INADVERTENT PARATHYROIDECTOMY AND TEMPORARY HYPOCALCEMIA: AN ADVERSE NATURAL OUTCOME OR A TRUE COMPLICATION DURING THYROIDECTOMY ?

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Objective. The aim of this study was to assess the factors that might predict patients at increased risk for inadvertent parathyroidectomy and postoperative symptomatic hypocalcemia during thyroidectomy.

Methods. Demographic data as well as the data on preoperative diagnosis, preoperative ultrasonography reports, operation reports, histological findings, and postoperative symptomatic hypocalcemia were collected. A total of 273 (83 male and 190 female patients) thyroid operations were included in this study.

Results. Histopathological examination identified inadvertent parathyroidectomy in 10 (3.7 %) cases. Statistical analysis identified the presence of cervical lymphadenopathy as detected by preoperative ultrasonography as a risk factor for inadvertent parathyroidectomy. In 57 patients (20.9 %) clinically symptomatic postoperative hypocalcemia was observed. However, the difference in the frequency of such hypocalcemia between the patients with and without inadvertent parathyroidectomy was not significant. Statistical evaluation identified total thyroidectomy as a risk factor for postoperative hypocalcemia ($p<0.005$).

Conclusion. Due to our experience, inadvertent parathyroidectomy is not a rare entity during thyroidectomy and the presence of cervical lymphadenopathy, as observed by preoperative ultrasonography, is the only risk factor for inadvertent parathyroidectomy. In contrast, no association between inadvertent parathyroidectomy and postoperative hypocalcemia was detected. Total thyroidectomy was found to be the sole risk factor for symptomatic temporary hypocalcemia.

Key Words: Thyroidectomy – Parathyroidectomy – Hypocalcemia – Complications

Every operation has a rhythm. The rhythm of thyroid surgery is, at the beginning, fast and flashy, with exposure of a large surgical field. The rhythm then suddenly slows down and the field of interest becomes much smaller, as the recurrent laryngeal nerve and parathyroid glands and their blood supply are identified and preserved. The operation requires strict rules including careful hemostasis, increased concentration and meticulous attention to detail at this stage. After this, the original rhythm is resumed, since the gland has been removed and the operation is going to be terminated. Surgeons having the least complications have an innate feeling for the changes in rhythm (FALK 1997). Nonetheless, even with meticulous dissection, every thyroid surgeon is occasionally surprised with a report revealing the presence of parathyroid tissue along with the thyroid specimen or symptomatic hypocalcemia after thyroidectomy (LIN et al. 2002).

The incidence of inadvertent parathyroidectomy during thyroid surgery was reported to range between 8-21 % (LEE et al. 1999; LIN et al. 2002; SAKORAFAS et al. 2005; GOURGIOTIS et al. 2006), whereas postoperative hypocalcemia, especially temporary hypocalcemia varies from 1.6 to more than 50 % (OLSON et al. 1996; SULIMAN et al. 1997; PATTOU et al. 1998).

This study was undertaken to assess the incidence and clinical significance of inadvertent parathyroid removal during thyroidectomy and to identify factors that

might predict patients at increased risk for inadvertent parathyroidectomy and postoperative symptomatic hypocalcemia.

Patients and Methods

We retrospectively reviewed all thyroid procedures performed in our Department of General Surgery between April 2001 and June 2006. A computer based data collection system was used. Demographic data of patients as well as these on their preoperative diagnosis, preoperative ultrasonographic evaluations, operation reports (details of surgical procedures), final histological diagnosis and postoperative symptomatic hypocalcemia were reviewed. Well documented final histopathological reports were examined specifically for the presence of parathyroid glands, the number of parathyroid glands removed, their location, and size.

Patients with recurrent or persistent thyroid disease and patients who were subjected to intentional parathyroidectomy were excluded. The patients were assessed in two groups for evaluating the association of the type of surgery with postoperative hypocalcemia and inadvertent parathyroidectomy. Thus, patients with total and nearly total thyroidectomy were included in Group 1 (n= 201) and these with total lobectomy or subtotal thyroidectomy were classified as Group 2 (n= 72).

The volume of each thyroid lobe separately and their total (data available in 172 cases), diameter of dominant nodule and cervical lympadenopathy (>1 cm) were estimated by grey-scale, real time, B-mode ultrasonography (US) using a 5-15 MHz transducer. Moreover, the age, gender, presence of thyroiditis or hyperthyroidism, type of surgery, and the final histopathological thyroid diagnosis were assessed as possible risk factors for inadvertent parathyroidectomy and postoperative hypocalcemia (data available in all cases).

The indications for surgery in patients were as follows: FNA suggesting malignancy, failure of medical treatment, rapid thyroid growth, compressive symptoms, cosmetic defects and hyperthyroidism with poor tolerance or compliance to medical treatment.

