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# Parathyroid Localization

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**ABSTRACT.** Twenty-nine consecutive patients with suspected primary hyperparathyroidism were examined preoperatively using ultrasound, sonographically guided fine needle aspiration, and aspirate immunostaining for PTH. In 25 patients, localization of enlarged parathyroid glands was successful. In 2 patients, the tumors were located retrosternally and, thus, could not be detected by ultrasound. One patient had a multinodular goiter which impeded localization. In 1 patient with renal osteodystrophy, 2 enlarged parathyroid glands in the neck were not

visualized preoperatively. Cytology was not diagnostic, although some cytological features were suggestive of parathyroid cells. Immunostaining of the aspirated smears for PTH, however, correctly diagnosed all preoperatively localized lesions. Ultrasound should be the routine procedure of choice for preoperative localization of abnormal parathyroid glands in primary hyperparathyroidism. Fine needle aspiration and immunocytochemistry can supply confirmation, if necessary. (*J Clin Endocrinol Metab* 63: 1390, 1986)

**P**REOPERATIVE localization of abnormal parathyroid glands in patients with primary hyperparathyroidism (pHPT) is still a challenge. Preoperative detection of abnormal parathyroid glands by ultrasound has been reported by many groups (1, 2, 4-7), and some have combined sonographic localization with sonographically guided fine needle aspiration (FNA) (3, 8). These aspirates have been examined cytologically and immunostained for PTH in attempts to make a morphological diagnosis. We combined ultrasound, sonographically guided FNA, cytology, and immunocytochemical PTH staining for preoperative detection of enlarged parathyroid glands.

## Materials and Methods

All patients (n = 29; 19 women and 10 men; age, 17-80 yr; mean age, 52 yr) who underwent parathyroid surgery between January 1983 until December 1985 with a diagnosis of pHPT were preoperatively evaluated for localization of the glands. The diagnosis of pHPT was based on serum calcium and PTH determinations (9). All patients were operated for pHPT for the first time, although 2 patients had previous surgery for nodular goiter. One patient had renal osteodystrophy.

The thyroid and neck were examined by ultrasound (SRT, linear MHz 5, General Electric, Rancho Cordova, CA). Sonolucent and echocomplex nodules outside the thyroid capsule were biopsied under sonographic guidance with a fine needle (od, 0.6-0.7 mm). In one patient, a suspicious sonolucent nodule

was seen within the thyroid and was aspirated. This patient had previously undergone bilateral subtotal thyroidectomy for nodular goiter. In all patients, biopsies from one or two areas (Table 1) were performed. In only a few patients was a second pass, to obtain sufficient material, necessary. Patients with coexisting nodular goiter were biopsied additionally a maximum of four times at sites that were nodular but not considered typical for parathyroid adenoma. The smears were air dried. Half were stained by the May-Grünwald-Giemsa technique for morphological evaluation. The other specimens were immunostained for PTH by a modification of the peroxidase-antiperoxidase technique described by Sternberger (10). A chicken C-terminal antihuman PTH-(44-65) antibody (IBL Co., Hamburg, West Germany) diluted 1:50 was applied and incubated for 9 h at 37 C. Antichicken immunoglobulin G antiserum conjugated with rabbit peroxidase (Medac Co., Hamburg, West Germany) diluted 1:25 was added, and incubation was carried out for 30 min at room temperature. To visualize the peroxidase reaction, staining was completed with 3,3'-diaminobenzidine solution (0.03% plus 0.03% H<sub>2</sub>O<sub>2</sub>) for 5 min. At these dilutions, the antisera did not cross-react with fresh postmortem cytological specimens obtained from liver, thyroid, and kidney.

## Results

The decision for surgery was based on clinical and biochemical grounds alone. All patients who had a preoperative diagnosis of pHPT, based on the presence of hypercalcemia (range, 2.7-4.0 mmol/liter; mean, 3.3; upper limit of normal, 2.7) and an inappropriately high serum PTH concentration (range, 300-30,000 ng/ml; upper limit of normal, 200) proved to have a parathyroid adenoma or primary parathyroid gland hyperplasia on

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TABLE 1. Clinical characteristics of patients with pHPT and maximal diameters of adenomas after surgical removal

