Parathyroid incidentaloma. Literature review about three case reports

Incidentalome parathyroïdien. Revue de la littérature à propos de trois cas

I. Benabbad a,*, b, A. Chraibi a, H. Iraqi a, b, B. Serji c, R. Mohsine c, L. Ifrine c, A. Belkouchi c, P. Bonnichon d, H.O. El Malki b, c, e

a Service d'endocrinologie, diabétologie et maladies métaboliques, CHU Ibn Sina, faculté de médecine et de pharmacie de Rabat, université Mohammed V Souissi, Rabat, Morocco
b Centre de recherche en épidémiologie clinique et essais thérapeutiques (CRECET), faculté de médecine et de pharmacie de Rabat, université Mohammed V Souissi, Rabat, Morocco
c Service de la clinique chirurgicale « A », CHU Ibn Sina, faculté de médecine et de pharmacie de Rabat, université Mohammed V Souissi, Rabat, Morocco
d Service de chirurgie endocrine, hôpital Cochin, 27, rue du Faubourg-Saint-Jacques, 75014 Paris, France
e Laboratoire de biostatistique et recherche clinique et épidémiologique (LBRCE), faculté de médecine et de pharmacie de Rabat, université Mohammed V Souissi, Rabat, Morocco

Abstract

Background. – Parathyroid incidentaloma is not a well-known entity. The aim of this study was to show its incidence and to discuss its management. Methods. – This was a prospective study analyzing cases of enlarged parathyroid glands discovered during thyroid surgery. The records of patients with parathyroid incidentaloma were reviewed. We also reviewed all cases of primary hyperparathyroidism (HPTPs) operated during the same period for comparison. Results. – Three cases of enlarged parathyroid were found. No clinical or biochemical features led us to suspect hyperparathyroidism before surgery, but a macroscopically enlarged parathyroid gland was discovered during the dissection and was removed in all three patients. Conclusions. – Enlarged parathyroid glands discovered at the time of surgery may represent an early pathological stage responsible for overt primary hyperparathyroidism. In absence of major risk for recurrent nerve palsy, we recommend removal of any enlarged parathyroid discovered during neck surgery in order to avoid the risks of future surgical procedures, preserving in the same time at least one normal parathyroid gland.

© 2010 Elsevier Masson SAS. All rights reserved.

Keywords: Parathyroid incidentaloma; Hyperplasia; Parathyroid adenoma; Thyroid; Parathormone

1. Introduction

The parathyroid incidentaloma is not as well documented as the adrenal or the pituitary incidentalomas. Only a few articles about it are found in the literature [1–3].
**Table 1**

<table>
<thead>
<tr>
<th>Preoperative Biological Features</th>
<th>Surgery Pathology</th>
<th>Postoperative Biological Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Case 1</strong></td>
<td>Thyroid hyperplasia and parathyroid adenoma</td>
<td><strong>Ca</strong>(^{2+}) mg/l N: 85–105</td>
</tr>
<tr>
<td>CAST [µg/l]</td>
<td>PTH [pg/ml]</td>
<td><strong>PTH</strong> pg/ml N: 10–65</td>
</tr>
<tr>
<td>65</td>
<td>57</td>
<td>91</td>
</tr>
<tr>
<td><strong>Case 2</strong></td>
<td>Nodular hyperplasia and parathyroid adenoma</td>
<td>91</td>
</tr>
<tr>
<td>65</td>
<td>57</td>
<td>80</td>
</tr>
<tr>
<td><strong>Case 3</strong></td>
<td>Nodular hyperplasia and parathyroid adenoma</td>
<td>91</td>
</tr>
<tr>
<td>65</td>
<td>57</td>
<td>80</td>
</tr>
</tbody>
</table>

N: normal; TSHus: thyreostimulating hormone; LT4: tetra-iodothyroxin; LT3: tri-iodothyronin. Ca\(^{2+}\): calcemia; P: phosphoremia.

