

Challenges in the Management of Parathyroid Cyst: A Mini-review

Lynnette RL Tan¹, Lau WL Joel², James WK Lee³, Bengt Fredrik Petersson⁴, Rajeev Parameswaran⁵

ABSTRACT

Parathyroid cysts are exceedingly uncommon but should remain a differential in the evaluation of a patient with a cystic neck lump. Case reports in the literature are few and far between and there are no universally defined guidelines as to the diagnosis and management of this condition. In this paper, we review the existing literature regarding the epidemiology, etiology, and clinical presentation of parathyroid cysts. We evaluate the existing diagnostic modalities, discuss their benefits and limitations, and discuss key considerations in the management of this little-known condition.

Keywords: Cyst, Hyperparathyroidism, Parathyroid.

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The paired parathyroid glands were discovered by the medical student, Ivor Sandstrom in 1880.¹ These glands secrete parathyroid hormone (PTH), which regulates the serum calcium by its action on bones, kidneys, and the gut. Pathological enlargement of the parathyroid glands due to an adenoma, hyperplasia, or carcinoma cause primary hyperparathyroidism. However, a clinician will on rare occasions, come across the uncommon entity called a parathyroid cyst. Parathyroid cysts account for only 0.5% of parathyroid lesions with 350 cases reported in the literature.^{2,3} In this review, we discuss the challenges in the diagnosis and management of parathyroid cysts.

Parathyroid cysts occur more commonly in the fourth and fifth decades of life and have a female preponderance.² They are postulated to arise from the vestigial remnants of the third and fourth branchial clefts,⁴ persistence of the Kürsteiner canals of the fetal parathyroids,⁵ the cystic degeneration of an adenoma,⁶ or the aggregation of microcysts.² They are most commonly located in the neck in the inferior parathyroid glands,⁷ or in the mediastinum,^{7,8} though occasionally are intra-thyroidal.⁹ The incidence appears to be higher in women in a ratio of 3:1 and more commonly in the middle age, and rarely seen in children.²

Parathyroid cysts present in many ways. Patients may be completely asymptomatic, learning of this finding during imaging procedures for other indications. When seen incidentally on imaging, they are usually seen on the left side and may be seen to be confused with a thyroid nodule or cyst.¹⁰ Symptoms vary with the size and location of the lesion. Large, centrally located mediastinal cysts may cause compressive symptoms.¹¹ Hyperfunctioning cysts which secrete PTH may present with hypercalcemic symptoms including bone pain, gastrointestinal, and neurological symptoms.^{12,13} The incidence of parathyroid cysts in MEN 1 has shown to be around 4%.¹⁴

Because parathyroid cysts are uncommon, there is a lack of guidelines on their diagnosis and management. There are no pathognomonic findings on history and clinical examination. Neck masses are palpable only when sizeable and even then, are difficult to distinguish from thyroid lesions. Ancillary investigations that can help obtain a diagnosis include:

¹⁻³Department of Endocrine Surgery, National University Health System, Singapore

⁴Department of Pathology, Yong Loo Lin School of Medicine, Singapore

⁵Department of Endocrine Surgery, National University Health System, Singapore; Department of Surgery, Yong Loo Lin School of Medicine, Singapore

Corresponding Author: Rajeev Parameswaran, Department of Endocrine Surgery, National University Health System, Singapore; Department of Surgery, Yong Loo Lin School of Medicine, Singapore, Phone: +6567724229, e-mail: rajeev_parameswaran@nuhs.edu.sg

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LABORATORY TESTS

Serum iPTH and calcium levels should be checked in all suspected parathyroid lesions to assess functional status. However, this does not indicate if the lesion is solid or cystic. FNA is increasingly performed with promising safety profiles. Parathyroid cysts classically yield “water-clear” aspirates; straw-colored fluid suggests a thyroid cyst and brown/hemorrhagic fluid occurs in parathyroid adenomas. Aspiration of the parathyroid cysts have generally a higher level of PTH and helps differentiate from a thyroid nodule,^{15,16} and other cystic lesions of the neck such as branchial cyst and esophageal duplication cyst. Serum iPTH levels, however, do not correlate with the size of the lesion, unlike in adenomas.

