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Supernumerary Parathyroid Glands: Frequency and Surgical Significance in Treatment of Renal Hyperparathyroidism

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Abstract. Supernumerary parathyroid glands (SPGs) are found in 13% of random autopsies. The high incidence of SPGs could explain the persistence or trigger recurrence of renal hyperparathyroidism after surgery. The aim of this study was to assess the frequency and clinical relevance of SPG in patients operated on for renal hyperparathyroidism (HPT). In this retrospective study we reviewed the medical records of 290 patients with renal HPT who were initially treated in our department. We examined the anatomic and pathologic findings during cervical surgical exploration and the outcome of HPT during follow-up. SPGs were identified in 87 patients (30%) during the initial cervicotomy, corresponding to intrathymic parathyroid cell islets (one to four) in 70 cases and to extrathymic SPG in 17 patients. Among 260 patients available for follow-up, 11 experienced persistent HPT (4%), and 34 developed recurrent HPT (13%). A total of 25 patients were reoperated on, and SPGs were responsible for 4 of 8 cases of persistent HPT and 4 of 17 cases of recurrent HPT, representing an overall frequency of 32%. The anatomic distribution of SPGs found during reoperations included thymus, retroesophageal grove, carotid sheath, and mediastinum. SPGs are thus present in 30% of patients with renal HPT and are situated mainly in the thymus. Thymectomy should be performed routinely during the first surgical exploration to prevent recurrences arising from anterior mediastinal glands. SPGs were also responsible for 32% of persistent or recurrent HPT. In that setting, frankly ectopic SPGs are not rare, and preoperative imaging appears highly desirable prior to embarking on surgical reexploration.

In patients with chronic renal failure, parathyroid cells are stimulated by vitamin D deficiency, hyperphosphatemia, and decreased serum calcium levels [1]. With time, progressive alteration of the parathyroid cell calcium and vitamin D receptors leads to inappropriate and uncontrolled hypersecretion of parathyroid hormone, causing renal hyperparathyroidism (HPT) [2, 3]. When surgical excision of hyperplastic parathyroid tissue becomes necessary, correct identification of all parathyroid tissue is mandatory prior to determining the optimal surgical strategy [4]. The frequency of supernumerary parathyroid glands (SPGs) in humans and their wide anatomic distribution has been well established by Akerström et al.'s autopsy studies [5] in accordance with parathyroid ontogeny. The aim of this study was to determine the frequency and distribution of SPGs in patients with renal HPT and their role in persistence or recurrence of the disease after surgery.

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Patients and Methods

Between February 1972 and December 1997 a total of 1852 patients were operated on for hyperparathyroidism (HPT) in the Department of General and Endocrine Surgery at our institution. Among them, 300 patients (female/male ratio 0.93) had renal HPT. End-stage renal failure had been treated by dialysis in 258 cases for a mean duration of 6.5 years (range 0–212 months). Nine patients did not develop prior end-stage renal failure. Thirty-three patients had a functional kidney graft at the time of parathyroid operation and were considered to be experiencing tertiary HPT. In this retrospective study, we reviewed the medical records of all patients with renal HPT who were initially treated in our department to examine the anatomic and pathologic findings during cervical surgical exploration and the outcome of HPT during follow-up.

All patients underwent an extensive bilateral cervical surgical exploration. The strategy for parathyroid excision adopted by our department has varied with time to include subtotal parathyroidectomy, total parathyroidectomy with autotransplantation as described by Wells, or total parathyroidectomy alone. With the exception of our initial experience, all patients had a routine thymectomy.

To evaluate the outcome of surgery, patients with clinical or biologic signs of HPT and parathyroid hormone (PTH) serum level exceeding four times the normal upper limit [6] within 6 months after surgery were defined as experiencing persistent HPT. When these signs occurred more than 6 months after surgery, patients were defined as experiencing recurrent HPT.

Table 1. Series and global results.

Operation	No.	Follow-up (no.)	Persistence		Recurrence	
			Treatment	No.	Treatment	No.
Subtotal Ptx						
With thymectomy	211	201	All	10 (4.4%)	All	20 (8.8%)
Without thymectomy	39	25	Medical treatment	3	Medical treatment	12
			Reduction of remnant	1	Remnant reduction/resection	6
			Resection of missing gland	2	Resection of missing gland	0
			Resection of 5 SPGs	4	Resection of 3 SPGs	2
Total Ptx						
With thymectomy	2	2	All	0	All	0
Without thymectomy	0	0				
Well's Ptx						
With thymectomy	29	27	All	1 (3.1%)	All	14 (43.7%)
Without thymectomy	9	5	Reduction of graft	1	Medical treatment	5
					Reduction of graft	7
					Resection of 2 SPGs	2
Total						
With thymectomy	242	230 (95%)	All	11 (4.2%)		27 (12%)
Without thymectomy	48	30 (62%)				7 (23%)

Ptx: parathyroidectomy; SPG: supernumerary parathyroid gland.

