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Pituitary Gland MR: A Comparative Study of Healthy Volunteers and Patients with Microadenomas

Brian W. Chong, Walter Kucharczyk, William Singer, and Susan George

PURPOSE: To compare the MR appearance of the pituitary glands of healthy volunteers with that of patients with microadenomas. **METHODS:** Unenhanced coronal T1-weighted MR of the pituitary gland was performed on 52 healthy adult volunteers and 14 consecutive patients with evidence of pituitary adenomas. The MRs were interpreted in a randomized, blinded fashion. Notation was made of pituitary gland size, symmetry, stalk position, and the gland's signal uniformity. **RESULTS:** Focal pituitary gland hypointensities were seen in 20 of 52 volunteers and in all 14 patients. In the volunteers, on average the areas of low signal were smaller and not as dark as in the patient group, but there was some overlap between the two groups. Pituitary gland size, symmetry, and stalk position did not differ between the two groups. **CONCLUSIONS:** Focal hypointensities are common incidental MR findings in the healthy population. On average they appear smaller and not as dark as microadenomas.

Index terms: Pituitary gland, magnetic resonance; Pituitary gland, neoplasms

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Magnetic resonance (MR) is frequently used for the evaluation of patients suspected of having pituitary microadenomas. On MR microadenomas are most often seen as small hypointense lesions relative to the normal anterior pituitary gland on T1-weighted spin-echo images (1-6). Before the widespread dissemination of MR systems, contrast-enhanced computed tomography (CT) was used as the main method of imaging pituitary microadenomas. On contrast-enhanced CT, focal hypodense areas in the pituitary gland were thought to be quite specific for the diagnosis of pituitary adenomas. This view changed when it was recognized that there was a high incidence of focal hypodensities in healthy volunteers (3, 7-11). Although some of these hypodensities were caused by asymptomatic microadenomas,

most were related to incidental cysts or similar lesions (8, 11).

Appreciation of the frequency of incidental findings in persons without clinically significant pituitary disorders puts the finding of pituitary hypodensities into the proper perspective. A hypodensity in the pituitary gland was recognized as consistent with the diagnosis of a pituitary microadenoma but not in itself diagnostic of such. The purpose of this study was to determine the frequency of incidental findings on MR of the pituitary gland and to compare the features of incidental findings with the features of microadenomas.

Patients and Methods

Fifty-two healthy volunteers were recruited for this study over a 3-month period based on an absence of clinical pituitary gland dysfunction. There were 30 men and 22 women with an average age of 34 years (range 22 to 68 years). Pregnant women and persons taking medications known to alter pituitary function were excluded. All volunteers also had assessments of serum prolactin, follicle-stimulating hormone, luteinizing hormone, and thyroid-stimulating hormone levels to exclude volunteers with asymptomatic functioning adenomas (it was recognized that this method could exclude patients with nonfunctioning adenomas). Alpha subunit was measured if any undue elevations in follicle-stimulating hormone levels suggested

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a gonadotropin-secreting tumor. Thyroid hormones were assayed if elevated thyroid-stimulating hormone levels were found. Growth hormone and adrenocorticotropin were not measured because the features of acromegaly and Cushing disease would not likely be missed, and stress-related hormone rises would make interpretation of single samples difficult. Over the same 3-month period 14 patients with amenorrhea or galactorrhea and serum prolactin levels exceeding 100 ng/ml (normal is less than 27 ng/ml) were referred to our institution for MR evaluation of the pituitary gland. These patients constituted the disease group for comparison with the healthy volunteers. All of the patients were women. The average age was 35 years (range 27 to 48 years).

All volunteers and patients underwent MR examination of their pituitary glands. MR was performed using a 1.5-T superconducting MR unit (Signa, General Electric Medical Systems, Milwaukee, Wis). After obtaining a sagittal localizer, coronal spin-echo 600/20/4 (repetition time/echo time/excitations), 3-mm-thick sections were imaged with a section gap of 0.5 mm. The field of view was 20 cm with a matrix of 256×256 . Pixel size was 0.8×0.8 and was constant throughout the study. Saturation pulses in the superior, inferior, anterior, and posterior locations were used to minimize pulsation artifacts from the adjacent vessels. Only unenhanced images were obtained.

