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Parathyroid adenomas: pre-operative localization with ultrasound combined with fine-needle biopsy

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Abstract

Sixteen patients with biochemically proven primary hyperparathyroidism (PHPT) underwent ultrasonography (US), fine-needle aspiration (FNA) for cytologic sampling (n = 9), or intact parathormone assay (n = 3) before operation (n = 15) in order to determine the accuracy of the methods. Pre-operative US was found sensitive (100 per cent), but two thyroid lesions were initially diagnosed as parathyroid tumours by US (i.e. false positives). Parathyroid cells were detected in six cytologic specimens, one sample was insufficient and another inconclusive, while one was diagnosed as thyroid tissue. Parathormone assay revealed a high hormone content in all three patients who underwent the procedure. We conclude that US is sufficiently sensitive to detect enlarged parathyroid tumours. Specificity can be improved by US-guided FNA for cytology or parathormone assay prior to neck exploration.

Key words: Parathyroid neoplasms; Ultrasonic diagnosis; Biopsy, needle

Introduction

Controversy exists as to whether pre-operative imaging methods, such as ultrasonography (US), computer-assisted tomography (CT), scintigraphy, magnetic resonance imaging (MR), should be performed before primary operation in patients with primary hyperparathyroidism (PHPT) (Karstrup *et al.*, 1987; Awwad *et al.*, 1988; Kairaluoma *et al.*, 1989; Uden *et al.*, 1990; Bergenfelz *et al.*, 1991). Imaging methods are non-specific and invasive methods are often needed to establish an accurate diagnosis. Guided biopsies are accurate in diagnosing various pathologies, but cytologic interpretation of specimens from endocrine organs such as the parathyroids is problematical and the literature on parathyroid fine-needle aspiration (FNA) for cytologic and histologic analysis and parathormone assay is scanty and controversial (Solbiati *et al.*, 1983; Rastad *et al.*, 1984a; Mincione *et al.*, 1985; Verbanck *et al.*, 1986; Karstrup *et al.*, 1987, 1989a; Bergenfelz *et al.*, 1991).

The aim of the present study was to evaluate the efficacy of pre-operative cervical US, cytologic sampling and aspiration for intact parathormone assay in 16 consecutive patients with proven PHPT.

Material and Methods

The study material comprised 16 consecutive patients with biochemically proven PHPT at the Central Hospital of Keski-Pohjanmaa, Kokkola, Finland. Fifteen patients (4 men and 11 women: mean age 54.5 years, range 32–72 years) were operated on and one 79-year-old woman was treated with percutaneous alcohol inactivation (Karstrup *et al.*, 1989b). The clinical symptoms and signs of the patients are given in Table I.

All 16 patients underwent cervical US, one patient underwent computer-assisted tomography (CT), nine patients underwent US-guided fine-needle aspiration (FNA) biopsy (0.8 mm) for cytologic sampling, and three patients underwent FNA for intact parathormone assay. For the US study we used a 7.5 MHz real-time sector or linear probe (Aloka SSD-720, Toshiba 270A). Patients were examined supine, with the neck hyperextended. Transverse and longitudinal scans were obtained with the acoustic gel as couplant. The CT study (Siemens Somatom DR) included both non-contrast and contrast (4 mm slice thickness, 4 mm intervals) examinations.

US-guided FNA was carried out with free-hand technique. The cytologic aspirate was fixed in 50 per cent alcohol and all cytologic specimens were examined by an experienced cytopathologist (M.A-S). The technique for CT-guided parathormone assay was originally described by Doppman *et al.* (1983). The aspirated material for hormone assay, usually one or two drops, was diluted in sterile water to a final volume of 1 ml and frozen immediately at −20°C prior to determination of intact PTH content (Bergenfelz *et al.*, 1991). Plasma level and aspirate content of parathormone were both determined with commercially available assays for intact parathormone. The aspirate hormone level was regarded as positive when higher values than those for plasma (10–50 ng/l) were obtained.

Exploration was performed in 15 patients. One patient was initially treated with percutaneous alcohol inactivation. Indications for the use of percutaneous alcohol

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TABLE I
CLINICAL PRESENTATION OF THE CASE MATERIAL

Incidental finding	5
Lassitude, general malaise	4
Ureterolithiasis	4
Abdominal pain	1
Arterial hypertension	1
Skeletal pain	1

inactivation were poor general condition and hypercalcaemic crisis (Case 13).

