

Incidentally discovered parathyroid lipoadenoma in thyroid surgery: a case report and review of the literature

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1. Introduction

Parathyroid lipoadenoma, one of the rare causes of primary hyperparathyroidism, is an uncommon type of parathyroid adenoma, described as a single parathyroid adenoma with more than 50% fat on histologic examination and an unknown etiology. There are currently 64 cases of parathyroid lipoadenoma reported on PubMed. We present a case that supplements and supports the rare literature data concerning the clinical and therapeutic aspects of occasional parathyroid lipoadenoma in thyroid cancer surgery in our treatment centre and review the relevant literature.

2. Case Description

The patient was a middle-aged male with a body mass index (BMI) of 38.4 who was hospitalized with thyroid nodules for 40 days. Physical examination showed that the thyroid gland was firm and no obvious mass was palpable; ultrasonography showed normal thyroid gland size, heterogeneous glandular echoes, patchy hypoechoic areas, the larger one was located in the right lobe, with a range of about 2.7×1.09 cm, a hypoechoic nodule was observed in the lower deep layer of the right lobe, with a size of about 0.61×0.60 cm, aspect ratio > 1 , regular borders, and punctate hyperechogenicity was observed; an anechoic nodule was observed in the middle superficial layer, with a size of about 0.28×0.34 , aspect ratio < 1 , regular borders, and no significant focal hyperechogenicity was observed; a solid hypoechoic nodule was observed in the lower grade of the left lobe, with a size of about 0.54×1.01 cm, aspect ratio < 1 , regular borders, and no significant focal hyperechogenicity was observed. No significant abnormal enlarged lymph nodes were found in bilateral neck. Cytological examination of the right thyroid lobe nodule showed atypical cells suggestive of papillary thyroid carcinoma. Thyroid function tests: thyroid stimulating hormone TSH 0.862 mIU/L (normal reference value 0.372 – 4.94 mIU/L); parathyroid hormone PTH 64.62 pg/ml (normal reference value 15 – 56 pg/ml); serum calcium Ca 2.42 mmol/L (normal reference value 2.2 – 2.65 mmol/L).

Resection of the right lobe and isthmus of the thyroid gland and central lymph node dissection were planned, during which the right lobe and isthmus of the thyroid gland were first removed, and grayish white nodules were observed in the right lobe of the thyroid gland by dissection, about 0.4 cm in diameter, and the remaining sections were grayish red and soft. During the resection, two masses measuring $1.5 \times 0.8 \times 0.7$ cm and $2.5 \times 1.5 \times 0.5$ cm were found in the dorsal and lateral aspect of the middle and upper parts of the right lobe, respectively. The texture was firm, the surface was smooth and the boundary was clear. The possibility of parathyroid gland mass was considered, so it was decided to remove the tissue for rapid pathological examination. The results showed that round cells were scattered in the fibroadipose tissue of the middle and upper dorsum of the right lobe, not excluding the mass of parathyroid gland origin; most of the tissues submitted to the lateral aspect of the middle and lower parts of the right lobe were fat, in which a few round cells were scattered. At the same time, the left thyroid gland was dissected to explore the tracheoesophageal groove of the lower pole of the thyroid gland in its dorsal pole, and no abnormal hyperplastic parathyroid tissue was observed. PTH values were 29.68 pg/ml and 35.71 pg/ml at 15 and

30 minutes after tumor resection, respectively, and serum calcium was 2.30 mmol/L on the first day after surgery. Postoperative paraffin pathology (Fig. 1.) revealed that the superior dorsal mass and the middle and lower lateral mass in the right lobe were consistent with parathyroid lipoadenoma, and immunohistochemistry (Fig. 2.) revealed PTH (+); CgA (+); SyN (-); CD56 (-); TTF-1 (-); Tg (-); Ki-67 (< 1% +), and the right lobe of the thyroid gland was papillary thyroid carcinoma 0.4 cm in diameter; there was one lymph node metastasis in the central group, and the diameter of the metastasis was 0.05 cm; the isthmus was nodular goiter. Euthyrox 50 µg was orally administered daily after surgery.

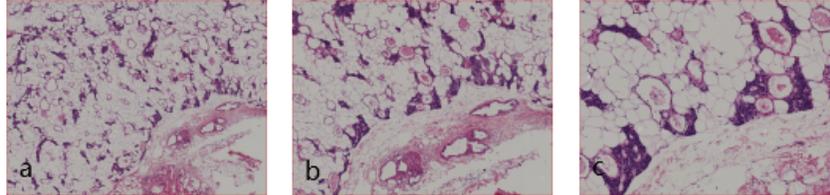


Fig. 1. Parathyroid adenoma, composed of > 50% mature adipose tissue, with principal cells arranged in nests between adipose tissues. Hematoxylin-eosin staining magnification × 20 (a), × 40 (b), and × 100 (c).

