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Case Report

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Recurrent renal hyperparathyroidism due to parathyromatosis

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Abstract
Parathyromatosis is the most severe type of recurrent secondary hyperparathyroidism (SHPT) after parathyroidectomy (PTX) in haemodialysis patients. It is difficult to completely remove all foci of parathyroid tissue and neck re-explorations are often required. Here, we report for the first time a case of recurrent SHPT due to parathyromatosis treated by radio-guided PTX.
A haemodialysed 48-year-old woman with recurrent SHPT due to parathyromatosis was treated by radio-guided PTX. Preoperatively Ultrasonography, ^{99}Tc-SestaMIBI scintigraphy and magnetic resonances of the neck and thorax were performed. The preoperative imaging techniques detected four parathyroid nodules, while intraoperative gamma probe identified six nodules (three in atypical site). No frozen sections were performed during surgery. Post-operative intact parathyroid hormone levels were stabilized in the range 300–500 pg/mL during the 26 month follow-up by means of cinacalcet and paricalcitol therapy. In cases of parathyromatosis, the preoperative imaging techniques are inadequate, while intraoperative gamma probe is useful to detect the parathyroid tissue and allows a more extensive cytoreduction because it ensures the removal of undetectable and ectopic parathyroid foci. The operative time is reduced and frozen sections are unnecessary. However, the radio-guided PTX do not rule out parathyromatosis recurrence and complementary medical treatment is appropriate.

Keywords: haemodialysis; parathyromatosis; radio-guided parathyroidectomy; secondary hyperparathyroidism

Introduction

Secondary hyperparathyroidism (SHPT) is a common complication of end-stage renal disease and parathyroidectomy (PTX) frequently becomes the ultimate option for treatment.

The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) stated that PTX should be recommended in patients with severe hyperparathyroidism [persistent serum levels of intact parathyroid hormone (iPTH) >800 pg/mL (88.0 pmol/L)], associated with hypercalcaemia and/or hyperphosphataemia that are refractory to medical therapy [1]. Recently, the Dialysis Outcome and Practice Pattern Study evaluated the situation and quality of haemodialysis therapy in European countries, the USA and Japan from 1996 to 2001. Baseline prevalence of PTX (%) and the incidence of PTX at follow-up per 100 patients per year in each country were as follows: France 14.3%, 1.8; Germany: 6.0%, 1.0; Italy: 5.0%, 0.9; Japan: 4.1%, 0.6; Spain: 5.7%, 1.5; UK: 9.2%, 1.5; USA: 4.0%, 0.5, respectively [2].

However, PTX is not always successful and the relapse of SHPT is frequent (10–30%). The most severe type of recurrent SHPT is a rare entity called parathyromatosis [3].

Parathyromatosis is a rare condition firstly described in 1975 as multiple foci of benign parathyroid hyperfunctioning tissue in the neck or mediastinum. Nowadays it is thought to be an irremediable and lethal condition because it is difficult to be detected and controlled by reoperation.

Case report

A 48-year-old woman on maintenance haemodialysis since 1992 developed SHPT refractory to medical therapy. This was based on calcitriol intravenously (3–6 μg/week), calcium-based phosphate binding (calcium carbonate 1–3 g/day) and aluminium hydroxide and magnesium hydroxide (20–40 mg/day). The calcium concentration in dialysis solution was 1.5 mmol/L.

