Size, Shape, and Appearance of the Normal Female Pituitary Gland

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AJNR Am J Neuroradiol 1984, 5 (3) 263-267
http://www.ajnr.org/content/5/3/263

Size, Shape, and Appearance of the Normal Female Pituitary Gland

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One hundred seven women 18–65 years old were studied who were referred for suspected central nervous system disease not related to the pituitary gland or hypothalamus. High-resolution, direct, coronal, contrast-enhanced computed tomography (CT) was used to examine the size, shape, and density of the normal pituitary gland. There were three major conclusions: (1) the height of the normal gland can be as much as 9 mm; (2) the superior margin of the gland may bulge in normal patients; and (3) both large size and convex contour appear to be associated with younger age. It was also found that serum prolactin levels do not appear to correlate with the CT appearances. Both low- and high-density areas were seen within the gland, and may be due to either tumors, cysts, infarcts, or metastases. Noise artifacts inherent in high-detail, thin-section, soft-tissue scanning may be a limiting factor in defining reproducible patterns in different parts of the normal pituitary gland.

Computed tomography (CT) has facilitated the radiologic recognition of pituitary gland enlargement. Direct coronal scans in which the interface between the gland and the suprasellar cistern can be seen clearly are preferable to axial scans with sagittal reconstruction because of the loss of spatial resolution inherent in reformatted images. The configuration of the superior surface of the gland, its height, the integrity of the sellar floor, and the position of the infundibulum are all important factors to be considered in diagnosing pituitary tumors.

Many authors have described the appearances of both the normal and abnormal glands [1–11]. While correlation of the CT appearances in life with postmortem examination of the glands is the most direct method for developing criteria of anatomic normality, examination of the CT scans of asymptomatic subjects with normal pituitary hormone assays represents the best indirect method for developing these criteria. We analyzed coronal CT scans of the pituitary gland in 107 women without suspected pituitary or hypothalamic dysfunction. Serum prolactin levels were obtained in 102 of the women and were correlated with the CT appearances.

Subjects and Methods

One hundred seven women 18–65 years old referred for suspected central nervous system disease not related to the pituitary gland or the hypothalamus consented to have direct coronal scans of the sella following their standard scans, under guidelines established by the institution's Human Investigation Review Committee. The studies were not consecutive since about 20% of the women contacted refused the additional scans. The scans were obtained after the intravenous injection of 300 ml of Renografin 30 by drip infusion over 5–10 min. One hundred two of the women also had blood drawn immediately before contrast infusion for the measurement of prolactin and alpha-subunit levels.

The scans were obtained on the Somatom 2 Siemens scanner operated at 46 mA, 10 sec, and 120 kV with 2 mm collimation. The pixel size was 0.5 mm^2. Scanograms, although available, were not obtained, since, after an initial scan approximately through the center of the sella turcica, appropriate positional corrections could easily be made. The scans extended

This article appears in the May/June 1984 issue of *AJNR* and the August 1984 issue of *AJR*.

Received August 25, 1983; accepted after revision December 21, 1983.

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***AJNR* 5:263–267, May/June 1984**
0195–6108/84/0503–0263 $00.00

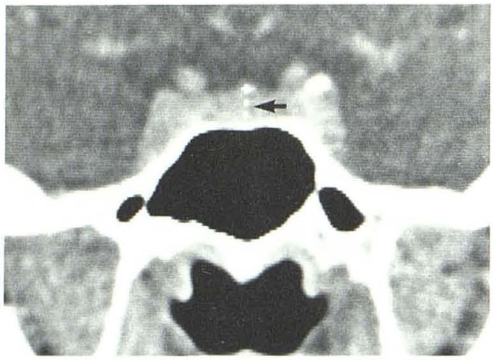

Fig. 1.—Frontal coronal view of sella turcica and pituitary gland. Height of gland (*arrow*) (distance between sellar floor and top of gland) is 7 mm.

from the dorsum sellae to the anterior clinoid processes. Between four and six scans were obtained per patient.

The heights of the glands were determined by measuring the greatest distance between the sellar floor as seen on a scan imaged with a wide bone window to the top of the gland as imaged with a soft-tissue window (fig. 1). The superior surfaces of the glands were classified as convex superiorly, flat, or concave superiorly. The density patterns of the glands were assessed in four different regions—through the anterior pituitary, the region of the pars intermedia, the posterior pituitary, and immediately in front of the dorsum sellae—by analyzing four contiguous scans.