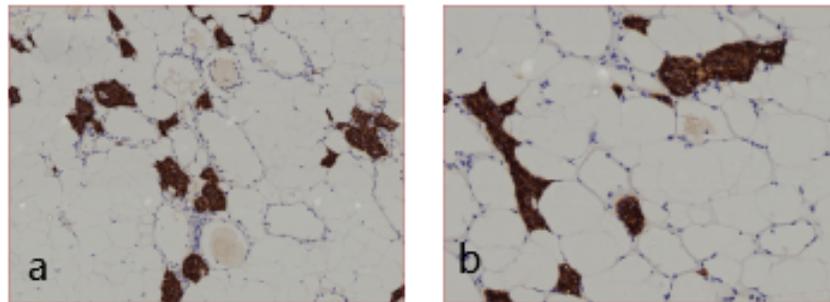


Fig. 2. Immunohistochemical sections of parathyroid lipoma demonstrating positive parathyroid hormone in the cytoplasm, magnified × 100 (a) and × 200 (b).

One month later, the patient came to our hospital for reexamination, without perioral numbness of four extremities, TSH 1.30000 mIU/L; PTH 28.51 pg/ml; Ca 2.59 mmol/L. At present, the patient came to our hospital for reexamination 9 months after operation, without related symptoms.

3. Discussion

Parathyroid lipoadenomas are rare and are incidentally detected during thyroid cancer surgery in this case. In this paper, 40 literatures with "parathyroid lipoademona" as search term on PubMed^[1,2,4,5, 7-42] and 65 cases of parathyroid lipoadenoma (including this case) were counted. After excluding 18 cases with missing clinical data, 47 cases had complete clinical data, including 30 females and 17 males, with a female-to-male ratio of about 1.8:1, that is, parathyroid lipoadenoma accounted for a higher proportion in females than in males. In addition, it has been reported in the literature that parathyroid lipoadenoma may account for a higher proportion in males than parathyroid adenoma^[1]. The age of onset of parathyroid lipoadenomas varies from 24 to 88 years, mostly located in the neck, but up to 15% of parathyroid lipoadenomas are ectopic or located in the mediastinum, much higher than common parathyroid adenomas^[2].

In 1958, Ober and Kaiser^[3] first described parathyroid lipoadenoma in a middle-aged man with a gradually enlarging neck mass that was painless and without manifestations of hyperparathyroidism. A large lipoma

was found under the sternum on neck exploration. Because the tumor was nonfunctional, they named it "parathyroid hamartoma". The concept of "parathyroid lipoadenoma" was first introduced in 1962 by Abul Haj [4] et al. Parathyroid lipoadenoma is a rare type of parathyroid adenoma with an incidence of 0.5% to 1.6% of primary hyperparathyroidism and contains fat, principal cells, and eosinophils, of which fat content is > 50%, unlike adenomas with fatty infiltration, and the fat component is an integral part of parathyroid lipoadenoma [5]. In 2022, the World Health Organization defined parathyroid lipoadenoma as "a tumor with simultaneous increases in parathyroid parenchyma and adipose tissue, and more than 50% of the glandular volume consists of adipose tissue" [6]. In the currently reported cases of parathyroid lipoadenoma, the origin of the adipose tissue component is unknown, and most of them are small brown lesions with the largest reported weight of 480 g. Some researchers have speculated that the factors of increased fat composition may be the same as those of increased parathyroid chief cells [7,8]. It has been suggested that fat may be present in adenomas by high BMI, and some speculations suggest that some adipogenic factors may be produced by adenoma epithelial or stromal cells, which in turn stimulate adipocyte proliferation [9]. Christofer Juhlin proposed that parathyroid lipoadenomas may be associated with hypertension [5].

Parathyroid lipoadenomas can be classified as functional and non-functional, with approximately 64 percent of previously reported cases symptomatic, 28 percent asymptomatic, and 7 percent suspicious [10,11], and four parathyroid lipoadenomas found on autopsy for which function is uncertain. Among them, the clinical features, laboratory tests and parathyroid adenomas of functional parathyroid lipoadenomas are similar, that is, patients show recurrent urinary stones and hip or shoulder fractures, but the increase in parathyroid hormone and blood calcium may not be as obvious as parathyroid adenoma, and a very small number of patients have asymptomatic hypercalcemia.