In October 1998 she underwent total PTX with autograft in the left sternocleidomastoideus muscle. At surgical exploration, five parathyroid glands (PTG) were removed and 2 min fragments (total volume corresponding to half of a normal PTG) of the smaller PTG without macroscopic evidence of nodular hyperplasia were implanted in the left sternocleidomastoideus muscle. Histological examination showed diffuse or nodular hyperplasia. Post-operative iPTH level was 99 pg/mL. In March 2001, the patient was scheduled for surgical re-exploration because of the high serum iPTH (1525 pg/mL) and calcium levels (>11.4 mg/dL). Preoperative ^{99}Tc SestaMIBI scintigraphy

(PS) showed an intense delayed tracer activity in the left inferolateral thyroid lobe. Two nodules, one within the left sternocleidomastoideus muscle and one below the left thyroid lobe, were surgically removed and histology confirmed PTG hyperplasia. Parathyroid hormone level dropped to 66 pg/mL in the early post-operative period and remained <500 pg/mL until December 2003. Since then, it raised progressively up to 1250 pg/mL in December 2005. In order to avoid further surgery, cinacalcet (180 mg) and paricalcitol (15 mcg/week) were administered but the iPTH level continued to increase. In January 2008, the PS showed four areas of elevated uptake and slow wash out of the tracer (Figure 1a). Neck US showed hypoechoic or heterogeneous oval nodules exterior to the thyroid capsule. The US showed four of six PTG surgically removed, while magnetic nuclear resonance only one PTG.

Consequently, we decided to use radio-guided techniques to facilitate the intraoperative PTG localization. Thirty minutes before surgery, we administrated 8 mCi ^{99m}Tc-sestamibI intravenously and a hand-held gamma probe was used to detect radioactivity before surgical incision. During surgery, every site showing an increase of gamma probe counts >20% compared to background (controlateral thyroid tissue: 60 counts/s) was considered as possible parathyroid tissue and excised.

Five PTG were localized as follows: one PTG (6 mm, cps 399) in subcutaneous tissue below the platysma muscle corresponding to the right upper third of the neck (Figure 1), one PTG over median cervical line (3 mm, 220 cps), one PTG close to left inferior thyroid artery (20 mm, 444 cps), one PTG on the lower edge of left thyroid lobe and one PTG within the left sternocleidomastoideus muscle (Figure 2). The nodule was positive for gamma probe were not examined with frozen sections. The intraoperative assay performed 30 min after the removal of five PTG showed that iPTH concentration was 300 pg/mL above the levels acceptable and therefore the search of additional parathyroid tissue using the gamma probe was extended. Pathological uptake was recorded at the left thyroid lobe and, although macroscopic nodules were not visible, a total thyroidectomy was performed. The final intraoperative iPTH level after thyroidectomy was 209 pg/mL and the intervention was concluded. The iPTH level at 24 h after surgery was further decreased (126 pg/mL). No complications (post-operative bleeding, recurrent laryngeal nerve paralysis) occurred. Histologic examination showed well-circumscribed nests of cytologically benign and densely packed parathyroid chief cells with a small amount of stromal fat. No cytological

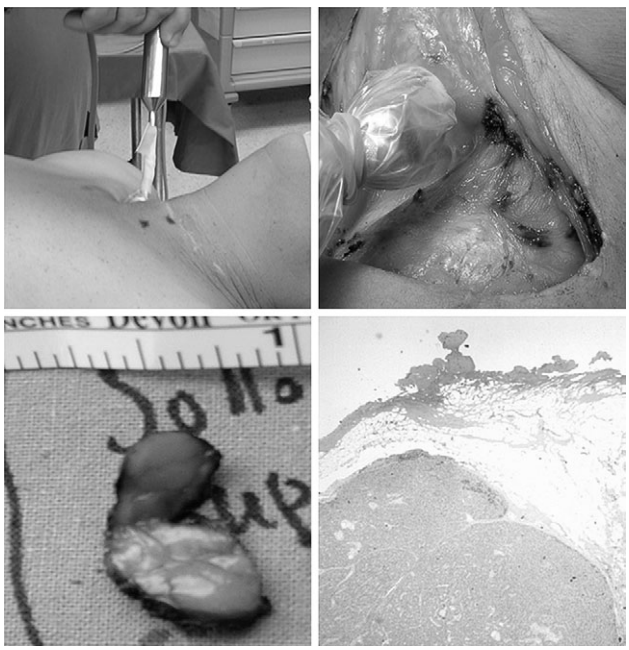

Fig. 1. A PTG was detected by gamma probe in the upper third of the right neck within subcutaneous tissue below the platysma muscle. Histology showed benign parathyroid nodule surrounded by muscle tissue.