The imaging findings and the cytologic and hormone assay results were correlated with the final histopathologic diagnoses (n = 15) or after 22 months follow-up (n = 1).

Results

Details of the case material are presented in Table II. Nineteen suspected parathyroid tumours were diagnosed by US and 16 of these were confirmed at surgery. Two of the lesions proved both at operation and at follow-up to be thyroid lesions (i.e. were false positive) and were not definitively diagnosed by primary US. CT was performed in one patient (Case 6) and the radiologic finding was comparable to US: a left retrothyroid solid 3 cm tumour that was enhanced less than thyroid tissue. All but one patient (Case 12) had one adenoma at operation. At US, all the tumours were hypoechoic (one partially cystic), oval or round.

US-guided FNA yielded parathyroid cells in six patients. The sample was insufficient in one patient and inconclusive in one other. Furthermore, one sample contained thyroid cells. Intact parathormone assay proved positive in three patients (Table II). One patient (Case 13) with hypercalcaemic crisis was successfully treated with percutaneous alcohol inactivation. The cytologic sample and hormone assay both proved positive for parathyroid tumour in this case.

Neither vocal fold paralysis nor persistent hypocalcaemia was detected either following the alcohol injections or post-operatively. During the follow-up period, spanning 3 months to 7 years (mean 2.5 years), no recurrences have been detected.

Discussion

Although exploratory surgery is successful in 90–95 per cent of PHPT patients, pre-operative localization of enlarged parathyroid adenomas is important for several reasons, of which the most important is to direct the initial surgical exploration to the affected side of the neck. Thus, the operative time and the risk of nerve damage during exploration is diminished and the incidence and severity of post-operative hypocalcaemia is reduced (Awwad *et al.*, 1988; Kairaluoma *et al.*, 1989; Uden *et al.*, 1990). High-resolution US proved a reliable method for imaging enlarged cervical parathyroid glands. Previous studies have reported the diagnostic accuracy of parathyroid US, varying from 50 per cent to 92 per cent (Graif *et al.*, 1987; Uden *et al.*, 1990). We saw no signs of ectopic or mediastinal parathyroid tumour in this study and the tumours were quite large and easy to locate, in agreement with a previous study (Rastad *et al.*, 1984a).

As visualized by US, most parathyroid adenomas are homogeneous, hypoechoic, round or oval. Morphological variations, such as cystic, calcified, multilobulated, and inhomogeneous, were present in 16–24 per cent of all adenomas (Graif *et al.*, 1987; Randel *et al.*, 1987). Moreover, concomitant thyroid disease reduces the specificity of the method. False-positive US interpretations accounted for some 8–24 per cent in three earlier studies (Solbiati *et al.*, 1983; Verbanck *et al.*, 1986; Uden *et al.*, 1990), compared with our figure of 10.5 per cent (2/19). Two advantages of US are that it is readily available, and also that direct visualization of the needle tip during insertion and aspiration is possible by US, but not by CT. Due to the limitations of the method, intrathoracic, retro-esophageal, or retrotracheal tumours cannot be detected (Rastad *et al.*, 1984a). Moreover, hyperplastic glands, thyroid nodules and enlarged lymph nodes may be difficult to distinguish from adenomas (Rastad *et al.*, 1984b). Thus, US is extremely operator dependent.

In such instances, FNA for cytologic analysis is impor-

TABLE II
DETAILS OF THE 16 PATIENTS WITH BIOCHEMICALLY PROVEN PRIMARY HYPERPARATHYROIDISM

Case no./ age and sex	Serum calcium (mmol/l)	Serum parathormone level (ng/l)	Lesion size (mm) and localization*	Aspirate hormone level	Cytology	Histology
1/59/F	3.02	140	13, LUP	—	—	Adenoma
2/72/F	3.08	280	23, LLP	—	—	Adenoma
3/49/F	2.88	60	12, RLP	—	—	Adenoma
4/35/F	3.90	55	45, LLP	—	Parathyroid cells	Adenoma
5/32/F	3.03	160	18, RLP	—	Parathyroid cells	Adenoma
6/44/M	3.17	280	30, LLP	—	—	Adenoma
7/63/F	3.00	—	13, RLP	—	—	Adenoma
8/61/F	3.17	460	50, RLP	—	Parathyroid cells	Adenoma
9/71/F	2.95	160	13, LLP	—	—	Adenoma
10/49/M	3.04	150	15, RLP	—	Insufficient	Adenoma
11/71/M	3.10	900	25, LLP	—	Parathyroid cells	Adenoma
12/62/F	2.87	170	30, LLP	—	Parathyroid cells	Hyperplasia
13/79/F	4.06	2800	30, LLP	50 000	Parathyroid cells	—
14/46/F	3.02	130	23, LLP	2280	Thyroid, lymph node or parathyroid cells	Adenoma
15/42/F	2.90	180	20, LLP	—	Thyroid cells	Adenoma
16/67/M	2.90	143	11, LLP	4155	—	Adenoma

LUP = left upper pole, LLP = left lower pole, RLP = right lower pole.

