CT of the Sella Turcica after Transsphenoidal Resection of Pituitary Adenomas

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A retrospective review of 120 patients undergoing transsphenoidal surgery for pituitary adenomas revealed that computed tomography (CT) was less sensitive and less specific than hormonal methods in identifying residual functioning adenomas. However, CT was the only useful method of evaluating nonfunctioning tumors, including pseudoprolactinomas. Enlargement of the pituitary stalk, when seen on preoperative CT, was 100% predictive of "cure" if the enlargement returned to normal size on a remote follow-up scan (n = 8) and was 100% predictive of residual tumor if the enlargement persisted or evolved (n = 8). Resolution of stalk displacement was the next most reliable predictor of cure (91%, n = 11), but persistent displacement was less reliable than abnormal intrasellar enhancement in predicting the presence of residual tumor (71%, n = 28, vs. 81%, n = 26). Enhancement in the postoperative sella by other than normal pituitary gland was presumed to be due to inflammation in 19% of patients. Inflammatory enhancement was observed in the presence of autograft and homograft muscle plugs and, unlike enhancement due to untreated tumors, was observed to decrease in size and intensity with time. Intrasellar enhancement was an unreliable criterion of success or failure in cases of microadenoma. All 14 patients with functioning adenomas and preoperative parasellar tumor extension had persistent tumor at postoperative evaluation. Of the 47 patients with resected functioning adenomas who had CT scans showing empty or partly empty sellas after operation, 22 (47%) had hormonally detectable residual tumor.

During the last decade, advances in computed tomography (CT), transsphenoidal microsurgery, immunohistochemistry, and radioimmunossay have improved the management of patients with pituitary adenomas. Radioimmunossay of blood hormone levels has proved to be a more specific and sensitive indicator of the presence or the persistence of functioning (endocrine hypersecreting) adenomas after operation than CT [1] because the features of normal and abnormal postoperative CT often overlap. CT remains the most reliable method of evaluating nonfunctioning tumors. In this report, we compared CT in patients whose tumors were successfully resected with CT in patients who had residual or recurrent tumor by independent hormonal criteria and determined the relative merit of CT findings so that they could be usefully applied to nonfunctioning tumors that had no hormonal markers. To date, very little has been reported on these subjects [2].

Materials and Methods

General

At the Mayo Clinic between May 1979 and June 1983, 521 patients had transsphenoidal surgery to remove pituitary adenomas. From this group, patients were selected who met two criteria: (1) had pathologic verification of tumor type (92%) or endocrine evidence suggestive of hormonally active tumor that was not surgically evident or pathologically proved (8%) and (2) underwent high-resolution preoperative and postoperative CT scanning (GE 8800 and 9800). These criteria delineated a subgroup from which 120 (78 females and 42 males aged
8–82 years) were chosen so as to match (within 4%) the proportions of tumor types seen in the larger surgical series (fig. 1). The proportions of tumor types in our series closely match those reported by others [3]. Functioning tumors were present in 95 patients and nonfunctioning tumors in 25 patients. All 25 nonfunctioning tumors were macroadenomas (>1 cm), while 37 of the 95 functioning tumors were macroadenomas and 58 were microadenomas (≤1 cm) (fig. 1).

Clinical

For the 95 patients with functioning tumors, cures and noncures could be identified by hormonal levels, with provocative tests used to further evaluate borderline cases. This methodology has been described [4–6]. Cure for the 25 patients with nonfunctioning tumors was based on CT criteria that were developed from cases with functioning tumors. Patients with obvious noncures could be further treated with irradiation or bromocriptine (or both), and those with Cushing disease could be treated with bilateral adrenalectomy [7].

