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MR of Corticotropin-Secreting Pituitary Microadenomas

N. Colombo, P. Loli, F. Vignati, and G. Scialfa

PURPOSE: To assess the accuracy of MR in the preoperative identification of corticotropin-secreting pituitary microadenomas. **METHODS:** Twenty-six patients with clinical and biochemical evidence of pituitary-driven Cushing disease in whom MR of the sellar region was performed were selected for this study. The MR examinations were retrospectively evaluated by a neuroradiologist who was aware of the presence of an adenoma at surgery but not of location and size of the lesion. **RESULTS:** Considering the whole group of MR examinations performed either without ($n = 26$) or without and with intravenous injection of gadopentetate dimeglumine ($n = 16$), overall 20 MR studies were judged to show disease. Seventeen of 26 microadenomas were adequately shown and located by MR (true-positive, 65.4%). In three cases the sides of the microadenomas were misjudged (false-positive, 11.5%). Six patients had negative MR studies (false-negative, 23%). Twelve of the 16 patients studied after gadopentetate dimeglumine injection had true-positive MR findings (75%). **CONCLUSIONS:** In our experience the accuracy of MR in detecting corticotropin-secreting microadenomas as small as 2 to 3 mm is 65% to 75%. Although precontrast images provide diagnostic information, the microadenoma can be better seen with administration of contrast material.

Index terms: Cushing disease; Adenoma; Sella turcica, magnetic resonance; Pituitary gland, neoplasms

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Cushing disease is caused by hypersecretion of corticotropin by the pituitary gland, with secondary bilateral adrenal cortical hyperplasia and hypercortisolism. Data from the literature suggest that 60% to 96% of patients with Cushing disease harbor a pituitary adenoma and that in most cases the adenoma is less than 5 mm in diameter (1, 2). Accurate location of the corticotropin-secreting pituitary microadenoma is of obvious relevance to the outcome of the transsphenoidal microsurgical procedure, which is generally considered the treatment of choice of pituitary-dependent Cushing disease (1, 2).

Over the last 10 years computed tomography has been the method of choice in the radiologic

evaluation of pituitary and parasellar lesions, despite some limitations related to the difficulty in detecting small pituitary lesions and the use of ionizing radiation (3-7). At present magnetic resonance (MR) is reportedly the most sensitive noninvasive imaging method in the preoperative location of pituitary microadenomas (8-11). The accuracy of MR in the identification of corticotropin-secreting pituitary microadenomas has not been definitely established (12-20).

To evaluate the accuracy of MR in the preoperative identification and location of corticotropin-secreting microadenomas, we evaluated 26 patients with clinical and biochemical evidence of pituitary-driven Cushing disease preoperatively with MR.

Materials and Methods

Among 40 patients referred to the Endocrine and Neuroradiologic Departments for Cushing disease during the last 6 years, records from 26 patients (18 female and 8 male, 16 to 64 years of age) were retrospectively evaluated. The criterion for inclusion in the study was the availability of surgical and pathologic demonstration of a cor-

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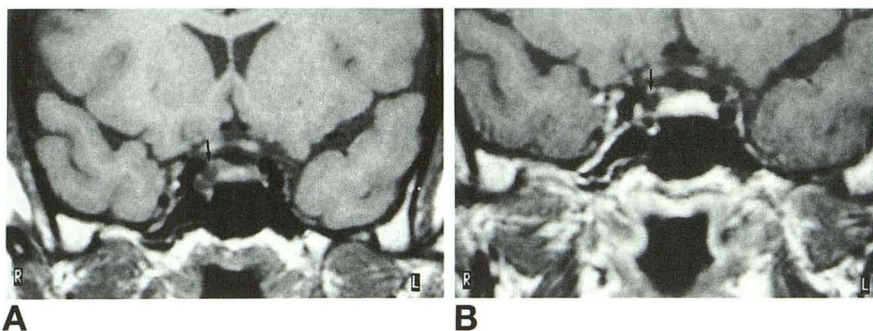
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Fig 1. Hypointense microadenoma.

A, MR coronal T1-weighted image (600/20/4). A focal area of low signal intensity (arrow) is seen in the right lateral aspect of the pituitary gland, associated with mild upward convexity of superior pituitary profile.