The MRs of the healthy volunteers were mixed with the MRs of the 14 patients. The images were then interpreted in a randomized, blinded fashion by a single neuroradiologist who noted gland size, stalk position, symmetry of gland size with respect to the midline, and the presence or absence of any focal increases or decreases of signal within the pituitary gland. A focal signal alteration was considered 4 pixels or larger in size. If there was a focal area of increased or reduced signal in the gland, the size and signal intensity of the area was measured on a cathode ray tube using standard software. The signal difference (SD) between the area of altered signal in the normal gland was measured using a region of interest cursor. This value was then divided by the noise in the system, which was taken as a standard deviation of a 1-cm region of interest measurement of air in the sphenoid sinus. This ratio is herein referred to as the SD/N. The signal difference between the area of altered signal and the rest of the normal gland was also compared with the signal difference between gray matter (GM) and white matter (WM) by taking a ratio of the two differences ($SD/(WM - GM)$). The gray matter and white matter signal intensities were obtained from the left temporal lobe on the coronal images of the sella turcica.

Results

Volunteers

The biochemical profiles of all the volunteers were normal. The MR features of the volunteers' pituitary glands are listed in Table 1. Of specific interest is that the MRs of 20 of 52 volunteers contained focal hypointensities in the pituitary

gland (Fig 1). No hyperintensities were observed. The size of these hypointensities varied from 2 to 5 mm (mean 3.9 mm). The degree of hypointensity (difference in intensity between the region of interest and the pituitary gland = SD) normalized for system noise (N) or for differences between white and gray matter ($WM - GM$) were 1.9 and 0.57, respectively. (Both values, listed in Table 2, are ratios without units.)

Patients

The serum prolactin levels of all the patients exceeded 100 ng/ml. The MR features of the patients' pituitary glands are listed in Table 1.

TABLE 1: Gland parameters

	Normal (n = 52)	Microprolactinomas (n = 14)
Height of left side	5.9 ± 1.6	7.0 ± 1.6^a
Height of right side	5.9 ± 1.4	6.5 ± 1.5
Width	15.5 ± 2.3	16.3 ± 1.9
Depth	10.4 ± 2.3	10.6 ± 2.0
Lesion size	3.9 ± 0.9^b	5.1 ± 2.1^c

^a $P = .02$ by Student *t* test.

^b Twenty of 52 of the healthy volunteers had focal hypointensities in the pituitary gland.

^c $P = .05$ by Student *t* test.

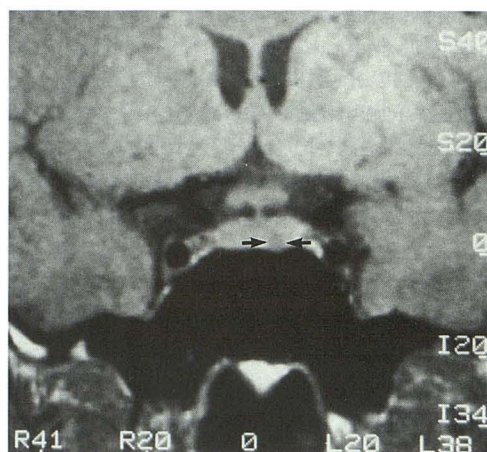


Fig. 1. Coronal T1-weighted MR of the pituitary gland of a healthy volunteer. In the left side of the gland there is a 3.8-mm focal hypointensity (arrows). SD/N ratio is 3.26. Serum biochemistry in this asymptomatic subject was normal.

TABLE 2: Comparison of SD/N and $SD/(WM - GM)$

	Normal glands	Microprolactinomas
SD/N	1.9 ± 0.9	6.2 ± 2.6^a
$SD/(WM - GM)$	0.57 ± 0.4	0.92 ± 0.4^b

^a $P = .0001$ by Student *t* test.

^b $P = .08$ by Student *t* test.

Every patient's gland contained a focal hypointensity with size varying from 2.5 to 9 mm (mean 5.1 mm) (Fig 2). The degree of hypointensity (SD) normalized for system noise (N) and gray matter/white matter differences (WM - GM) were 6.2 and 0.92, respectively (Table 2).

