ULTRASONICALLY GUIDED FINE-NEEDLE ALCOHOL INJECTION AS AN ADJUNCT TO MEDICAL TREATMENT IN SECONDARY HYPERPARATHYROIDISM

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Summary

In 12 uraemic patients with symptomatic secondary hyperparathyroidism, 13 parathyroid hyperplasias, detected by sonography and confirmed by fine-needle aspiration biopsy, were treated by ultrasonically-guided percutaneous injection of absolute ethanol, in order to reduce the gland mass.

Only in the larger glands were significant volume reductions recorded, whereas in the smaller ones evident structural changes were observed.

In most cases with single lesions, a reduced incidence of vitamin D hypercalcaemia and a permanent improvement in bone alkaline phosphatase and PTH were documented. This technique can be usefully employed either as an alternative to surgery in selected cases, or as support to medical therapy in single lesions.

Introduction

In uraemic patients the incidence of secondary hyperparathyroidism (sHPT) is very high, affecting bone metabolism, cardiac and endocrine functions [1]. Medical treatment with active vitamin D metabolites does not seem to achieve a definite improvement of sHPT [2] and can seldom influence the parathyroid hyperplasia which sustains this syndrome.

Therefore the reduction of the gland mass by parathyroidectomy (PTX) is considered an effective method to create a new starting point for pharmacological treatment [3].

For the same purpose, as an alternative to PTX and in cases resistant to medical therapy, we have performed ultrasonically-guided percutaneous fine-needle alcohol injection (UGFNA) of enlarged parathyroid glands.

In this paper we report our preliminary results in a small group of patients.

Material and methods

Twelve out of 101 uraemic patients with symptomatic sHPT and one or more enlarged parathyroid glands detected by sonography were selected for UGFNA.
The patients had been on haemodialysis treatment from 65 to 176 months; their age ranged from 34 to 69 years. In all cases diagnostic confirmation of the lesions was obtained by fine-needle aspiration biopsy with ultrasonic guidance with cytological examination (11 cases), according to the technique previously described [4], and/or parathyroid hormone assay of the aspirated material (4 cases), as reported by Doppman et al [5]. Serum parathyroid hormone levels (iC-PTH) were estimated by a radioimmunological method (Sorin Biomedica, Saluggia, Italy); bone alkaline phosphatase isoenzymes were determined on cellulose acetate [6].

In 7/12 cases one enlarged parathyroid gland was shown by high-resolution real-time sonography. In the remaining five two glands were detected: in 4/5 only the larger gland was injected with alcohol, whereas the fifth had both glands treated. The dimensions of the glands ranged from 0.9 to 2.5 cm in diameter. Serum levels of either parathyroid hormone or bone alkaline phosphatase were significantly increased in all patients. Reduction of the gland mass was considered necessary because of severe sHPT (4 cases), mixed bone disease with fractures (2), hypercalcaemia (3), itching and hyperphosphataemia (2), or vascular calcification (1). UGFNA was preferred to surgery when there was hyperplasia of a single gland (4 cases), recurrence after subtotal PTX (2), high surgical risk (3), or refusal of surgery (3).

Informed consent was obtained from all patients. Bleeding parameters were carefully evaluated and in all cases prophylactic treatment with Deamino-8 D-Arginine Vasopressin (0.3 μg/kg) was administered, as in previous studies [7].

For the ultrasonic guidance real-time sector scanners with lateral biopsy guides were employed, either with a 7.5 MHz probe (Advanced Technology Laboratories) or a 10 MHz intra-operative probe (Diasonics). We used commercially available 22 gauge, 9.5 cm needles connected to 5 ml syringes.

High-resolution real-time monitoring allowed precise control of needle penetration: the needle-tip was always guided into the anterior portion of the lesion, in order to avoid injury to the recurrent laryngeal nerve which lies posterior to the parathyroid glands. The quantity of injected alcohol was 1 ml per 2–2.5 cc of glandular volume approximately calculated for both oval and round-shaped glands.

All the procedures were carried out between dialyses, attention being paid to maintenance of a controlled administration of heparin during the following dialysis.

Fifteen, 30, 60, 180 and 240 days after the procedure the patients were sonographically and biochemically assessed.

Results

Thirteen hyperplastic parathyroid glands in 12 patients were treated with UGFNA and significant results were obtained in nine cases. In four glands the procedure was unsuccessful: in two the injected alcohol diffused anteriorly to the gland, in one case the lesion had partially calcified walls which prevented an adequate intra-glandular injection of the alcohol, and in one case the patient
did not co-operate sufficiently. In the other nine glands either a significant volume reduction or changes in the echopattern were observed following the alcohol injection. The maximum reductions, ranging from 20 to 100 per cent (Figure 1) of the initial volume, were recorded after six months. Changes in the echopattern were increasingly evident in successive controls. Early changes (15–30 days after the procedure) consisted of high-level internal echoes and focal marginal irregularities appearing in all the glands.

