

# Diagnostic pitfalls in a cystic ectopic intrathyroidal parathyroid adenoma mimicking a nodular goiter

## A care-compliant case report

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### Abstract

**Rationale:** Cystic parathyroid adenomas are rare and seldom arise in ectopically located glands which may be found within the carotid sheath, mediastinum, thymus, or thyroid gland. They cannot be detected consistently by any imaging methods. Unusual symptoms may bring about certain pitfalls and difficulties for the diagnosis of primary hyperparathyroidism (PHPT) caused by cystic parathyroid adenomas. Until now, there are no specific guidelines on the management of cystic ectopic intrathyroidal parathyroid adenoma (ETPA).

**Patient concerns:** An 82-year-old male musician presented abrupt thyroid enlargement, hoarseness, and trachea compression when he was playing the clarinet. Thyroid and renal function tests were normal. Serum-free calcium and parathyroid hormone (PTH) were in high concentration. Thyroid ultrasonography (US) detected a giant and cystic nodule within right thyroid lobe, which is the very image of cystic nodular goiter. Parathyroid US was negative. The cystic nodule had a decreasing radioactive uptake of Technetium-99m-methoxyisobutylisonitrile (<sup>99m</sup>Tc-MIBI). At patient's request, the invasive fine-needle aspiration (FNA) was not conducted.

**Diagnoses:** The patient was initially diagnosed as cystic nodular goiter and inconclusive PHPT.

**Interventions:** Enucleation of solitary cystic intrathyroidal nodule was conducted.

**Outcomes:** The cystic nodule strongly resembled a nodular goiter grossly, but it was proved cystic ETPA by histopathology. Postoperative follow-ups found that serum-free calcium and PTH decreased sharply into normal range, and hoarseness and trachea displacement were obviously improved.

**Lessons:** The diagnosis of cystic ETPA is easily overlooked for its rarity. Diagnostic pitfalls, including atypical symptoms, inconclusive imaging manifestation, and unidentified gross specimen, are highlighted. They make the diagnosis of PHPT caused by cystic ETPA challenging. Patients would rather choose surgical excision directly than invasive FNA. Acute hemorrhage of the preexisting ETPA may account for the cystic degeneration.

**Abbreviations:** <sup>99m</sup>Tc-MIBI SPECT = Technetium-99m-methoxyisobutylisonitrile single photon emission computed tomography, CT = computed tomography, ETPA = ectopic intrathyroidal parathyroid adenoma, FNA = fine-needle aspiration, PHPT = primary hyperparathyroidism, PTH = parathyroid hormone, TSH = thyroid stimulating hormone, US = ultrasonography.

**Keywords:** cystic thyroidal lesion, diagnosis, ectopic intrathyroidal parathyroid adenoma, primary hyperparathyroidism

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## 1. Introduction

Superior and inferior parathyroid glands originate from 4th and 3rd branchial pouches, respectively. Anatomic variation makes thyroid to be one of ectopic implantation sites during migration.<sup>[1–3]</sup> Cystic parathyroid adenomas are reported to take up 1% to 2%<sup>[4]</sup> of primary hyperparathyroidism (PHPT) cases, but the cystic ectopic intrathyroidal parathyroid adenoma (ETPA) is exceedingly rare with about 7 cases having been reported so far. Depending on their capability to secrete parathyroid hormone (PTH), cystic parathyroid is categorized as functioning and nonfunctioning.<sup>[5]</sup> The pathological mechanisms of cystic ETPA are still uncertain. We report one of the largest cystic ETPAs among published papers. We also reveal some rare clinical characteristics of PHPT which is caused by cystic ETPA.