B, MR coronal T1-weighted image (600/20) after gadolinium injection. The microadenoma shows no enhancement (arrow) in comparison with the normal pituitary gland.



ticotropin-secreting pituitary microadenoma, including confirmation that the adenoma did not exceed 10 mm in maximum diameter. Before surgery all patients had undergone extensive evaluations, including low-dose and high-dose dexamethasone suppression tests and corticotropin-releasing hormone stimulation tests, the results of which were consistent with the diagnosis of corticotropin-dependent Cushing disease.

MR was performed with a 1.5-T unit; 3-mm sagittal and coronal T1-weighted images (600/20/4 [repetition time/echo time/excitations]) were acquired by using a 22-cm field of view and a 256 × 256 matrix. In 16 patients, T1-weighted coronal images were repeated immediately after intravenous injection of gadopentetate dimeglumine (0.1 mmol/kg body weight).

MR scans of the 26 patients were retrospectively reviewed by a neuroradiologist who was aware that in each patient an adenoma was found and removed at surgery but was unaware of its size and location. The MR images were considered positive if there was (a) an intraglandular focal area of low signal intensity before and/or after injection of gadopentetate dimeglumine with or without upward convexity of the superior pituitary profile (Figs 1 and 2); or (b) asymmetrical enlargement of the gland on the side of the lesion even in the absence of focal signal abnormality. The latter parameter was evaluated in a semiquantitative way: differences of 2 mm or more in pituitary height, measured on both sides of midline, were considered significant.

Nineteen of 26 patients also had undergone bilateral and simultaneous catheterization of inferior petrosal sinuses for corticotropin determination as a part of the diagnostic workup for Cushing disease. At the end of the diagnostic workup all patients underwent transphenoidal

microsurgery. In all cases an adenoma was removed; 24 patients had selective adenomectomy, and two patients had total hypophysectomy. Surgical results were summarized by neurosurgeons' sketches drawn in the coronal planes describing size and location of the microadenoma.

Relying on the surgical diagrams, 24 adenomas had maximum diameters of 2 to 6 mm, whereas two measured 9 and 10 mm in diameter, respectively. Fourteen microadenomas were located in the right sides of the glands (4 with midline extension); 10 microadenomas were found in the left sides (4 with midline extension); and 2 were midline lesions.

MR results were compared with the neurosurgeons' findings summarized in diagrams, which were considered the standard of reference. In this context, MR readings were defined as true-positive when they matched the surgical findings, false-positive when they showed an adenoma on the side opposite the surgical locations, and false-negative when they failed to show the adenoma.

Results

The results are given in Table 1. Overall, 20 MR examinations, performed either without or without and with gadolinium injection, were considered abnormal; 17 of 26 microadenomas were adequately detected and located with MR (true-positive, 65.4%), whereas on the bases of MR studies, in 3 cases the sides of the microadenomas were misjudged (false-

Fig 2. Iso/hypointense microadenoma.

A, MR coronal T1-weighted image (600/20) before gadolinium injection. A left-sided focal volume increase of the hypophysis with mild low signal is shown (double arrows).

B, Postcontrast MR coronal T1-weighted image (600/20). The left adenoma (double arrows) is better seen with respect to hyper-signal of a normal gland.

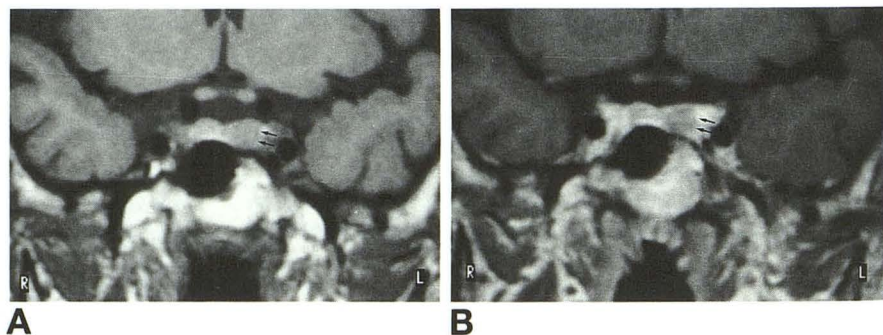


TABLE 1: MR results in 26 patients with corticotropin-secreting microadenomas

Patient	MR -	
	Before Gadolinium	After Gadolinium
1	Normal	...
2	Abnormal	...
3	Normal	...
4	Abnormal	Abnormal
5	Abnormal	Abnormal
6	Normal	Normal
7	Abnormal ^a	Abnormal ^a
8	Abnormal	Abnormal
9	Abnormal	Abnormal
10	Normal	Abnormal
11	Normal	...
12	Normal	...
13	Abnormal	Abnormal
14	Abnormal	Abnormal
15	Abnormal ^a	Abnormal ^a
16	Abnormal ^a	Abnormal ^a
17	Normal	...
18	Abnormal	...
19	Abnormal	Abnormal
20	Normal	Abnormal
21	Normal	Abnormal
22	Abnormal	...
23	Abnormal	Abnormal
24	Abnormal	...
25	Abnormal	Abnormal
26	Abnormal	...