![Graph showing parathyroid size before and after UGFNA](image)

**Figure 1.** Parathyroid size before and six months after UGFNA ([●] patient subsequently submitted to PTX who showed extensive necrotic change in the greatest gland)

Subsequently (4–6 months) the glands were replaced by echogenic tissue, either partially (2 cases) or totally (2), or by liquid areas (2 cases) (Figure 2). In the three lesions larger than 2cm only a volume reduction was noted, without any structural change.

In the 5/7 cases of single gland hyperplasias with successful injection the sonographic changes were accompanied by an improvement in the clinical condition and a decrease in serum levels of PTH and bone alkaline phosphatase (Figure 3).

The procedure was generally well tolerated: side effects were limited to spontaneously remitting local pain in 10/12 patients. In one patient mild dysphonia was recorded over the following 24 hours and in the last patient, who erroneously received dialysis only 12 hours after the manoeuvre, a small haematoma was documented in the site of injection.

**Discussion**

Medical treatment of sHPT with vitamin D can improve both clinical and biochemical patterns, but does not seem to affect the volume of the hyperplastic
Figure 2. Sagittal scan of inferior parathyroid gland (a) before and (b) 90 days after UFGNA. The gland volume is decreased from 1.8 cm (calipers) to 0.8 cm and its structure is highly echogenic due to fibrosis.
gland. Moreover in the most severe forms of sHPT the concomitant hypercalcaemia may preclude any pharmacological treatment. Therefore surgical reduction of gland mass is thought to be necessary in order to obtain greater responsiveness to medical therapy. The therapeutic usefulness of the injection performed on enlarged parathyroid glands was suggested by the reported unexpected remission of the symptoms of hyperparathyroidism following aspiration biopsy. We have also observed internal haemorrhagic or necrotic changes in four surgically removed parathyroid tumours which had previously undergone fine-needle aspiration biopsy.

Absolute ethanol was chosen as the therapeutic agent because it is already being employed to infarct renal neoplasms [8], to obliterate oesophageal varices [9] and to sclerose the walls of renal cysts [10]. Its action is likely to be based on endothelial damage and thrombosis of small vessels.

In our initial experience both sonographic and clinical effects of UGFNA were recorded. With sonography the same early structural changes were observed in the nine glands successfully injected, whereas the late changes appeared related to the initial size of the glands. In the smaller glands the parenchyma was mostly replaced by either dense high-level echoes or liquid areas. We believe the former was due to fibrous tissue, the latter to cystic or necrotic changes. In fact in two patients who underwent surgery (previously refused) after sHPT the pathological examination of the treated glands showed extensive necrotic changes in one case and fibrous tissue in the other.

In the larger glands the volume decreased significantly, but no structural change was observed; however a therapeutic effect was obtained, proved by a lowering of serum PTH. We feel that in these glands a larger amount of alcohol is needed and a second percutaneous injection may be attempted.

Figure 3. Parameters of hyperparathyroidism before and six months after UGFNA ([●] recurrence after subtotal PTX)
Significant clinical results were obtained in cases of single hyperplasias: serum calcium fell, allowing increased doses of vitamin D to be administered. At later times the serum levels of PTH and bone alkaline phosphatase slowly fell. Even in the most responsive cases, however, recurrence of parathyroid hyperplasia may occur. Adequate medical treatment should therefore be prolonged after UGFNA in order to control the multiple risk factors.

In conclusion, in patients with sHPT the percutaneous injection of alcohol into the enlarged parathyroid glands seems to be a useful aid to prolong dietary and medical therapy before submitting patients to surgery.

In recurrences after PTX and in patients in poor clinical condition UGFNA is likely to be a therapeutic alternative to surgery.

References


Open Discussion

GOODWIN (Chairman) I think many of us are very impressed by our ability to demonstrate glands. I would like to ask you if you were to scan a group of patients with chronic renal failure are you able regularly to demonstrate three, four, five glands with confidence?

GIAGRANDE It is not infrequent to find two glands in the patient. In the last year with improved techniques and with the possibility of using a 10mmHz probe we have often succeeded in finding four glands. This means that the sensitivity of the procedure is about 0.5cm.

GOODWIN Thank you, that was beautifully clear.

WALLS (Leicester) I suspect that you have the answer to my question. You are obviously aspirating these glands. Would you like to tell us what your various aspires show and whether you can differentiate between hyperplasia and adenoma?

GIAGRANDE I do not think we can differentiate hyperplasia from adenoma. It is useful to differentiate thyroid nodulae from parathyroid hyperplasia and we used two techniques which we have already published*.

*Solbiati L, Montali G, Croci F. Radiology 1983; 148: 793
KERR (London) Have you had to operate on any of these patients after your procedure and what did the surgeons think of the operating field?

GIAGRANDE Yes, some surgeons like the preliminary echographic documentation of the glands and on some occasions some surgeons don't like the damage after fine needle aspiration biopsy. After the ultrasonically guided fine needle alcohol injection the damage is a little more. We have operated on three patients after this procedure and the surgeon has not had any problems in localising the lesion. There is some damage which is not limited just to the gland. Some diffusion of the alcohol may produce some necrosis which may give some problem to the surgeon.

GOODWIN It sounds as if you have to treat your surgeon very carefully to get his collaboration with this technique.