Comparison of Patient and Volunteer MRs

There were no statistical differences in pituitary size or stalk position between the patient and volunteer groups (Table 1). The left side of the gland was larger than the right in the microprolactinoma group, probably because most of the microadenomas happened to be in the left side of the gland. There were significant differences in the size of focal hypointense areas and the degree of hypointensity of these areas with respect to the pituitary gland. These characteristics are graphically illustrated in Figures 3 and 4.

Although there was an overlap in size and degree of hypointensity, the patient group had significantly larger hypointensities ($P = .05$) and greater degree of hypointensity than the healthy group ($P = .0001$) (Tables 1 and 2). This is illustrated graphically in Figure 5.

There were no significant differences between the degree of hypointensity normalized for gray matter/white matter differences (Table 2).

Discussion

Microadenomas are most often visualized as focal areas of reduced signal intensity on T1-weighted spin-echo MR (1-6). However, because

there is a high incidence of small asymptomatic lesions in the pituitary gland, it would be expected that focal areas of hypointensity could also be caused by incidental pituitary cysts, other focal pituitary disease (such as infarcts and metastases), voxel-to-voxel heterogeneity in normal pituitary tissue, and MR system noise.

In this study we found that approximately 40% of healthy young adults, without clinical or biochemical evidence of a pituitary endocrinopathy, had focal areas of low signal intensity. Although the incidence of these findings in volunteers was not nearly as great as in patients with evidence of pituitary disease, our results indicate that a focal area of low signal is in itself not specific for pituitary adenoma.

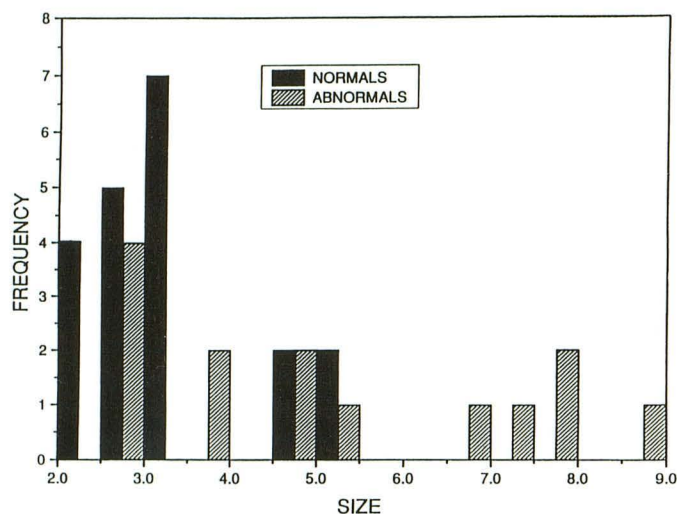
Analysis of the size and degree of hypointensity allowed some discrimination between volunteers and patients. The hypointensities in the volunteers were on average smaller and more similar in intensity to that of the pituitary gland (that is, they were not as dark). Despite some overlap in size and degree of hypointensity, in no case did a volunteer have a hypointense area larger than 5 mm or signal difference (relative to pituitary gland) normalized to noise greater than 4. The degree of hypointensity discriminated better between the two groups than the size of the hypointensity.

Recognizing the impracticality of measuring signal intensities on a routine basis, we normalized the signal intensity difference to the gray matter/white matter difference of the temporal lobes. Using this internal standard, the image contrast of the hypointensities in healthy volunteers was usually less than the gray matter/white matter contrast. In the patient group the image contrast of the hypointensities was equal to or greater than the gray matter/white matter contrast. However, this difference between the groups was not statistically significant.

It may be argued that techniques other than unenhanced T1-weighted spin-echo sequences, in particular contrast-enhanced studies, would have been more appropriate to evaluate for applicability to modern MR image interpretation. Although the use of supplementary contrast-enhanced MR does increase the sensitivity of adenoma detection (12, 13), we believe that the incidence of false-positive results would increase with contrast-enhanced studies because MR contrast agents distribute in a manner entirely analogous to the iodinated agents used with CT. Therefore, it would be reasonable to expect that



Fig. 2. Coronal T1-weighted MR of the pituitary gland of a patient with elevated prolactin, 254 ng/ml. There is a 9-mm hypointensity in the center of the gland (arrows). SD/N ratio is 9.03.