The increase in the volume of the parathyroid glands is usually due to a parathyroid adenoma, or hyperplasia involved in a genetic context or less frequently due to a parathyroid cancer [4]. Clinical and biological investigations establish the diagnosis before the localization of the pathological parathyroid(s) is recognized. It generally presents as hyperparathyroidism, which is an overactivity of the parathyroid glands, with an excess production of parathyroid hormone (PTH) leading to hypercalcemia [4,5]. In a few cases, this increase in volume is discovered fortuitously in a patient with no clinical signs undergoing a sonography exploration or surgery for thyroid disease [1,2,6,7].

This entity is defined as parathyroid incidentaloma, by analogy with increased gland volume, without increased hormone secretion, in adrenal or pituitary incidentalomas.

The aim of our study, conducted within the framework of a prospective open study, was to evaluate the incidence of fortuitously discovered enlarged parathyroid glands in patients undergoing surgery for thyroid disease, and to discuss subsequent management.

### 2. Methods

This prospective opened study included all patients who underwent thyroid surgery from 2000 to 2006 in a general surgery department (Surgery A) in the University Hospital Ibn Sina of Rabat and who had enlarged parathyroid glands incidentally discovered during surgery.

Serum calcium and phosphorous levels were measured in all patients preoperatively and only those with normal levels were included.

Calcemia was also determined systematically the first and the second day after surgery. Vitamin D and calciuuria were not determined, unless there were clinical signs before the thyroid surgery.

The hospital laboratory determined serum calcium, phosphorus and PTH levels using the Achitech® kit (Aeroset – Abott). The calcium assay was based on a colorimetric reaction using Arsenazo III and spectrophotometry analysis at 660 nm. Normal range: 85–105 mg/l. Serum phosphorus was based on a colorimetric reaction using phosphomolybdate and ultraviolet analysis at 340 nm. Normal range: 25–45 mg/l. Serum PTH level was determined only in patients who presented a calcium level over 100 mg/l. The method was based on an immunologic reaction with PTH antibodies and chemoluminescence analysis. Normal range for PTH: 10–65 pg/l. Patients with marked hypercalcemia (Ca\(^{2+}\) > 105 mg/ml) and a high PTH level were not retained for analysis.

During the same period, we checked all the patients who underwent surgery for primary hyperparathyroidism.

Thyroidectomies were performed in patients presenting one or more suspicious nodules or hyperthyroidism. Procedures were performed after achieving clinical and biological euthyroid status. A standard surgery protocol was rigorously applied [8].

The same team performed all cytology exams, reported the histology of thyroid and parathyroid tissue surgical specimens. The diagnosis of adenoma was retained when a tumor with few...
fat cells was identified and well separated from the normal gland tissue by a distinctive “ring”. The diagnosis of hyperplasia was retained in the presence of diffuse involvement of the gland loaded with numerous fat cells [3,6].

Early and late follow-up findings were recorded. After surgery, patients were carefully monitored for clinical and biological signs of hypocalcemia and recurrent nerve palsy. Long-term follow-up visits were scheduled at one, two, and five years.

3. Results

Among the 357 patients who underwent thyroid surgery, we found two cases of hypercalcemia with a high serum level of PTH before surgery. These patients were excluded.

An enlarged parathyroid gland (> 6 × 4 × 2 mm) that had not been recognized in the preoperative investigations was found in three patients during surgery.

Mean patient age was 44 ± 12 years. The three women did not exhibit any clinical manifestations of hyperparathyroidism. They did not have any personal or family history of urinary stones, nor of gastric or duodenal ulcer, as well as no signs of multiple endocrine neoplasia.

All of them showed normal clinical or chemical thyroid features.

Serum calcium was 105 mg/l in one patient but the PTH level was normal before surgery. Table 1 summarizes the laboratory results for the three patients.

Surgery consisted of a total intracapsular thyroidectomy in two patients associated with excision of the enlarged parathyroid gland found incidentally during the course of the operation.

In the third patient, isthmolobectomy was performed for an isolated simple thyroid nodule with the excision of the homolateral parathyroid gland. The digital exploration of the controlateral lobe did not reveal any thyroid dystrophy.

