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The Diagnostic Accuracy of Preoperative CT Scanning in the Evaluation of Pituitary ACTH-Secreting Adenomas

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Between 1980 and 1985, 35 patients (26 women and nine men) who had coronal CT scans of the sella turcica for suspected ACTH-secreting pituitary adenoma underwent transsphenoidal exploration. The CT examinations were performed with a fourth-generation EMI scanner (CT 7070). The reports of the preoperative CT examinations were compared with the findings at transsphenoidal exploration; in cases with negative CT scans, the decision to operate was based on biochemical evidence of Cushing's disease. In 27 patients, distinct adenomas were found at surgery; in the eight others, total hypophysectomy (four cases) or resection of the central core of the pituitary gland (four cases) was performed. Three patients had macroadenomas, all of which had been identified correctly on preoperative CT scan. Among the 24 microadenomas (<10 mm diameter), 14 had been correctly identified on preoperative CT scan while 10 were found in patients with negative scans. The CT examinations in these 35 patients showed probable adenomas in 20 cases, of which 17 (85%) were confirmed at surgery. In the other three cases (15%), adenomas were not found. Among the 15 patients with negative CT scans, 10 (66.6%) had distinct adenomas found at surgery. Coronal CT scans for ACTH-secreting adenomas had a sensitivity of 63%, a specificity of 62.5%, and an overall accuracy rate of 62.8%. Thus, in our experience, CT scanning with current state-of-the-art equipment has poor diagnostic accuracy in Cushing's disease. The possible reasons for this are that most of the adenomas in this series were microadenomas less than 6 mm in diameter, and that ACTH microadenomas probably show almost the same degree of enhancement with contrast medium as the surrounding normal pituitary tissue.

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 scant information about the diagnostic accuracy of this procedure, especially in regard to the identification of adenomas in Cushing's disease [1–6]. Over a period of 5 years between 1980 and 1985, 35 patients who had coronal CT scans of the sella turcica at the Montreal General Hospital for suspected ACTH-secreting adenoma underwent transsphenoidal exploration. We reviewed the findings in these patients in order to document the reliability of the CT imaging technique for identifying the lesion preoperatively.

Subjects and Methods

The patients included in this study had been referred for CT of the sella turcica because of clinical and biochemical evidence of pituitary-dependent cortisol hypersecretion. 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) in order 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 (5 mm slice width was only used for the three macroadenomas, which appeared obvious on the initial plain scans), slice overlap 1 mm, scan

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wedge 250 mm. The final pixel size was 0.22–0.31 mm. Scans were obtained both with and without contrast enhancement for 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. Before 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 iodine, maximum) given as rapidly as possible (usually 3–4 min) by hand injection through a gauge-19 butterfly needle. Twelve patients were scanned in this manner. Subsequently, 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 a total of about 20 g of iodine. With either technique the examination was usually completed within 20 min after injection of the first bolus of contrast.

ACTH-secreting microadenomas were diagnosed by CT scanning as areas of low density within a contrast-enhanced pituitary gland. Hypodense areas were considered to be summations of streak 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 diagnostic at the time of reporting for purposes of clinical management of the patients.

The data concerning the interpretation of CT scans were gathered by reviewing the reports 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 at the time the scans were performed and interpreted. Four patients had more than one CT scan before surgery, and in these cases the study closest to the date of surgery was the one included in the series.

Our series consists of 35 patients (26 women and nine men) who underwent transsphenoidal exploration between 1980 and 1985. In patients with negative CT scans, the decision to operate was based on biochemical evidence of pituitary-dependent Cushing's disease. All transsphenoidal explorations were performed by the same neurosurgeon. The size and location of the adenoma reported by the neurosurgeon and confirmed by pathologic studies were taken as the standard against which the CT findings were compared. Cases in which microscopic adenomas were found in the pathologic specimens but were not visible to the neurosurgeon were considered for purposes of statistical calculations to have no adenoma.