Surgical

Exact details of the surgical procedure have been described elsewhere [8–10], but factors affecting the postoperative CT appearance are summarized below. After the tumor was removed, in order to promote hemostasis, stop cerebrospinal fluid leaks, and seal the sellar floor, 91% of the sellae turcicae were packed with a plug of homograft muscle, 8% with an absorbable gelatin sponge (Gelfoam), and 1% with homograft fat. The plugs were usually supported by a stent of nasal septal bone (87%), cartilage (12%), or acrylic bone cement (11%). With macroadenomas, subarachnoid air was frequently introduced via a lumbar needle to prolapse the diaphragma sellae and the superior aspects of the tumor into the operative field. In 19 sellae, a surgical clip was placed, either for dural hemostasis to repair defects in the diaphragma sellae or as a marker to be followed on plain skull radiographs.

Eight patients had had prior operations (four transsphenoidal and seven transfrontal) and were seen with evidence of residual or recurrent tumor (3 weeks to 31 years later). Reexploration 0–39 days postoperatively was necessary in three other patients because of iatrogenic cerebrospinal fluid leaks.

Pathologic

In each case, the pituitary adenoma or the postoperative sellar contents were microsectioned and stained with hematoxylin and eosin, Gomori reticulin, and periodic acid-Schiff. Serial microsections were stained immunocytochemically by the peroxidase-antiperoxidase method, as described by Sternberger et al. [11]. Antisera to growth hormone, prolactin, adrenocorticotropic hormone (ACTH), follicle-stimulating hormone, luteinizing hormone, and thyroid-stimulating hormone were applied (Immukol, Carpenteria, CA). Pituitary glands that were normal at autopsy served as positive controls; substitution of specific primary antiserum with normal rabbit serum served as negative controls.

Because a nonfunctioning macroadenoma may falsly elevate the serum prolactin level by compressing the pituitary stalk (pseudoprolactinoma) [12], immunostaining was performed on the surgical specimens in all cases with elevated prolactin levels. Eight pseudoprolactinomas were identified, including six that presented as Forbes-Albright syndrome (amenorrhea-galactorrhea). Preoperative blood prolactin levels in these patients were as high as 85.5 ng/ml (normal, <23). Because the elevation of prolactin level in patients with pseudoprolactinomas is related to distortion of the pituitary stalk rather than intrasellar tumor, their cures can be defined only by CT.
Radiologic enhancement during the immediate postoperative period and scanning the tumors.

Hormone levels 16–18 in 8 were from preoperative bromocriptine therapy, which was discontinued postoperatively.

Most sellae were scanned with 3-mm slices at 3-mm intervals, although 1.5-mm slices with 1.5-mm intervals in the axial plane were used for reconstruction when direct coronal views could not be obtained.

A total of 369 CT scans were reviewed retrospectively: 136 preoperative and 233 postoperative. Intrasellar contents were evaluated for the presence of normal pituitary gland or for alterations from normal. The location, size, and pattern of any density or enhancement change, as well as the presumed cause (such as air, blood, hemostatic agents, bone, cartilage, muscle, fat, or tumor), were recorded. Suprasellar and parasellar structures, including the pituitary stalk, carotid siphon, cavernous sinus, suprasellar cisterns, optic chiasm, and the sphenoid sinus, were similarly evaluated, and the findings (including displacement and size) were recorded. The CT findings were separated into those seen during initial hospitalization and those seen later on follow-up scans.

Results

Clinical

Of the 95 patients with functioning adenoma, 48 (51%) were "cured" by surgery alone, whereas 45 (47%) had hormonal evidence of residual tumor. Of the 25 patients with nonfunctioning tumors (necessarily evaluated by CT criteria only), eight (32%) were cured by surgery and 10 (40%) had incomplete resection. The clinical status of seven patients with nonfunctioning and two with functioning tumors was indeterminate, pending follow-up CT or hormonal testing (fig. 3).