Nodular thyroid hyperplasia was found at the cytology examination for all three patients. For the parathyroid tissue, the histology was adenoma in 2 patients and hyperplasia in the third.

All three patients were free of clinical features of hypoparathyroidism or hyperparathyroidism after surgery and remained so during the follow-up. Serum PTH was assayed and was normal.

During the same period, 50 patients underwent parathyroidectomy for primary hyperparathyroidism. Their mean age was 48 ± 11 years.

4. Discussion

Discovery of parathyroid incidentaloma during thyroid surgery is a relatively rare event. The first case was reported in 1937. In our experience, we observed an incidence of 0.84% since we diagnosed three cases of enlarged parathyroid gland during surgery among 357 thyroidectomy procedures performed during six years. In autopsy series of subjects without primary hyperparathyroidism or any thyroid diseases, Alveryd and Akerstrom found an incidence of enlarged parathyroid of, respectively, 1.9% (among 129 patients) and 9.4% (among 422 patients) [3,6,10]. In Akerstrom et al.’s histological findings, 2.4% of parathyroid adenomas and 7% of hyperplasias were confirmed by immunohistochemical methods. Carnaille et al. report an incidence of 0.6% [9] in their study. Hellman et al. have an incidence of 2% [6] and the most recent study (Abboud et al.) an incidence of 1.9% [11]. The incidence of primary hyperparathyroidism revealed by a hypercalcemia in our study is 1% according to the literature [11].

Parathyroid incidentalomas appear to be more common in women as in primary hyperparathyroidism. Their mean age seems to be younger than in primary hyperparathyroidism [9,11,12]. In our study, the mean age for patients admitted for thyroid surgery was 44 years, similar to the age of 48 years of patients admitted for primary hyperparathyroidism during the same period.

None of our three patients with enlarged parathyroid gland had clinical signs suggesting hyperparathyroidism. This might suggest that the glands were not functional at that moment. Indeed, some authors implied that the parathyroid incidentalomas may represent the early stage of a hyperfunctioning parathyroid gland, before the biological findings [1,2,6,9,11].

Hellman has noted a reduction of E11 antibody expression that recognizes the calcium receptor of hyperfunctional parathyroid cells. These glands would also present a decreased response to intracellular calcium related to the rise of the extracellular calcium. The same is true with primary hyperparathyroidism [6,13].

Parathyroid gland enlargement could also result from a genetic cause, e.g., inactivating mutation polymorphisms of the calcium-sensing receptor gene [14].

Our standard work-up did not include systematic assessment of calcium-phosphorus-PTH preoperatively because our patients had thyroid disease and were scheduled for thyroid surgery; none of them had a history or clinical signs suggesting parathyroid disease.

Many authors advise resection of enlarged parathyroid glands found incidentally during a thyroid operation [1,2,9,11,12,15]. The risk of hypocalcemia after surgery remains low, as we found in our series, despite total thyroidectomy [9,11]. The rationale for preventive resection of incidentalomas is mainly based on the risk of recurrent nerve palsy during a second surgery, with an increased risk of complications. Another reason is that it is difficult to monitor an enlarged parathyroid gland. Finally, immunohistochemical studies have suggested that incidentalomas would be a prepathological state. After surgery, it would be reasonable to keep the parathyroid glands for possible immunohistochemical studies and molecular biology, in particular genetic study of the calcium-sensing receptor to determine the etiological diagnosis.

5. Conclusion

In conclusion, systematic search for the parathyroid glands during thyroid surgery to ensure their preservation leads to the discovery of a parathyroid incidentaloma in approximately 1% of patients. Since data on the functional outcome of these incidentalomas is lacking, it is recommended to remove any
enlarged parathyroid discovered during neck surgery, even without primary hyperparathyroidism, in absence of major risk for the recurrent nerve. Furthermore, the preservation of the other normal parathyroid glands is of course recommended.

**Conflict of interest**

The authors have not conflict of interest.

**References**