Results

Ten patients who were reoperated on in our department for persistent or recurrent HPT but who were not initially treated in our department have been excluded from this study. The characteristics of the initial operation and the outcome of HPT after surgery in the remaining 290 patients are summarized in Table 1. The outcome of surgery was unknown in 30 patients lost to follow-up when this study was completed. Complete records were available for 260 patients (90%) who had been followed for a mean duration of 5.5 years (range 1–22 years).

First Cervicotomy

At the first operation SPGs were identified in 87 patients (30%). In 70 cases parathyroid cell islets (one to four) were identified by the pathologist in the thymus specimen, routinely excised during surgery in 242 cases. None of these supernumerary parathyroid foci had been macroscopically suspected by the operating surgeon. Conversely, in 17 patients one or two (one patient) SPGs were clearly identified during cervical exploration in various extra thymic locations (Fig. 1). Pathologic examinations of these 18 SPG revealed diffuse parathyroid hyperplasia ($n = 14$), nodular parathyroid hyperplasia ($n = 14$), or a normal parathyroid gland ($n = 2$). Four patients had preoperative parathyroid localization studies with sonography, a sestamibi scan, or both; but none of their SPGs were suspected prior to surgery.

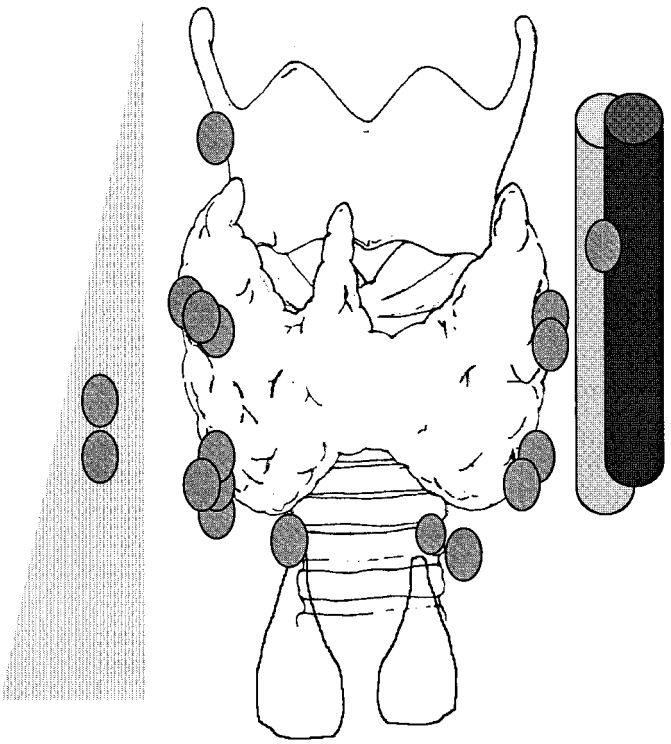

Fig. 1. Location of 18 extrathymic supernumerary parathyroid glands found during initial surgical exploration of 17 patients with renal hyperparathyroidism (HPT). Individual glands ($n = 18$) are represented as dark gray dots. Two glands were found within the sternocleidomastoid muscle (triangle at left) and one in the carotid sheath (light gray tube).

Reoperations

As detailed in Table 1, persistent HPT after the initial cervicotomy was noted in 11 patients (4%): once after total parathyroidectomy and autotransplantation and in 10 cases after subtotal parathyroidectomy. Conservative treatment was chosen for three patients, and eight patients underwent reoperation on one or two (three patients) occasions. In one patient antebrachial graft resection was attempted unsuccessfully. In another patient reduction of the parathyroid remnant after subtotal parathyroidectomy cured the HPT. In two patients identification and excision of an abnormal parathyroid gland that had been missing at the first operation cured the disease. In four patients excision of one or two (in one patient) SPGs was performed and led to cure in three. These SPGs were located in the proximal carotid sheath and associated with a sixth intrathymic gland in one patient (behind the esophagus, under the innominate venous trunk) or in the

aortopulmonary window in others. The latter gland was excised via thoracoscopy, but the patient remained in a hyperparathyroid state probably because of capsular rupture and parathyroid cell seeding during excision.