Results

In 27 of the 35 patients, distinct adenomas were found at surgery, while in the eight others total hypophysectomy (four cases) or resection of the central core of the pituitary gland (four cases) was performed. Histologic examination revealed microscopic distinct adenomas in one total hypophysectomy specimen and in one core resection specimen.

CT scans of the three patients with macroadenomas all showed changes in gland height, superior contour, stalk position, and appearance of the bone of the sella turcica. One lesion was approximately 30 mm in diameter with a large suprasellar extension and virtually complete destruction of the sella floor, and the pituitary stalk was unrecognizable. Of the two others, one showed a gland height of 9 mm with convex contour, displacement of the stalk to the right, and lowering of the sella floor on the left; the other showed a gland height of 14 mm with upward bulging and displacement of the stalk to the left and thinning of the bone.

Among the other 32 cases, gland height was not measurable in three cases; it was 3 mm in one case, 4 mm in two cases, 5 mm in eight cases, 6 mm in nine cases, 7 mm in three cases, and 8 mm in six cases. A convex superior contour was seen in three cases, all with a gland height of 8 mm; in one of these cases the stalk was displaced to the right and there was a hypodense lesion that proved to be an adenoma at surgery. Of the other two cases with a midline stalk, one showed a hypodense defect but both patients underwent core resections because no distinct adenoma could be found by the surgeon. In 10 cases the superior contour of the gland was concave and in all the stalk was midline. In five cases hypodense lesions were reported—one in association with generalized thinning of the sella floor and another with localized thinning of the floor on the right side—four of which were confirmed at surgery. The patient with the localized thinning of the floor underwent total hypophysectomy. In the five cases without hypodense lesions, no bone changes were observed and among these one was found at surgery to have a distinct 5-mm adenoma while three had total hypophysectomies and one had a negative exploration without total hypophysectomy. In 18 cases the superior contour was flat; bone changes were seen in only one of these, which had lowering of the floor on the left side but a central 4-mm hypodense lesion that was confirmed at surgery. Stalk deviation was seen in two cases, one associated with a hypodense lesion susequently confirmed to be an adenoma and the second with an otherwise negative scan; the latter patient had a gland height of 6 mm and stalk deviation to the right. At surgery she was found to have an adenoma measuring 3 mm in diameter in the center of the gland.

Overall, among the 15 patients who did not have hypodense lesions on CT scan, one had a gland height of 8 mm with convex superior contour, and no distinct lesion was found at surgery; one only had stalk deviation, and an adenoma was found at surgery; while in nine other cases without any detectable CT changes, distinct adenomas were subsequently found by the neurosurgeon at surgery. Thus, it appears that CT changes other than hypodense lesions were not helpful in diagnosing ACTH adenomas; and in the statistics presented below, positive CT findings refer only to hypodense lesions.

Table 1 compares the surgical and CT findings in this series. Three of the patients had macroadenomas (>10 mm in diameter), and all had been correctly identified on CT scan. Of 17 microadenomas suspected on the basis of the CT scan, 14 (82.4%) were confirmed at surgery; in the other three cases gross adenomas were not found. Among the 15 patients with negative CT scans, 10 (66.6%) had distinct adenomas found at surgery. Five patients had negative CT scans and no gross adenomas at surgery. Eight patients with negative CT scans had tumors found at surgery; in two other patients lesions had been suspected on the preoperative CT

scans but the adenomas found at surgery were in a location different from that described on the CT scan—thus, these CT scans were considered negative for purposes of statistical calculations. Consequently, in the present series, coronal CT scans for ACTH-secreting adenomas had a sensitivity, or true positive rate, of 63%; a specificity, or true negative rate, of 62.5%; and an overall accuracy rate of 62.8%.

For the group of microadenomas the sensitivity was 58.3%, the specificity 62.5%, and the accuracy 59.4%. Comparison of the results with dynamic scanning versus the nondynamic technique shows that for the 12 patients studied with the single-injection method sensitivity was 87.5% and specificity 75%, whereas for the 20 patients examined with dynamic scanning the sensitivity and specificity were 43.8% and 50%, respectively; there is no statistically significant difference between these two subgroups by chi-squared analysis.

