Impaired Vision

Visual field deficits were documented in 60 patients, and acuity was impaired in 26 (43.3%) of them. Abnormalities of ocular motility were found in 12 patients (4.8%). The majority (65%) of field defects were produced by nonsecreting tumors and, as expected, 80% of all abnormal fields represented some variation of bitemporal hemianopsia.

In the early postoperative period, visual fields either returned to normal or improved in 40 patients (66.7%). The visual fields were unchanged in 19 patients at the time of their discharge from the hospital. In a single patient who had presented with rhinorrhea 9 years after craniotomy and radiotherapy, vision deteriorated 48 hours after operation. At last follow-up examination (3 weeks after operation), his vision was only slightly impaired relative to the fixed preoperative deficit and was improving. Five patients (41.6%) recovered fully from preoperative extraocular palsies. Late postoperative recovery of vision will be reported subsequently.

HGH-Secreting Adenomas

We have analyzed the preoperative and postoperative endocrine status of 25 patients evaluated in our Metabolic Research Unit.24 For all patients, transsphenoidal adenectomy was the initial therapy for active acromegaly. The mean age was 42 years with a mean duration of symptoms of 6.7 years. The mean preoperative HGH value was 49 ng/ml. Pneumoencephalography established suprasellar extension in eight cases, three of which were associated with visual field defects.

Postoperatively, 23 patients (92%) had HGH values in the normal range (less than 10 ng/ml). In both patients whose postoperative HGH values were reduced but remained elevated above normal, the preoperative values exceeded 150 ng/ml. Only one patient developed hypopituitarism as a result of the operation, whereas normal gonadal function was restored in two of the three patients with preoperative hypogonadism. All complications were transient: diabetes insipidus,8 syndrome of inappropriate antidiuretic hormone (ADH) secretion,1 CSF leak,1 and diplopia.1 Observation extending up to 6 years, with annual re-evaluation, has given no indication of tumor recurrence.

Endocrine data were less detailed for some of the remaining patients harboring HGH-secreting adenomas, but of particular interest were 18 patients who had received prior therapy. By endocrine criteria, transsphenoidal cures were effected in all four patients with prior radiotherapy; in five of 10 patients with prior cryosurgery, with or without added radiotherapy; and in only one of four patients with prior craniotomy, with or without postoperative radiotherapy. From this experience, we have concluded that prior radio-
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therapy does not affect the likelihood of successful transsphenoidal tumor removal at a later time, whereas invasive intrasellar procedures (cryosurgery and craniotomy) create anatomical distortion and greatly reduce the prospects for a successful secondary transsphenoidal operation.

Two acromegalic patients died of complicating heart disease, one 6 weeks and the other 2 1/2 years after operation.

Prolactin-Secreting Adenomas

These tumors fall into two main categories with a few intermediate forms. The larger category contains the microadenomas (3 mm to 9 mm), which cause the Forbes-Albright syndrome of amenorrhea and galactorrhea. Chang, et al.,4 have analyzed 34 patients evaluated by our Reproductive Endocrinology Group (the majority of PRL-secreting adenomas coming to operation). Of the 17 patients with microadenomas, 16 were either menstruating or pregnant 1 year after operation, and their galactorrhea had ceased. Except for hydrocortisone in the early postoperative period, none received supplemental hormones.

The second category includes larger tumors characterized by marked expansion of the sella, suprasellar extension, dural erosion with sphenoidal extension, or invasion of the cavernous sinus and orbit. Results in this group were poor, with cures in only two of seven patients treated by operation alone.

Two males, a child and an adult, both with gynecomastia and galactorrhea, harbored tumors that produced symptomatic hyperprolactinemia. The child had a microadenoma and was cured by operation.26 The adult’s large tumor was not completely removed.

ACTH-Secreting Adenomas:
Cushing’s Disease

Twenty of the 23 patients with Cushing’s disease underwent transsphenoidal exploration. Two patients are not included in this series because in both instances exploration was impossible due to large dural venous sinuses. When the same situation was encountered in a third patient, the tumor was destroyed by applying a cryoprobe to the partially exposed anterior lobe. In another patient the adenoma was not identified after thorough exploration and, by prior agreement, the entire pituitary gland was removed and sectioned serially. The pathologist identified a 1.5 mm basophilic adenoma.

Sixteen patients harbored microadenomas. Hypercortisolism was cured in all of these patients; normal pituitary function was preserved in 15 of them. The two patients undergoing cryohypophysectomy and surgical hypophysectomy were cured, but at the cost of panhypopituitarism.

One patient took her own life on the evening before scheduled admission. Upon sectioning the pituitary gland, the coroner identified a 3-mm adenoma.

ACTH-Secreting Adenomas:
Nelson’s Syndrome

The typical tumor in patients with Nelson’s syndrome has been large and often invasive. In this group of 18 patients, only two have achieved postoperative values of ACTH in the normal range. One patient died as a consequence of massive infratentorial extension and the remainder have active tumors, despite irradiation either before or after operation. The poor results obtained in treating these biologically aggressive tumors argue for the surgical removal of microadenomas from patients with Cushing’s disease, and total hypophysectomy for those with Nelson’s syndrome, when the tumor is confined to the sella.

Complications

The single death occurred in a patient who had a large suprasellar tumor and deteriorating vision after two earlier courses of radiotherapy and craniotomy. Hospitalization was prolonged because of postoperative meningitis, and he died of massive pulmonary embolism.