The presence of clinical symptoms or signs of hypocalcemia included facial paresthesia, positive Chvostek's or Trousseau's signs, muscular spasms, cardiac arrhytmias etc. were assessed. Total plasma calcium and parathyroid hormone levels were determined postoperatively, and in cases of hypocalcemia, an infusion of calcium gluconate was administered. Oral calcium carbonate and 1,25-dihydroxyvitamin D_3 supplements were prescribed simultaneously. All patients with hyperthyroidism were treated with Propylthiouracil until their free thyroxine and triiodothyronine levels were normalised before operation.

In our Department of General Surgery, all surgeons perform the same thyroidectomy technique with meticulous dissection along the thyroid capsule attempting to identify and preserve the parathyroid glands with their vascular supply, as well as the recurrent laryngeal nerves. Due to the concept of our clinic, in relation with unilateral attempts, at least two parathyroid glands are identified and preserved in situ and also, in relation to bilateral attempts, at least four parathyroid glands are identified and preserved in situ routinely. In addition, all resected specimens are subjected to immediate routine macroscopic examination in the operation room to identify accidentally removed parathyroids and to perform immediate parathyroid autotransplantation. Parathyroid tissue submitted separately for histopathological evaluation was not considered in this study.

Statistical evaluation. Data analysis and statistical evaluation was carried out by an independent statistical company. Statistical tests included Mann-Whitney U test, Fisher's exact test, Pearson chi-square test, and logistic regression. The level of $p<0.05$ was considered statistically significant.

Results

In summary, 273 (83 male and 190 female patients; median age of 44 years, range: 20-76) thyroid operations performed during the study period were included in this study.

Total lobectomy was performed in 69 (25.3 %) patients, subtotal thyroidectomy in 3 (1.1 %) patients, total thyroidectomy in 90 (33 %), and nearly total thyroidectomy (leaving no more than 2 g of residual thyroid parenchyma) in 111 (40.7 %) patients. Well documented final histopathological examination of resected thyroid specimens has revealed the presence of malignant thyroid disease in 15 (5.5 %) cases and benign thyroid disease in 258 (94.5 %) cases. Neither wound infection nor mortality was noted.

In removed tissues the histopathological examination identified parathyroid tissue in 10 (3.7 %) cases. In each of such cases, only one accidentally removed parathyroid gland was identified and in all cases normal parathyroid tissue was found. Mean diameter of such accidentally removed parathyroid glands was 3.5 mm, the location of 8 (80 %) glands being extrathyroidal and that

Table 1
Patient demographics and incidence of inadvertent parathyroidectomy according to potential predictive variables

VARIABLE		n=273, (100 %)	Inadvertent parathyroidectomy n= 10, (3.7 %)	No parathyroidectomy n=263, (93.6 %)	P value
Sex	Male Female	83 (30.4%) 190 (69.6%)	3 (30%) 7 (70%)	80 (30.4%) 183 (69.65%)	1.0
Age	Mean Range	45.27 20-76	44.90 28-68	45.28 20-76	0.846
Procedure	Total/Near total Thyroidectomy Lobectomy/ Subtotal Thyroidectomy	201 (73.7%) 72 (26.4%)	8 (80%) 2 (20%)	193 (73.4%) 70 (26.6%)	0.413
Final thyroid pathology	Benign Malignant	258 (94.5%) 15 (5.5%)	8 (80%) 2 (20%)	250 (95.1%) 13 (4.9%)	0.098
Volume	Right Lobe Volume (mm^3) (Mean)	47563.74	50424.11	47406.77	0.280
	Left Lobe Volume (mm^3) (Mean)	43571.66	48813.75	43311.19	0.929
	Total Thyroid Volume (mm^3) (Mean)	90275.95	100410.88	89775.46	0.471
Dominant nodule	Dominat Nodule Diameter (mm)	31.99	38.60	31.74	0.135
Thyroiditis	With Thyroiditis Without Thyroiditis	29 (10.6%) 244 (89.4%)	0 (0%) 10 (100%)	29 (11%) 234 (89%)	0.607
Lymphadenopathy on preoperative US (LAP)	With LAP Without LAP	18 (6.6%) 255 (93.4%)	4 (40%) 6 (60%)	14 (5.3%) 249 (94.7%)	**0.002***
Status	Hyperthyroid Euthyroid	106 (39.1%) 165 (60.9%)	8 (80%) 2 (20%)	104 (39.8%) 157 (60.2%)	0.325
Postoperative Hypocalcemia	With Without	57 (20.9%) 216 (79.1%)	1 (10%) 9 (90%)	56 (21.3%) 207 (78.7%)	0.693

