

Parathyroid Adenoma Completely Impacted Within the Thyroid: A Case Report and Literature Review

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1. Introduction

Primary hyperparathyroidism (PHPT) is the most common cause of hypercalcemia, causing oversecretion of parathyroid hormone from adenomas, hyperplasias or carcinomas. Enlarged parathyroid glands are usually detected by ultrasonography or scintigraphy. After making a diagnosis based on laboratory examinations and imaging studies, the patients with PHPT can be easily treated with surgery to remove the enlarged gland, and 95% of such operations are curative (1-3).

However, we sometimes encounter enlarged parathyroid glands located in uncommon regions, such as within the thyroid, in the thymus, in the mediastinum, in the posterior cervical triangle or in other locations, making it hard to detect the parathyroid.

We recently experienced a case of PHPT whose parathyroid adenoma was completely impacted within the thyroid. Based on the sonographic and scintigraphic features of the lesion, the size and location of the parathyroid gland could be estimated before the surgery. We have also established a hypothesis for how some of the parathyroid glands become located in uncommon regions.

This chapter describes uncommon locations of parathyroid adenoma, particularly within the thyroid. We also report a case and review the pertinent literature regarding its generation.

2. Case presentation

A 58-year-old female underwent surgery for breast cancer a year prior to her current presentation. After the operation, she had received chemotherapy with anthracycline for three months and radiotherapy for one and a half months. After these treatments, she had not been on any medications, such as anti-cancer agents or hormone therapy. The laboratory examination during her first annual check-up after the surgery revealed a high corrected serum calcium level of 11.4 mg/dl. Additional laboratory parameters showed high serum

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intact parathyroid hormone (iPTH) of 114 pg/ml. Her serum alkaline phosphatase level, 332 U/L, was within the normal limits. She was suspected to have hyperparathyroidism.

She had experienced two pregnancies and delivered twice. Her family history revealed no parathyroid disease, other endocrine disease, nor any malignancies. She had not received radiation to the head and neck area during childhood. She had no complaints such as a loss of appetite, nausea, vomiting, constipation, confusion or impaired thinking and memory, feelings of weakness, fatigue, depression, nor aches and pains. Objectively, neither symptoms of bone thinnings nor kidney stones were present.

Ultrasonography revealed a solid and isoechoic mass, 6.0 x 12.7 x 9.8 mm in size, with a regular shape and contour in the middle of the right lobe of the thyroid. The tumor showed a homogeneous internal echo with a high degree of Doppler signaling and was completely embedded in the thyroid, thus suggesting a thyroid tumor (Figure 1a). A technetium-99m MIBI scintigram demonstrated a focal accumulation in the middle of the right lobe of the thyroid from the early phase to the delayed phase (Figure 1b). These findings suggested that the right lower parathyroid gland might be morbid and it could be inside the thyroid parenchyma.