In general, about two-thirds of all patients with microadenoma and one-third of all patients with macroadename were cured by surgery alone. Of the 55 patients in whom surgery failed, 16 (29%) were further treated by irradiation, 15 (27%) by bromocriptine, and 13 (24%) by a combination of irradiation and bromocriptine. Three patients (5%) had persistent Cushining disease after operation and were treated with bilateral adrenalectomy, while eight (15%) other surgical failures were...
untreated either because the residual tumor remained indolent or because of the patient's age.

The maximal preoperative prolactin and growth hormone levels of 63 patients with prolactinomas and 17 with acromegaly were compared. Even without provocative testing, postoperative hormonal levels separated patients with cures from those with residual functioning tumors fairly well (fig. 4). Similar methods were used to identify success in patients with Cushing disease.

Fig. 6.—Bony stent was almost always seen (arrow) on early postoperative scans (day 4). Muscle plug, blood, and residual tumor often overlapped (B and C) and could not be distinguished without serial scans.

Surgical

The surgeon's impression of residual or grossly invasive tumor was generally accurate, in that 10 patients with functioning tumors said to be invasive at surgery and five with functioning tumors said to be incompletely resected had elevated hormonal levels postoperatively. However, 14 of 48 patients with tumors considered to be "completely" removed had hormonal evidence of residual tumor.
Fig. 8—Sequential early postoperative scans demonstrate decreasing attenuation of blood and reabsorption of air. Residual tumor is demonstrated on follow-up scans at 3½ months. Contrast medium would have added little in immediate postoperative period to identify residual tumor.

Fig. 9—After successful removal of ACTH microadenoma, low density (arrow) seen in sella at 2 weeks (A) but not at 15 months (B) may represent either Gelfoam (which contains air) or free air introduced at surgery. Sphenoid fluid level or debris, seen at 2 weeks, was a common finding in early postoperative period, and its subsequent disappearance was also typical.

Pathologic

A homograft muscle plug removed from a patient with a cerebrospinal fluid leak at 39 days histologically demonstrated early signs of an inflammatory reaction and fibrosis. Dense fibrous tissue with nonspecific chronic inflammation was found in the reoperated sellae of two other patients with diffuse intrasellar enhancement on preoperative CT. One patient had undergone transsphenoidal surgery elsewhere 5½ months before, and the sella was packed with autograft muscle (fig. 5), and the second patient had undergone transfrontal craniotomy and radiotherapy 16 months before.

Radiologic

The CT appearance of the sella after operation depended on the size of the tumor, amount of tissue resected, surgical technique, materials inserted into the operative site, interval since surgery, and postoperative therapy.

Early Postoperative Period (0–21 Days) (47 Patients)

Because most early scans were obtained without contrast medium, enhancing structures, such as the pituitary gland, pituitary stalk, residual tumor, carotid siphons, and cavernous sinus, could not be evaluated. In addition, meaningful conclusions regarding the optic chiasm and suprasellar cisterns were often impossible because of disturbance from surgical manipulation.

Alterations of intrasellar attenuation were increased by the bony stent; increased or isodense by blood, tumor, or muscle; and decreased by air, fat, or Gelfoam.

The septal bone stent was almost always evident on the axial scan as a linear or curvilinear calcific density (figs. 6 and 7). Hemorrhage occupied the tumor bed in 23 of 40 cases of macroadenoma but in only one of seven cases of microadenoma. In cases with serial studies, blood exhibited decreasing attenuation, regressing toward isodensity, even in this short (21 day) time span (fig. 8). The appearance of muscle plug, blood, and residual tumor ranged from hyperdense to isodense, and frequently these three entities could not be distinguished with a single examination (fig. 6).

Air was present in the tumor bed or subarachnoid space in 22 of 40 cases of macroadenoma but was not encountered in any of the seven cases of microadenoma. In almost all cases, detectable intrasellar air was reabsorbed within 21 days. In one case, postoperative deterioration of the muscle plug and seal was accompanied by a sudden increase of intracranial air and massive cerebrospinal rhinorrhea. Unlike intrasellar fat, air and Gelfoam were usually reabsorbed and not seen on later scans (fig. 9), with one exception (fig. 7).

