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Diagnostic Accuracy of Preoperative CT Scanning of Pituitary Prolactinomas

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Between 1980 and 1985, 102 patients (84 women and 18 men) who had coronal CT scans of the sella turcica for suspected prolactin adenoma underwent transsphenoidal exploration. The CT examinations were performed with a fourth-generation EMI scanner (CT 7070), and reports of the preoperative CT examinations were compared with the findings at transsphenoidal exploration. The same neurosurgeon performed all the operations. In 97 patients distinct adenomas were found at surgery, among which were 36 macroadenomas (diameter larger than 10 mm) and 62 microadenomas (one patient had two coexisting microadenomas). All macroadenomas were identified correctly on the preoperative CT scans. Preoperative CT scans correctly localized 58 microadenomas in 57 of 62 patients, for a sensitivity rate of 91.9%; this included correct localization in four patients with recurrent microprolactinomas and in the one patient with two coexisting adenomas. Three patients in whom the adenomas were found in a location other than that reported on the preoperative CT scan were considered to have false-negative scans for the purpose of statistical calculations; two other false negatives occurred in patients whose scans had been interpreted as entirely normal and who were subsequently found to have adenomas at operation. Four patients had negative surgical explorations and the preoperative CT scan was correct in one, for a specificity of 25%. The overall accuracy rate was 92.1% for the entire group of patients and 87.7% for the subgroup of microadenomas.

In our experience, coronal CT scanning has high diagnostic accuracy in patients with pituitary prolactinomas.

In recent years, high resolution CT of the sella turcica has almost completely replaced all other imaging techniques in the investigation of abnormalities of the pituitary gland. However, there is rather scant information about the diagnostic accuracy of this procedure with fourth generation equipment in regard to the identification of prolactin adenomas [1–7].

Over a period of 5 years, between 1980 and 1985, 102 patients who had coronal CT scans of the sella turcica for suspected prolactinoma underwent transsphenoidal exploration. We reviewed the findings in this group of patients to document the reliability of the CT imaging technique for identifying the lesion preoperatively.

Subjects and Methods

The patients included in this study were referred for CT examination of the sella turcica because of clinical and biochemical evidence of prolactin hypersecretion; all patients were evaluated by an endocrinologist prior to referral for CT scan examination, and causes of hyperprolactinemia such as pregnancy, medications, or primary hypothyroidism were excluded. Serum prolactin levels varied between 30 and 7000 ng/ml (normal <15 ng/ml) in the male patients, and between 40 and 3800 ng/ml (normal <25 ng/ml) in the female patients. The clinical presenting manifestations in this group of patients are shown in Table 1. Although secondary amenorrhea and galactorrhea in women and sexual dysfunction in men were the most common clinical features, several patients had more unusual presentations, such as arrested puberty, primary amenorrhea, and epistaxis from a voluminous tumor associated

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TABLE 1: Clinical Findings in Patient Population

Finding	Women (n = 84)	Men (n = 18)
Microadenoma	58	6
Galactorrhea	68	1
Amenorrhea	68	—
Amenorrhea/galactorrhea	54	—
1° amenorrhea	4	—
Oligomenorrhea	7	—
Gynecomastia	—	2
Decreased libido	11	9
Impotence	—	9
Impotence and/or decreased libido	—	14
Headache	15	5
Infertility	4	1
Arrested puberty	2	1
Visual defect	3	2
Epistaxis	—	1
Serendipitous detection	—	2

with a serum prolactin of 1050 ng/ml that filled the sphenoid sinus and protruded into the nose [8]. In two patients the problem first came to attention as sellar enlargement on X-ray films requested for investigation of sinusitis symptoms. The CT examinations were performed with a fourth-generation scanner (EMI CT 7070). The patients were placed on the scanner couch in the prone position with the neck hyperextended. The scanner gantry was angled 90° to a line connecting the outer canthus of the eye to the external auditory meatus (canthomeatal line) to obtain direct coronal views.