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tant for differential diagnosis. In five previous studies, sufficient material for cytologic analysis was obtained in 86.5 per cent to 100 per cent of cases and a definitive diagnosis of parathyroid neoplasia in 73 per cent (Solbiati *et al.*, 1983; Rastad *et al.*, 1984a; Mincione *et al.*, 1986; Verbanck *et al.*, 1986; Karstrup *et al.*, 1988). While parathyroid cells can be identified in the cytological aspirate, differential diagnosis of adenoma or hyperplasia cannot be performed cytologically (Solbiati *et al.*, 1983). In this study, six of nine aspirates proved positive for parathyroid cells. Follicular thyroid neoplasms may make cytologic differential diagnosis difficult (Mincione *et al.*, 1986) as in one of our patients. Moreover, one sample contained only thyroid tissue, possibly due to a missed target during aspiration. While histological specimens may be more familiar to the general pathologist, in one study a 21-gauge cutting needle failed to provide an adequate histologic specimen in 47 per cent of the patients (Karstrup *et al.*, 1989a).

In this study intact parathormone assay proved a specific and reliable method, in agreement with two previous studies (Bergenfelz *et al.*, 1991; Mäkäräinen *et al.*, 1991). In contrast to two previous studies, we omitted CT-guidance, repeated the aspiration, used local anaesthesia, or injected saline into the suspected enlarged parathyroid gland. We did not take control samples from sternocleidomastoid muscle or thyroid tissue, or measure the mid-region parathormone (Doppman *et al.*, 1983; Karstrup *et al.*, 1987). US-guided intact parathormone assay may be even more specific than cytologic sampling and the specificy of US is increased. Post-biopsy haematoma and fibrosis are the only reported complications to this procedure (Bergenfelz *et al.*, 1991; Mäkäräinen *et al.*, 1991), although we had no complications at all.

CT has an accuracy of 75–81 per cent in detecting pathological parathyroids (Awwad *et al.*, 1988; Cates *et al.*, 1988). However, tortuous vessels, thyroid adenomas, oesophagus and atypical parathyroid adenomas may cause diagnostic errors. Neither CT nor MR is a specific technique for the detection of parathyroid adenoma (Spritzer *et al.*, 1987; Cates *et al.*, 1988), but CT, MR and technetium–thallium subtraction scintigraphy are known to be effective in detecting mediastinal and ectopic parathyroid tumours (Awwad *et al.*, 1988). Nevertheless, thyroid adenomas can give false-positive scintigraphic results (Foster *et al.*, 1989) as at US. At our hospital, US combined with FNA is the primary imaging method for thyroid and parathyroid diseases and the results of this study support this procedure.

Chemical parathyroidectomy may be an alternative treatment for patients in poor clinical condition and with severe hypercalcaemia or advanced age and for those few patients who refuse surgery (Karstrup *et al.*, 1988). The diagnosis of HPT must be definitive and the detected parathyroid tumour confirmed either with US-guided cytologic specimen or intact parathormone assay.

Accurate pre-operative localization of parathyroid tumours is of the utmost advantage for the surgeon. We conclude that US combined with FNA for cytology and intact parathormone assay is a safe and accurate diagnostic procedure in patients with primary hyperparathyroidism when neck exploration is planned.

References

Awwad, E., Archer, C., Krebs, F. (1988) Parathyroid adenomas; computed tomographic imaging and the importance of preoperative imaging. *Computerized Medical Imaging and Graphics* **12:** 305–314.

Bergenfelz, A., Forsberg, L., Hederström, E., Ahren, B. (1991) Preoperative localization of enlarged parathyroid glands with ultrasonically guided fine needle aspiration for parathyroid assay. *Acta Radiologica* **32:** 403–405.

Cates, J., Thorsen, K., Lawson, T., Middleton, Wm., Foley, W., Wilson, S., Krubsack, A. (1988) CT evaluation of parathyroid adenomas: diagnostic criteria and pitfalls. *Journal of Computer Assisted Tomography* **12:** 626–629.