Prolactin levels were measured by double antibody radioimmunoassay with antibody obtained from the National Hormone and Pituitary Program of the National Institutes of Health and the University of Maryland with standards purchased from Serono using minor modifications of published techniques [12]. Alpha-subunit levels were measured by double antibody radioimmunoassay with antibody and standards obtained from the National Hormone and Pituitary Program using previously published methods [13].

Results

The heights and configurations of the glands and their relations to the age of the patients are set out in table 1 and figure 2. The heights varied between 1 and 9 mm (mean 5.7 mm). Larger glands were seen in the younger women. The superior margins of the glands were convex in 19, again more often in the younger than in the older women. The superior margins of the glands were concave in 33 patients, more often in the older than in the younger women (table 1). Empty sellae (gland heights 2 mm or less with the infundibuli extending down to the superior margins of the sellar contents) were seen in six patients, all aged 43 or more. Partially empty sellae (gland heights 3–4 mm) were seen in a further 13 patients.

The density of the glands in the four different regions is set out in table 2. The most frequent pattern seen was that of a heterogeneous density (i.e., mottled appearance of both high- and low-density areas less than 3 mm in diameter) usually throughout the gland and involving the pars intermedia and the posterior pituitary regions. The pre–dorsum sellae region, however, was usually of a homogeneous density. An analysis of the seven patients with low-density areas greater than 3 mm in diameter (fig. 3A) revealed that the anterior region was involved in two patients, the pars intermedia region in all seven patients, and the posterior pituitary region in five patients. In one of these seven, a patient with peripheral neurofibromatosis, the serum prolactin was elevated to a value of 36.2 ng/ml (normal <25 ng/ml); the prolactin levels were normal in the other six patients. Focal high-density areas, greater than 3 mm in diameter (fig. 3B) and involving both the pars intermedia and the posterior pituitary region, were seen in five patients. In one patient with a lesion larger than 3 mm, the serum prolactin level was elevated to 48 ng/ml (table 3).

TABLE 1: **Pituitary Gland Surface and Height versus Age in 107 Women**

Superior Surface	No.	Height (mm)	Age 18–36	Age 37–70
Convex	19	6–9	14	5
Flat	55	4–8	28	27
Concave	33	1–7	12	21

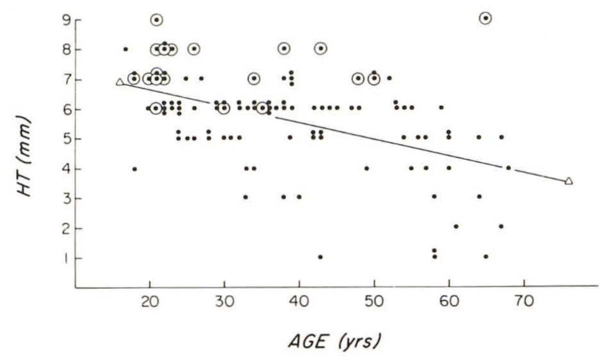

Fig. 2.—Least squares fit relation of gland height and patient age in 107 women. Each dot represents one patient; encircled dots represent glands with convex superior margins. Linear correlation coefficient (r) = 0.047; $p < 0.001$.

TABLE 2: **Density Patterns of the Pituitary Gland in Four Different Anatomic Regions**

Density Pattern	No. Patients by Anatomic Region* 1	2	3	4
Heterogeneous	37	60	62	24
Homogeneous	1	4	1	46
Focal hypodensity†	2	7	5	0
Focal hyperdensity†	0	5	5	0
Empty‡	5	6	6	6
Central hyperdensity with paracentral hypodensity	0	1	2	0

Note.—Only scans without artifacts were selected for analysis. *Hypodensity* and *hyperdensity* are relative to the rest of the gland. Absolute Hounsfield numbers were not considered important because such values varied among patients depending on the relation between time of contrast administration and time of scan. Low-density values, however, were greater than cerebrospinal fluid and ranged between 23 and 56 H; high-density values were 86–122 H.

* Region 1 = anterior pituitary; 2 = pars intermedia; 3 = posterior pituitary; 4 = pre–dorsum sellae.

† Areas greater than 3 mm in diameter.

‡ Pituitary contents 2 mm or less in height.