Recurrence of HPT was observed during follow-up in 34 patients (13%). Fourteen patients with recurrent HPT were initially treated by total parathyroidectomy and autotransplantation. Conservative management was chosen for five patients, and nine have undergone reoperation. The excision, eventually sequential, of the antebrachial parathyroid graft in seven patients allowed cure in five. In two patients, an SPG was identified at reoperation 15 and 18 years after the first cervicotomy and was successfully excised. One was found in the initially unresected thymus and the other behind the upper thyroid pole.

Twenty patients had recurrent disease after subtotal parathyroidectomy, and eight of them have undergone reoperation. Excision of the parathyroid remnant in two cases allowed cure in both. Reduction of the parathyroid remnant cured two of four patients. Three SPGs were identified and were excised in two patients. One was found at the proximal carotid sheath, and the patient was cured for 3 years prior to another HPT recurrence. In the other patient, two glands were found behind the cricothyroid cartilage and behind the manubrium.

In summary, SPGs were responsible for 4 of 8 cases of persistent HPT and 4 of 17 cases of recurrent HPT, representing overall 8 of 25 cases (32%). All 10 SPGs found in these patients were abnormal, with a mean weight of 3126 mg (range 450–6635 mg). Their anatomic distribution is summarized in Figure 2. In all cases, these SPG could be suspected by preoperative sestamibi scans. None of these patients had a scintigraphy performed prior to the initial cervicotomy.

Technical Considerations

The carotid sheath was not explored routinely during the first cervicotomy. In 19 patients (9%) one or both carotid sheaths were extensively explored because of a missing parathyroid gland, but it was never successful. In one case a macroscopically obvious SPG was found in the upper carotid sheath during the first exploration. In case of reoperation, the exploration of one or both carotid sheaths was performed in six patients and was successful in four, leading to excision of two missing glands and two SPGs.

Prior to 1981 a total of 48 patients did not have a routine thymectomy during the initial operation. In this group, among the 30 patients who were not lost to follow-up, one had persistent HPT (3%) and seven had recurrent HPT (23%). Two of the latter underwent reoperation, and an intrathymic SPG was found in one of them.

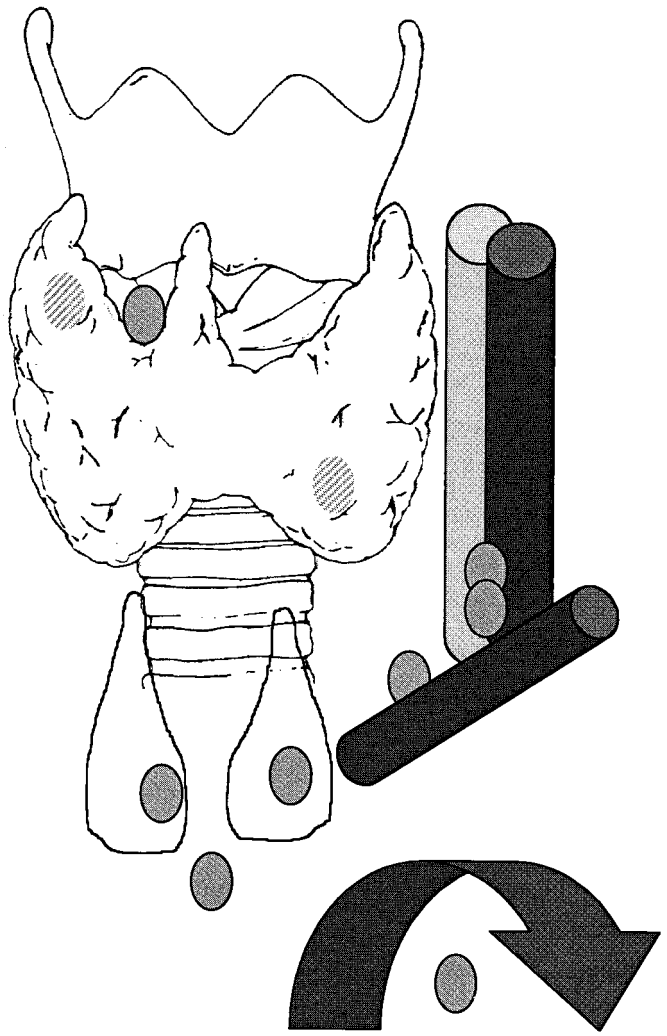

Fig. 2. Location of 10 extrathymic supernumerary parathyroid glands found during reoperations in eight patients with persistent or recurrent renal HPT. Individual glands ($n = 10$) are represented as dark gray dots or light gray (hatched) dots when found within the thyroid. Two glands were found in the carotid sheath (light gray tube), one behind the innominate vein (oblique dark tube) and one in the aortopulmonary window (arrow at bottom).