Technical factors were chosen so as to optimize image quality and contrast resolution while confining the examination time to a reasonable duration: 120 kVp, 80–99 ma, scan time 3 or 6 sec, slice width 3–5 mm, slice overlap 1 mm, scan wedge 250 mm. Slice width of 5 mm was used only for the macroadenomas and for 17 microadenomas that appeared obvious on the initial plain scans. For the other cases of microadenoma the slice widths used were 2 mm in four patients, 3 mm in 13, and 4 mm in 27, while in five cases this information is not available. The final pixel size was 0.22–0.31 mm. Scans were obtained both with and without contrast enhancement in each patient. After completion of the plain scans, contrast material was injected as a rapid bolus through an indwelling IV catheter and contrast-enhanced images were obtained immediately. Prior to August 1982, patients received 2.2 ml of 60% iothalamate (Conray-60) per kg body weight up to a maximum of 150 ml (about 42 g I maximum) given as rapidly as possible (usually 3–4 min) by hand injection through a 19-gauge butterfly needle. Forty-one patients were scanned in this manner. Subsequently, for cost considerations, the contrast material was changed to 76% diatrizoate (Renografin 76 or MD 76%) and the technique of contrast enhancement was modified. After the rapid injection of 30 ml of MD 76%, several slices were taken and then further aliquots of 15–20 ml were injected for every three slices, resulting in the administration of about 20 g I; 61 patients were examined with this modified technique after August 1982. With either technique the examination was usually completed within 20 min after the first bolus of contrast. There were no significant differences in the results for these two subgroups of patients.

Prolactin-secreting microadenomas were diagnosed by CT scanning as areas of low density within a contrast-enhanced pituitary gland. Hypodense areas were considered to be artifacts rather than adenomas if: (1) they had a linear shape and traversed adjacent extrasellar structures or (2) their size and shape corresponded to adjacent areas of dense bone, such as the junction of a sphenoid septum or lateral sphenoid wall to the floor of the sella turcica. Small changes in gland height or in the contour of the sellar floor alone were not considered to be diagnostic at the time of reporting for purposes of clinical management of the patients.

Data concerning interpretation of CT scans were gathered through a review of the reports that had been made by the examining neuroradiologist before the transsphenoidal surgical interventions. The neuroradiologists had access to clinical information such as history, physical findings, and results of biochemical tests, and they were able to see the patients while obtaining and interpreting the scans. Four patients had more than one CT scan before surgery. In these cases the study closest to the date of surgery was the one included in the series. Tumor size and location were assessed prospectively in all cases; data regarding gland height and contour, stalk position, bone changes, and slice width and incrementation were gathered retrospectively by reviewing the hard copies (films) of the examinations.

In patients with negative CT scans, the decision to proceed to surgery was based on findings of significant clinical problems attributable to hyperprolactinemia and unsatisfactory results with medical dopamine agonist therapy due either to unacceptable adverse effects or to insufficient prolactin-lowering effect at the maximum tolerated dose. All transsphenoidal explorations were performed by the same neurosurgeon. The size and location of the adenoma reported by the neurosurgeon and confirmed by pathology reports were taken as the standard against which the CT findings were compared.

Results

In 97 of the 102 patients distinct adenomas were found at surgery. CT scans of the 36 patients with macroadenomas all showed obvious changes in gland height, superior contour, stalk position, and appearance of the bone of the sella turcica. Macroadenomas were most commonly isodense with brain on the preinjection scans, and showed variable degrees of enhancement with contrast (25 cases). Nine macroadenomas were hypodense and poorly enhancing, one contained calcification (Fig. 1), and one was hyperdense on plain CT and enhanced moderately after administration of contrast material (Fig. 2). The latter tumor did not contain any fresh blood at surgery 2 days later, and grossly it was soft; but electron microscopy revealed, in addition to typical prolactin secretory granules, the presence of intra- and extracellular concretions. Five of the nine large hypodense tumors were found to contain areas of necrosis or hemorrhage at surgery, while four of the 25 isodense lesions contained such areas. Among the microadenomas, all of which were hypodense on CT scan, 11 were partially cystic, necrotic, or hemorrhagic at surgery.