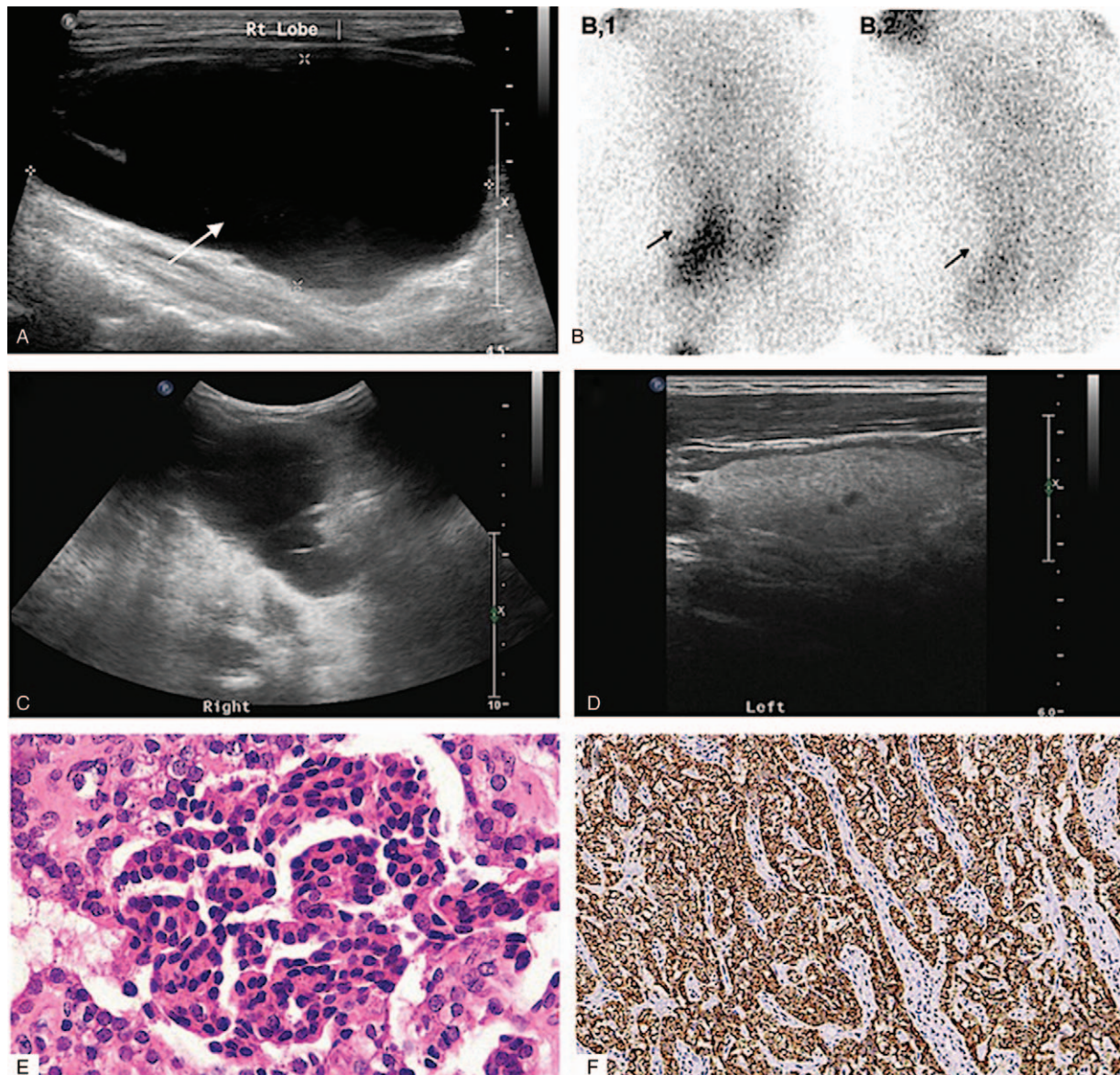
## 2. Case report

The institutional review board (Peking Union Medical College Hospital) approved this work, and written informed consent was

provided by the patient. The 82-year-old man, a musical artist, suffered from abrupt thyroid enlargement and neck mass with concomitant symptoms of hoarseness and trachea compression when playing the clarinet. Classical PHPT symptoms such as bone pain, osteoporosis, urinary calculi, and peptic ulcer were not observed. Past clinical history was negative and family history was insignificant for any similar sickness or other endocrine dysfunctions. Physical examination found a second-degree enlargement of right thyroid gland and trachea displacement to left side. The serum-free calcium level was 1.43 mmol/L (normal range 1.08–1.28 mmol/L) and the PTH level was 210.4 pg/mL (normal range 12.0~68.0 pg/mL), whereas thyroid and renal function tests were all within normal range. Computed tomography (CT) observed a giant and cystic intrathyroidal nodule within right thyroid parenchyma and trachea displacement to left side. Thyroid ultrasonography (US) revealed a

giant and predominantly cystic intrathyroidal nodule with a maximum volume of 6.9 cm × 5.2 cm × 4.8 cm (Fig. 1A), which was the very image of cystic nodular goiter in right thyroid lobe. Technetium-99m-methoxyisobutylisonitrile ( $^{99m}\text{Tc}$ -MIBI SPECT) (Fig. 1B) showed the cystic intrathyroidal nodule with a decreasing radioactive uptake of MIBI. Parathyroid US revealed no pathological parathyroid lesions in cervical parathyroid regions (Fig. 1C and D). The fine-needle aspiration (FNA) was seldom used in Peking Union Medical College Hospital and we suggested the patient to do this manipulation in other hospital. However, he rejected the invasive manipulation and preferred surgical treatment directly to relieve cervical compressive symptoms especially hoarseness and neck appearance.

