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Research Article

Intrathyroid Parathyroid Adenoma: Should Preoperative Imaging Tests Help Guiding Scheduled Operation? Report of Two Cases

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Abstract

Background: Intrathyroid parathyroid adenoma is a rather rare condition. The incidence rates reported in the world literature varies from 1.4% to 3.2%. The aim of the study is to present the surgical management of two patients with intrathyroid parathyroid adenomas and particularly to assess the contribution of preoperative imaging tests in intrathyroidal localization of ectopic parathyroid adenomas preoperatively.

Methods: Two Caucasian females were admitted in our department for a scheduled parathyroidectomy. In both patients preoperative imaging was unclear. Cervical ultrasound showed solitary thyroid nodules, while in the same areas Technetium^{99m} Sestamibi scintigraphy revealed parathyroid adenomas.

Results: In both patients neck exploration was performed and resulted negative for parathyroid adenomas. Blind thyroid lobectomy was performed on the side of the undetected adenomas to both patients. The intraoperative and histopathologic findings revealed intrathyroid parathyroid adenomas. Patients were discharged normocalcemic and asymptomatic.

Conclusion: Preoperative imaging tests, such as Technetium^{99m} Sestamibi scintigraphy, high resolution US and color Doppler, frequently fail to localize accurately intrathyroid parathyroid adenomas. Combination of these diagnostic modalities may imply the presence of ectopic intrathyroidal adenoma. Furthermore, intraoperative localization of missing parathyroid adenomas needs specific strategy by the surgeon who often alters the typical parathyroidectomy to blind thyroid lobectomy.

Keywords: Parathyroid adenoma; Ectopic parathyroid; Intrathyroid parathyroid adenoma; Hyperparathyroidism; Blind thyroid lobectomy

Introduction

Surgery for hyperparathyroidism has made significant progress during the last decades. In particular, minimally invasive parathyroidectomy should be the initial target by the surgeon, in terms of reduced operation and hospitalization time. Despite the progress that has been made, one of the major challenges in parathyroid surgery remains the situation where parathyroid glands cannot be assessed in the normal anatomic sites. An even more challenging question is whether standard imaging modalities are adequate in predicting ectopic parathyroid glands preoperatively.

These ectopic glands are commonly found in the retroesophagealretropharyngeal area and in the superior mediastinum. Other possible ectopic locations are posterior mediastinum (2%), low anterior mediastinum (1%-2%), thymus (20%), carotid sheath (1%) and the thyroid gland (1.4% - 3.2%) [1]. Intrathyroid localization of a parathyroid gland appears in ~0.2% of cases in autopsy studies [2].

The aim of this study is to describe two cases of intrathyroid parathyroid adenoma and to discuss the management of these patients and the potential benefits of the combination of preoperative diagnostic modalities in revealing the ectopic parathyroid location and guiding the scheduled operation.

Materials and Methods

Case 1

A 54 years old Caucasian female was admitted for a scheduled right inferior parathyroidectomy. She was referred to us two months ago, by her cardiologist, who during blood tests for general fatigue showed elevated serum calcium levels (12.9 mg/dl). Further exploration revealed elevated parathormone and urine calcium levels (PTH: 27.9 pmol/l range 1.6 – 6.9 pmol/l, Urine Calcium: 624 mg/24h), while cervical ultrasound showed an intrathyroid nodule in the lower pole of the right lobe of the thyroid gland. Sestamibi scintigraphy revealed a hyperfunctioning right inferior parathyroid gland, implying the presence of an adenoma (Figure 1).

Unilateral neck exploration was performed with no evidence of the adenoma. Fat tissue and a suspicious right superior parathyroid gland were removed but the frozen-section analysis showed fat and normal parathyroid gland respectively. In addition, quick PTH levels remained elevated (25.3 pmol/l). A palpable nodule was

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Figure 1: Case 1 preoperative sestamibi scintigraphy: Arrow shows the hyperfunctioning right inferior parathyroid gland.

found on the inferior pole of the right thyroid lobe and therefore, a blind right thyroid lobectomy was decided and performed. A small yellowish solid mass, inside the inferior pole of the right thyroid lobe was detected and this was assumed to be the missing parathyroid adenoma (Figure 2).

