Chirurgia (2015) 110: 425-429
No. 5, September - October

Technical Factors Involved in Parathyroid Surgery

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Rezumat

Factori tehnici implicați în chirurgia paratiroidiană

Lucrarea își propune investigarea frecvenței glandelor paratiroide ectopice și supranumerare în seria noastră de pacienți cu hiperparatiroidism renal. Din octombrie 2011 până în noiembrie 2014, 202 pacienți cu insuficiență renală cronică și SHPT avansat, refractar la tratamentul medicamentos au fost internați pe secția Chirurgie Generală a Spitalului de Nefrologie Carol Davila. La acești pacienți au fost efectuate 188 paratiroidectomii totale (93%), respectiv 14 paratiroidectomii subtotale (7%) în departamenul nostru. Dintre aceștia, reintervenția a fost realizată la 14 pacienți (7%), la care s-au identificat glande paratiroide ectopice și supranumerare. Detaliile operatorii și rezultatele anatomopatologice au fost colectate și analizate prospectiv după ce s-a obținut consimțământul informat al pacienților pentru utilizarea datelor și imaginilor. La 188 din cei 202 pacienți (93% cazuri), au fost găsite cel puțin patru sau mai multe glande paratiroide la operația inițială. În 14 cazuri (7%) nivelul crescut al PTH-ului a persistat postoperator. În 22 cazuri (11%) au fost decelate glande paratiroide supranumerare la operația inițială și în 6 cazuri (3%) la a doua intervenție. În concluzie explorarea cervicală extensivă în asociere cu o explorare imagistică preoperatorie adecvată (ecografie paratiroidiană, scintigrafie cu tc sestamibi, CT cervico-mediastinal poate reduce rata recurenței hiperparatiroidismului secundar.

Cuvinte cheie: Hiperparatiroidism secundar, paratiroidectomie, ectopic, supranumerar

Abstract

We aimed to investigate the frequency of ectopic and supernumerary parathyroid glands in our series of renal hyperparathyroidism. From October 2011 to November 2014, 202 patients with chronic renal failure and advanced SHPT nonresponsive to medical therapy were hospitalized in the General Surgery Department of the Carol Davila Nephrology Hospital. These patients underwent a number of 188 (93%) total parathyroidectomies and a number of 14 patients (7%) subtotal parathyroidectomies. Of these 202 patients, reoperation was carried out for 14 patients (7%) in which we identified ectopic and supernumerary parathyroid glands. Operative details and pathology results were prospectively collected and reviewed after we obtained informed consent for data and pictures use. In 188 patients (93% cases), four or more parathyroid glands were removed at the first operation. In 14 cases (7%) high PTH level persisted after the initial operation. In 22 of them (11%), supernumerary glands were found at the first operation and in 6 of them (3%) at the second operation. We conclude that extensive cervical exploration in addition with preoperative imaging tests, parathyroid ultrasound; scintigraphy with Tc will reduce secondary hyperparathyroidism surgery.

Key words: secondary hyperparathyroidism (SHPT), parathyroidectomy, ectopic & supernumerary

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Introduction

It had been demonstrated that 30% are chronically dialyzed patients develop Secondary hyperparathyroidism (SHPT). Surgical therapy is the only viable solution. The aim of this article is to present our experience in SHPT treatment and to investigate the frequency of ectopic parathyroid supernumerary glands located infrathymic, paraesofageal, intrathyroidian.

To avoid persistent and recurrent HPTS, all parathyroid glands including supernumerary and ectopically ones should be removed at the initial operation. A missed gland may be an ectopic gland or a very small one.

It is well known that chronic renal failure induces SHPT, which is one of the serious complications influencing the mortality and quality of life in patients with chronic renal failure. Despite advances in medical prophylaxis and treatment, in many patients SHPT is refractory to medical treatment such as calcimimetics, new phosphate binders, less calcemic vitamin D analogs. These cases then consequently require parathyroidectomy (1). The incidence of advanced SHPT gradually increases with the duration of hemodialysis treatment. Total parathyroidectomy is the most successful treatment for advanced SHPT and has positive effects on symptoms and biochemistry (1). Subtotal parathyroidectomy and total parathyroidectomy with auto transplantation of parathyroid tissue are currently considered standard surgical procedures, the last procedure being the most successful treatment for advanced SHPT with positive effects on symptoms and biochemistry (1)

It is possible that with the ongoing stimulus of renal failure, microscopic rests proliferate over time to manifest later as supernumerary glands serve as a cause of recurrent hyperparathyroidism (9–11).