* Fisher's exact test

of 2 (20 %) cases intrathyroidal. There was no significant correlation (p>0.05) between the inadvertent parathyroidectomy on one side and the type of surgery, age, gender, left thyroid lobe volume, right thyroid lobe volume, total thyroid volume, diameter of dominant nodule, presence of thyroiditis, presence of hyperthyroidism, and final histopathological type of thyroid disease (benign/malignant) inadvertent parathyroidectomy on the other. Statistical evaluation showed the presence of cervical lymphadenopathy observed at preoperative US examinationas as a risk factor for inadvertent parathyroidectomy (p = 0.002, odds ratio = 9.934) (Table 1). Significant correlation between the final histopathological type of thyroid disease and inadvertent parathyroidectomy was not detected (p>0.05), but a higher risk of inadvertent parathyroidectomy was found in patients with malignant thyroid disease (odds ratio of 2.442).

In 57 (20.9 %) patients one of whom was with inadvertent parathyroidectomy, clinically symptomatic hypocalcemia was observed. No case of persistent hypocalcemia was detected in this study. There was no significant difference regarding the postoperative hypocalcemia between the patients with and without inadvertent parathyroidectomy (p>0.05).

Statistically significant correlation between the above mentioned criterion with postoperative symptomatic

Table 2
Incidence of symptomatic hypocalcemia according to potential predictive variables

VARIABLE		No hypocalcemia n=216 (79.1 %)	Symptomatic hypocalcemia n=57 (20.9 %)	P value
Sex	Male Female	66 (30.6 %) 150 (69.4 %)	17 (29.8 %) 40 (70.2 %)	0.915
Age	Mean Range	45.47 20 – 76	44.51 27 – 76	0.314
Procedure	Total/near total thyroidectomy Lobectomy/ subtotal thyroidectomy	147 (68.1 %) 69 (31.9 %)	54 (94.7 %) 3 (5.3 %)	**0.0001***
Final thyroid pathology	Benign Malignant	206 (95.4%) 10 (4.6%)	52 (91.2%) 5 (8.8%)	0.322
Volume (mm^3 ; mean)	Right lobe Left lobe Total thyroid	48346.15 43168.68 90154.07	44687.84 45060.47 90729.64	0.541 0.167 0.476
Dominant nodule	Dominant nodule diameter	32.23	31.09	0.459
Thyroiditis	With thyroiditis Without thyroiditis	22 (10.2 %) 194 (89.8 %)	7 (12.3 %) 50 (87.7 %)	0.648
Lymphadenopathy on preoperative US (LAP)	With LAP Without LAP	16 (7.4 %) 200 (92.6 %)	2 (3.5 %) 55 (96.5 %)	0.381
Status	Hyperthyroid Euthyroid	80 (37.4 %) 134 (62.6 %)	26 (45.6 %) 31 (54.4 %)	0.258

* Yates chi-square test

hypocalcemia was not found (p>0.05), except for type of surgery. The postoperative hypocalcemia was significant in the Group 1 (p = 0.0001) (Table 2). The subgroup analysis of Group 1 revealed that total thyroidectomy was the sole risk factor for postoperative hypocalcemia (p = 0.005). Parathyroid autotransplantation was performed in three patients, none of whom developed temporary or permanent hypocalcemia.

Discussion

Complications in thyroid surgery can be kept to a minimum by a through knowledge of the thyroid and parathyroid anatomy and its variations, by understanding thyroid pathology, and by meticulous hemostasis and delicate surgical technique (Falk 1997). Most authors agree that accidental parathyroidectomy may occur even in the hands of the more experienced thyroid surgeons and the intracapsular or intrathyroidal location of parathyroid glands contributes the risk of accidental parathyroidectomy (Lin et al. 2002). On the other hand, theoretically, meticulous identification of parathyroid glands during thyroid surgery can result in a lower risk of incidental parathyroidectomy.

Despite of advanced surgical techniques and experience in thyroid surgery as much as up to 8-21.6 % accidentally removed parathyroid glands have been reported in the literature. Not to regard as too little, up to 40-50 % of these are intrathyroidal (Sakorafas et al. 2005; Gourgiotis et al. 2006). In our study, we observed inadvertent parathyroidectomy in 10 (3.7 %) cases and 20 % of these were intrathyroidal. In cases with intrathyroidal parathyroid, inadvertent parathyroidectomy has been considered to be inevitable. Strikingly, in our study, only one of these patients with inadvertent parathyroidectomy experienced temporary clinical hypocalcemia.