Discussion

During the first cervicotomy in patients with renal HPT, we identified more than four parathyroid glands in 87 cases (30%). The most frequent location of this supernumerary parathyroid tissue was the cervical thymus (80%). Indeed parathyroid cell islets were found within the thymic specimen in 29% of patients who underwent routine thymectomy. This frequency is much superior to the figures suggested by autopsy studies reported by Akerström et al. [5] (13%) or Delattre et al. [7] (20%). In patients with renal HPT, the frequency of SPGs has been reported by others to be 2.3% to 19% [8–11]. The discrepancies with the results of present study may be explained by a less extensive search for intrathymic parathyroid tissue. Indeed, Courant et al. had reported that most of these SPGs were located in the cervical thymus [11].

Thymectomy appeared justified because of the frequent occurrence of intrathymic parathyroid SPGs (9%), as reported by Akerström et al. [5]. Conversely, it is difficult to appreciate the clinical outcome of the minute intrathymic parathyroid cells if they are not resected and left under chronic stimulation by ongoing renal insufficiency. Although the group of patients without routine thymectomy have been followed for a longer period, it is noteworthy that their risk for recurrent HPT (7/30, 23%) appeared to be much higher than for the rest of our patients (27/230, 12%). The discovery of an authentic intrathymic SPG in one of two patients who was reoperated on further indicates the rele-

vance of thymectomy. We therefore strongly recommend that bilateral thymectomy is performed routinely in all patients undergoing cervical exploration for renal HPT. At the very least, this policy can greatly simplify the strategy in cases of persistent or recurrent HPT during follow-up. In accordance with others, we found a 6% frequency of extrathymic SPGs. In most cases these SPGs were found in the immediate vicinity of another, normally located parathyroid gland. This frequent particularity may indicate a division of a normal parathyroid gland during ontogeny, as suggested by the bi- or trilobular shape of some glands described by Akerström et al. [5] or the 24% frequency of rudimentary SPGs found by Numano et al. [12]. Other locations of SPGs, including the external aspect of prethyroidal muscles, the carotid sheath, and the inferior and superior thyroid poles, have been described [5, 7, 11] and may give rise to persistent or recurrent HPT [13]. Most of these locations are easily explored during cervicotomy, and discovery of an SPG is often incidental. In contrast to Numano et al. [12], we did not find any preferential side for SPGs.

Extensive exploration of the carotid sheath is demanding and carries its own morbidity. In our series the only SPG found in the carotid sheath during the initial operation was large enough (297 mg) to be detected by the surgeon. In all other cases and even in a case of a missing gland, exploration of the carotid sheath remained negative. In contrast to others' results [12], the results of this study do not support routine exploration of both carotid sheaths during a first cervicotomy for renal HPT. Routine exploration of the carotid sheaths appeared much more useful in the case of reoperation, allowing excision of an ectopic parathyroid gland in 50% of patients, which corresponded in two cases to an SPG.

In accordance with others [12], we found that mediastinal localization of extrathymic SPGs was initially low but its incidence rose to 30% in case of reoperation. SPG excision here may necessitate sternotomy or thoracoscopy. The sensitivity of preoperative localization studies has been extensively studied by Numano et al. [12], who found them to be disappointing prior to the initial operation, detecting only 8% of SPGs. As confirmed in this study, the sensitivity of the sestamibi scan is greatly increased in cases requiring reoperation. In that setting, the responsible lesion is often unique, and its traced uptake appears superior [14–18].

Our results and the physiopathology of renal HPT clearly advocate excision of all SPGs incidentally found during the initial cervicotomy, although there is no evidence supporting routine extensive exploration of ectopic sites, such as the carotid sheaths, when the four glands have been identified. The routine preoperative parathyroid localization study does not appear useful before a first cervicotomy given its low sensitivity in that setting [14]. In the case of renal insufficiency, the return of PTH serum levels to normal after successful parathyroidectomy is delayed [19] and the intraoperative PTH assay remains controversial [20]. We found that most extrathymic or cervical SPGs display pathologic characteristics similar to other abnormal parathyroid glands in renal HPT. The clinical impact of SPGs was also well documented in this series, as they accounted for 32% of persistent or recurrent reoperated HPT. In the case of reoperation, frankly ectopic SPGs are not rare, and preoperative imaging appears highly desirable prior to embarking on surgical reexploration [16].

Conclusions

This study documented the clinical importance of SPGs in renal HPT. Given the frequency of intrathymic parathyroid tissue, our results strongly support routine thymectomy during the initial surgery for renal HPT. Recurrence of the disease in the parathyroid remnant after subtotal parathyroidectomy or on the parathyroid graft in case of total parathyroidectomy and autotransplantation was also frequent. Eventually this clinical reality may also support total parathyroidectomy without transplantation as the procedure of choice for patients who are not candidates for renal transplantation, as suggested by some authors [21, 22].