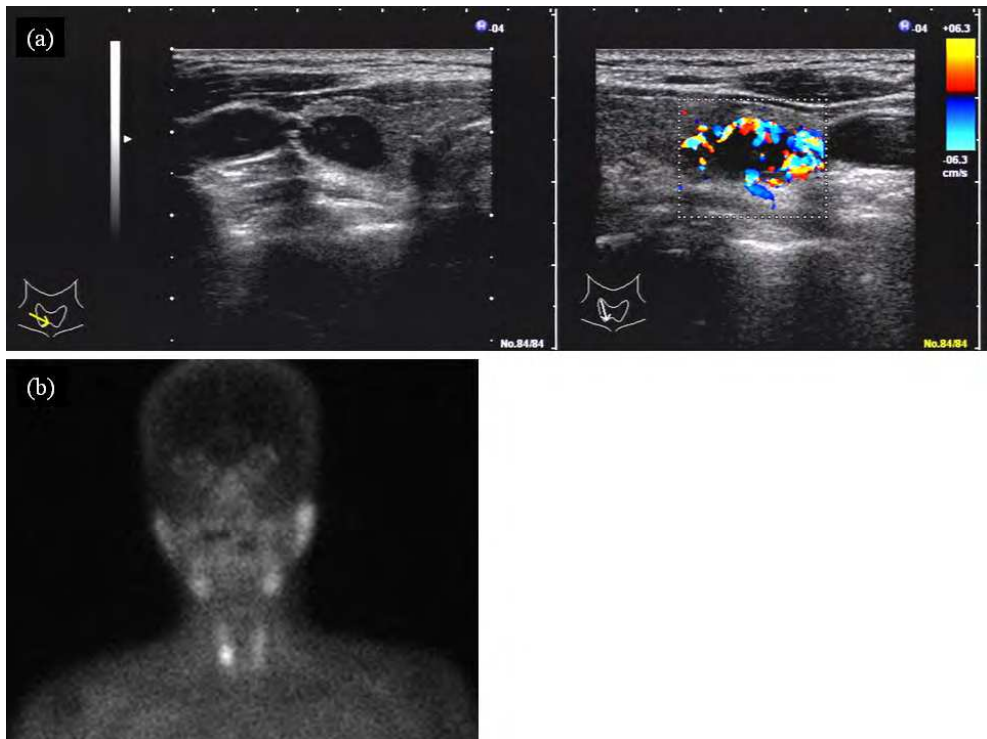


Fig. 1. a) Ultrasonography of the right lobe of the thyroid showing a hypoechoic and hypervascular Doppler signaling mass impacted within the thyroid.
b) A technetium-99m MIBI scintigram demonstrated a focal accumulation in the middle-lower part of the right lobe of the thyroid.

We diagnosed the patient with asymptomatic PHPT and predicted that its location was in the right lobe of the thyroid. The observations during the surgery revealed a morbid parathyroid gland as predicted. It was completely impacted within the right lobe of the thyroid. A right lobectomy of the thyroid was performed, and the right upper parathyroid gland was also removed. The right upper gland located at the cricothyroidal junction was normal.

The histopathological findings of the specimen were as follows: A tumor measuring $9 \times 6 \times 5$ mm in size was located in the middle portion of the right lobe (Figure 2a). The enlarged parathyroid gland had proliferated, displacing the thyroid parenchyma. Microscopically, fat was displaced by the proliferation of chief cells with pale clear cytoplasm arranged in sheets in a solid-alveolar or sinusoidal pattern. Deposits of hemosiderin and cystic changes were also present in the tumor. Mitoses were difficult to detect. All of the tumor cells remained within a fibrous capsule that surrounded the tumor, without direct invasion to the thyroid parenchyma. No capsular or vascular invasion was observed (Figure 2b). The right upper parathyroid and the thyroid parenchyma showed no abnormal findings. The diagnosis was adenoma of the right lower parathyroid gland.

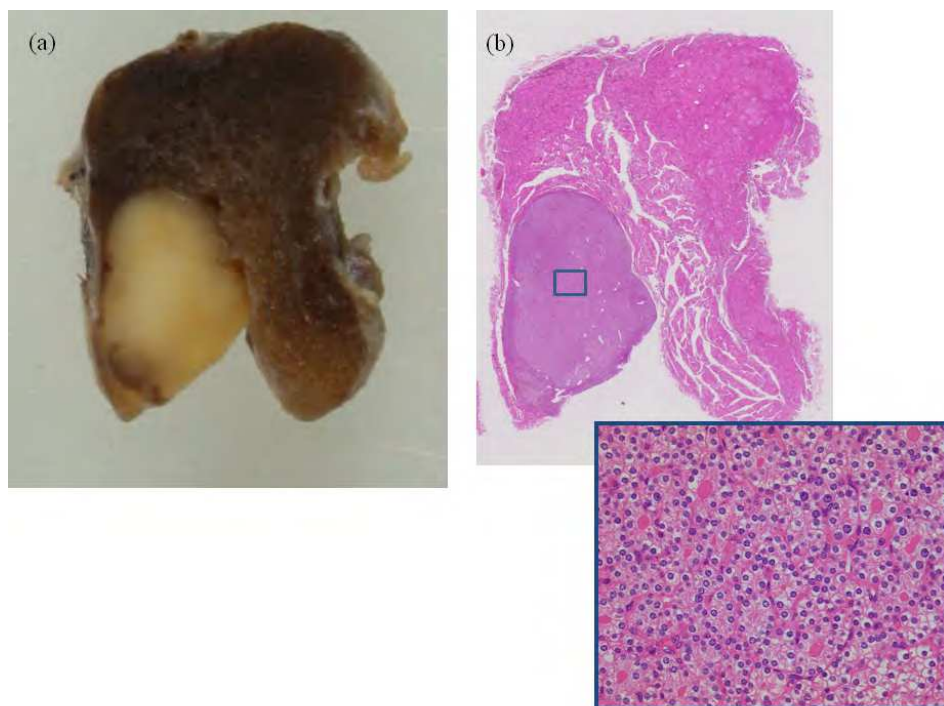


Fig. 2. a) Macroscopic appearance of the specimen showing a tumor measuring $9 \times 6 \times 5$ mm in size located in the middle portion of the right lobe of the thyroid.
b) Microscopic appearance of the tumor diagnosed as parathyroid adenoma, showing the proliferation of chief cells with pale clear cytoplasm arranged in sheets in a solid-alveolar or sinusoidal pattern without mitoses.