In the microadenoma group there was a preponderance of very small lesions, with 23 of the 24 tumors found by the neurosurgeon measuring 6 mm or less in diameter (Fig. 1). The location of the adenomas was classified as central, paracentral, or lateral. Of the 14 microadenomas with the true positive CT scan findings, eight were central, three were paracentral, and three were lateral (Fig. 2). Among the tumors identified by the neurosurgeon in patients whose CT scans had been classified as negative, nine were central and one was lateral. Of the two tumors discovered only on pathologic study of hypophysectomy or biopsy specimens, one was lateral and the other central. Thus, of the 26 microadenomas identified at surgery or by histology, 18 were centrally located, three were paracentral, and five were lateral.

TABLE 1: ACTH-Secreting Adenomas

Tumors	Operation		CT Scan	
	+	−	+	−
Macroadenomas	3		3	
Microadenomas	14	3	17	
	8	5		13
	2			2*
Total	27	8	20	15

* Two tumors found in locations not corresponding to suspected CT lesions.

Discussion

In our experience, CT scanning with current state-of-the-art equipment and technique is much less helpful in Cushing's disease than in prolactinomas [7]. A similar discrepancy has been reported from another center [6], although the total

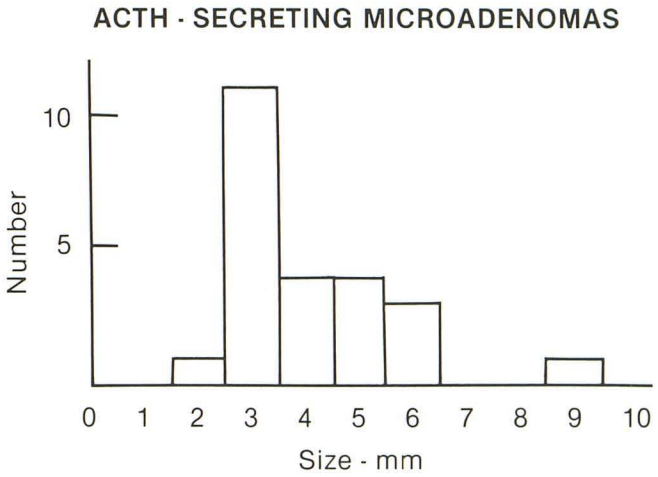

Fig. 1.—Size distribution of 24 ACTH microadenomas visible during transsphenoidal surgery.

