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Original Research Article

Evaluation for the Coexistent of Thyroid Nodules and Primary Hyperparathyroidism

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Abstract

Background: The coexistence of primary hyperparathyroidism (PHPT) and thyroid disease (TD) is a well-known entity**.** The aim of our study is to report our experience, to evaluate the prevalence of this association with review of the literature. ***Methods:*** We retrospectively examined the operative database over the past 03 years. We looked for patients who underwent parathyroid surgery. All patients underwent preoperative neck US and Tc99m sestamibi scintigraphy and /or CT scan or MRI. ***Results:*** Among the 43 patients who underwent a parathyroidectomy. Preoperative thyroid US revealed that 62, 79 % of patients with PHPT had thyroid abnormalities. 58, 14 % patients underwent parathyroidectomy, whereas 41, 86 % patients underwent both parathyroidectomy and thyroidectomy. Postoperative histopathology results showed that 62.96% of patients had benign thyroid disease and 3.70 % of patients had malignant thyroid disease. ***Conclusion:*** In our study, we found a high prevalence of concomitant thyroid disease and PHP T. however, one patient had a micro papillary carcinoma and that emphasize the importance of careful judgment to avoid over-treatment.
Keywords: Primary hyperparathyroidism; thyroid disease; parathyroidectomy; papillary micro carcinoma.

INTRODUCTION

Primary hyperparathyroidism (PHPT) is an endocrine disorder characterized by autonomous production of parathyroid hormone (PTH). It is the third most common clinical endocrine disorder after diabetes and thyroid disease [1]. Its incidence increases with age with a peak in the fifth to sixth decades of life [2]. Coexistent thyroid pathology discovered during neck exploration in patients with PHPT has been well described in the literature [3]. In different studies, the rate of benign thyroid diseases concomitant with PHPT ranges from 17% to 84% [4, 5]. Besides, the incidence of synchronous thyroid cancer in patients with PHPT ranges between 2% and 24% [6]. The first cases of concomitant nonmedullary carcinoma of the thyroid in patients with PHPT were reported by Ogburn and Black in 1956 [7]. That is why a warrant careful preoperative and intraoperative evaluation of thyroid and parathyroid glands, in order to obviate reoperation. High-resolution ultrasonography (US) and dual phase technetium 99m sestamibi scintigraphies (Tc-MIBI) are widely accepted methods for preoperative localization of parathyroid lesions [8]. Ultrasonography enables screening of the thyroid gland while simultaneously localizing the parathyroid adenoma [9].These concomitant preoperative findings require surgical attention. The aim of our study is to report our experience, to evaluate the prevalence of this association with review of the literature and comparison with prior reports discussed.

Design and Study

We retrospectively examined the operative database of our department of endocrinology in Hassan II University Hospital of Fez over the past 03 years from 2015- 2018. We looked for patients who underwent parathyroid surgery.

We excluded from our study all patients who are younger than 15 years old, patients with a previous history of thyroid or parathyroid operations, patients suffering from secondary hyperparathyroidism, patients with a surgical contraindication associated with co morbid diseases or who refused surgery. In our department, all operation indications were discussed in multidisciplinary (surgeons, endocrine specialists, and nuclear medicine specialists).

Data collected included demographics (sex, age); serum calcium levels (mg/l; normal range: 88–105); phosphorus (mg/l; normal range: 25–45), vitamin D (ng/ml), preoperative PTH value (pg/ml; normal range: 15–65), the 24-hour urine Ca (mg/day); results of preoperative parathyroid localization by neck US and Tc99m sestamibi scintigraphy and /or CT scan or MRI. Our patient underwent also examens for identifying the

thyroid disease (TSHus, FT3, FT4, anti- TPO, US, fine-needle aspiration biopsy [FNAB]).

Besides, dual energy X-ray absorptiometry (DEXA) and renal US were indicated to evaluate bone mineral density and nephrolithiasis, respectively. The surgical approach was a conventional "open" thyroidectomy" with a wide bilateral parathyroid exploration.

Statistical Analysis

Statistical analysis was performed using Microsoft Excel and Epi info 7.