Most surgeons hesitate to operate giant goitres, with an inappropriate expectation of technical difficulties resulting in postoperative complications such as recurrent laryngeal nerve palsy and hypoparathyroidism. Nevertheless, as the majestic size of thyroid often scares the surgeon, in our study the volume of thyroid and the diameter of dominant nodule were not found to be the independent risk factors for postoperative hypocalcemia and inadvertent parathyroidectomy ($p>0.05$). Malignant thyroid disease is another factor accused for inadvertent parathyroidectomy, whereas a statistically significant correlation was not demonstrated in our study.

According to our data, the statistical analysis identified the presence of cervical lymphadenopathy as found by preoperative US as a risk factor for inadvertent parathyroidectomy ($p< 0.002$, odds ratio = 9.934). This might be attributed to the similarity of small lymph nodes and parathyroid glands (colour and location), which might cause confusion to differentiate these structures. In these circumstances, surgeons might consider the parathyroid gland as a lymph node which might result in inadvertent parathyroidectomy.

Lin et al. (2002) reported a significant association of accidental parathyroidectomy with the operations for recurrent or persistent malignancy and the patients who had tracheoesophageal groove node dissection. This may be attributed to the technical difficulties resulting from the formation of scar tissue and fibrosis more often encountered in revision operations. However, in our study, we have excluded the patients who underwent reoperation for recurrent and persisted thyroid disease.

Hypocalcemia, especially transient one is not a rare problem after thyroid surgery. In the literature, the incidence of hypocalcemia varied from 1.6 to more than 50 % (Olson et al. 1996; Al Suliman et al. 1997; Pattou et al. 1998). The incidence of symptomatic transient hypocalcemia in our series was found to be 20.9 %.

Recently, Abboud et al (2002) reported that the etiology of hypocalcemia seems to be a multifactorial phenomenon, but the most important factor is the iatrogenic surgical trauma to parathyroid glands, closely related to the extent of operation. Among 57 hypocalcemic patients in our series, 54 (94.7 %) had undergone Group 1 type thyroidectomy and, among these 33 (61.1 %) were subjected to total thyroidectomy. The extent of operation creates a higher risk for parathyroid function (de Roy et al. 1995). The physical preservation of parathyroid tissue is essential, but such preservation does not guaranty the recovery of its function in all cases. Extensive and aggressive surgery may result not only in compromising parathyroid arterial and venous blood supply, but also in the disruption of parathyroid gland, and/or in a direct injury to the parathyroid gland as well (Demeester-Mirkine et al. 1992; McHenry et al. 1994; Shaha et al 1998; Glinoer et al. 2000; Bhattacharyya et al 2002; El-Sharaky et al. 2003). In accordance with the literature (Sason et al. 2001; Bhattacharyya et al 2002), statistical analysis of our data identified total thyroidectomy as a true risk factor for postoperative hypocalcemia ($p<0.05$).

Some authors suggest that hypocalcemia is more frequent in cases of thyroidectomy for thyroid malignancy (Falk 1997; Sasson et al 2001), In our study, we did not find any significant association of these circumstances. However, many studies by others underestimate the fact that patients with malignant thyroid disease are more likely to undergo total thyroidectomy and that in such cases the true variable predicting hypocalcemia might be in fact the extent of surgery. In our study, final histopathological diagnosis in 6 of 15 (40 %) malignant cases was an occult papillary carcinoma. The extent of surgery in these cases was limited.

Some authors suggest hyperthyroidism as a risk factor for developing hypocalcemia after thyroid surgery (See 1997; Wilkin et al. 1997; Abboud et al. 2002). However, in our series such difference was not statistically significant. In these patients in which normal parathyroid function can be documented, the hungry bone syndrome appears to be the most likely cause of hypocalcemia. Nevertheless, most of these studies were retrospective and the precise documentation of parathyroid function was frequently impossible. In this respect, the true reason responsible for hypocalcemia might not be achieved. As a consequence it is not feasible to attribute it as a true risk factor in circumstances of insufficient documentation.

Elevation of serum calcitonin secondary to manipulation of the thyroid was also initially suspected to participate in hypocalcemia (See 1997), but was not confirmed by the other studies (Percival et al. 1985; McHenry et al. 1994).

In conclusion, due to our experience, inadvertent parathyroidectomy is not rare during thyroidectomy and the presence of cervical lymphadenopathy on preoperative US is a risk factor for inadvertent parathyroidectomy. In contrast, no association between inadvertent parathyroidectomy and postoperative hypocalcemia was detected. Total thyroidectomy was found to be the true risk factor for symptomatic temporary hypocalcemia. Hypocalcemia an adverse effects of thyroidectomy, is either a natural sequel or a true complication. Until the

true pathogenesis will be determined, the question of whether temporary hypoparathyroidism is an adverse natural sequel or a true complication of thyroidectomy remains unanswered.

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