Five minutes after the excision, quick PTH levels dropped at 7.4 pmol/l and the frozen section revealed the intrathyroid parathyroid adenoma. Postoperative course was compensatory and the patient was discharged, 48 hours after the operation. Parathormone and calcium levels returned to normal values 24 hours after operation. The pathological report confirmed the intrathyroid localization of the parathyroid adenoma (Figure 3).

Case 2

A 58 years old female patient was managed for primary hyperparathyroidism. Preoperative blood tests revealed high levels of PTH (PTH: 93.92 pg/ml), and high serum and urine calcium as well (Ca (serum) 12.5 mg/dl, Ca (urine) 310 mg/24h). Symptoms were mild and the rest of the routine blood tests were normal. The cervical ultrasound was negative for an enlarged parathyroid gland, but an intrathyroid nodule in the upper pole of the right lobe of the thyroid gland was detected. Preoperative sestamibi scintigraphy revealed the presence of a right superior parathyroid adenoma (Figure 4). Intraoperatively, the right superior parathyroid gland was not detected but the right inferior parathyroid was found and was removed. Frozen section showed normal parathyroid gland and quick PTH remained elevated (79.37 pg/ml). After negative neck exploration, a blind right thyroid lobectomy was performed and frozen section demonstrated the missing parathyroid adenoma inside the upper pole of the right thyroid lobe. Serum Ca and parathormone levels returned to normal 24h after the operation (8.6 mg/dl and 32.7 pg/ml respectively) and the patient was discharged on the 2nd postoperative day. The pathological report showed the intrathyroid adenoma (Figure 5).

Discussion

Several studies have tried to explain the intrathyroid localization of parathyroid glands and most of them conclude in their embryological origin. More specific, the superior parathyroid glands originate from the epithelium of the dorsal portion of the fourth pharyngeal pouch and descend posteriorly through the neck with the ultimobrachial to



Figure 2: Case 1 right thyroid lobe with incised inferior pole showing the intrathyroid parathyroid adenoma.



Figure 3: Case 1 pathological findings: Thick arrow shows parathyroid gland surrounding from thyroid tissue (thin arrow). H-E X 100.



Figure 4: Case 2 preoperative sestamibi scintigraphy: arrow shows the location of the parathyroid adenoma (right superior parathyroid gland).

their final destination, which is the dorsal surface of the thyroid lobe [1,3]. The inferior parathyroid glands originate from the dorsal aspect of the third brachial pouch and descend through the neck, usually stopping at the lower border of the inferior thyroid lobe, where they adhere to the thyroid capsule [1]. Wang et al suggested that the primordium of the superior gland on one side might be trapped within the thyroid lobe, as the lateral lobe fuses with the median lobe, resulting in an intrathyroid parathyroid gland [4,5]. This condition refers mostly to the superior glands. However, Thompson et al reported that all intrathyroid parathyroid adenomas involve the inferior parathyroid glands [6]. This study reinforces the theory that





either superior or inferior parathyroid glands may be trapped into the thyroid [1,6,7]. Special consideration should be given to the fact that, in some cases, the parathyroid gland lies in a deep thyroid sulcus and is not a true intrathyroid parathyroid adenoma, but rather an intracapsular one, which should be strictly distinguished from the intrathyroid parathyroid adenoma [1].

In order to detect an intrathyroid parathyroid gland, specific strategy is necessary pre- and intra-operatively. Beus et al reported that thyroid lesions co-exist with hyperparathyroidism in 15-70% of cases whereas co-existence of thyroid cancer and hyperfunctioning parathyroid glands vary from 1.7% to 6% of patients [8]. In such cases, if a hypersecreting parathyroid gland is undetectable, after a standard neck exploration, the surgeon needs to proceed to ipsilateral blind thyroid lobectomy. The excised lobe is detected carefully with parallel incisions in order to localize the adenoma. In most of the cases, the intrathyroid parathyroid adenoma is palpable. Proye et al reported that among 1200 consecutive patients who underwent surgery for hyperparathyroidism, 34 of 47 histologically proven intrathyroid parathyroid glands (43 patients, 3.6%) were visible at the thyroid surface [9]. The intrathyroid existence of the parathyroid adenoma can be verified in frozen sections. Quick PTH can also verify this entity when it is immediately decreased after the excision of the thyroid lobe with the adenoma. Blind thyroid lobectomy should be performed on the side of the missing parathyroid gland even if no nodule is palpable in the thyroid gland.

