Case Report

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Cystic parathyroid lesion: case report of rare entity

Pietro Princi, MD[a], Ludovica Di Fede[b,*], Serena Elisa Tempera, MD[a], Giulia Salvi, MD[a], Maria De Ninno, MD[c], Miriam Veleno, MD[b], Casimiro Nigro, MD[a]

Introduction and importance: Parathyroid cysts are rarely encountered in neck surgery and often misdiagnosed. We review the case incidence and treatment of parathyroid cystic lesions among all neck procedure in two single institutions operated on by a single surgeon.
Case presentation: We report two female patients presenting with neck swallowing, dysphagia, choking and occasional dysphonia. Ultrasound US (ultrasound) imaging revealed two neck masses of 66 × 44 mm and 44 × 25 × 23 mm; serum iPTH (intact Parathyroid Hormone) levels were 238 and 699 ng/mL respectively and sestamibi scintiscan results were negative for both masses. Intra-cystic fluid evaluation of PTH showed elevated value (>5000 ng/ml). Both patients underwent parathyroidectomy along with total thyroidectomy and thyroid lobectomy. Post-operatively I-PTH and serum calcium levels became normal. Final histology confirmed a benign parathyroid cystic adenoma with concomitant benign thyroid disease.
Clinical discussion: Parathyroid cyst is of rare entity and a diagnostic challenge.
Conclusions: This case report demonstrates that fine needle aspiration (FNA) fluid with intra-cystic parathyroid analysis shows to be fundamental and supports surgery for hyperparathyroidism resolution.

Keywords: case report, cystic parathyroid lesion, endocrine surgery, parathyroid cyst, parathyroid surgery

Introduction

Parathyroid cysts are rare clinical entities that can be easily misdiagnosed both in endocrinology and endocrine surgery. Since the first case described in 1880 by Sandstrom[1] and the first one operated by Goris in 1905[2] the disease's genesis and classification have come under scrutiny. Case report or small series did not clarify the two previous points of discussion (etiology and classification) even if McCoy *et al*[3] in a large series achieved a clear classification based on parathyroid cyst etiology[4].

We would like to report two cases operated on by the same surgeon and to discuss about this question and more. This case report has been reported in line with the SCARE Criteria.[5]

Case report

Among 1714 patients operated on for thyroid and parathyroid surgery by the same surgeon (P.P.) in two different institutions (Division of Surgical Oncology – Campobasso and Cristo Re General Hospital – Rome) between 2010–2016 and 2021–2023, two patients were selected and included in the present study.

Patient 1

The first patient was a 44-year-old female referred to our surgical division because of neck swallowing. Upon suspicion of an esophageal diverticulum the patient was sent for a gastrointestinal endoscopy, which only revealed chronic gastritis *Helicobacter* positive. Ultrasonography of the neck showed an ipo-anecoic neck mass of 44 × 25 × 23 mm on the left thyroid lobe without clear clivage plane. Serum evaluation reported elevated levels of calcium (10.6 mg/dL, normal value 8.5–10.1), of PTH (238.6 pg/mL, normal value 10–65) and antibody titer, suggesting thyroiditis. The Sesta-mibi scintiscan test result was negative; but PTH levels in the intracystic fluid sample were above 5000 pg/mL.

Patient 2

The second patient, a 52-year-old female, has been referred to us for severe neck compression symptoms with swallowing and dysphonia. The patient reported history of hypertension, severe osteoporosis, and chronic renal disease without dialysis treatment. Ultrasonography of the neck showed (Fig. 1) a large anecoic mass of 7 cm located in left thyroid bed and the gland showed multinodular goiter. Serum evaluation reported elevated levels of calcium (13.8 mg/dL, normal value 8.5–10.1) and PTH (699.3 pg/mL, normal value 10–65). Sesta-mibi scintiscan showed low accumulation of radioactive tracer in lower pole of left thyroid gland without clear identification of pathologic parathyroid tissue. Fine needle agobiopsy confirmed intracystic level of PTH elevated (>5000 pg/mL).

The first patient underwent left inferior parathyroidectomy combined with left thyroid lobectomy, while the second patient had left inferior parathyroidectomy and total thyroidectomy for nodular goiter. Intra-operative (io-PTH) level decreased to

[a] *Multifunctional Center of Endocrine Surgery, Cristo Re General Hospital, Rome, Italy,* [b] *Catholic University of Sacred Heart, Rome, Italy and* [c] *Division of Histopathology, Responsible Research Hospital, Campobasso, Italy*

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**Corresponding author. Address: Ludovica Di Fede, Catholic University of Sacred Heart, L.go Gemelli, 8, 00168 Rome. Italy. E-mail: ludovica.difede01@icatt.it.*