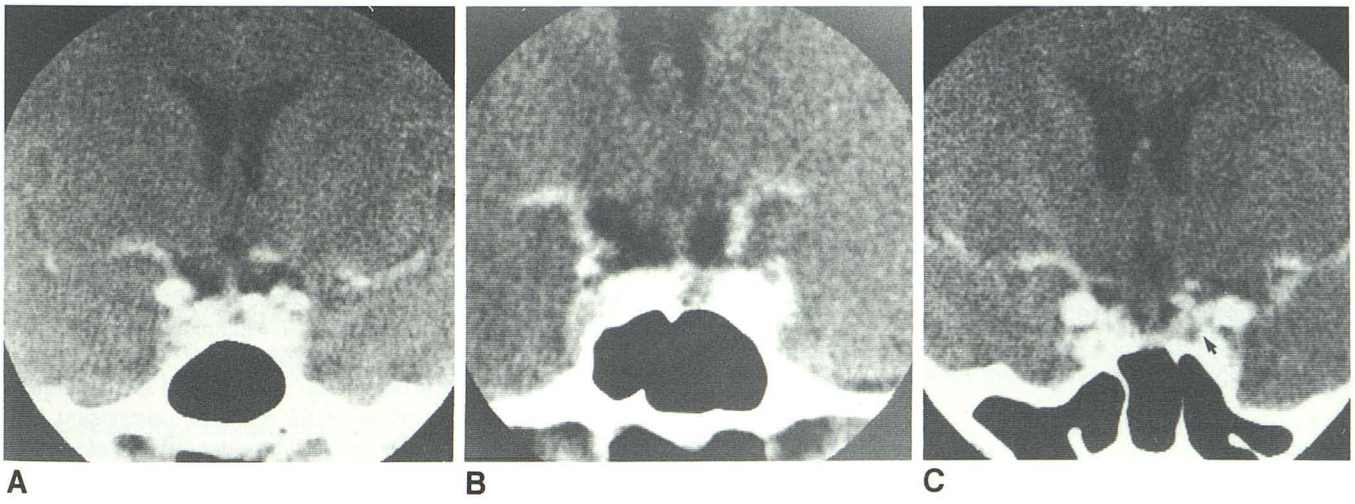

Fig. 2.—*A*, Example of a centrally located ACTH microadenoma.
***B*, Example of an ACTH microadenoma classified as paracentral.**
***C*, Example of a lateral ACTH microadenoma (*arrow*) in left side of pituitary gland. Note coexistent, partially empty sella.**

number of cases is smaller and the sensitivity rates in each type are lower. The possible reasons for this are that most of the adenomas in this series were microadenomas less than 6 mm in diameter and that some ACTH microadenomas probably enhance with contrast medium in a manner similar to normal pituitary tissue. Ten of the 32 patients (31.3%) suspected of harboring microadenomas had a concave superior gland contour indicative of a partially empty sella turcica; this proportion is not unusual when compared with the general population [8–11], and coexistence of adenomas with partially empty sellae has been reported previously [12–15]; the rate of detection of adenomas in these 10 patients—sensitivity and specificity both 80%—was no worse than for the group as a whole. The finding that CT changes other than hypodense lesions were infrequent and not helpful in diagnosing ACTH microadenomas is in agreement with the report of Davis et al. [6] and might also be explained by the small size of many of the lesions in this group as well as by the variations in normal pituitary anatomy [9].

Other reports in the literature also document a preponderance of small microadenomas in recent series of patients with Cushing's disease [5, 6, 16, 17]. Information about the accuracy of CT scanning is scant, but in one series of 12 patients [4] the sensitivity was approximately 18% and the false-negative rate was approximately 73% for microadenomas, while in a second series [6] the sensitivity was 22% in a group of nine microadenomas. Better sensitivity was found in a group [18] in which 12 of 19 patients with biochemical abnormalities suggestive of ACTH pituitary adenomas were found to have hypodense lesions on coronal CT. Since only cases with positive CT were explored surgically, actual sensitivity and specificity cannot be calculated; microadenomas were found in eight of these, with four scans considered to be false positive. Statistics such as these have provided an impetus for attempts to develop other diagnostic techniques, such as inferior petrosal venous sampling [5].

The predominantly central location of ACTH-secreting pituitary microadenomas found in this series is consistent with surgical findings previously reported on another group of patients without preoperative CT scans [19] and is in agreement with CT findings reported by Bonafe et al. [2]; however, it is in contradiction to the experience reported by three other groups [5, 20, 21].

Our conclusions from this study are that in the present context a positive pituitary CT scan in a patient with clinical and biochemical evidence of Cushing's disease is very helpful, but a negative CT scan should not be considered a contraindication to transsphenoidal surgical exploration in centers with expertise in this procedure [19, 22].