All patients had alterations in the sphenoid sinus, with changes ranging from complete opacification to moderate membrane thickening. In one-fifth of the patients, fluid, debris, or occasionally bone fragments were evident (fig. 9).
Fig. 10.—ACTH macroadenoma at 9 (A) and 18 (B) months (6 and 15 months postirradiation, respectively). Typical decrease in contrast enhancement of residual tumor usually occurs 6–12 months after irradiation. Nonfunctioning adenoma at 6 (C) and 13 (D) months (3 and 10 months postirradiation, respectively). Persistent enlargement and displacement of stalk (arrows), despite decreased enhancement and size of residual tumor after irradiation.

Contrast enhancement was used in 11 of the 47 cases and enabled the detection of enlargement of the pituitary stalk (to a diameter equal to or larger than the basilar artery at the level of the dorsum sellae) in four cases (two with preoperative enlargement) and stalk displacement in one case (also present preoperatively). Contrast medium was of no particular help in evaluating the other structures.

Remote Postoperative Period (39 Days–56 Months) (108 Patients)

Findings (in order of prevalence) on the late follow-up CT scans of the 95 patients with functioning tumors included normal-appearing pituitary gland in 60, empty or partially empty sella in 47, displaced stalk in 28, enhancing intrasellar tissue other than normal gland in 26, enlarged stalk in 10, acromegalic soft-tissue changes in seven, and inferior migration of the optic chiasm in four.

Of the 60 patients with no enhancing tissue other than normal-appearing pituitary gland, 20 (33%) had residual tumor by hormonal criteria. About half of all patients (including 47 of the 95 with functioning tumors) had an empty or partly empty sella postoperatively. The secondary empty sella developed after resection of the functioning macroadenoma in 18 patients and after removal of a microadenoma in 29. Of the 47 patients, 22 (eight with empty and 14 with partially empty sellae) had hormonal evidence of residual tumor, even though most of them lacked evidence of tumoral enhancement.

Tumor enhancement, when seen, varied in character and could be described in different cases as diffuse, mottled, peripheral, focal, or nodular [14] (fig. 10). Such enhancement was absent in 17 (81%) of 21 cases of microadenoma and in three (15%) of 20 cases of macroadenoma, despite hormonal

<table>
<thead>
<tr>
<th>Finding</th>
<th>No. of Patients</th>
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<tr>
<td>Finding Present on Preoperative CT</td>
<td>Finding Improved on Postoperative CT</td>
</tr>
<tr>
<td>Cutis gyrata</td>
<td>4</td>
</tr>
<tr>
<td>Eye muscle enlargement</td>
<td>7</td>
</tr>
<tr>
<td>Pituitary stalk enlargement</td>
<td>7</td>
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Note.—Follow-up was 5 days to 42 months (mean, 16.7 months). No improvement in these features was seen in any of five other patients with residual tumor.

Fig. 11.—Because of normal prolactin levels after removal of prolactin microadenoma, we concluded that postoperative enhancement seen here at 17 months (A) was due to inflammation. B. Follow-up scan 10 months later. Decrease in enhancement is uncharacteristic of untreated tumor.
Acromegalic soft-tissue changes such as cutis gyrata (arrows) and enlargement of eye muscles and pituitary stalk were observed to disappear postoperatively in cured patients (see table 1).

Evidence of residual tumor. Surgical clips, which would have obscured any enhancement, were present in two of the latter three cases. Similar enhancement was seen about the floor of the sella near the homograft muscle plug in five (11%) of 46 patients in whom functioning tumors had been surgically "cured" and in the previously mentioned patient with an autograft muscle plug. Unlike neoplastic enhancement, this inflammatory change decreased in subsequent scans (fig. 11).