There were no complications due to the surgery. After the operation, her serum calcium and iPTH levels were maintained within the normal limits.

3. Parathyroid glands

There are four parathyroid glands, with average weights of 30-40 mg, although the weights vary somewhat with age and sex. Since the glands are soft and pliable in consistency, they are easily shaped and molded by the adjacent tissue. The consistency of morbid parathyroid glands varies (4). In case of adenoma and hyperplasia, accounting for more 85-% of PHPT, the parathyroid glands are relatively hard compared to the normal glands, although they are generally as soft as the thyroid parenchyma. In cases of parathyroid carcinoma, accounting for 1-% to 5-% of PHPT (5), the glands are elastic and hard, which facilitates the diagnosis before and during the operation. Although it can be difficult, we try to make a differential diagnosis between benign and malignant parathyroid disease using real-time tissue elastography before surgery. Elastography shows that the parathyroid carcinomas are definitely harder than the thyroid parenchyma, whereas the adenomas and hyperplasia are as soft as the thyroid parenchyma (Figure 3).

4. Common locations of the parathyroid glands

The expected locations of the parathyroid glands are behind the thyroid parenchyma. They adhere behind the thyroid parenchyma on the bilateral, upper and lower sides of the thyroid. The upper parathyroid glands are located one-third or halfway from the upper poles of the thyroid, and 80-% of the upper parathyroid glands are located within 1 cm around the 1 cm caudal portion from the crossing point of the recurrent laryngeal nerve and the inferior thyroid artery. They sometimes seem to float within the cyst in the thyroid capsule around the upper border of the cricoid cartilage, or posteriorly around the cricothyroid junction. The glands are often intimately associated with the recurrent laryngeal nerve and adjacent vascular branches.

The lower glands are more widely distributed than the upper glands. These glands are distributed between the lower pole of the thyroid and the thymus. It has been estimated that 95-% of the lower glands are located within a 2 cm region around the lower poles of the thyroid. They are found in the anterior or lateroposterior surface of the thyroid. Approximately 40-60-% of the glands adhere to the thyroid parenchyma, and these glands are frequently hidden between the thyroid creases, with 25-40-% being located within the neck of the thymus. They are commonly located in front of the recurrent laryngeal nerves.

Although almost all the parathyroid glands on each side, 80-90-% of the upper glands and 64-70-% of the lower glands are located symmetrically, however, the left parathyroid glands are occasionally located somewhat inferior to the right glands (4, 6).

5. Uncommon locations of the parathyroid glands

a. On the basis of embryological development

The parathyroid glands begin to form from the epithelium of the third and fourth pharyngeal pouches. The upper glands begin in the fourth pouch, and fall back to the upper one-third of the thyroid. If the upper gland lies in an atypical location, it will generally be