Patient no.	Age (yr)/sex	Serum PTH (ng/ml)	Serum CA (mmol/liter)	Location	Maximal diameter (cm)
1	47 F	1,335	3.2	LL	2.5
2	51 F	300	3.0	LL, LR	2.8, 2.1
3	36 F	364	3.6	UL	2.0
4	64 F	1,908	2.7	T	2.3
5	54 M	6,140	3.9	LL	4.2
6	17 M	1,229	3.1	LR	3.8
7	36 F	840	3.5	LL	5.2
8	27 F	1,820	2.8	LL	1.9
9	38 F	616	4.0	UL	2.8
10	76 F	300	3.3	UL	3.7
11	72 M	380	3.2	UR	2.2
12	80 M	1,000	2.8	UL	4.6
13	46 F	716	3.7	LL	3.8
14	22 M	311	3.2	LL, UR	2.9, 2.2
15	38 M	346	3.1	LL	1.9
16	47 F	30,000	2.9	UL	2.7
17	25 F	346	4.0	LR	4.1
18	76 M	1,029	3.1	LL	1.1
19	71 F	832	3.1	UR	2.8
20	52 M	458	3.2	LL	3.7
21	68 F	802	3.6	LL	1.3
22	70 F	1,442	3.1	LL	5.3
23	36 M	927	2.8	UR	1.8
24	75 F	456	3.0	LL	4.1
25	53 F	720	3.5	LR	3.8
26 <sup>a</sup>	43 F	1,500	4.0	R	3.2
27 <sup>a</sup>	52 F	3,500	2.7	UL	7.8
28 <sup>a</sup>	74 F	752	2.9	R	3.6
29 <sup>a</sup>	68 M	1,853	3.3	UL, UR	1.6, 1.8
Normal	range	<200	<2.7		

R, Retrosternally; T, intrathyroidal; LL, lower left lobe; UL, upper left lobe; LR, lower right lobe; UR, upper right lobe.

<sup>a</sup> Adenomas, not localized sonographically.

histological examination (the maximal diameter of the surgical specimens ranged from 1.1–5.3 cm). Pertinent clinical data are illustrated in Table 1. In 23 patients solitary adenomas and in 2 patients (patients 2 and 14) 2 enlarged parathyroid glands were identified preoperatively. Subsequent surgical findings agreed with the preoperative ultrasonographic localization and the approximate predicted dimensions (Fig. 1). In 4 patients, abnormal parathyroid glands were not located preoperatively. Two of these patients had adenomas that were retrosternal and, thus, not accessible to ultrasonographic detection (patients 26 and 28). In the third patient (no. 27), detection of abnormal parathyroid tissue was not possible due to the presence of multiple sonolucent nodules in a goiter; this patient had 1 adenoma. The fourth patient (no. 29) had renal osteodystrophy, and 2 enlarged hyperplastic parathyroid glands were found at the time of surgical exploration.

Definite cytological discrimination between thyroid and parathyroid cells was not possible. Lymphocytes and cells from other tissues of nonthyroid origin, however, could be identified. Some cytological features were suggestive of parathyroid cells. Thus, parathyroid cells have lighter, often foamy and more narrow cytoplasm, and their nuclei are larger and more marginally situated compared to thyroid cells (Fig. 2).

Positive PTH immunostaining was seen in cells from all aspirates (Fig. 3). In one patient in whom a parathyroid adenoma was located within the thyroid gland, cytology was not diagnostic, but the aspirate stained with anti-PTH. Thus, immunocytochemistry made the correct preoperative diagnosis in this patient.

After transient postoperative calcium replacement therapy, serum calcium and PTH concentrations returned to normal levels in all patients.

### Discussion

Preoperative localization of abnormal parathyroid glands has been attempted by various invasive and non-invasive procedures. Selective angiography and venous catheterization with determination of serum PTH concentrations are invasive and technically difficult (11). Imaging procedures employing subtraction scanning with <sup>210</sup>-thallium and <sup>99m</sup>-technetium have been successfully employed, but further experience with these techniques is necessary (12). Computerized tomography is costly and has a relatively low yield (13, 14). Ultrasonographic localization has been reported by various researchers to be useful (1, 2, 4–7), and attempts to improve its specificity by FNA have been made. However, the ability of cytologists to differentiate between thyroid and parathyroid cells is questionable (15, 16). Other groups have assayed the biopsy material for PTH content, with useful results (3, 17). PTH immunostaining, however, relates the PTH to the cells. A comparison of RIA and immunostaining with regard to sensitivity and specificity is needed.