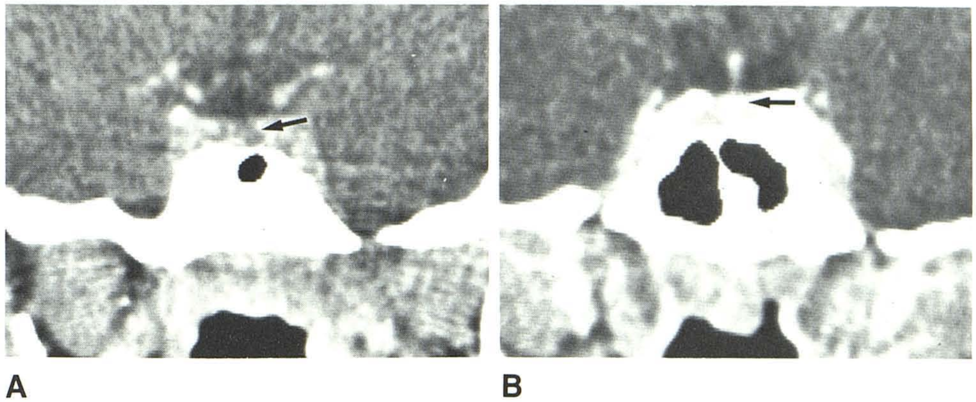

Fig. 3.—**A**, Low-density area measuring 4 × 4 mm (*arrow*) is seen in left half of gland in pars intermedia region. **B**, High-density area (*arrow*) is seen in center of gland. Although scan was obtained at end of, not during, administration of contrast material, appearances suggest opacification of hypophyseal capillary bed.

TABLE 3: **Surfaces, Heights, and Prolactin Levels in Seven Women with Low-Density Areas and Five Women with High-Density Areas within the Pituitary Gland**

Density, Superior Surface	Height (mm)	Prolactin (ng/ml)
Low, convex	9	5
	8	5.2
Low, flat	6	36.2
	6	8.4
Low, concave	6	12.8
	6	12.4
	5	12.6
High, convex	6	4.4
	6	3.3
High, flat	8	14
	5	15.7
High, concave	3	48

Note.—High-density areas were all greater than 3 mm in diameter.

The patient had a melanotic melanoma metastatic to the brain, and the high-density area may represent a pituitary metastasis.

The serum prolactin levels were initially elevated in eight patients (table 4). On repeat testing, however, the levels remained elevated in only four patients. No specific relation between the gland heights, the configuration of the top of the glands, the density patterns of the glands, and the elevated serum prolactin levels were found. One of the four hyperprolactinemic patients had idiopathic seizures, a second had peripheral neurofibromatosis, and a third probably had optic neuritis. These patients may have had idiopathic hyperprolactinemia, but also remained suspect for harboring prolactinomas. The fourth patient, the patient with a melanotic melanoma metastatic to the brain, had also undergone cranial irradiation—a known cause of hyperprolactinemia [14]. Alpha-subunits were not elevated in the four patients.

Discussion

The size of the normal female pituitary gland varies widely. According to Syvertsen et al. [1] the height varied between 2.7 and 6.7 mm in a series of 14 women without known sellar or parasellar lesions who were referred for CT studies of the temporal bone and skull base. Another report on direct coronal scans in 50 normal female volunteers indicated a normal maximum height of 9.7 mm [10]. On reformatted sagittal images of patients of both genders with symptoms of orbital disease but no clinical pituitary disease, Chambers et al. [9] determined that the height of the normal gland averaged 5.3 mm (±1.7 mm). The same authors sectioned the sphenoid bones of 100 cadavers in the sagittal plane and found the height of the pituitary gland to average 5.2 mm (±2 mm). In an autopsy series of 205 pituitary glands, Muhr et al. [15] found the mean gland height of the females to be 6 mm (SD 1 mm). In a CT series of 15 normal adult females, Peyster et al. [8] found the mean height to be 4.8 mm (SD 1.7 mm) and in an in vivo study of 30 female patients, Roppolo et al. [11] found the mean height to be 4.2 mm (±1.4 mm).

Our data correlate well with this past experience. We also agree that the top of the normal gland may be convex as has been stated by others [8, 10], but found the maximum height to be greater than in all previous studies except that of Swartz et al. [10]. The relation between the heights of the glands, their superior configurations, and the ages of the patients probably represents the childbearing potential of the younger patients.