^a False-positive.

positive, 11.5%). Six patients had normal MR studies (false-negative, 23%).

In the group of 17 true-positive MR examinations, 9 microadenomas were hypointense, and 8 were isointense with respect to the surrounding normal pituitary tissue on nonenhanced images (Table 2). Twelve of these 17 patients also had postcontrast MR studies; 6 hypointense lesions were conspicuous both before and after contrast administration; 3 microadenomas were isointense both before and after gadolinium injection, but they became more evident after contrast administration, being better demarcated from the normal contrast-enhanced pituitary tissue; in 3 patients with negative nonenhanced images a microadenoma could be detected after gadolinium injection as a focal area of hypointensity in comparison with normal glands (Fig 3).

False-positive MR examinations were obtained in three patients both before and after gadolinium injection (Fig 4 and Table 2). One of the 6 patients with false-negative precontrast studies was examined also after contrast injection

without identification of the microadenoma. Overall, of 16 patients with postcontrast images, 12 have proved true-positive (75%). Displacement of the pituitary stalk contralateral to the side of the microadenoma was observed in only 3 of our cases.

Discussion

It is now well recognized that 60% to 96% of patients with pituitary-driven Cushing disease harbor a pituitary adenoma that is responsible for corticotropin hypersecretion and hypercortisolism (1, 2); however, until recently the reported accuracy of neuroradiologic imaging methods in identifying such lesions has been rather limited. This is possibly because of the frequent very small size of corticotropin-secreting adenomas.

An accurate endocrine diagnostic workup is mandatory for the diagnosis of Cushing disease and for subsequent surgery; although the accuracy of the diagnosis has improved since the development of corticotropin determination in blood taken from the inferior petrosal sinuses to differentiate between pituitary and ectopic sources of corticotropin (21), a correct preoperative neuroradiologic identification of the pituitary tumor is of obvious relevance. In fact, because of their frequently very small size, corticotropin microadenomas can escape detection during exploration of the pituitary, even by experienced neurosurgeons.

The sensitivity of computed tomography in the detection of corticotropin-secreting microadenomas varies between 17% to 57%, owing to the frequent small size and isodensity of the tumors with respect to the adjacent normal pituitary tissue (3-7, 22). Positron emission tomography is equally as effective as MR in detecting pituitary microadenomas (22). However, its use is restricted by high cost and limited availability.

The sensitivity of MR is still to be defined; the number of patients with pituitary-driven Cushing disease is small, and a limited number of cases had been studied after administration of gadopentetate dimeglumine (12-20). From these preliminary reports, MR seems to be more effective than computed tomography in the detection of corticotropin-secreting microadenomas, especially when postcontrast images are acquired (13, 14, 16-22).

In our experience precontrast MR has a sen-

TABLE 2: MR and surgical findings in the group of 20 patients with abnormal MR studies

Patient	MR			Surgical Findings of Adenomas		Catheterization of Inferior Petrosal Sinuses	Stalk Deviation
	Signal on T1-Weighted Image		Side	Size, mm	Side		
	Before Gadolinium	After Gadolinium					
1	Hypointense	...	Right	6	Right paramedian	No side	None
2	Isointense	Isointense	Left paramedian	3-4	Left paramedian	Left	Right
3	Hypointense	Hypointense	Right	5	Right	No side	None
4	Hypointense ^a	Hypointense ^a	Left paramedian	4	Right paramedian	Right	Right
5	Isointense-Hypointense	Hypointense	Right paramedian	5	Right paramedian	Right	None
6	Isointense	Isointense	Median	4	Median	Right	None
7	Normal	Hypointense	Right	6	Right	Right	None
8	Hypointense	Hypointense	Right	3	Right	No side	Left
9	Hypointense	Hypointense	Left	5-6	Left paramedian	No side	None
10	Hypointense ^a	Hypointense ^a	Right	6	Left	Left	Right
11	Isointense-Hypointense ^a	Hypointense ^a	Left	4	Right	Right basal/ Left postCRF	None
12	Hypointense	...	Right	5	Right	...	None
13	Hypointense	Hypointense	Right	4	Right	...	None
14	Normal	Hypointense	Right	5	Right	...	None
15	Normal	Hypointense	Right	3-4	Right	...	None
16	Isointense	...	Right paramedian	9	Right paramedian	...	None
17	Hypointense	Hypointense	Left	4	Left	...	None
18	Isointense	...	Left median	5	Median	...	None
19	Isointense	Isointense	Left paramedian	8	Left paramedian	Right	None
20	Isointense-Hypointense	...	Left paramedian	10	Left paramedian	...	None