Microscopically, parathyroid cysts have a smooth inner surface wall with membranous lining, a single layer of cuboidal epithelium, and parathyroid tissue within the cyst wall (Figs 1 and 2). Atypical parathyroid cystic adenomas may mimic parathyroid carcinoma and it is important to look for vascular and capsular invasion in the submitted specimen to differentiate the two.¹⁷ Sometimes heterotopic salivary gland tissue may be seen around the cyst.¹⁸

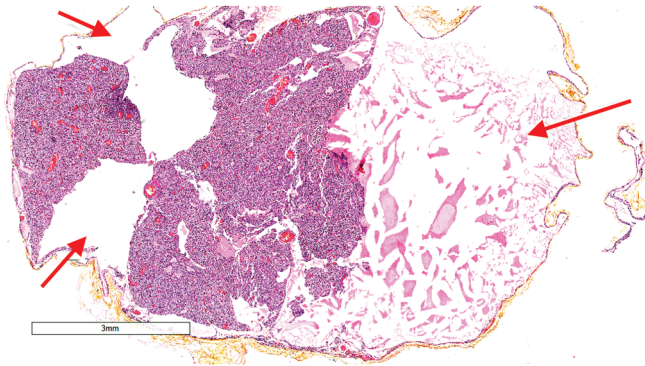


Fig. 1: Microscopy showing the parathyroid with cystic component

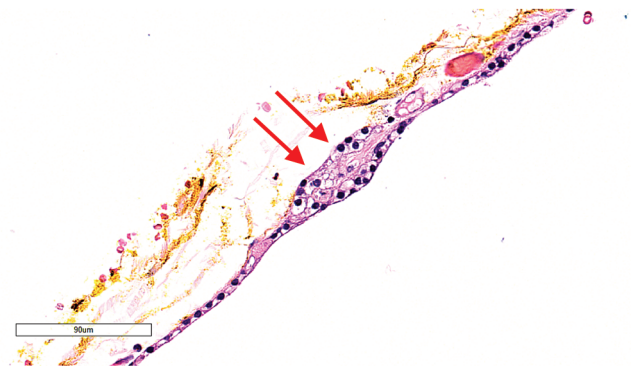


Fig. 2: High microscopy showing a parathyroid cyst with a smooth inner surface wall with membranous lining, a single layer of cuboidal epithelium

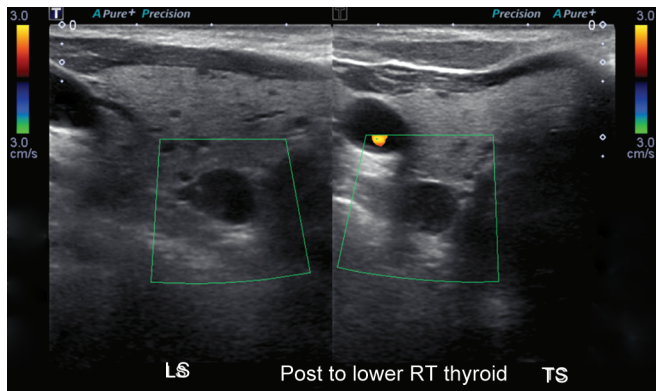


Fig. 3: US showing the cystic parathyroid at the postero-inferior pole of the thyroid



Fig. 5: CT scan of the same patient showing the parathyroid lesion at the inferior pole of the thyroid

IMAGING

Ultrasonography (US) is non-invasive, inexpensive, and often the first-choice option.¹⁹ Parathyroid cysts are usually posterior and/or inferior to the thyroid (Fig. 3), are hypoechoic and hypervascular with a prominent polar feeding vessel from a branch of the inferior thyroid artery. Ultrasonography demonstrates the anatomical relation of the parathyroid cyst to other neck structures and is useful intraoperatively when prior neck surgery creates a scarred surgical field making the location of the parathyroid cyst challenging. However, accuracy is reduced in inexperienced hands, in obese patients, and cysts that are smaller or located in the mediastinum posterior to the clavicles.²⁰