Among the other 66 cases, midline gland height was 2 mm in five patients, 3 mm in five, 4 mm in six, 5 mm in 15, 6 mm in 13, 7 mm in nine, 8 mm in one, 9 mm in three, 10 mm in three, 11 mm in one, 12 mm in one, and 14 mm in one. It was unmeasurable in three cases. A convex superior contour was seen in 14 cases, a local bulge in 10, and a concave superior contour (partially empty sella) in 15 patients. Thinning or asymmetry of the bony sella floor was seen in 19 cases, and the pituitary stalk was displaced to the left in five patients and to the right in six patients. Secondary findings such as stalk displacement, bone changes and bulging, or convex gland contour were always in agreement with the position of the

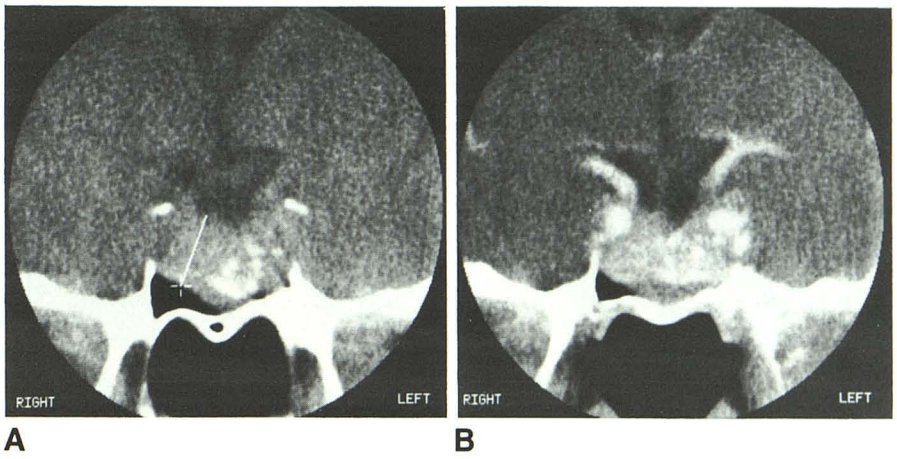

Fig. 1.—Partially calcified prolactin-secreting macroadenoma on plain scan (*A*) and after contrast enhancement (*B*).

hypodense area, except for one case in which the floor was lower on the side opposite the adenoma and there was also coexistent arachnoidocoele. In none of the five false-negative scans were there any such changes that might have given a clue about the true location of the microadenoma. Thus, it appears that CT changes other than hypodense lesions were not helpful in diagnosing prolactin adenomas. In the statistics that appear below, positive CT findings refer only to hypodense lesions.

Table 2 compares the surgical and CT findings in this series. Thirty-six of the patients had macroadenomas (>10 mm in diameter), and all had been correctly identified on CT scan. Of 60 patients thought to have microadenomas on the basis of the CT scan, 57 (95%) were confirmed at surgery while the three others had negative explorations. Among three patients whose scans were considered normal before surgery, one had a negative exploration and two were found to have microadenomas. In three other cases lesions had been suspected on CT scan, but the adenomas found at surgery were in different locations from the hypodense areas seen on CT; these scans were therefore classified as negative (false negative) for the purposes of statistical calculations. Among the tumors correctly localized on preoperative CT were four recurrent microprolactinomas and two coexisting microprolactinomas in a single patient (Fig. 3). Thus, in the present series coronal CT scans permitted correct preoperative identification of prolactin-secreting adenomas in 93 of 98 patients, for a sensitivity, or true-positive rate, of 94.9%. For the group of microadenomas the sensitivity was 91.9% (57 of 62 patients). Four patients had negative surgical explorations and the preoperative CT was negative in one, for a specificity of 25%. The overall accuracy rate was 92.1% for the entire group of patients and 87.7% for the subgroup of microadenoma patients.

The size of adenomas as measured on CT scan was within 2 mm of the dimensions determined at surgery, except for two cases. These two patients' tumors each appeared to measure 6 mm on CT scan, but were found to be 12 and 13 mm, respectively, at surgery and were thus classified as macroadenomas in this series. The size distribution of the microadenomas found by the neurosurgeon is shown in Figure 4. The location of the adenomas was classified as central, paracentral, or lateral. Of the 57 microadenomas with true-positive CT scan findings, six were central, four were paracentral, and the others (82.4%) were lateral.