RESULTS

Clinical characteristics and Preoperative Evaluation

There were 43 patients evaluated and enrolled, 35 (81, 40%) were female and 8(18, 60%) were male with a sex-ratio H/F: 0, 23. The mean age of the patients was 55;34 ± 13,64 years (range 26- 79 years). Laboratory evaluation confirmed hypercalcemia with hypophosphatemia. The mean level of serum Calcium and phosphorus were 126 ±18,40 and 20,15 ± 7,17 mg/l. Mean levels of serum PTH and 25-OH vitamin D were 737,80pg/ml ± 656,96 (range 110- 2500 pg/ml; median, 514 pg/ml) and 10,49± 6,93ng /ml respectively. The mean 24-hour urinary Ca excretion was 262, 25 mg/day (Table-1). All patients underwent preoperative Neck US and only 72,09 %, 48,84 % underwent Tc99m sestamibi scintigraphy and neck and mediastinum MRI or CT scan respectively. Based on ultrasonography, 47, 61% of the parathyroid adenomas were on the left side and 76, 74 % were located inferiorly. The mean parathyroid adenoma size was 29, 75 ± 19,06mm (range, 7- 85 mm). Besides, Tc99m sestamibi scintigraphy identified an ectopic parathyroid adenoma in four patients and double parathyroid adenomas in one patient.

Preoperative Thyroid evaluation (Table-2)

Ultrasound examination showed co-existent thyroid abnormalities with parathyroid adenomas in 62, 79 % (n=27). 37, 21% (n= 16) had diffuse multinodular goiter (MNG). 25, 58% (n=11) had thyroid nodules.

TI-RADS classification of thyroid nodules showed TIRADS 2 in 6, 98% (n=3), TIRADS 3 in 23, 26% (n=10) and finally TIRADS 4 in 32, 56% (n=14). The median size thyroid nodule was 1, 5 cm for all patients with thyroid pathology. Concerning biological evaluation, 38 (88, 30%) patients had a normal thyroid function and 5 (11, 62%) had thyrotoxicosis. The thyroid peroxidase antibody positivity rate was 6, 97 %.

Postoperative Results (Table-3)

25 (58, 14 %) patients underwent parathyroidectomy, whereas 18 (41, 86%) patients underwent both parathyroidectomy and thyroidectomy.

Based on the parathyroid histopathology results: 41 (95, 34 %) patients had parathyroid adenomas; one patient had atypical adenoma and one patient had hyperplasia. No parathyroid carcinoma was finding in our cases.

However, the postoperative thyroid histopathology results showed that 97, 67 % of patients had benign thyroid disease and one patient had malignant thyroid disease. This last had microcarcinoma.

Table-1: Patient demographics with pre-operative laboratory and radiographic results

Demographics	**Patients (n = 43)**
Age; mean in SD (y)	55; 34± 13,64
Gender (female: male)	35:8
Preoperative laboratory evaluation	**Mean ±SD**
Serum calcium (mg/ L)	126± 18,40
PTH (pg/mL)	737,80 ± 656,96
phosphate	20,15 ± 7,17
Urine calcium (mg/ day)	262,25
25 OH vit D (ng/ml)	10,49 ± 6,93
Preoperative radiographic results	
Site of parathyroid adenoma	n (%)
Right	22 (50, 06)
Left	20 (47, 61)
Bilateral	1(2,33)

Table-2: Pre-operative thyroid evaluation

Thyroid function	**n (%)**
Hypothyroidism	0 (0 %)
Thyrotoxicosis	5 (11, 62%)
Euthyroid	38 (88, 30%)
thyroid peroxidase	3 (6, 97 %)
Neck US thyroid evaluation	**n=43**
Normal thyroid	**16**
Multinodular goiter	**15**
Thyroid nodules	**11**
Chronic thyroidite	**1**

Table-3: Operation types and postoperative parathyroid and thyroid histopathological results

Variables	n (%)
Operation type:	
Parathyroidectomy	25 (58,14)
Parathyroidectomy + lobectomy/isthmectomy	8 (18,60)
Parathyroidectomy + Total thyroidectomy	10 (23,25)
Parathyroid histopathology	
Adenoma	41(95, 34%)
Atypical adenoma	1 (2, 33%)
Hyperplasia	1 (2, 33%)
Carcinoma	0(0%)
Thyroid histopathology	
Benign	17 (62, 96%)
Malignant	1 (3,70%)