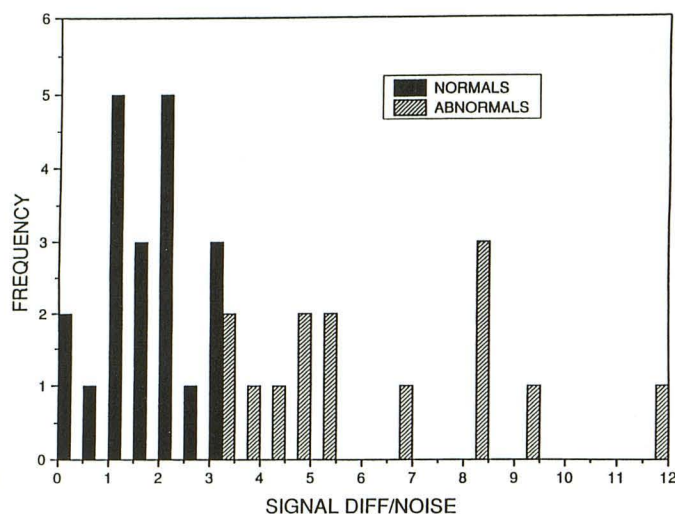


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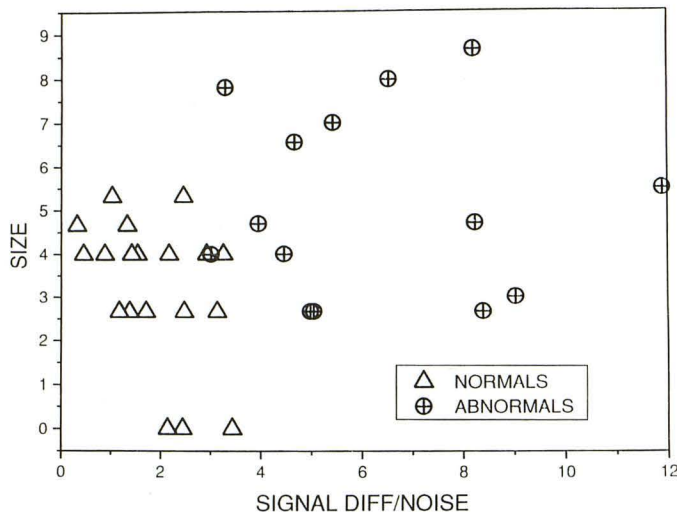
Fig. 3. Frequency distribution of the size of the hypointensities seen in the pituitary glands of healthy volunteers and in glands with microprolactinomas. Note the considerable overlap between the groups. Hypointensities greater than 6 mm are seen only in the microadenoma group.

Fig. 4. Frequency distribution of SD/N ratios measured from the hypointensities in the pituitary glands of healthy volunteers and those with microprolactinomas. There are two patients with microadenomas who have SD/N ratios of 3, along with three volunteers. No volunteer has an SD/N ratio of 4 or greater.

Fig. 5. Comparison of size and degree of low signal areas in volunteers and patients. The hypointensities seen in the glands with microadenomas are larger and more hypointense than those seen in healthy volunteers. The degree of hypointensity discriminates between the two groups better than the size of the hypointensity.



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contrast-enhanced MR would show at least as great a number of incidental findings, and possibly more, as previously reported on CT (3, 7–11). On this basis we do not believe that contrast-enhanced MR would permit any greater discrimination between incidental findings and microadenomas than unenhanced T1-weighted studies.

The selection of the patient group for comparison with the healthy volunteers warrants comment. In our institution the vast majority of patients with microadenomas are treated medically. This precludes obtaining pathologic confirmation of diagnoses in most patients with microadenomas. Restricting the patient group to persons with serum prolactin levels greater than 100 ng/ml virtually ensures that these patients truly do harbor adenomas, because it is rare for any other type of disease to cause such high serum levels (14, 15).

To summarize, small areas of low signal intensity are observed on unenhanced T1-weighted spin-echo MR of the pituitary gland in approximately 40% of healthy persons. In most cases these can be discriminated from pituitary microadenomas by their smaller size and less marked degree of signal difference relative to the pituitary gland. In a minority of cases these incidental findings have imaging features that overlap with these of microadenomas and cannot be discriminated from them.

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