Non-functional parathyroid cyst masquerading as a thyroid cyst: Report of two cases and review of the literature

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ABSTRACT
Parathyroid cysts are rare and can pose a diagnostic challenge. We describe two cases of patients who presented with cystic anterior neck masses and underwent hemithyroidectomy for clinically and radiologically presumed thyroid cysts. The final diagnosis was only established postoperatively on histological examination. A review of the literature on parathyroid cysts and a discussion of suggested management for suspected cases are included.

INTRODUCTION
Parathyroid cysts are rare clinical entities and may be mistaken for thyroid cysts [1]. They are typically classified as functional or non-functional, depending on their association with hyperparathyroidism [2]. The majority of cases are non-functional [3]. This report illustrates the diagnostic conundrum associated with a non-functional parathyroid cyst mimicking a cystic thyroid nodule. We review diagnostic aspects and management of suspected cases.

CASE REPORT 1
A 39-year-old woman presented with a right-sided anterior neck swelling. This had remained largely asymptomatic until 12 months prior to her presentation when she began to experience progressive effects of local compression including dyspnoea, dysphagia and a noticeable change in her voice. She had no significant past medical history and there was no family history of thyroid disease.

Clinical examination showed a smooth swelling of the right thyroid lobe, which was more prominent towards the inferior pole with normal movements of the vocal cords. There were no clinical features suggestive of hyperthyroidism or hyperparathyroidism and routine blood tests, including thyroid function, were within normal reference range.

Ultrasound examination of the neck confirmed a 5 × 4 cm well-defined cystic nodule that appeared to be in the right lobe of the thyroid gland. There was associated tracheal deviation to the left. No adverse features of the thyroid nodule were seen and there was no evidence of cervical lymphadenopathy. Salivary glands appeared normal, as did the left lobe of the thyroid. The overall ultrasound appearance was thought to be consistent with a benign colloid cystic nodule of the right thyroid lobe.

Over the following months, the patient developed worsening problems requiring hospital admission on one occasion with stridor and dyspnoea. She underwent fine-needle aspiration (FNA) of the cyst with removal of 46 ml of clear, watery fluid resulting in resolution of her symptoms. A follow-up ultrasound scan of the neck was arranged as an outpatient three months later which demonstrated reaccumulation of the cystic fluid (Figure 1(a)).

She subsequently underwent a planned right hemithyroidectomy with excision of the cyst. Intraoperatively, the right thyroid gland appeared normal on inspection and palpation. An approximately 4–5 cm floppy, thin-walled cyst with clear fluid content was found. This was located between the inferior pole of the thyroid and the thymus but seemed to be separate from both structures.

Histological examination of the specimen showed a right thyroid lobe with an attached cyst weighing...
31.2 g (Figure 2(a)). The thyroid lobe itself measured 35 × 20 × 22 mm. The cut surface of it was deep red and uniform throughout. No intra-thyroid cysts or focal lesions were identified and no papillary nuclear features were seen. No parathyroid glands were identified within the specimen. Attached to the lower pole of the thyroid was a thin-walled unilocular cyst measuring 56 × 43 × 12 mm and containing clear fluid. The cyst had a thin fibro-collagenous capsule with a small amount of attached fat and small amounts of thymic tissue seen at the deep aspect of the cyst wall. Within the cyst wall there were bland and, in places, rather degenerate small solid nests of cells with moderate amounts of clear cytoplasm. The cyst lining epithelium showed patchy positive staining with cytokeratin (CK) 5/6 but was negative for epithelial membrane antigen (EMA), tumour protein 63 (p63), thyroid transcription factor 1 (TTF1) and thyroglobulin. The cell nests within the cyst wall were positive for chromogranin and parathyroid hormone (PTH) consistent with a parathyroid origin. There was some renal cell carcinoma (RCC) marker expression in both the solid cell nests in the cyst wall and the cyst lining epithelium. The significance of this was uncertain, and cluster of differentiation 10 (CD10) and EMA markers were negative. Morphologically, there were no features

Figure 1. Ultrasound scan of the neck. (a) Reaccumulation of cystic fluid following fine-needle aspiration (patient 1). (b) Thin-walled cystic lesion (patient 2).

Figure 2. Macroscopic appearance. (a) Resected right thyroid lobe with attached cyst (patient 1). (b) Resected left thyroid lobe with attached cyst (patient 2).
suggestive of a metastatic renal cell carcinoma, hence, this was thought to be aberrant staining. Therefore, a benign parathyroid cyst with incidental attached thymus was deemed to be the diagnosis (Figure 3(a)).

The patient made an uneventful recovery and was discharged from hospital on postoperative day one. She remained asymptomatic with no recurrence at four-month follow-up.

Case report 2

An otherwise fit and well 59-year-old woman presented with a two-week history of left lower neck swelling. She reported no other associated symptoms.

Physical examination showed a smooth, firm, mobile and non-tender left-sided goitre measuring approximately 5–6 cm with no evidence of cervical lymphadenopathy. Routine blood tests, including thyroid function, were unremarkable.

Ultrasound examination of the neck revealed chronic atrophic thyroiditis as well as what appeared to be a thin-walled cystic lesion arising from the lower pole of the left lobe of the thyroid. The radiological findings were presumed to be in keeping with a benign colloid cyst of the thyroid gland (Figure 1(b)).