Material and Methods

From October 2011 to November 2014, 202 patients with chronic renal failure and advanced SHPT refractory to medical therapy, were hospitalized the General Surgery Department of the Carol Davila Nephrology Hospital. These patients underwent total parathyroidectomies a number of 188 patients (93%) and respectively subtotal parathyroidectomies a number of 14 (7%) patients. Of these 202 patients, reoperation was carried out for 14 (7%) patients in whom we identified ectopic and supernumerary parathyroid glands. Operative details and pathology results were prospectively collected and reviewed after we obtained informed consent for use data and pictures.

Results

In 188 patients (93%), four or more parathyroid glands were extirpated at the first operation.

In all these cases, the intact PTH level dropped under the normal upper limit indicating that an essential hyperplastic parathyroid gland was not left behind (normal range: 10-70 pg/ml).

The number of removed gland was confirmed by histopathological examination at the initial operation. Intact PTH levels were measured the 1st postoperative day.

Table 1. *Intervention type*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	PS	14	7	7	7
	PT	188	93	93	100.0
	Total	202	100.0	100.0	

In 14 patients (7%) who had undergone subtotal parathyroidectomy the fourth parathyroid gland was not found in these cases being necessary a second operation witch detected ectopically parathyroid glands: infrathyimic 4 patients (29%), close to aortic arch, deep within the mediastinum one patient (7%), on the surface of thyroid lobe 5 patients (36%), in paraesofageal fat tissue 4 patients (28%). (*Table 1*)

In 14 cases (7%) high PTH level persisted after the initial operation. In 22 of them (11%), supernumerary glands were found at the first operation and in 6 of them (3%) at the second operation.

Subtotal thyroidectomy was necessary in 8 patients (4%) diagnosed with chronic Hashimoto thyroiditis. In order to remove all parathyroid glands, including supernumerary ones, localization by preoperative noninvasive image diagnosis were required the following order Us, S, CT and MRI. All patients demonstrated biochemical criteria of SHPT. They were referred for surgery by the consultant nephrologist. Their data were collected prospectively and stored. In the study, we reviewed the medical records, the anatomic and pathological findings during cervical surgical exploration, together with their pathology reports and outcomes of SHPT during follow-up.

We establish an algorithm for brought the surgical indications gathering PTH levels higher than ten times the normal upper limit (normal range: 10-70 pg/ml), for us PTH > 800 pg/ml, osteopathy, osteoporosis, calciphylaxis, calcifications of vessels and soft tissues, fractures in pathological bone, medical history medical treatment administration for a period of six months persistent hypercalcemia and/or hyperphosphatemia (30, 31).

There were 91 men (45.05%) and 111 women (54.95%) with mean age of 51.51 years (range: 21–77) (*Table 2*).The mean ± SD time from the start of dialysis to parathyroidectomy was 7.36 years. In 190 cases (94%) underwent hemodialysis and 12 cases (6%) had peritoneal dialysis (*Table* 3). The mean ± SD of intact pre operatory PTH was 1684.20 (range: 355-4120 pg/ml) and intact post operatory was 98.47 (range: 3-985 pg/ml) (*Table 4, Table 5*).

All surgical procedures were performed under general anesthesia. In addition, since small rudimentary microscopic glands may be concealed in fat, the tissue surrounding the

Table 2. *Sex distribution*

		Frequency	Percent
Valid	Male	91	45.05
	Female	111	54.95
	Total	202	100.0

Table 3. *Dialysis type*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Peritoneal dialysis	12	6	6	6
	hemodialysis	190	94	94	100.0
	Total	202	100.0	100.0	

glands was routinely excised (32). In patients with less than four parathyroid glands identified extensive neck exploration was routinely performed.

The pathology results certificated nodular hyperplasia in 9 patients (4% of cases), diffuse hyperplasia in 103 patients (51% of cases) and mixed hyperplasia in 70 patients (35% of cases). Mixed hypertrophy was found in 20 patients (10% of cases) (*Figs 1, 2, 3*).