Discussion

In our experience, CT is very helpful in localizing pituitary prolactinomas. This finding is in contradiction to the experience reported by Davis et al. [5] in a blind retrospective study of 51 patients suspected of harboring prolactinomas. In their series hypodense lesions were also the only significant diagnostic criterion, but the sensitivity was 48.7% and the specificity was 16.7%. On the other hand, Hemminghytt et al. [4] reported 100% incidence of hypodense lesions on coronal CT scans in a group of 25 patients with surgically proved microprolactinomas. The reasons for these discrepancies are unclear. One possible reason for the high sensitivity in our series may be the preliminary endocrinologic investigations that may have precluded CT scan examinations in patients with clinical findings and hyperprolactinemia attributable to causes other than pituitary prolactinomas, such as medication-related hyperprolactinemia or primary hypothyroidism. In the report by Hemminghytt et al. it is unclear whether patients with negative CT scans were not considered for surgery and therefore excluded from their series, and also whether patients with negative surgical explorations were excluded. It is unlikely that systematic exclusion of patients with negative CT scans from surgical therapy has occurred in our series, since only two patients with persistent hyperprolactinemia have had negative CT scans and have been advised against surgery on that basis during this period of time. All other patients who did not have neuroophthalmologic complications were offered the options of transsphenoidal surgery or medical therapy; those who chose medical therapy did so out of personal preference or apprehension about surgery rather than by medical advice based on CT scan criteria.

The third possibility is that the differences in diagnostic accuracy relate to the scanning techniques or characteristics of the instruments used. In this series of patients all scans were closely monitored by a radiologist and it was possible

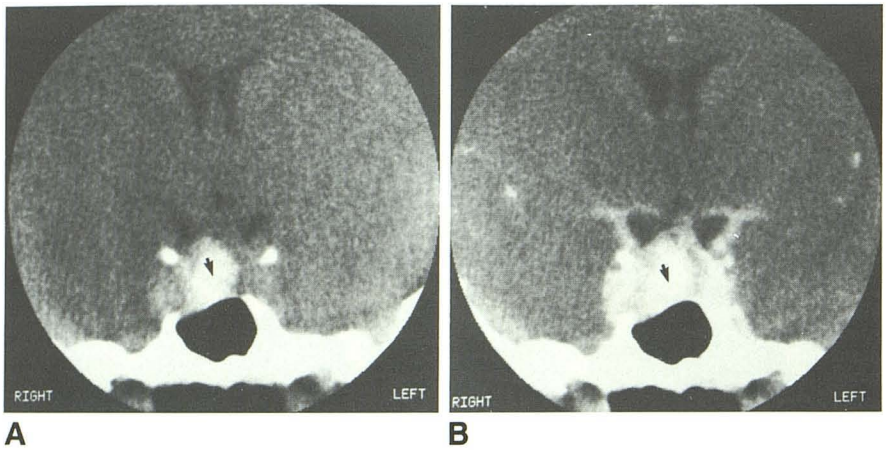

Fig. 2.—Macroadenoma (*arrow*) showing (*A*) hyperdense appearance on plain CT scan (125 H) and (*B*) enhancement after contrast (165 H). This tumor was subsequently found to contain microscopic calcification.

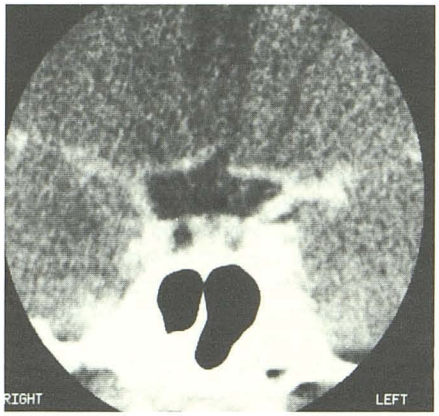

Fig. 3.—CT scan of two coexisting microprolactinomas, subsequently confirmed at surgery.

TABLE 2: Correlation of CT and Surgical Findings

Tumor Type	CT		Surgery	
	+	−	+	−
Microadenomas	60		57	3
		3[a]	3	
		3	2	1
Total	60	6	62	4
Macroadenomas	36		36	

[a] Lesions suspected on CT at wrong location.