Displacement of the stalk from its usual midline position, seen preoperatively in 38 patients, persisted in 27 and disappeared in 11. Twenty of the 27 patients had residual tumor, as did one other in whom displacement evolved. By contrast, 10 of the 11 patients in whom stalk displacement disappeared were cured (four had microadenoma and six had macroadenoma).

Enlargement of the stalk, seen preoperatively in 12 patients, persisted in four and disappeared in eight. All four with persistent enlargement and four others in whom enlargement evolved had residual tumor. Again, contrast-enhanced studies revealed that all eight patients in whom the enlargement disappeared were cured (six had microadenoma and two had macroadenoma).

Of 37 patients with functioning macroadenoma, 14 had extension into the parasellar regions on preoperative CT examination, and none of the 14 was cured surgically. Of 11 patients with nonfunctioning macroadenoma, with similar ex-
tension preoperatively, seven were not cured and four had indeterminate outcomes pending follow-up CT. If the experience with functioning macroadenomas is applicable to these nonfunctioning adenomas, we would expect these four patients to have residual tumor.

Preoperative or postoperative nonsurgical therapy—radiation, bromocriptine, or a combination of the two—in addition to reducing the levels of prolactin and growth hormone [15], frequently caused a decrease in tumor enhancement and size, which was typically visible on CT 6–12 months after commencement of treatment (fig. 10). In general, the effects on enhancement were seen only with radiation or the combination-type therapies. All methods usually led to shrinkage of tumor bulk most strikingly demonstrated in prolactin microadenomas, which were radiologically detectable in only 33% of patients treated with bromocriptine preoperatively, compared with 75% of the patients without such treatment.

In acromegalic patients who were cured, soft-tissue changes, such as cutis gyrata and eye muscle or stalk enlargement, were observed to disappear postoperatively (table 1) (fig. 12). Other less frequent alterations seen in all tumor types included inferior migration of the optic chiasm associated with the postoperative empty sella and alterations in and about the bony stent. In one patient with residual tumor, the stent disappeared, whereas in four others, the stent appeared to act as the nidus for deposits of ectopic calcification, from which it was separated by a lucent zone in two patients (figs. 13 and 14).

Finally, surgical clips, present in 19 sellae, rendered CT indeterminate in most cases, even despite hormonal evidence of residual tumor in five.

Discussion

As a result of the selection criteria applied in this study, the observed cure rates were lower than those reported by Laws and coworkers [1, 6, 8–10, 16] for their overall surgical experience. Patients whose hormone levels returned promptly to normal after removal of a proved functioning tumor generally had persisting normalization of pituitary function. This was not necessarily true for patients with pseudoprolactinoma, whose decreased levels of prolactin may simply reflect an elimination of the mass effect. Residual functioning tumor was diagnosed by elevated blood hormone levels, even when tumor could not be resolved by CT. Furthermore, when preoperative levels of prolactin exceeded 400 ng/ml or growth hormone levels exceeded 90 ng/ml, surgery was uniformly unsuccessful at completely ablating the tumor (fig. 4).

To understand the postoperative CT changes within the sella, one must appreciate that certain foreign materials were implanted at surgery. Since in our patients the foreign material most often was homograft muscle, we initially assumed that CT enhancement observed in 11% of hormonally cured patients represented an inflammatory reaction due to tissue mismatch. We have, in fact, histologically documented such a response in the presence not only of homograft muscle but also of autograft (nonforeign) muscle (fig. 5). Therefore, we have concluded that CT enhancement in the absence of residual tumor is due in part to an inflammatory response to these tissues. Of the 26 cases with postoperative intrasellar enhancement, five (19%) were presumably due to inflammation and 21 (81%) to tumor. The fact that most muscle plugs were not observed to enhance may merely reflect a variability in the time course and severity of the inflammatory reaction, in addition to the possible effect of tissue mismatch.