^a False-positive.

sitivity of 65.4%, which increases to 75% after gadolinium injection. A focal area of hypointensity within the pituitary and an asymmetrical enlargement of the gland without signal abnormality, detected on coronal images, have turned out to be the most significant signs of the presence of the microadenoma. Our results agree with the previously reported limited value of sagittal images (8).

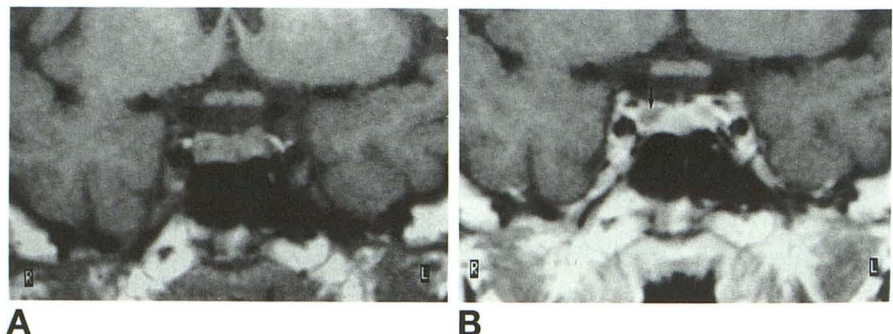
The existence of pituitary microadenomas that are isointense with normal pituitary tissue at MR examination justifies the routine use of gadopentetate dimeglumine when precontrast

images are negative in patients suspected of having a pituitary microadenoma; indeed, reacquisition of images immediately after administration of paramagnetic contrast can provide better demarcation of the adenoma with respect to the surrounding tissue, taking advantage of the different characteristics of enhancement (peak of enhancement within 3 minutes for normal pituitary, later peak for the adenoma). This was the case in three of our patients, who had completely normal precontrast images. It is worthy of note that some adenomas may show the same enhancement characteristics as the

Fig 3. Confirmation of MR findings after contrast injection.

A, MR coronal T1-weighted image (600/20) before contrast administration. An uncertain microadenoma is in the right side of the gland.

B, MR coronal T1-weighted image (600/20) after gadolinium injection. A right-sided microadenoma of low signal is recognized (arrow), in comparison with the normal bright signal of the pituitary.



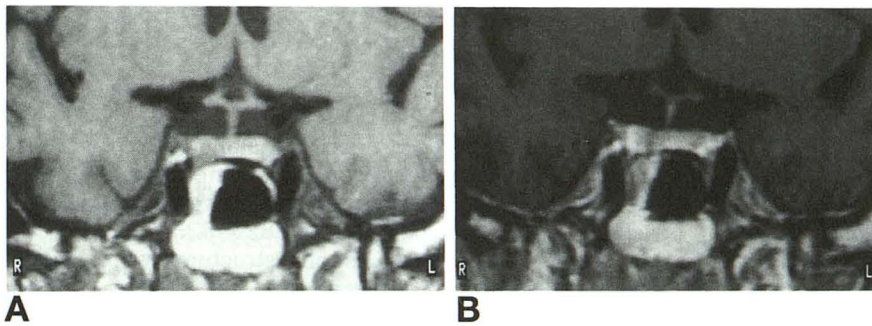


Fig 4. False-positive MR study. T1-weighted (600/20) coronal images without contrast (A) and with contrast (B). A right-sided microadenoma was reported by the neuroradiologist, but a left-sided adenoma was found at surgery.

normal pituitary at any time after gadolinium injection (14). The latter observation, as well as the very small size of some corticotropin-secreting microadenomas, could explain the false-negative results recorded in ours as well as in others' studies.

In conclusion, our data suggest that MR can detect corticotropin-secreting microadenomas as small as 2 to 3 mm with an accuracy of 75%. Although precontrast images may provide diagnostic information, a more confident detection of lesions can be expected immediately after administration of contrast material.

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