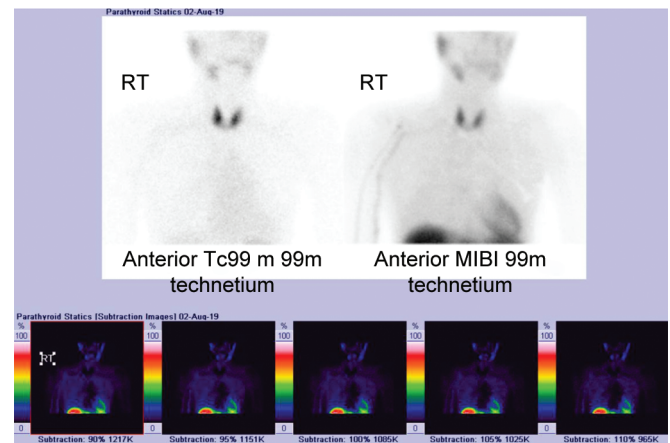


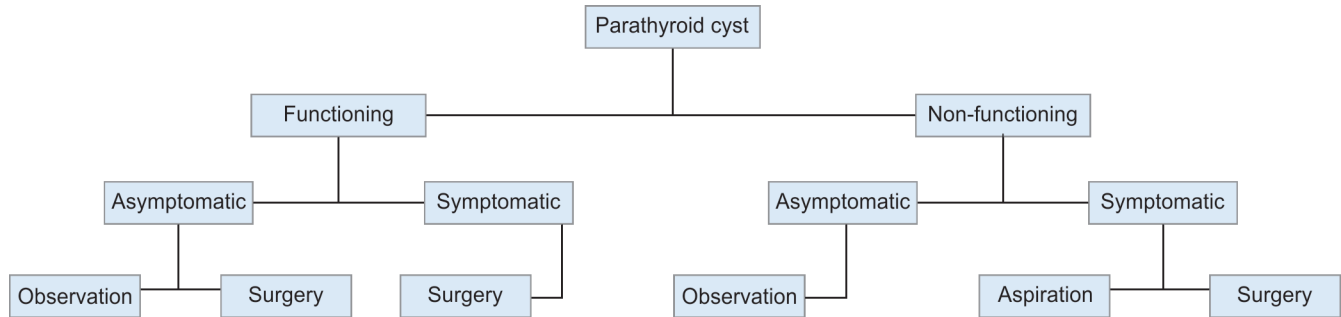
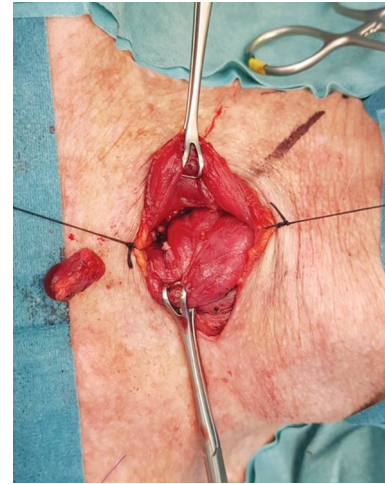
Fig. 4: Negative Technetium Sestamibi scan imaging along with SPECT for the same patient

^{99m}Tc-MIBI works based on radiotracer uptake and retention by mitochondria-rich oxyphil cells in parathyroid glands²¹ but is associated with significant false-negative rates particularly in small, superiorly located glands²² and parathyroid cysts (containing fewer oxyphil cells) (Fig. 4).²³

In contrast, 4D-CT with volume-rendering reconstruction has statistically significant higher positivity and accurate localization rates.²⁴ Parathyroid cysts demonstrate less enhancement in the arterial phase and little washout in the delayed phase compared with adenomas (Fig. 5). 3D-reconstructed images help facilitate surgical planning. Radiation exposure—→ 50-times that of MIBI!—with elevated long-term risk of developing head and neck cancers remains a significant deterrent, particularly in younger patients.