Doppman, J., Krudy, A., Marx, S., Saxe, A., Scheined, P., Norton, J., Spiegel, A., Downs, R., Schaaf, M., Brennan, M., Scheiner, A., Aurbach, G. (1983) Aspiration of enlarged parathyroid glands for parathyroid hormone assay. *Radiology* **148:** 31–35.

Foster, G., Bekerman, C., Blend, M., Byrom, E., Pinsky, S. (1989) Preoperative imaging in primary hyperparathyroidism. *Archives of Otolaryngology, Head and Neck Surgery* **115:** 1197–1202.

Graif, M., Itzchak, Y., Strauss, S., Dolev, E., Mohr, R., Wolfstein, I. (1987) Parathyroid sonography: diagnostic accuracy related to shape, location and texture of the gland. *British Journal of Radiology* **60:** 439–443.

Kairaluoma, M., Mäkäräinen, H., Salo-Zetterman, E., Kairaluoma, M., Ståhlberg, M. (1989) Cost effectiveness of ultrasound in primary hyperparathyroidism. *British Journal of Surgery* **76:** 596–597.

Karstrup, G., Glenthoj, A., Torp-Pedersen, S., Hegedus, L., Holm, H. (1987) Ultrasonically guided fine needle aspiration of suggested enlarged parathyroid glands. *Acta Radiologica* **29:** 213–216.

Karstrup, S., Lohela, P., Apaja-Sarkkinen, M., Borgmästars, H., Holopainen, O. (1988) Non-operative inactivation of a parathyroid tumour in a patient with hypercalcemic crisis. *Acta Medica Scandinavia* **224:** 187–188.

Karstrup, G., Glenthoj, A., Hainau, B., Hegedus, L., Torp-Pedersen, S., Holm, H. (1989a) Ultrasound-guided, histological, fine-needle biopsy from suspect parathyroid tumours: success-rate and reliability of histological diagnosis. *British Journal of Radiology* **62:** 981–985.

Karstrup, S., Transbol, I., Holm, H., Glenthoj, A., Hegedus, L. (1989b) Ultrasound-guided chemical parathyroidectomy in patients with primary hyperparathyroidism: a prospective study. *British Journal of Radiology* **62:** 1037–1042.

Mäkäräinen, H., Takalo, R., Kairaluoma, M., Salmela, P., Reinilä, M. (1991) Lisäkilpirauhassairauden varmistaminen kaikuohjauksen avulla otetuilla hormooninäytteillä. *Duodecim* **107:** 1613–1618 (in Finnish).

Mincione, G., Borrelli, D., Cicchi, P., Ipponi, P., Fiorini, A. (1986) Fine needle aspiration cytology of parathyroid adenoma. *Acta Cytologica* **30:** 65–69.

Randel, S., Gooding, G., Clark, O., Stein, R., Winkler, B. (1987) Parathyroid variants: US evaluation. *Radiology* **165:** 191–194.

Rastad, J., Johansson, H., Lindgren, P., Ljunghall, S., Stenkvist, B., Åkerström, G. (1984a). Ultrasonic localization and cytologic identification of parathyroid tumors. *World Journal of Surgery* **8:** 501–508.

Rastad, J., Fransson, A., Lindgren, P., Johansson, H., Ljunghall, S., Malmaeus, J., Åkerstrom, G. (1984b) Ultrasonic appearance of adenomatous and hyperplastic parathyroid glands. *Acta Radiologica* **25:** 471–474.

Solbiati, L., Montali, G., Croce, F., Bellotti, E., Giangrande, A., Ravetto, C. (1983) Parathyroid tumors detected by fine needle aspiration biopsy under ultrasonic guidance. *Radiology* **148:**793–797.

Spritzer, C., Gefter, W., Hamilton, R., Greenberg, B., Axel, L., Kressel, H. (1987) Abnormal parathyroid glands: High-resolution MR imaging. *Radiology* **162:** 487–491.

Uden, P., Aspelin, P., Berglund, J., Lilja, B., Nyman, U., Olsson, L., Zederfeldt, B. (1990) Preoperative localization in unilateral parathyroid surgery. *Acta Chir Scand* **156:** 29–35.

Verbanck, J., Clarysse, J., Loncke, R. (1986). Parathyroid aspiration biopsy under ultrasonographic guidance. *Archives of Otolaryngology, Head and Neck Surgery* **112:** 1069–1073.

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