Our results demonstrate that preoperative ultrasonographic localization is a safe, noninvasive, inexpensive, and reliable method for the detection of enlarged parathyroid glands located in the neck. Due to the limitation of the method, one cannot detect intrathoracic tumors. Sonography has further limitations in patients who have large multinodular goiters. The smaller the parathyroid gland, the more difficulties will arise in locating it. Therefore, hyperplastic parathyroids in patients with chronic renal failure are often difficult to detect (7). Despite the fact that the resolution of ultrasound now reaches approximately 1 mm, small tumors can be easily missed by this method.

Although the addition of cytology to ultrasound seems to be promising, more experience must be obtained con-

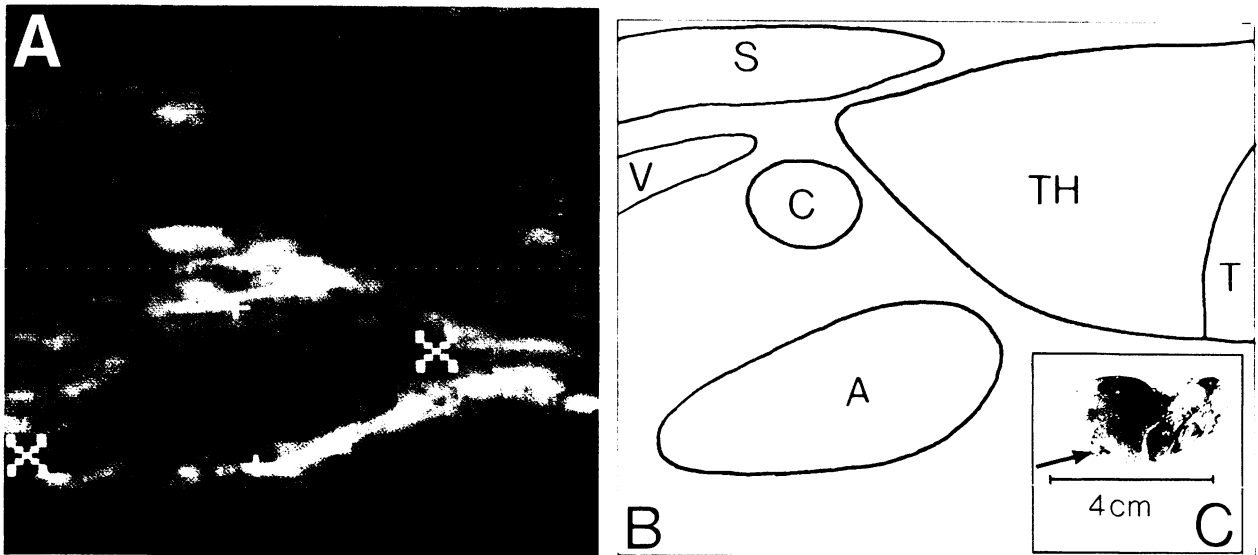


FIG. 1. A, Right transverse sonogram of the thyroid and the typical sonolucent parathyroid adenoma, as indicated in B, in patient 17. B, Schematic drawing of the sonogram. TH, Thyroid; C, carotid artery; A, parathyroid adenoma; S, sternocleidomastoid muscle; T, trachea; V, jugular vein. C, Surgical specimen of the enlarged parathyroid gland (4 cm) with the lesion (*arrow*) caused by preoperative FNA.

FIG. 2. Smear from FNA of a parathyroid adenoma (May-Grünwald-Giemsa; original magnification,  $\times 480$ ).