¹⁸F-fluorocholine positron emission tomography (FCh-PET) computed tomography has demonstrated excellent detection rates, sensitivity, and spatial resolution than conventional scintigraphy and CT.²⁵ It is advantageous in localizing small, hyperplastic parathyroid glands, regardless of their histopathological composition.²⁶ However, FCh-PET is non-specific for parathyroid disease and false positives can occur in cases of malignancy and inflammation.

Magnetic resonance imaging (MRI) has no radiation and has evaluated parathyroid cysts with some success although comparative studies with other modalities are lacking. Modern MRI technology utilizes fast imaging tools such as time-resolved

Flowchart 1: Classification of parathyroid cysts**Fig. 6:** Intraoperative image of the parathyroid cyst at the inferior pole of the thyroid on the right side**Fig. 7:** The excised parathyroid specimen in the same patient

imaging with stochastic trajectories (TWIST), improved parallel imaging techniques, and fat-suppression techniques.²⁷ Dynamic 4D contrast-enhanced MRI exploits the hypervascular nature of parathyroid lesions, distinguishing them from thyroid tissue and lymph nodes with good diagnostic accuracy. Although parathyroid cysts are less vascular, their fluid component yields a high T2WI signal that is easily detectable on MRI and this is an area that can be explored.

Our approach to the management of parathyroid cysts is outlined in Flowchart 1.

Treatment for asymptomatic functioning cysts is based on principles of management of primary asymptomatic hyperparathyroidism. Patients should be offered surgery if any of the criteria are fulfilled:

- Serum adjCa >1 mg/dL.
- T-score < -2.5 on BMD.
- Vertebral fracture(s) on imaging.
- Renal impairment (CrCl < 60 mL/minute).
- 24-hour urinary calcium >400 mg/day.
- Presence of nephrolithiasis/nephrocalcinosis on imaging.

The gold-standard treatment for symptomatic functioning cysts is surgery. Access depends on cyst characteristics. Most can be removed through a cervical incision (Figs 6 and 7) but larger mediastinal cysts may require thoracotomy or median sternotomy.²⁸ Thoracoscopic²⁹ and robotic³⁰ approaches have also been described. Care must be taken to avoid injury to the

ipsilateral recurrent laryngeal nerve, especially in large cysts. Cysts should ideally be removed intact or decompressed empirically to avoid spillage as there is a risk of parathyromatosis³¹ and recurrent hyperparathyroidism. Patients should be monitored closely for postoperative hypocalcemia;³ this generally occurs in those with larger cysts but all patients should have intravenous access and calcium replacement on standby nonetheless.

Patients with symptomatic non-functioning cysts should consider aspiration or surgery. Aspiration is less invasive, performed under local anesthetic, and a safer option in patients with comorbidities and high risk for general anesthesia. There is a risk of intra-cystic hemorrhage which can exacerbate hypercalcemia, and the possibility of recurrence.^{32,33} Sclerosing therapy with tetracycline and ethanol have been proposed to minimize recurrence,^{34,35} however, are associated with risks of peri-cystic fibrosis and damage to the recurrent laryngeal nerve. When carcinoma cannot be ruled out, FNA is discouraged because of the risk of malignant seeding along the percutaneous tract.³⁶ Surgical resection can be considered if recurrences occur after repeated aspirations.

Patients with asymptomatic non-functioning cysts can be left alone. However, there is the possibility of cyst enlargement and symptom development over time, therefore patients should remain under follow-up, with repeat imaging and/or blood tests when clinically indicated. In a study of eight asymptomatic non-functional parathyroid cysts treated with aspiration, all of them recurred and eventually underwent surgery.³³

CONCLUSION

Parathyroid cysts remain a rare entity. However, as diagnostic modalities continue to improve and existing practices are refined, we are optimistic that parathyroid cysts can be diagnosed with greater accuracy, and clearer guidelines on the management of parathyroid cysts will be developed in time to come.

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