Complications are summarized in Table 1. Visual complications among patients with normal preoperative vision and ocular motility were infrequent; only one patient experienced postoperative visual impairment. She had a huge, intrasphenoid, prolactin-secreting tumor without significant suprasellar extension. Postoperative bilateral visual loss prompted evacuation of an intrasellar hematoma. Her vision improved and became functionally adequate, but examination at the time of discharge revealed slightly impaired
TABLE 1
Mortality and morbidity during the 6-week postoperative period

<table>
<thead>
<tr>
<th>Mortality &amp; Morbidity</th>
<th>Cases (%)</th>
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<tr>
<td>mortality</td>
<td>0.4</td>
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<tr>
<td>major morbidity</td>
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<td>early CSF leak</td>
<td>4.4</td>
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<tr>
<td>late CSF leak</td>
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<tr>
<td>extraocular muscle palsy</td>
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<tr>
<td>pneumonia</td>
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<tr>
<td>bacterial meningitis</td>
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<tr>
<td>increased field deficit (transient*)</td>
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</tr>
<tr>
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<td>1.2</td>
</tr>
<tr>
<td>mental change</td>
<td>1.6</td>
</tr>
<tr>
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<tr>
<td>false aneurysm</td>
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<tr>
<td>minor morbidity</td>
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<td>transient partial ADH insufficiency</td>
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<tr>
<td>persistent partial ADH insufficiency†</td>
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</tr>
<tr>
<td>corneal abrasion</td>
<td>0.4</td>
</tr>
</tbody>
</table>

*Full recovery except in one patient with minimal defect still improving (see text).
†Only one of five patients required replacement beyond 6 months.

acuity and partial bitemporal field loss to red test objects.

Three patients acquired extraocular muscle palsies. Of these, one had a transient sixth nerve palsy, and one had a sixth nerve palsy that returned fully 1 year later. The third patient acquired an oculomotor palsy secondary to excessive packing of the sella; except for slight ptosis and mydriasis, recovery was complete within 3 months.

Among the 60 patients with impaired vision before operation, six acquired added deficits. In three cases the delayed appearance of monocular visual loss suggested edema of the optic nerve. In these cases, full recovery followed treatment with steroids but the cause and effect relationship remains open to question. Two patients developed intracapsular hematomas: after re-operation, vision returned to, and later improved beyond, preoperative levels. The sixth patient, who had preoperative rhinorrhea, has been discussed above in the section on patients with impaired vision.

The three postoperative hematomas were recognized and evacuated promptly, and each patient’s vision returned. Four elderly patients became confused after operation. Confusion was transient in two patients and persisted in two, one of whom improved after shunting of presumed occult hydrocephalus aggravated by operation. The other, who had a large suprasellar tumor accompanied by a mild organic mental syndrome preoperatively, remained confused; he was transferred to a convalescent facility, where he died later from a myocardial infarct.

One acromegalic patient developed a transient hemiparesis and oculomotor palsy (described above) due to overzealous packing of the sella; angiography demonstrated compression of the carotid artery.

A false aneurysm led to delayed epistaxis requiring emergency carotid ligation at another institution. During the course of the transsphenoidal operation for acromegaly, a large branch had been avulsed from the cavernous portion of the carotid artery; bleeding was controlled by packing. Postoperative angiography had failed to demonstrate any defect in the carotid artery.

Of the five patients with persistent total ADH insufficiency (requiring replacement therapy), only one had significant diabetes insipidus at the end of 6 months. The remaining complications indicated in Table 1 require no additional comment.

**Discussion**

Pituitary tumors present themselves in three different situations: 1) intrasellar secretory masses, 2) entirely intrasellar nonsecretory masses, and 3) masses with extrasellar extension.

Masses extending outside the sella, regardless of related endocrinological abnormality, are best handled by an operation followed by irradiation for incompletely removed tumors. While anatomic considerations should dictate the type of approach employed, in our own experience most of these tumors have been suited for transsphenoidal removal.

Intrasellar nonsecretory masses present a distinct diagnostic and therapeutic problem. At present, individual preference determines the choice among one of the following three possibilities: 1) observation for evidence of progression in size or the appearance of pituitary hypofunction, 2) irradiation, and 3) transsphenoidal or transfrontal operation.
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The uncertain outcome of irradiation without a histological diagnosis leads us to advise against this choice; in most cases, we have advised and performed transsphenoidal exploration. Following this practice, we have encountered a sterile abscess, benign non-neoplastic cysts, and several removable microadenomas.

Intrasellar secretory masses are identified as adenomas by their elaborated products, allowing an accurate diagnosis without histological confirmation. For such cases, four major therapeutic modalities are available: megavoltage irradiation,\textsuperscript{3,7,14,22} heavy particle irradiation,\textsuperscript{13,16} selective transsphenoidal resection,\textsuperscript{9,16} and cryohypophysectomy.\textsuperscript{1} Proponents of each modality cite comparable success rates. The relative advantages and disadvantages are matters for discussion, and are beyond the scope of this report.

Selective transsphenoidal removal of microadenomas has a high probability of accomplishing endocrine cure with preservation of normal pituitary function and an acceptable morbidity. The excellent results achieved with removal of microadenomas producing the Forbes-Albright syndrome and Cushings disease contrast with the significantly inferior outcome of operative removal combined with irradiation of both the large PRL-secreting adenomas and aggressive ACTH-secreting tumors in patients with Nelson's syndrome. The contrast argues forcefully for early transsphenoidal exploration. The increasing volume of patients referred with microadenomas reflects the endocrinologists' awareness that these small tumors can be identified, even in the presence of a normal sella turcica, and that transsphenoidal removal is an effective and acceptable form of treatment.

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