The correlation of the serum prolactin levels with the appearances of the glands was undertaken in an attempt to determine whether a substantial number of the patients had silent prolactinomas. These tumors, which are estimated to be present in 6%–13% of the normal population [16, 17], may be seen as either low- or high-density areas [6]. While persistent elevated prolactin levels were seen in four patients, in only three of them (one with a low-density area greater than 3 mm in diameter) could we state that tumors were possibly present by endocrinologic criteria. Elevated alpha-subunits, which are said to be secreted by some tumors otherwise characterized as nonsecretory [18, 19], were not found in any patient in our study.

It is known, however, that prolactin levels are not consistently elevated in patients with prolactinomas [20]. Conceivably therefore prolactinomas could be present in the seven patients with large, low-density areas and in the five patients with large, high-density areas, which would correlate well with the expected incidence of silent prolactinomas in the normal female population. Furthermore, some of these patients could

TABLE 4: **Pituitary Gland Characteristics in Hyperprolactinemic Patients**

Age (years)	Pituitary			Prolactin (ng/ml)		Reason for CT	Etiology of Hyperprolactinemia
	Density	Surface	Height (mm)	Initial	Repeat		
25	Iso	Flat	5	106.0	32.8, 37.8	Seizures	Idiopathic
38	Iso	Concave	6	26.1	12.8	Meningioma with multiple infarcts	...
20	Low	Flat	6	36.2	33.4	Neurofibromatosis	Idiopathic
37	Iso	Flat	6	29.0	26.5	Probable optic neuritis	Idiopathic
38	High	Concave	3	48.0	42.8	Metastatic melanoma	Cranial irradiation
26	Iso	Convex	8	26.3	11.0, 9.0	Pseudotumor of orbit	...
42	Iso	Concave	5	25.5	15.0, 20.0	Headaches	...
22	Iso	Flat	6	27.8	6.7, 6.6	Optic atrophy	...

have silent nonsecretory microadenomas, which were found in 7%–14% of unselected autopsy specimens [16, 17]. However, some of the low-density areas seen in our patients may also be due to Rathke cleft cysts, infarcts, metastases, epidermoid cysts, or abscesses [9, 21, 22]. Some of the high-density areas may be due to transsellar communicating arteries between the cavernous carotid arteries or intercavernous sinus venous connections [23]. A high-density midline area may also be due to the secondary hypophyseal capillary bed, which can be seen on dynamic scans [24].

The density patterns in the four different regions of the pituitary glands have been studied by others. Roppolo et al. [11] analyzed 13 autopsy specimens and 30 normal pituitary glands with high-detail coronal CT and defined different CT density variations in different parts of the gland. Four specific patterns were seen. Scans through the anterior pituitary often showed a heterogeneous pattern; scans more posteriad through the pars intermedia often showed midline lucent areas due to colloid cysts. Further posteriad, scans through the posterior pituitary gland showed a homogeneous central dense area flanked on both sides by lucent areas due to the diverging pars intermedia. Finally on the most posterior scan, immediately in front of the dorsum sellae, the posterior lobe was seen as a nonhomogeneous cystic area. The authors did not mention the incidence of these four patterns in their 30 patients. We could not confirm these patterns in our patients.

The amount of random noise in the different scanners may be a factor accounting for our different results. Roppolo et al. [11] found that the standard deviations of frontal horn cerebrospinal fluid densities were 3.76–5.73 H, whereas we found that the standard deviations were 6.3–9.8 H. A more likely cause for the different results may be the different techniques used. The Somatom 2 routinely is operated at 460 mAs, whereas the GE scanner used by Roppolo et al. was operated at 614–960 mAs. To reproduce the results of Roppolo et al. with the Somatom 2 scanner, assuming the two scanners have similar spatial resolutions and reconstruction algorithms, it may be necessary therefore to double the radiation dose to the patient. However, only four of the 30 patients of Roppolo et al. were examined with 1.5-mm-thick coronal scans, although they stress that such scans are the most informative, whereas all the patients in our series were examined with 2 mm slices. Before the results of Roppolo et al. are acceptable it would be necessary to have a far larger series of 1.5 mm direct coronal scans analyzed.

In conclusion our results suggest that the height of the normal gland can be as much as 9 mm, that the superior margin of the gland may bulge in normal patients, and that both of these factors appear to be related to the age of the patient. Estimation of the serum prolactin levels does not appear to correlate with the scan appearances, at least in the normal population. Low- and high-density areas seen within the gland may be due to tumors, cysts, infarcts, or metastases. The noise inherent in high-detail, thin-section, soft-tissue scanning may be a limiting factor in defining reproducible patterns in different parts of the pituitary gland.

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