In addition to parathyroid glands the fat, thymus and thyroid resected specimens were sent for histological examination. Thymus, adipose tissue, lymph nodes, thyroid and other specimens were fixed in buffered 10 % formaldehyde, embedded in paraffin and sectioned serially at 5 μm. The sections were stained with hematoxylineosin. Microscopic slides were examined at X20 to X200 magnifications under the light microscope by the same pathologist.

Reoperation was carried out in 14 patients with persistent HPT related to parathyroid remnants. In a patient with persistent HPT, the remnant was removed and parathyroid tissue which was implanted into the anterior cervical region in selective cases.

Supernumerary parathyroid glands (14%) were responsible for recurrent HPT. The hyperplastic supernumerary gland and remnant were resected and the parathyroid tissue was transplanted into the cervical region.

Discussion

The optimal surgical treatment in patients with refractory renal hyperparathyroidism (RHP) on hemodialysis for end stage renal disease is still a point of controversy (28).

It should be acknowledged that due to the complex development during embryogenesis the parathyroid gland may be located ectopically.

When overlooked during parathyroidectomy, the ectopic gland may cause persistent or recurrent hyperparathyroidism. Anomalies in the location of parathyroid glands, particularly in that of inferior ones are not rare. Autopsy examinations indicate that the percentage of cases with less than four parathyroid glands is 3.65 to 19% (2-6)

The inferior parathyroid glands and the thymus arise from the embryonic third pharyngeal pouch

During the course of normal development, the complex

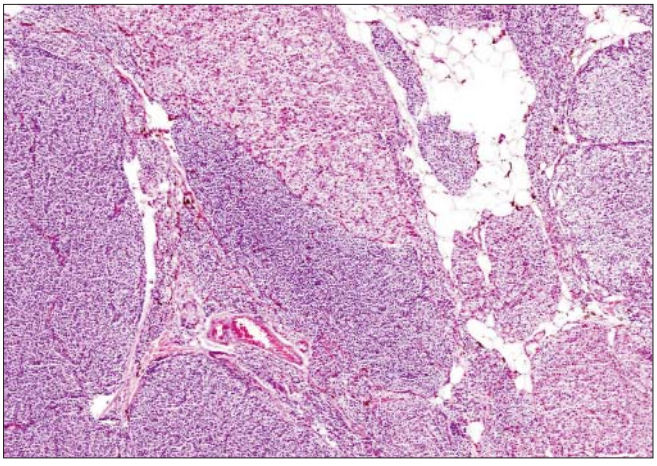

Figure 1. *Mixed hyperplasia*

Table 4. *Pre operatory PTH*

N	Valid	202
	Missing	0
Mean		1684.20
Median		1585.00
Mode		1450[a]
Std. Deviation		514.736
Minimum		355
Maximum		4120

Table 5. *Post operatory PTH*

N	Valid	202
	Missing	0
Mean		98.4748
Median		30.6500
Mode		3.00
Std. Deviation		168.58461
Minimum		3.00
Maximum		985.00