DISCUSSION

The coexistence of primary hyperparathyroidism (PHPT) and thyroid disease (TD) is a well-known entity [10]. Until now; there is no guidelines dedicated to this coincidental entity. In this present study, we targeted to evaluate the prevalence of concomitant thyroid disease in patients who underwent surgical treatment for PHPT. We also aimed to determine the clinical impact of preoperative Tc99m sestamibi and neck US in patients with PHPT. The prevalence of concomitant PHPT and thyroid disease in the review of the literature is ranges between 18% to 84.3%; [11, 12]. This is consistent with the finding in our study (27/ 43; 62, 79%). On the other hand, we found in our series one case of micro papillary carcinoma with a prevalence of 3, 70%. The coexistence of parathyroid adenoma and incidental papillary carcinoma is reported to be rare (13).the first case has been reported by Ogburn *et al*., in 1956 [7]. In several studies, the frequency of this association has been reported as 1.3-17.6% [14, 15]. Strichartz and Giuliano evaluated the coexistence of PHPT and thyroid disease in 308 patients and and revealed that 17% of patients had histologically proven thyroid disease and 4% of patients had differentiated thyroid cancer as seen in our study [16]. The standard surgical management of primary hyperparathyroidism has been bilateral neck exploration. This approach allowed for examination of both 4 parathyroid glands and thyroid gland. However, the surgical management of PHPT has evolved over the last decade into a more minimally invasive approach (MIA) [17]. This procedure was widely developed because of the use of both Tc 99 sestamibi and ultrasound to confirm abnormal parathyroid tissue and the introduction of a rapid intra operative PTH (IO-PTH) assay [18]. In our study, All patients underwent preoperative Neck US and only 72, 09 %, 48, 84 % underwent Tc99m sestamibi scintigraphy and neck and mediastinum MRI or CT scan respectively.

MIA presents several advantages: firstly; the possibility to use local anesthesia and reduction the time of the operation. Secondly; the reduction of surgical trauma and the already low complication rate of parathyroidectomy. Finally; decrease of hospitalization time [9, 19].

A MIA would not be discussed in a patient with a history of neck irradiation, a family history of thyroid cancer, or a non localizable parathyroid abnormality on preoperative imaging studies. Therefore, the main challenge of MIA is concomitant thyroid nodules because clinical decision and management of patients may change [20, 21]. The principal advantage of combined operative management of simultaneous thyroid and parathyroid is to avoid a second neck exploration particularly in patient with unexpected thyroid malignancy that can be treated safely at the time of initial operation for PHPT. In our hospital, the department of surgeon still uses the bilateral neck exploration because the impossibility of assessing immediately intra operative PTH. In our study, 10 (23, 25%) and 8 (18, 60%) patients underwent total thyroidectomy and isthmo-lobectomy respectively because of the toxic MNG / MNG or nodular thyroid. For technical reason, one patient only had Fine-Needle aspiration Biopsy (FNAB). Several studies have revealed that thyroid lesions of less than 1 cm are missed in 94% of patients and that lesion 1- 2cm are missed in 50% of patients with neck exploration [6]. In fact, US neck is recommended before parathyroid surgery for preoperative localization of Coexistent thyroid pathology. Some studies suggest that patients with a history of radiation to the head and neck need a careful evaluation for underlying thyroid malignancy. Hedman and Tisell studied 484 patients treated surgically for either PHPT non medullarythyroid cancer, or both conditions over an 8-y period; 73 patients (15%) had a history of radiation to the head and neck. These individuals were found to have a significantly increased incidence of synchronous PHPT and non medullary thyroid cancer (P <0.001) [22].

None of the patients studied had undergone a radiation of neck or head. Nevertheless, some other authors have suggested that this relationship may be explicated by an increase of endogenous Ca concentration, growth factors, epithelial growth factor, or goitrogenic factors [21].

CONCLUSION

The routine use of thyroid ultrasound en preoperative of hyperparathyroidism may aid in the timely diagnosis and treatment of coexisting thyroid disease and thus determine the best surgical strategy. In our study, we found a high prevalence of concomitant thyroid disease and PHP T. however, one patient had a micro papillary carcinoma and that emphasize the importance of careful judgment to avoid over-treatment. More data are needed with a long follow-up. These would be important

For the development of clinical guidelines for the management of incidental thyroid nodules in patients undergoing parathyroidectomy**.**

Declaration of Interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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