She underwent elective left hemithyroidectomy with excision of the cyst. Intraoperatively, the left thyroid gland appeared normal in size. An approximately 6–7 cm thin-walled cyst attached to but separate from the inferior pole of the left thyroid gland was noted.

Histological examination of the specimen showed a left thyroid lobe measuring $40 \times 20 \times 18$ mm with a loosely attached thin-walled unicocular cyst measuring $55 \times 50 \times 25$ mm (Figure 2(b)). The cut surface of the thyroid gland was uniformly fleshy. It showed lymphocytic infiltration of the parenchyma associated with atrophy of follicles showing focal Hurthle cell change consistent with autoimmune thyroiditis. The cyst, which was attached to the lower lateral pole of the thyroid gland, contained clear fluid on slicing and did not show any evidence of mural nodules. It was lined by bland cuboidal cells of variable thickness containing uniform round nuclei and pale moderate cytoplasm. The cyst wall was fibrotic and focally contained similar bland cells forming small clusters and nests. No mitoses or necrosis were seen. The cell nests within the cyst wall were positive for chromogranin and PTH. There was some RCC marker expression in both the solid cell nests in the cyst wall and the cyst lining epithelium. Again, this was thought to be aberrant staining. Overall, the features were consistent with a benign parathyroid cyst (Figure 3(b)).

Postoperatively, the patient developed a weak voice. Flexible nasendoscopy confirmed sluggish movements of the left vocal cord. Swallowing assessment was satisfactory. She was discharged from hospital on postoperative day 2. At one-month follow up, her voice had returned to normal and she remained well.

Discussion

Parathyroid cysts are rare lesions found in the neck and mediastinum [4]. First described by Swedish anatomist Ivar Sandström in 1880, only around 300 cases have been reported in the medical literature to date [5]. They tend to occur in the fourth and fifth decade of life with a female to male ratio of 2.5:1 [6]. Two types have been recognised: functional and non-functional, the former being associated with features of primary hyperparathyroidism. Non-functional cysts account for approximately 80% of cases [3].

The pathogenesis of parathyroid cysts remains poorly understood. Several theories have been proposed which suggest that they may develop from
embryological remnants of the third or fourth branchial pouch, coalescence of microcysts, simple retention of parathyroid secretions, or cystic degeneration of pre-existing adenomas [3].

Clinically, a parathyroid cyst may present as an asymptomatic neck mass, result in effects of local compression, or produce features of hyperparathyroidism in cases of functional cysts [3]. More commonly than not, they are found as solitary cysts located near the lower poles of the thyroid gland [2].

Ultrasonography is considered to be the first line imaging modality as part of the diagnostic workup [7]. The sensitivity and specificity of this is operator-dependent but is likely to reveal a cystic nodule that can often be difficult to differentiate from a thyroid cyst [8]. The absence of comet tail artefacts, which, if present, would indicate a colloid cyst, as well as the lack of other cystic lesions within the thyroid lobes may raise the suspicion of a parathyroid origin [9]. However, differentiation of parathyroid cysts from thyroid cysts based on radiological findings is challenging [1].

Fine-needle aspiration (FNA) plays an essential role in the confirmation of the diagnosis. A colourless and watery aspirate with high levels of PTH is strongly suggestive of a parathyroid cyst, irrespective of whether the cyst is functional or non-functional [1]. It is, however, recommended that carboxyl-terminal fragments of parathyroid hormone (C-PTH) is measured rather than intact PTH. This is because non-functional parathyroid cysts can produce large quantities of PTH, which is then rapidly degraded into the biologically inactive C-PTH. Analysing the aspirate of a non-functional cyst for intact PTH level may therefore lead to a potentially false negative diagnosis [10].

In the first case we presented, FNA was required on an urgent basis to achieve symptomatic relief for the patient. However, the aspirate was not sent for biochemical analysis as, at the time of presentation, the diagnosis of parathyroid cyst was not suspected clinically or radiologically. For the same reason, FNA was not performed in the second case.

Various approaches to the treatment of parathyroid cysts have been described in the literature, including fine-needle aspiration, sclerotherapy, and operative management [11]. In cases of uncomplicated, non-functional parathyroid cysts, fine-needle aspiration has been advocated as the management of choice [12]. This can be effective in leading to long-term cyst regression although reaccumulation of fluid remains a significant problem, as was illustrated in our case (Figure 1(a)). Sclerotherapy may be considered as an alternative approach to reduce recollection of cystic fluid [13]. This technique involves the injection of a sclerosing agent, such as ethanol, into the cyst which induces an inflammatory reaction, scarring, and obliteration of the cyst. In cases of functional parathyroid cysts as well as those presenting with compressive symptoms, the favoured treatment approach remains surgical excision [14].

Conclusions

Parathyroid cysts are uncommonly encountered in clinical practice. Nevertheless, they should be considered in the differential diagnosis of a patient presenting with a cystic neck mass, especially one involving the lower poles of the thyroid gland. Clinical and radiological features, particularly of non-functional cysts, can be equivocal, often making the diagnosis challenging, as was illustrated by our two cases. Fine-needle aspiration and cystic fluid carboxyl-terminal fragments of parathyroid hormone (C-PTH) offer a valuable diagnostic tool. Management options to consider include percutaneous aspiration, sclerotherapy, and surgical excision.

Disclosure statement

No potential conflict of interest was reported by the authors.

Written consent for publication was obtained from both patients.

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