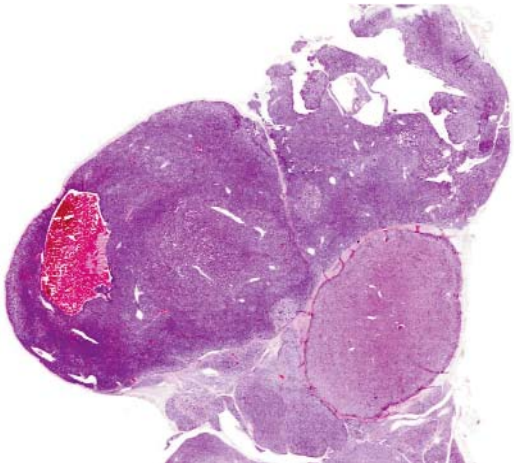

Figure 2. *Nodular hyperplasia*

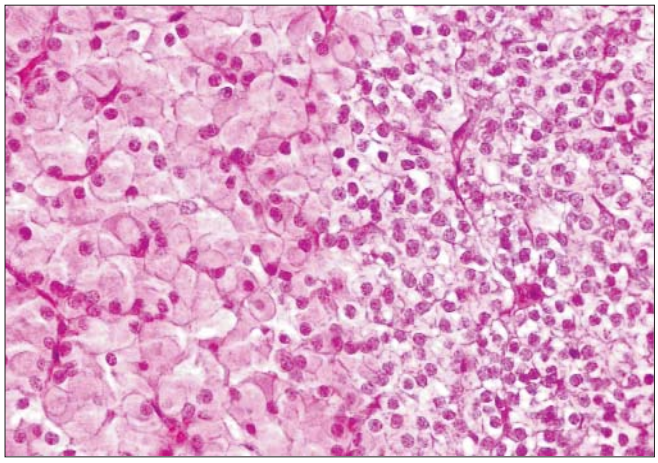

Figure 3. *Diffuse hyperplasia*

of the inferior gland and thymus migrate through the entire extent of the embryonic neck. Because of this embryologic relation of inferior parathyroid with the thymus, a missing lower gland is most likely to be found in the thymus (12, 21, 22). Uno et al (5) noted that in cases with renal hyperparathyroidism, 29.8 % of patients had only inferior glands and 8.6 % of patients had either inferior and supernumerary glands detected infrathymic or paraesofageal.

Based on 160 autopsies, Wang (8) reported that the frequency of supernumerary and ectopic parathyroid glands was 41%.

Also in 503 autopsies, Akerstrom et al (7) demonstrated that at least 13 % of all normal persons have supernumerary and ectopic parathyroid glands, half of which should be proper ones while the other half are rudimentary islets of parathyroid tissue.

Hyperplasia of all parathyroid tissues including microscopic rests develops as a result of continued parathyroid stimulation by chronic renal failure, possibly because hyperplastic glands can be recognized easier (13, 23). Thus, the supernumerary and ectopic glands are more important in SHPT than in primary HPT (15, 16).

The incidence of supernumerary and ectopic glands has been reported to be 10-30% in patients who underwent parathyroidectomy for SHPT (3, 5, 6, 17). The most frequent location of supernumerary and ectopic parathyroid tissue in autopsy series was in the thymic tongue, thyroid gland, carotid sheath, paraesofageal, mediastinum and paratracheal (3, 6, 24).

Numano et al (3) detected supernumerary and ectopic glands in 16.5 % of patients who under-went parathyroidectomy for SHPT while 51 % of those glands were located infratimic, intrathyroid.

Both subtotal parathyroidectomy and total parathyroidectomy with or without auto transplantation are accepted operations for SHPT.

Total parathyroidectomy with auto transplantation is the best procedure for treating recurrences but the increased risk of hypoparathyroidism must be kept in mind (1, 3, 21, 17, 19, 20). Based on 53 publications in literature, Richards et al (18) reviewed 501 patients who had undergone a reoperation for persistent or recurrent SHPT. They identified reported a significantly higher rate of recurrent SHPT in patients with auto grafts than in those with in situ remnants (49 % vs 17 %) (18).

Although the most common causes for recurrence include hyperplasia of the subtotal remnant or auto graft in SHPT, supernumerary and ectopic glands and account for up to 32 % of recurrences (6, 18). In both subtotal parathyroidectomy and total parathyroidectomy with auto transplantation, it is very important to identify all parathyroid glands including supernumerary and ectopic glands at the initial operation (3, 6).

In SHPT, the stimuli of the parathyroid cells persist after initial parathyroidectomy, leading to enlargement of small glands and parathyroid rests for long periods; therefore the rudimentary islets of parathyroid tissue in SHPT become important (10, 25). It has been observed that following total parathyroidectomy aimed at removing all macroscopic parathyroid tissue, plasma parathyroid hormone initially falls to undetectable concentrations but subsequently rises again with time (26, 27). This supports the presence of microscopic residual parathyroid rests able to respond to a stimulation of renal failure. Although they are missed, supernumerary and ectopic parathyroid glands are usually small, and may gradually enlarge due to continuous stimulation. Thus, a removal may be required during the long-term follow-up period (21).

Uno et al (5) reported that the incidence of patients with infrathymic, intrathyroid, paraesofageal, paratraheal parathyroid glands was 45.3 %. In our study extensive cervical neck exploration contributed to the treatment of about 93 % of patients.

Parathyroidectomy is effective for long intervals as symptomatic therapy in cases of RHPT appearing in uremic patients on hemodialysis or after renal transplant but the optimal technique must be individualized on each case and still to be debated (29).

Conclusions

We conclude that in order to minimize the risk of missing parathyroid glands, extensive cervical bilateral neck exploration in addition with superior mediastinum remains the prerogative of collective surgical involved in SHPT and the parathyroidectomy is the only curative therapy.

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