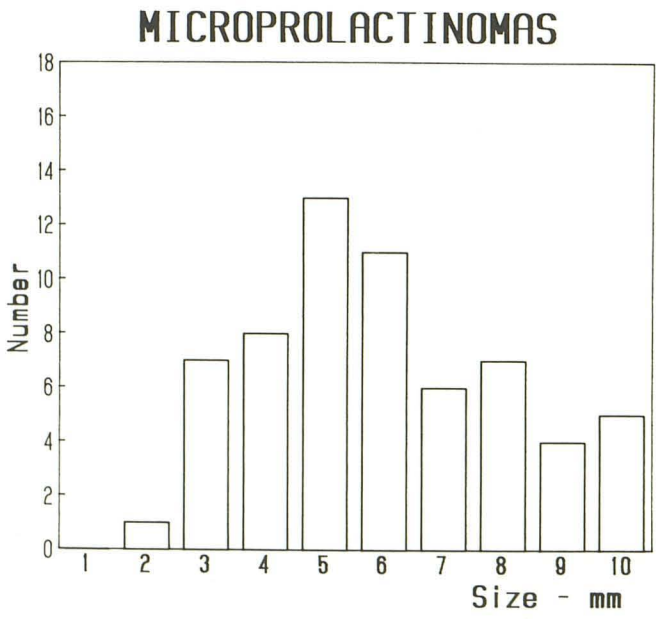

Fig. 4.—Size distribution of 62 microprolactinomas as determined at surgery.

to make changes in slice width or in scanning technique partway through the examination, depending on the findings in the initial images. The gantry on our scanner can be angled up to 30° from the vertical plane.

Fourteen (22.6%) of the 62 patients with microprolactinomas had a concave superior gland contour indicative of partially empty sella on CT scan. This proportion is not unusual when compared with the general population [9–11], and coexistence of prolactinomas with partially empty sella has been reported previously [12, 13]. Partially empty sella was present in one false-negative scan and in one false-positive scan, but in view of the small number of false-positive and negative examinations in the series, there is no statistically significant difference in the accuracy of diagnosis of prolactinomas in the presence or absence of empty sella.

The fact that CT changes other than focal hypodense lesions did not increase the accuracy of detecting microadenomas in this series is inconclusive in view of the small number of false-negative scans. However, this finding is in concordance with the report by Davis et al. [6], and is not at all surprising in view of the variability in normal gland heights reported in other CT studies [1, 14–18] and in normal cadaver pituitaries [14, 19], and of the variability found with age among asymptomatic women [20]. Although the superior gland surface is usually flat or concave, convex bulging is not rare in asymptomatic patients [18, 21, 22], especially young women [17]. Lack of correlation between the position of microadenomas and areas of cortical thinning or depressions of the sellar floor is also common [23–25].

It is difficult to explain the marked difference between the high accuracy of CT scanning we obtained for microprolactinomas and the poorer results we have seen with ACTH-secreting microadenomas [26]. Perhaps the slightly larger average size of the prolactinomas may be a contributing factor. However, we suspect, as did Hemminghytt et al. [4], that the marked difference in sensitivity is most probably due to the difference in the enhancement characteristics of the

two types of tumors. Microprolactinomas enhance poorly with contrast injection while ACTH microadenomas tend to enhance to a degree similar to normal pituitary tissue. This renders many ACTH tumors "invisible" on CT scans. The reason for the difference in enhancement characteristics is not related to technical factors in our series, and remains unknown.

Based on our findings in this series of patients we suggest that coronal CT scanning with contrast infusion is the radiologic procedure of choice in patients suspected of harboring prolactinomas. At the present time, experience with MR imaging is limited, and the diagnostic accuracy reported in the literature for microadenomas [27, 28] is considerably lower than that which we have observed with CT scanning. Although it appears that the use of gadolinium-DTPA paramagnetic contrast medium for MR imaging gives good results—sensitivity 83.3%, specificity 33% in a group of 13 patients—for ACTH-producing pituitary adenomas [29], there is no published experience yet with microprolactinomas.

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