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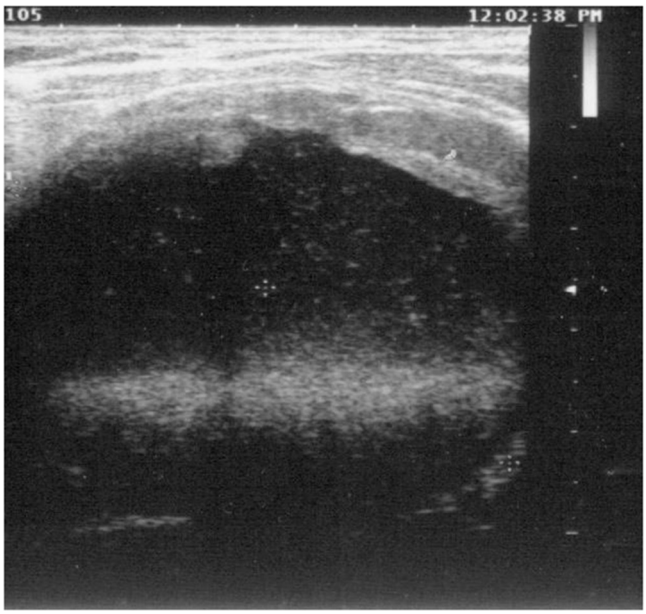

Figure 1. Ultrasound evaluation of cyst parathyroid mass.

normal value 10–20 minutes (according to Rome criteria) after removal of the parathyroid cystic gland. Final histology for both patients revealed parathyroid adenoma with central cyst degeneration in the first patient, and parathyroid tissue within the capsule of a completely cystic lesion in second one (Fig. 2).

Immunohistochemistry evaluation showed positivity for PTH (3+), as reported in Figure 3, and chromogranin A (3+) with low mitotic and proliferative activity (Ki < 1%). Thyroid disease was benign in both cases. Post-operatively, one patient needed oral calcium and vitamin D supplementation for less than 6 months (*transient hypoparathyroidism*). After a follow-up of 132 and 98 months, respectively, no recurrence was observed, and both patients maintained normal serum calcium and i-PTH values.

Discussion

Cystic parathyroid lesions (CPLs) have been reported as case reports or small case series. Older literature used to believe that

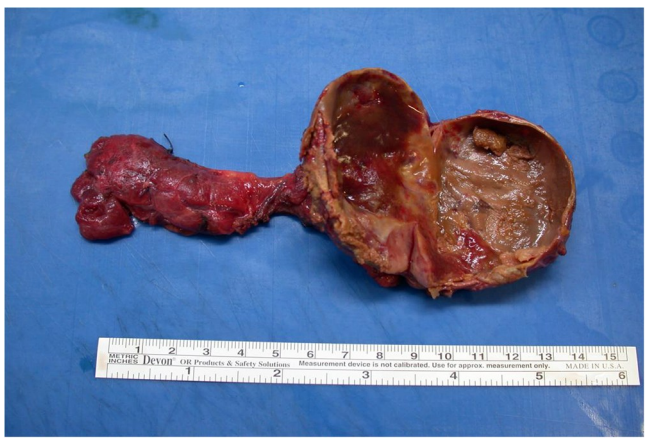

Figure 2. Cystic parathyroid lesion: specimen at final histology.

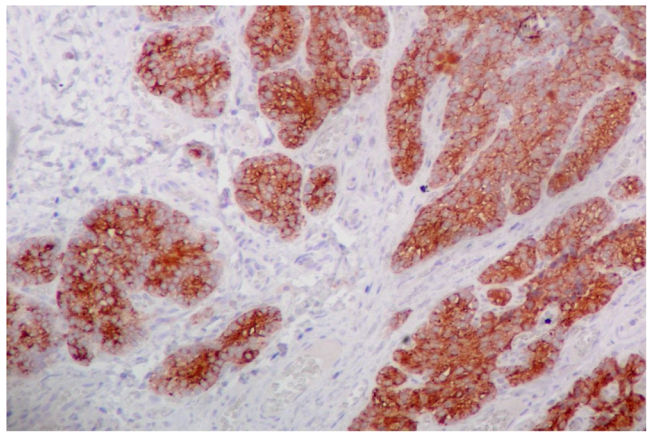

Figure 3. Cystic parathyroid lesion: immunohistochemistry for PTH.

this kind of lesion arise more frequently in men than in women, that the inferior parathyroid gland is the one more affected and older patients more than younger ones[6,7].

The study of McCoy *et al*[3] referred a larger frequency of less than 3% with 48 patients among 1769 cases operated for hyperparathyroidism in a single institution and no difference between sex, side and inferior or superior parathyroid glands is reported. However, this report is the image of a referral center for the treatment of hyperparathyroidism, and this doesn't reflect the real incidence of CPLs.

According to a literature review by Papavramidis *et al*[8], CPLs are classified into two categories: functioning and non-functioning. Non-functioning, which are more common, exhibit non-specific physical and radiological features and are reported to be twice as prevalent in women, particularly in their fourth to sixth decades of life. Clinical presentation shows compressive symptoms such as neck swallowing, dyspnea, and hoarseness[4]. Recurrent nerve palsy as initial presentation of CPLs has been documented in 11 patients[9,10]. At the clinical examination the lesion is a cervical soft mass, mobile, usually located in the neck or superior mediastinum[7].