Preoperative diagnosis of intrathyroid parathyroid pathology remains controversial. High-resolution ultrasonography is a highly sensitive and cost-effective examination, especially when it is performed by an experienced radiologist [7,10-13]. Additionally, color Doppler sonographic detection of the feeding vessels may differentiate the hypervascular parathyroid adenomas from the nodular lesions of the thyroid. The sensitivity of this method varies worldwide, from 70% to 92.5% and the specificity ranges between 50% - 100%, though in patients with multinodular thyroid disease the sensitivity falls off (~64%) [7]. Technetium-99m-sestamibi scintigraphy is a complementary tool, particularly when US fails to identify the adenoma. The overall sensitivity of this method is ~75% in the patients without co-existence of thyroid lesions and ~70% in those with additional thyroid pathology [7,14]. Many structures can mimic a parathyroid adenoma, causing imaging methods to fail, such as esophageal diverticulum, small vessels, lymph nodes and thyroid nodules [7]. Furthermore, another diagnostic technique is the intraoperative use of handheld gamma probe in detecting intrathyroid parathyroid adenomas. However, Saaristo et al showed that in unselected patients with primary parathyroidism, preoperative Technetium^{99m} Sestamibi imaging is more accurate than intraoperative gamma probe in localization of undetected parathyroid adenomas [15].

The first description of a rapid intraoperative assay for PTH in patients undergoing neck exploration for hyperparathyroidism was by Nussbaum et al, who modified the IRMA (ImmunoRadioMetric Assay), by increasing the temperature of incubation and employing a kinetic enhancer, changing the turnover time to approximately 15 minutes [16]. Subsequently, several other rapid intraoperative PTH assays has been developed, with further reduction of the turnover time. To date, the ICMA (ImmunoChemiluminoMetric Assay) is been used as a base for different kits, which measure the biological active molecule of PTH (1-84) [17]. The simple technique of taking blood sample from a peripheral site (e.g. antecubital vein) and measuring the decrease of PTH at 5, 10 and 20 minutes after excision of the pathologic gland is widely performed [17]. Several criteria for interpreting the intraoperative use of quick PTH have been proposed but most surgeons agree that the excised parathyroid is the pathologic one when a drop of 50% of PTH below preoperative baseline at 10 post-excision minutes is achieved [18]. Apart from the fact that quick PTH is a useful tool for the identification of the pathological side, in correlation with preoperative localization imaging, for the success of a minimally invasive parathyroidectomy and the correct exploration in reoperation cases, it can be grossly beneficial in finding ectopic overactive parathyroid glands, therefore in intrathyroidal existence of parathyroid adenoma. Furthermore, Perrier et al have proposed the PTH measurement in the tissue sample after FNA for intrathyroid node coexisting with hyperparathyroidism and thus a more accurate diagnosis of a possible intrathyroid parathyroid adenoma [17].

In our cases, preoperative cervical ultrasonography failed to identify pathologic intrathyroid parathyroid glands whereas an intrathyroid node was detected in both patients. Further evaluation with Technetium^{99m} Sestamibi scintigraphy revealed the presence of parathyroid adenomas without detecting the intrathyroid location in both patients. These findings are consistent with the overall inadequacy of these methods, when trying to distinguish the intrathyroid parathyroid adenoma from thyroid nodules. The combined ultrasonographic and scintigraphic results showed the possibility of the intrathyroid localization of the adenomas, which helped to the more accurate planning of the surgery towards minimally invasive operation. Further neck exploration which would have caused prolonged operating time and possible higher morbidity has been avoided, in favor of minimally invasive procedure.

Conclusion

Intrathyroid parathyroid adenoma is a rare entity with controversial preoperative imaging results. Preoperative cervical ultrasonography with sestamibi scintigraphy combined with intraoperative rapid PTH measurement is a standard procedure. Blind thyroid lobectomy concerning the ipsilateral thyroid lobe with the suspicious parathyroid gland, is the necessary procedure when the hyperfunctioning parathyroid gland cannot be assessed.

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