The difficulty of parathyroid lipoadenoma is mainly diagnosed by preoperative imaging localization. 29 of 64 patients (45%) had lesions localized using imaging studies. Ultrasonography was performed in 24 cases, and lesions or suspected lesions were found in 14 (58%) of them. Computed tomography (CT) was reported in 12 cases, of which 9 (75%) detected or suspected lesions. Technetium-99m sestamibi scintigraphy was reported in 15 cases, of which 8 (53%) reported detection or suspicion of lesions. In one of them, an X-ray was performed and the tumor was found to be located in the mediastinal cavity. Positron emission tomography (PET) scans were used in 6 cases, of which 3 (50%) were reported as lesions. Because of the high adipose tissue content, lipomas tend not to be detected by preoperative imaging techniques. On ultrasound, typical parathyroid adenomas are homogeneous hypoechoic lesions, however, fat-rich variants of parathyroid adenomas sometimes present as hyperechoic lesions [9], resulting in reduced accuracy, and ultrasound examination of this patient showed no parathyroid lesions; they can be localized as lipomatous masses on CT, and Johnson et al [12] reported cases in which CT scans of parathyroid lipoadenomas had CT values of - 60 to - 90 HU, consistent with lipoma density, proposing the possibility of parathyroid lipoadenomas on such CT scans in similar cases of non-local primary HPT. However, CT may also be confused with lipomas, lymph nodes, or other fat-rich lesions; the accuracy of dual-phase Sestamibi scanning of the parathyroid depends on the proportion of parathyroid chief cells, which are more than 50% fat in parathyroid lipoadenomas and have less principal cell content than normal parathyroid tissue, resulting in reduced accuracy of Sestamibi scanning; however, there are cases [13] indicating the usefulness of using 99Tcm-MIBI imaging in localizing the diagnosis, reoperation, and persistent hyperparathyroidism, and they propose speculation that the lesion may be shown based on the space-occupying appearance, or that the target may have a low signal ratio to the background. Cases showed a good target-background signal ratio in Tc-99m sestamibi imaging, which may be due to the relatively large size of the lesion, as well as the fact that the main part of the lesion consists of parathyroid chief cells; the sensitivity of syngeneic SPECT for parathyroid lipoadenoma was significantly reduced [12]. However, Sabri et al. [1] concluded that although SPECT is not as effective as parathyroid adenoma in the diagnosis of parathyroid lipoadenoma, it may be superior to ultrasound. Cholinergic PET-CT imaging is superior to ultrasound and CT in the localization of parathyroid adenoma, but there is no relevant report for parathyroid lipoadenoma.

Primary hyperparathyroidism is most commonly caused by solitary parathyroid adenomas, accounting for more than 80 – 85%; less commonly, parathyroid hyperplasia, parathyroid carcinoma, and multiple parathy-

roid adenomas^[2]. Parathyroid lipoadenoma is a very rare cause of primary hyperparathyroidism with an incidence of 0.5% to 1.6% of primary hyperparathyroidism. In parathyroid lipoadenomas, the sensitivity of imaging is significantly reduced by low parathyroid cell concentration and excessive fat content. Abundant adipocytes in parathyroid tissue can be found in the following conditions: normal tissue, lipohyperplasia, lipoadenoma, and cancer infiltrating the surrounding adipose tissue. It is difficult to differentiate these diagnoses by intraoperative rapid frozen section. Therefore, definitive diagnosis of parathyroid lipoadenoma should include pathologic diagnosis of parathyroid hyperplasia within adipose tissue, as well as a significant decrease in hormone following intraoperative removal of the parathyroid gland. Increases in parathyroid gland weight (> 40-60 mg) may also represent parathyroid lipoadenomas in appropriate morphologic and clinical settings^[6]. Parathyroid lipoadenomas should be considered when no lesions are reported on ultrasound but clearly identified by CT or SPECT. Parathyroid carcinoma infiltrating in adipose tissue may be misdiagnosed as parathyroid lipoadenoma, so careful pathological examination is still required for differential diagnosis.

4. Conclusions

Parathyroid lipoadenoma is a rare cause of primary hyperparathyroidism, which is mainly manifested as infiltration of a large amount of adipose tissue in the gland, and due to excessive fat content, its sensitivity in imaging localization diagnosis is reduced, and the difficulty of parathyroid lipoadenoma is still in preoperative localization diagnosis, so we believe that parathyroid lipoadenoma needs to rely on paraffin pathology to make a final diagnosis. This case report serves as a reminder that patients with preoperative unprovoked primary hyperparathyroidism and negative imaging findings may have a parathyroid lipoadenoma. During intraoperative thyroidectomy or lymph node dissection, it is important to carefully examine the adipose tissue for the possibility of parathyroid lipoadenoma, as this can lead to postoperative hypoparathyroidism or even intractable hypocalcemia.

Declarations

Ethical Approval:

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Competing interests:

The authors have no conflicts of interest to declare.

Authors' contributions:

- (I) Conception and design: Yihan Wang
- (II) Administrative support: Yantao Fu
- (III) Provision of study materials or patients: Yantao Fu
- (IV) Collection and assembly of data: Yihan Wang
- (V) Data analysis and interpretation: Yihan Wang
- (VI) Manuscript writing: All authors
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In this paper, 40 literatures with "parathyroid lipoademona" as search term on PubMed and 65 cases of parathyroid lipoadenoma (including this case) were counted.

This case comes from the Department of Thyroid Surgery, China-Japan Union Hospital of Jilin University, we do not wish to share the data for the sake of patient privacy protection principles.

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