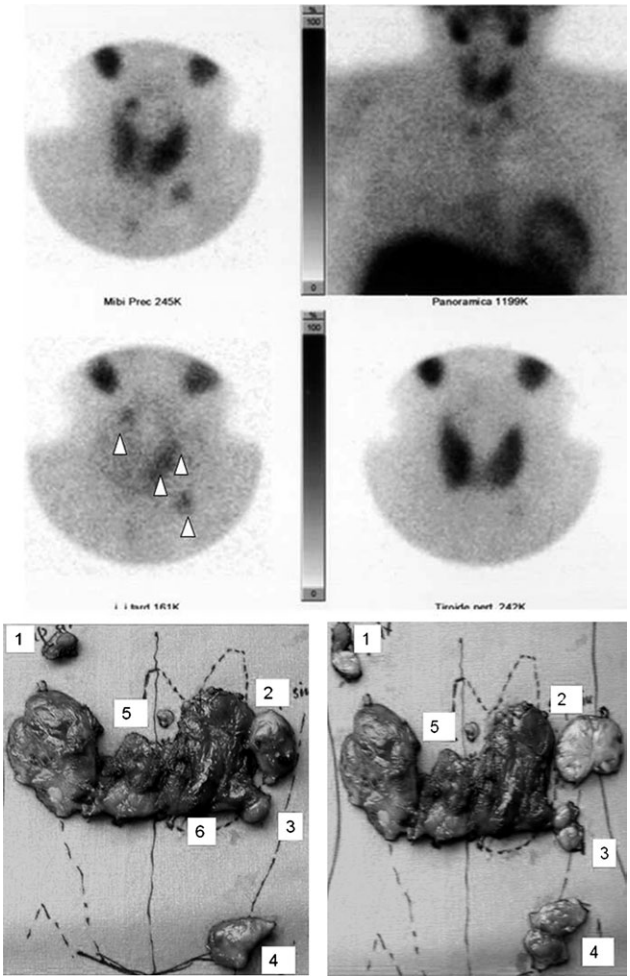

Fig. 2. Upper panel. Dual phase ^{99}Tc SestaMIBI scintigraphy: four areas of elevated uptake and slow wash out of the tracer in the tardive phase suggestive of the presence of parathyroid tissue are shown. Lower panel. Parathyroid glands (PTG) removed during surgical exploration: intact PTG (left), longitudinal section (right). A PTG (Number 1) was detected within subcutaneous tissue below the platysma muscle corresponding to the right upper third of the neck; two nodules of soft, yellow–white parathyroid tissue are scattered around the left thyroid lobe (Numbers 2 and 3); one PTG (Number 5) over median cervical line; a PTG (Number 4) was detected within the left sternocleidomastoideus muscle. Finally, a PTG (Number 6), macroscopically non-visible, was detected by gamma probe and confirmed by histology of the thyroid gland. The PTG 5 and 6 were not detected by preoperative imaging techniques but were identified by intraoperative gamma probe.

atypia, mitotic activity or giant cells were identified. Neither vascular invasion nor infiltrative features were detected. Nests of parathyroid cells within the thyroid parenchyma and the adjacent skeletal muscle were also observed. After intervention, vitamin D (paricalcitol) with low dose of cinacalcet (30 mg/day) were administered and the iPTH concentrations remained stable in the range 300–500 pg/mL during the 26-month follow-up.