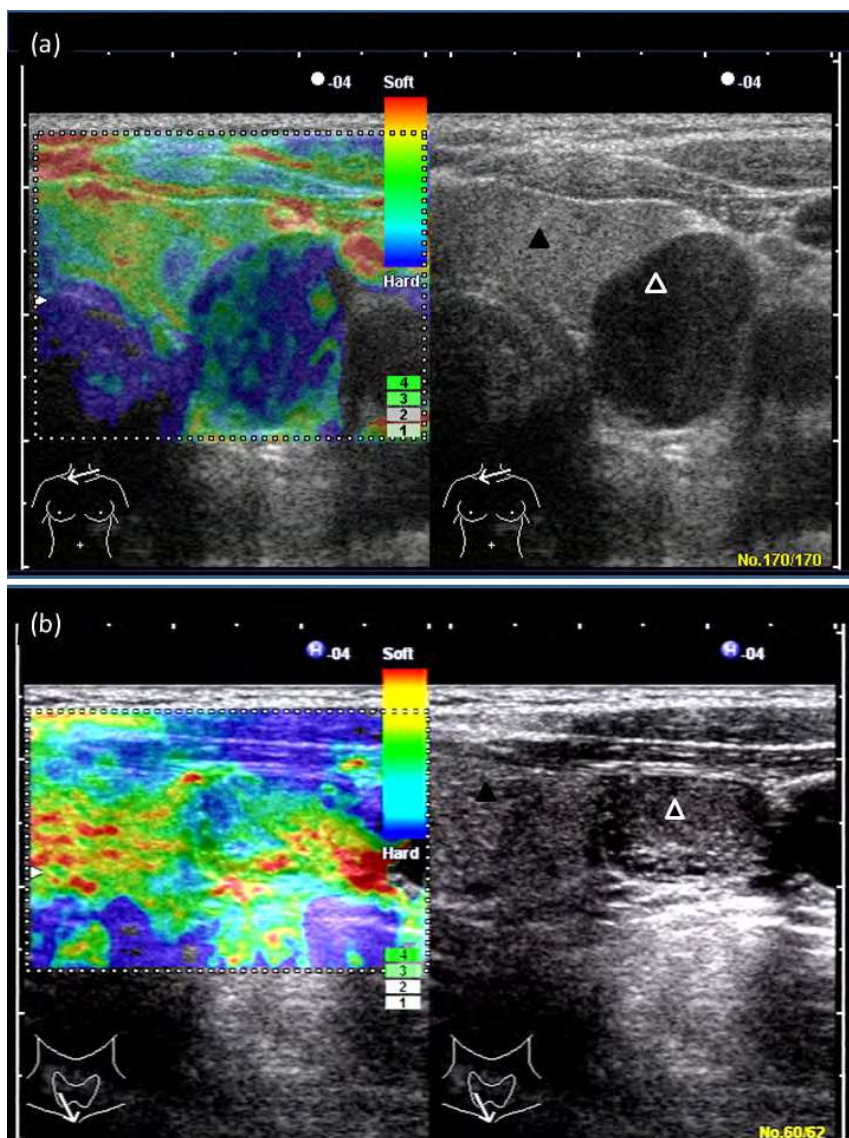


Fig. 3. (a) Elastography of the parathyroid carcinoma showing hard elasticity of the mass
(b) Elastography of the parathyroid hyperplasia showing soft elasticity of the mass
(▲; thyroid parenchyma. Δ; parathyroid gland)

found in the back of the upper pole of the thyroid, rarely below the lower thyroid artery, and extremely rarely above of the thyroid pole, retropharyngoesophagus space, or in the thyroid parenchyma.

The lower parathyroid glands and thymus begin from the epithelium of the third pharyngeal pouch. As a complex, they descend caudally through the lateral side of the thyroid. They separate, and then the lower parathyroid gland dissociates from thymus and localizes to the anterior or lateroposterior aspect of the lower thyroid pole, and the thymus localizes inside of the mediastinal space. Since the lower glands descend a long distance, there are frequent positional aberrations. For example, if they never descend, they lie in the submandibular space on the lateral side of the common carotid artery and the internal jugular vein, the so-called lateral triangle, or within the carotid sheath. If they descend incompletely, they are called an "undescended parathymus". If they do not separate, the parathyroid glands descend with the thymus into the mediastinum, or may be left high in the neck as a result of early developmental arrest. In nearly half of the cases, the lower gland remains within the thymic tongue at the thoracic inlet. Thus, the lower gland may be found anywhere from the angle of the jaw to the pericardium. Some rare reports have demonstrated even more unusual locations for the parathyroid gland, such as on the base of the heart, in the front of the heart sac, and in the aorto-pulmonary window (4).

b. The cases where enlarged parathyroid glands descend due to of the effects of gravity

Although parathyroid carcinoma or parathyroid hyperplasia caused by renal dysfunction may induce adhesion to the surrounding organs, so that they rarely descend, parathyroid adenoma or primary hyperplasia of the parathyroid may lead the glands to descend caudally because they have no supporting structure except for the feeding vessels. The upper parathyroid glands are commonly located behind the recurrent laryngeal nerves, and sometimes are located between the esophagus and trachea. The lower glands are commonly located on the anterior side of the recurrent laryngeal nerves.