Neck ultrasound examination is crucial in the diagnostic workup[8], but as noted in literature[11] while it is sensitive, it may lack specificity in accurately identifying the cysts. On the other hand, CT scan (computed tomography) and MRI (magnetic resonance imaging) do not often lead to a correct diagnosis[12] but can reveal homogenous areas of cystic nature. 4DCT and 4DMRI offer high-resolution images, but 4DCT carries a higher radiation risk for thyrotoxicity and 4DMRI is preferred for parathyroid adenomas. In the future, F-fluorocholine (FCH) PET/MRI could improve dynamic structural imaging.[13] Sestamibi scinti-scan or other nuclear medicine technique rarely detect the functioning CPLs with an accuracy rate lower than 68%[3,14-16].

In combination with US examination, FNA is considered the best method to accurately diagnose PTH cysts[17]. CPLs show clear-watery colorless fluid[3,11,17]; if is turbid suggests prior hemorrhage. However, elevated i-PTH levels remain key to increase specificity for CPLs.

When evaluating CPLs, they should be included in the differential diagnosis with thymic cyst, thyroid adenoma, and parathyroid carcinoma and thyroid cyst[18]. The final histology for CPLs

reports that the functioning ones are generally lined by cuboidal or columnar epithelium and are thin-walled white cysts. The non-functioning, instead, lack this kind of epithelium and are described as pseudocysts. Immunohistochemistry assay highlights positivity for parathormone peptide, glycogen, and focally for chromogranin[8]. As reported in previous studies[4,19], two different subgroups of CPLs, based on their etiology, are registered in clinical practice: (a) degeneration of an adenoma or hyperplastic gland and (b) true cyst with epithelial layer. Ippolito *et al* defined "true cysts" exclusively the non-functioning parathyroid lesions, in their opinion the hyperfunctioning ones derive from a cystic degeneration of a parathyroid adenoma or a hyperplastic gland[4]. There are two other theories explaining the origin of CPLs: one suggests that small microcysts form within a parathyroid gland, while the other hypothesizes that varying numbers of epithelial tubules, arising near thymic tissue, develop into canalicular or glandular tissue layers in postnatal life.

In our two cases, different microscopic findings suggest distinct origins. In the first case, the pathological finding (Fig. 3), aligns with cystic degeneration due to intraglandular hemorrhage, with a small amount of insular parathyroid tissue detached from the cystic wall. In the second case, the cystic wall is composed of a few stratified parathyroid cells uniformly lining the CPL. This finding suggests a true parathyroid cyst, potentially derived from an embryological remnant[4].

According to these three different subgroups of CPLs are identified: (a) cystic degeneration of parathyroid adenoma or of a hyperplastic gland; (b) true non-functioning parathyroid cysts; and (c) "rare" functioning true parathyroid cyst.

The treatment for CPLs is deeply discussed among surgeons and physicians; an optimal one could be FNA alone, but recurrence has been registered[4]. In cases of recurrence surgical excision is the definitive treatment. Sclerosis with tetracycline or ethanol ablation has been proposed[19-21], especially for non-functioning CPLs. According to the literature, it was preferred over surgery after recurrence in FNA treatment, for cosmetic reasons. Another paper reported optimal results after ethanol ablation in 12 patients without major complication (only localized pain) even if two patients relapsed and needed a second ethanol treatment[21]. Nevertheless, authors still confirm surgical excision after recurrence or failed sclerosis, especially, in patients with compressive symptoms[19,20]. The difference between surgical excision and FNA as far as recurrence rate (27.83%) is statistically non-significant.[8]

An alternative approach for non-functioning CPLs includes minimally invasive video-assisted parathyroidectomy (MIVAP) and open minimally invasive parathyroidectomy (OMIP)[22]. These techniques allow for cystic fluid aspiration, reducing the risk of rupture and minimizing the potential for persistent disease (parathyromatosis)[23,24]. Other studies suggest that MIVAP may offer advantages over OMIP, including reduced post-operative pain, improved patient satisfaction, and better cosmetic outcomes[25].

Conclusion

It's necessary to underline that diagnosis of CPLs is a real challenge in clinical practice and sometimes is referred to as "forgotten diagnosis in neck mass"[26]. I-PTH washing of intra-cystic fluid should be performed to confirm diagnosis. US evaluation, CT scan, MRI and Sesta-mibi scintiscan showed low accuracy and specificity.

The final treatment for these lesions should be excisional surgery in case of functioning CPLs. For non-functioning CPLs, FNA can be considered the first line treatment. In the event of recurrence, surgery should be preferred, particularly in symptomatic patients, due to the potential risks associated with parathyroid fine needle aspiration[24].

Ethical approval

Not applicable.

Consent

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 Editor-in-Chief of this journal on request.

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Author's contribution

All listed authors have contributed to the work, design data collection and interpretation and analysis. P.P. contributed to the ideation of the paper and data collections as also review of the final manuscript. L.D.F. curated the writing and application of the paper. M.D.N. worked on histological analysis. E.T., G.S., and C.N. worked on data collection and analysis.

Conflicts of interest disclosure

All the authors declare to have no conflicts of interest relevant to this study.

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Presentation

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