Discussion

Parathyromatosis is a rare complication of subtotal and total PTX with autograft, firstly described by Palmer *et al.* [4] in 1975 and classified by Reddick *et al.* [5] in 1977. Given the paucity of parathyromatosis cases reported, it is difficult to determine whether the risk is greater after subtotal PTX or after total PTX + autotransplantation. Matsuoka *et al.* [3] reported that the frequency of parathyromatosis after total PTX with forearm autograft was 0.11% (2/1837), and in the subtotal PTx group, it was 5% (1/20). Therefore, the authors concluded that the risk for developing parathyromatosis was lower after total PTx with forearm autograft than after subtotal PTX ($P < 0.05$). On the contrary, Falvo *et al.* [6] reported five cases of parathyromatosis due to the autografted parathyroid tissue in all cases.

Parathyromatosis differs histologically from atypical adenoma and cancer [7] and is classified as follows: Type 1, defined as parathyroid rests left behind during ontogenesis that develop under physiologic pressure; Type 2, defined as the result of improper handling of the glands during surgical extirpation. Regarding our case, both theories could apply because the patient underwent an initial total PTX with autograft of parathyroid tissue in the left sternocleidomatoideus muscle. In this site, we removed the parathyroid tissue tenaciously adhering to muscle. These patterns are indicative of Type 2 parathyromatosis.

The prognosis of parathyromatosis remains severe because it is difficult to detect preoperatively and to remove all parathyromatosis foci at re-exploration [8].

During neck re-exploration for recurrent SHPT, the surgeon should keep well in mind the possible presence of parathyromatosis and make every effort to prevent recurrence or treatment failure. During surgery, it is mandatory to avoid injury of the PTG capsule that causes seeding of parathyroid cells into the surgical field. The introduction of radio-guided surgery represents an important advance in the surgical management of parathyroid disease. The present report shows that radio-guided surgery is useful in recurrent SHPT due to parathyromatosis and in evidenced parathyroid tissue in atypical sites not usually explored by the surgeon. In fact, radio-guided surgery allows a greater cytoreduction and the removal of foci of parathyroid tissue not evident at gross examination. This indirectly means that gamma probe investigation has some sensitivity limit. In the present case, the paricalcitol/cinacalcet administration was shown to be effective after removal of five PTG, thyroid and adipose tissue containing nests of parathyroid tissue. They may turn out to be an integral part of the integrated medical and surgical treatment of parathyromatosis.

In conclusion, the present case report suggests that radio-guided surgery is useful for patients undergoing surgery for parathyromatosis.

Conflict of interest statement. None declared.

References

1. National Kidney Foundation. K/DOQI clinical practice guidelines for bone metabolism in chronic kidney disease. *Am J Kidney Dis* 2003; 42 (Suppl 3): S1–S202
2. Young EW, Albert JM, Satayathum S *et al.* Predictors and consequences of altered mineral metabolism: the dialysis outcomes and practice patterns study. *Kidney Int* 2005; 67: 1179–1187
3. Matsuoka S, Tominaga Y, Sato T *et al.* Recurrent renal hyperparathyroidism caused by parathyromatosis. *World J Surg* 2007; 31: 299–305
4. Palmer JA, Brown WA, Kerr WH *et al.* The surgical aspects of hyperparathyroidism. *Arch Surg* 1975; 110: 1004–1007
5. Reddick RL, Costa JC, Marx SJ. Parathyroid hyperplasia and parathyromatosis. *Lancet* 1977; 5: 549
6. Falvo L, Catania A, Sorrenti S *et al.* Relapsing secondary hyperparathyroidism due to multiple nodular formations after total parathyroidectomy with autograft. *Am Surg* 2003; 69: 998–1002
7. Fernandez-Ranvier GG, Khanafshar E, Jensen K *et al.* Parathyroid carcinoma, atypical parathyroid adenoma, or parathyromatosis? *Cancer* 2007; 110: 255–264
8. Tominaga Y, Katayama A, Sato T *et al.* Re-operation is frequently required when parathyroid glands remain after initial parathyroidectomy for advanced secondary hyperparathyroidism in uremic patients. *Nephrol Dial Transplant* 2003; 18: 65–70

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