REFERENCES

1. Syvertsen A, Haughton VM, Williams AL, Cusick J. Computed tomography of the normal pituitary gland and microadenomas. *Radiology* **1979**; 133:385–391
2. Bonafe A, Sobel D, Salandini AM, et al. Diagnostic value of CT scanning in pituitary microadenomas (abstr). *Neuroradiology* **1982**;20:263
3. Gardeur D, Naidich TP, Metzger J. CT analysis of intrasellar pituitary adenomas with emphasis on patterns of contrast enhancement. *Neuroradiology* **1981**;20:241–247
4. Hemminghytt S, Kalkhoff RK, Daniels DL, Williams AL, Grogan JP, Haughton VM. Computed tomographic study of hormone-secreting microadenomas. *Radiology* **1983**;146:65–69
5. Oldfield EH, Chrousos GP, Schulte HM, et al. Preoperative localization of ACTH-secreting pituitary microadenomas by bilateral and simultaneous inferior petrosal venous sinus sampling. *N Eng J Med* **1985**;312:100–103
6. Davis PC, Hoffman JC Jr, Tindall GT, Braun IF. CT-surgical correlation in pituitary adenomas: evaluation in 113 patients. *AJNR* **1985**;6:711–716
7. Wee R, Marcovitz S, Chan JD, Hardy J. The diagnostic accuracy of CT scanning in the evaluation of pituitary prolactinomas (abstr). *Ann Royal Coll Phys Surg Can* **1984**;17:309
8. Busch W. Die morphologie der sella turcica und ihre beziehungen zur hypophyse. *Virchows Arch [A]* **1951**;320:437–458
9. Bergland RM, Ray BS, Torack RM. Anatomical variations in the pituitary gland and adjacent structures in 225 human autopsy cases. *J Neurosurg* **1968**;28:93–99
10. Kaufman B, Chamberlain WB Jr. The ubiqitous "empty" sella turcica. *Acta Radiol [Diagn] (Stockh)* **1972**;13:413–425
11. Renn WH, Rhoton AL. Microsurgical anatomy of the sellar region. *J Neurosurg* **1975**;43:288–298
12. Sutton TJ, Vezina JL. Co-existing pituitary adenoma and intrasellar arachnoid invagination. *AJR* **1974**;122:508–510
13. Ganguly A, Stanchfield JB, Roberts TS, West CD, Tyler FH. Cushing's syndrome in a patient with an empty sella turcica and a microadenoma of the adenohypophysis. *Am J Med* **1976**;60:306–309
14. Molitch ME, Hieshima GB, Marcovitz S, Jackson IMD, Wolpert S. Coexisting primary empty sella syndrome and acromegaly. *Clin Endocrinol (Oxf)* **1977**;7:261–263
15. Domingue JN, Wing DS, Wilson, CB. Coexisting pituitary adenomas and partially empty sella. *J Neurosurg* **1978**;48:23–28
16. Boggan JE, Tyrrell JB, Wilson CB. Transsphenoidal microsurgical management of Cushing's disease. *J Neurosurg* **1983**;59:195–200
17. Salassa RM, Laws ER Jr, Carpenter PC, Northcutt RC. Transsphenoidal removal of microadenoma in Cushing's disease. *Mayo Clin Proc* **1978**;53:24–28
18. Kuwayama A, Kageyama N. Current management of Cushing's disease I. *Contemp Neurosurg* **1985**;7(2):1–6
19. Hardy J. Cushing's disease: 50 years later. *Can J Neurol Sci* **1982**;9: 375–380
20. Kuwayama A, Kageyama N. Current management of Cushing's disease II. *Contemp Neurosurg* **1985**;7(3):1–6
21. Ludecke DK, Niedworok G. Results of microsurgery in Cushing's disease and effect on hypertension. *Cardiology* **1985**;72:91–94
22. Bigos ST, Robert F, Pelletier G, Hardy J. Cure of Cushing's disease by transsphenoidal removal of a microadenoma from a pituitary gland despite a radiographically normal sella turcica. *J Clin Endocrinol Metab* **1977**;45:1251–1260

Addendum

In the interval since this paper was accepted for publication, a report by S. C. Saris, N. J. Patronas, J. L. Doppman, et al. about the accuracy of pituitary CT scanning in Cushing's syndrome was published (*Radiology* **1987**:162:775–777). These authors found a sensitivity of 30% and a diagnostic accuracy of 39% in a group of 57 patients, comprising 50 patients with surgically proven pituitary adenomas and seven patients with ectopic ACTH-producing tumors.