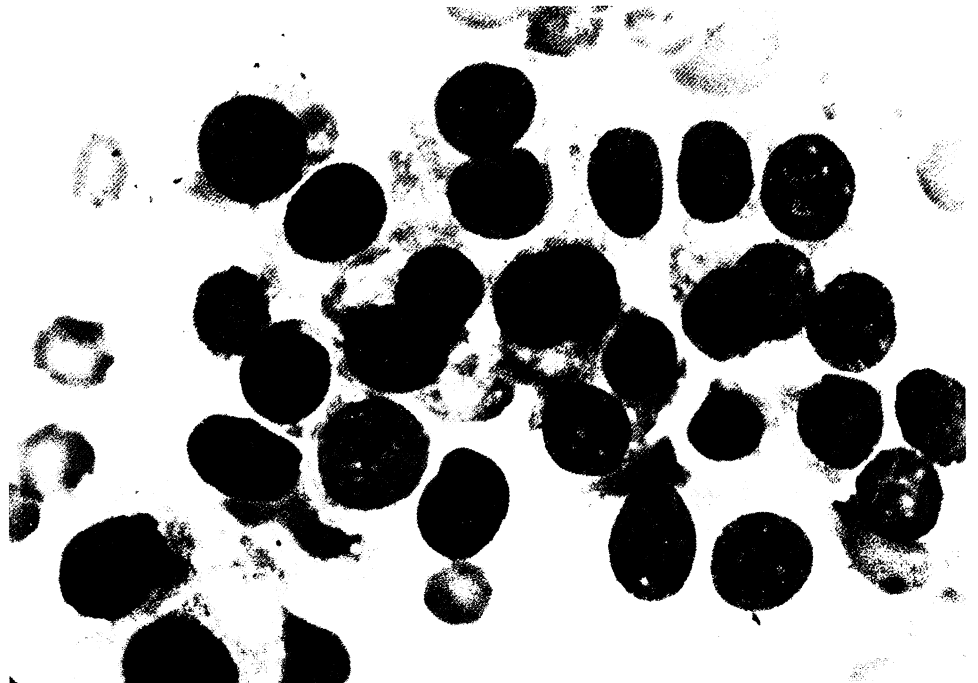
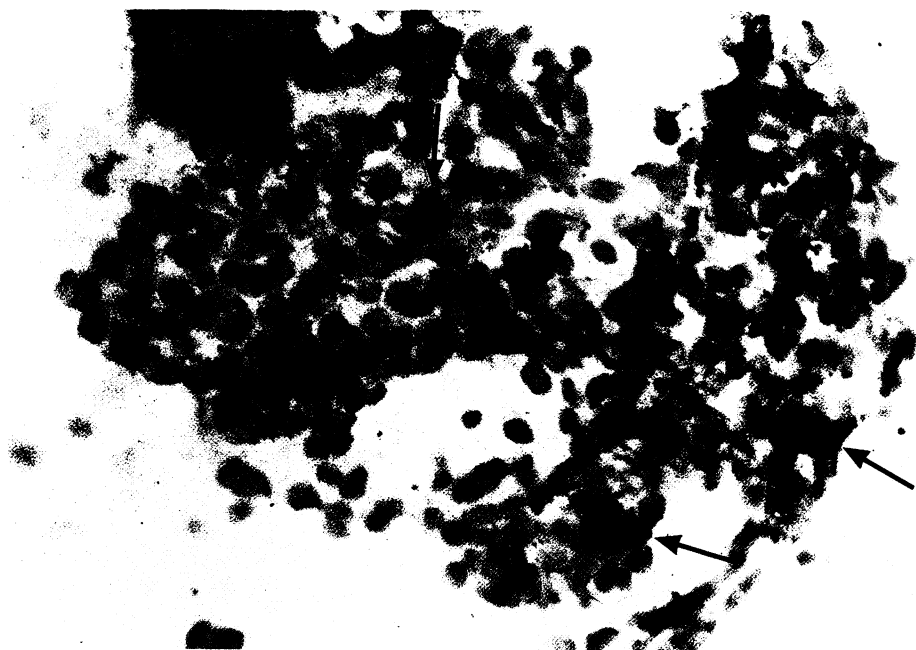


FIG. 3. Smear from FNA of parathyroid adenoma immunostained for PTH (original magnification,  $\times 120$ ). The arrows indicate PTH immunostaining.



cerning the details of parathyroid cell morphology. At present, the benefit of cytology is to identify the aspirated cells as parathyroid and/or thyroid cells. Since immunocytochemistry is gradually becoming a routine procedure, addition of this method may help to establish the correct final diagnosis.

In conclusion, we believe that sonography is the procedure of choice for preoperative localization of abnormal parathyroid glands in patients with pHPT. Immunocytochemistry can supply confirmation, if necessary. The utility of these procedures for identifying parathyroid tissue in patients who had a previously unsuccessful operation is not known.

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