c. Supernumerary parathyroid glands

The usual number of parathyroid glands is four. Some reports have indicated that only three glands could be detected, although it is sometimes difficult to conclude whether this was the true number in that case or represented a failure during the search for the glands. On the other hand, supernumerary glands (five or more glands), are often detected. The clinical significance of this condition is that can be a cause of continuing hyperparathyroidism (2, 4). The most common cause of supernumerary glands is when a part of the parathyroid gland is detached during the process of the embryological development of the parathyroid gland. In approximately two-thirds of the cases, the supernumerary gland is found below the thyroid, in association with the thyrothymic ligament or the thymus, while one-third of these glands are found in the vicinity of the thyroid (2). The separated glands are called "rudimentary glands", which are only minimally (less than 5 mg) separate from the parathyroid gland, or "split glands", which are separated evenly. In general, these supernumerary glands are smaller than the normal glands.

6. The uncommon location in this case

In the present case, the enlarged parathyroid gland was considered to be the right lower gland, although Wang et al reported that the intrathyroidal parathyroid was generally the upper gland (4). They indicated that the primordium of the parathyroid gland in the fourth branchial pouch is trapped between the lateral and the median thyroid prior to their embryological fusion. Indeed, most intrathyroidal parathyroid glands are located in

the middle or the lower third of the thyroid. In the 1980s, there was a disagreement about the embryonic origin of intrathyroidal parathyroid adenoma. However, a contrary opinion, considering that the intrathyroidal parathyroid adenomas were derived from the lower gland, was also estimated by some researchers. Recently, some reports have shown that the intrathyroidal parathyroid gland can correspond to upper, lower or supernumerary glands (7).

In our case, the upper gland was normal, which suggests that the intrathyroidal parathyroid can be considered to be the lower gland. Our hypothesis is that the lower parathyroid descended incompletely in the sinus of the middle of the thyroid lobe, and the crease had sealed over time. However, regardless of whether an intrathyroidal parathyroid gland is the upper, the lower or a supernumerary gland, we consider that the parathyroid descent to the crease or the sinus of the thyroid and develop toward the inside of the thyroid parenchyma during the embryonic process.

7. Discussion

The incidence of the intrathyroidal parathyroid glands is about 1-4%, and adenoma is the most common cause of persistent hyperparathyroidism among hyperparathyroid patients (5, 7). Moreover, most of the affected glands are located in the right lobe. The choice of treatment for complete resection of intrathyroidal parathyroid adenoma is hemithyroidectomy, instead of parathyroidectomy, because it decreases the incidence of the rupture of the capsule of the parathyroid gland, which could result in a local recurrence.

Despite their wide distribution, the parathyroid glands fall into a definite pattern. Preoperative findings of ultrasound and scintigram studies may be helpful for identifying localized lesions of intrathyroidal parathyroid adenoma, as well as for intraoperative assessment, which can facilitate the selection of appropriate treatment.

8. Acknowledgements

Written patient's informed consent was obtained for publication of this report.

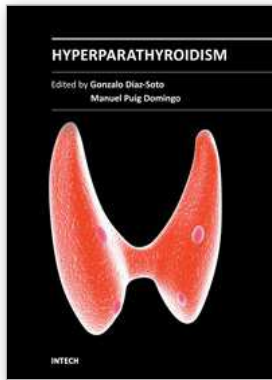
9. Abbreviations

Primary hyperparathyroidism; PHPT, intact parathyroid hormone; iPTH

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Hyperparathyroidism

Edited by Dr. Gonzalo Diaz Soto

ISBN 978-953-51-0478-0

Hard cover, 96 pages

Publisher InTech

Published online 04, April, 2012

Published in print edition April, 2012

This book is the result of the collaboration between worldwide authorities of different specialities in hyperparathyroidism. It aims to provide a general but deep view of primary/secondary and tertiary hyperparathyroidism, from a physiological basis to hyperparathyroidism in hemodialyzed patients, as well as new treatment approaches, techniques and surgical scenarios. We hope that the medical and paramedical researchers will find this book helpful and stimulating. We look forward to sharing knowledge of hyperparathyroidism with a wider audience.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Yuko Tanaka, Hisato Hara and Yuzuru Kondo (2012). Parathyroid Adenoma Completely Impacted Within the Thyroid: A Case Report and Literature Review, *Hyperparathyroidism*, Dr. Gonzalo Diaz Soto (Ed.), ISBN: 978-953-51-0478-0, InTech, Available from: <http://www.intechopen.com/books/hyperparathyroidism/parathyroid-adenoma-completely-impacted-within-the-thyroid-a-case-report-and-literature-review>

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