The time course of various postoperative intrasellar changes has implications for optimizing the conduct of CT examinations. In the early postoperative period, intrasellar attenuation may be increased by blood, tumor, or muscle plug. Hemorrhage is of the most immediate clinical concern and cannot be distinguished from residual tumor on contrast-enhanced scans, so we have generally elected to use noncontrast CT. Intrasellar and subarachnoid air was normally present in many cases but was usually reabsorbed by 3
weeks after operation. Persistent or increasing amounts of air on serial scans beyond this time imply the presence of a fistulous communication and should be cause for concern.

Serial CT scans are valuable during the remote postoperative period to distinguish the usual progressive atrophy and fibrosis of a muscle plug—leading to a partly and then completely empty sella—from the persistence of tumor mass. If contrast medium is added, serial CT may also identify inflammatory enhancement that, unlike the enhancement of untreated residual tumor, decreases in size and intensity with time (fig. 11).

While untreated residual tumors may show increasing size and enhancement, the use of irradiation or bromocriptine postoperatively usually reversed these effects, with enhancement and size decreasing after irradiation or combination therapy and size alone affected by bromocriptine [17]. These effects were obtained 6–12 months after irradiation and considerably earlier after bromocriptine therapy. The substantial decrease in the CT detection rate of prolactin microadenomas before operation in patients treated with bromocriptine suggests that CT localization of microadenomas should be carried out routinely before bromocriptine therapy. The decreased enhancement after irradiation may be due in part to attenuation of the inflammatory response.

Enlargement or displacement of the pituitary stalk was correlated with the presence of functioning microadenoma and macroadenoma in cases of acromegaly, Cushing disease, and, to a lesser extent, prolactinoma. The enlargement of the pituitary stalk to a diameter equal to or greater than the basilar artery at the level of the dorsum sellae, if seen on preoperative CT, was 100% predictive of cure if the enlargement returned to normal on a remote follow-up scan and was 100% predictive of failure if the enlargement persisted or evolved. These findings did not apply to the immediate postoperative period (table 2).

Resolution of stalk displacement that was seen preoperatively was the second most reliable predictor of cure, but displacement that persisted or evolved postoperatively was less reliable than parasellar extension on preoperative CT or abnormal intrasellar enhancement in predicting the presence of residual tumor. The CT findings that were most predictive of curative surgical resection and failure are summarized in table 2. These observations should also be applicable to the evaluation of nonfunctioning tumors.

In addition to having enlargement of the pituitary stalk, acromegalic patients exhibited enlargement of other soft tissues: scalp (cutis gyrata) and extracranial muscles. When a surgical cure was attained, these alterations regressed on postoperative scans (fig. 12) (table 1).

In general, our surgical colleagues were correct in predicting persistent tumor if they observed gross tumor invasiveness. They also greatly assisted the radiologist by eschewing the use of intrasellar surgical clips (unless absolutely necessary). These metallic clips create CT artifacts, the most common cause of diagnostic difficulty. Of the patients with microadenoma, surgical cures were attained in 100% (seven of seven) of acromegalic patients, 77% (10 of 13) of patients with Cushing disease, and 50% (19 of 38) of patients with prolactinoma. These variations may reflect differences in detectability at surgery, bromocriptine pretreatment, or multifocality and diffuseness of some tumors.

Of 36 successfully resected microadenomas, 16 were seen on preoperative CT as positive-enhancing areas and eight as low-density areas, but 12 were not seen definitely. These areas correlated with tumor locations noted in the operative reports, and the abnormalities were absent on postoperative scans. The absence of abnormal enhancement postoperatively was not a reliable criterion of cure, however, in that 81% of residual functioning microadenomas lacked evidence of abnormal enhancement in the postoperative period. If the tumor extended into the parasellar region on preoperative CT, it was virtually always refractory to cure.

Tumor calcification was rarely seen, and although the bony stent varied in appearance with time, its true nature is obvious and should not be misidentified as a neoplastic deposit.

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