Résumé

Fond du problème: Les glandes parathyroïdes surnuméraires (GPS) se voient dans 13% des autopsies faites au hasard. Cette incidence élevée pourrait expliquer la persistance ou être à l'origine de la récidive d'hyperparathyroïdie (HPT) dite «rénale» après chirurgie. Le but de cette étude a été d'évaluer la fréquence et l'impact clinique des GPS chez les patients opérés pour HPT rénale. Méthodes: Dans cette étude rétrospective, nous avons revu les dossiers médicaux de 290 patients ayant une HPT rénale, traités initialement dans notre département; nous avons examiné les données anatomiques et anatomo-pathologies de l'exploration cervicale et tenu compte de l'évolution de l'HPT. Résultats: On a identifié au moins une GPS chez 87 patients (30%) ayant eu une cervicotomie, correspondant à des îlots cellulaires parathyroïdiennes intrathymiques (une à quatre) dans 70 cas, et à des GPS extrathymiques chez 17 patients. Parmi les 260 patients disponibles pour évaluation postopératoire, il y avait 11 cas d'HPT persistante (4%) et 34 ont développé une récidive d'HPT (13%). On a réopéré 25 patients; des GPS étaient responsables de 4 des 8 cas de HPT persistante et de 4 des 17 cas de HPT récidivante, représentant une fréquence globale de 32%. La localisation anatomique des GPS retrouvées pendant les réopérations était le thymus, le sillon rétro-œsophagien, la gaine vasculaire de la carotide et le médiastin. Conclusion: On retrouve des GPS chez 30% des patients ayant une HPT «rénale» et la plupart sont localisées dans le thymus. Il faut réaliser une thymectomie de façon systémique pendant la première exploration chirurgicale pour éviter les récidives à partir des GPS médiastinales antérieures. Les GPS sont également responsables de 32% de HPT persistantes ou récidivantes. Dans ces éventualités évolutives, les GPS ectopiques ne sont pas rares et l'imagerie préopératoire apparaît hautement souhaitable avant de pratiquer une re-exploration chirurgicale.

Resumen

Antecedentes: En el 13% de las necropsias se descubren glándulas paratiroideas aberrantes o supernumerarias (SPG). La gran frecuencia de SPG puede explicar la persistencia o recidiva postoperatoria de los hiperparatiroidismo renales. El objetivo del presente trabajo fue averiguar la incidencia y la relevancia clínica de las SPG en pacientes intervenidos por hiperparatiroidismo (HPT) renal. Métodos: Se efectúa un estudio retrospectivo revisándose 290 historias clínicas de HPT renal, tratados por vez primera, en nuestro Centro. Se reexaminaron los hallazgos anatomopatológicos y quirúrgicos

tras exploración cervical y los resultados del tratamiento del HPT durante el periodo de seguimiento. Resultados: Paratiroides supernumerarias o aberrantes se descubrieron al efectuar la exploración quirúrgica inicial (cervicotomía) en 87 pacientes (30%); intratímicas, como islotes celulares paratiroideos (1–4) en 70 casos; paratiroides supernumerarias extratímicas se registraron en 17 pacientes. Entre los 260 casos que pudieron ser sometidos a un seguimiento prolongado, 11 (4%) presentaron un HPT persistente, y 34 (13%) desarrollaron un HPT recidivado. Fueron reintervenidos 25 pacientes, encontrándose que las SPG eran responsables de 4 de los 8 HPT persistentes y de 4 de los 17 HPT recidivados, cifras que suponen una frecuencia global del 32%. La reintervención demostró que las glándulas paratiroideas supernumerarias (SPG) se localizaban no sólo dentro del timo sino también, en el espacio retroesofágico, dentro de la capa adventicial carotídea y en el mediastino. Conclusión: Las SPG se encuentran en el 30% de los pacientes con HPT renal y se localizan preferentemente dentro del timo. Por tanto, durante la primera intervención quirúrgica deberá realizarse, de forma rutinaria, una timectomía con objeto de evitar recividas producidas por glándulas paratiroideas supernumerarias sitas en el mediastino anterior. Las SPG fueron las causantes del 32% de los casos de HPT persistente o recidivado. En estos casos, glándulas paratiroideas supernumerarias, francamente ectópicas no son infrecuentes; de ahí, que sea necesaria su visualización y localización exacta, antes de embarcarse en una reexploración quirúrgica.

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