The diagnosis was initially considered as giant and cystic nodular goiter and inconclusive PHPT. During the surgery on



**Figure 1.** Neck US for thyroid demonstrates a cystic nodule within the right thyroid lobe (A, arrow);  $^{99m}\text{Tc}$ -MIBI SPECT demonstrates a cystic intrathyroidal nodule with decreasing radioactive uptake both 20 minutes later (B, 1, arrow) and 2 hours later (B, 2, arrow). Neck US for parathyroid observes no abnormal parathyroid lesions in parathyroid regions (C, right and D, left); postoperative paraffin pathology examination (E) and immune histochemical staining for PTH (F) confirm the cystic nodule to be ETPA.  $^{99m}\text{Tc}$ -MIBI SPECT = technetium-99m-methoxyisobutylisonitrile single photon emission computed tomography, ETPA = ectopic intrathyroidal parathyroid adenoma, PTH = parathyroid hormone, US = ultrasonography

July 10, 2018, the giant and cystic intrathyroidal nodule was identified in the right thyroid lobe and it was surrounded by thyroid parenchyma. Enucleation of solitary cystic intrathyroidal nodule was performed to solely excise total intrathyroidal nodule with circular and smooth appearances, which looked like a cystic nodular goiter grossly. However, it incidentally ruptured and a large amount of unclear and bloody fluid flowed out which was cleared away by a vacuum extractor. As the diagnosis of cystic ETPA was overlooked and the cystic nodular goiter was considered according to our clinical experiences, we did not collect cystic fluid for assay of PTH. Parathyroid exploration operation in suspicious regions, including resected thyroid tissue, carotid sheath, carotid bifurcation, thymus, anterior mediastinum, and esophagus, was also performed but no pathological parathyroid lesions were observed.

Postoperative paraffin pathology (Fig. 1E) and immune histochemical staining (with a result of Ki-67 (index 2%), TTF-1 (-), Thy (-), PTH (+) (Fig. 1F)) proved the cystic intrathyroidal nodule to be ETPA. Trachea compression recovered 3 days after surgery. Hoarseness was mildly improved 3 days after surgery and recovered about 1 month after surgery. Serum-free calcium and PTH returned to normal range within 3 days and about 1 month after surgery. (Table 1).

### 3. Discussion

Different literatures have reported that the incidence rate of ETPA is 0.2% to 6.0%.<sup>[5-7]</sup> Cystic parathyroid adenomas take up 1% to 2%<sup>[4]</sup> of PHPT cases. Colsa-Gutiérrez et al<sup>[8]</sup> considered that cystic parathyroid adenomas could be caused by embryological remnants of the 3rd or 4th pharyngeal pouches and preservation of glandular secretion. However, in this case, it is inferred that acute hemorrhage of preexisting ETPA could explain abrupt cystic degeneration and neck mass.

PHPT patients usually present typical symptoms such as bone pain, bone deformity, nephrolithiasis, and peptic ulcer. Acute neck mass and thyroid enlargement with concomitant symptoms of hoarseness and trachea displacement are exceedingly interesting and unusual. Owing to rarity, lack of clinical experience, and unusual characteristics, the cystic ETPA is easily overlooked and misdiagnosed as a cystic nodular goiter.

CT, US, and <sup>99m</sup>Tc-MIBI SPECT are necessary for preoperative diagnosis and localization studies of ETPA. A basic feature of abundant blood supplying to parathyroid adenomas cannot be seen in most cystic adenomas especially in cystic ETPA, which lead to inconclusive and atypical imaging performances. The accuracy of US scan has been reported to be less for cystic parathyroid adenomas.<sup>[9]</sup> It is quiet challenging for thyroid or parathyroid US scans to distinguish cystic intrathyroidal parathyroid nodules with a great amount of fluid histologically according to their location, size, and blood supply. <sup>99m</sup>Tc-MIBI

SPECT could distinguish parathyroid adenoma and thyroid tissue since the absorption and elution time of solid or predominantly solid parathyroid adenoma are far more than those of thyroid tissue, which cannot be seen in cystic cases. Tresoldi et al<sup>[10]</sup> reported that sensitivity and positive predictive value of parathyroid lesions are, respectively, 68% and 100% for <sup>99m</sup>Tc-MIBI SPECT, 91% and 98% for combinations of <sup>99m</sup>Tc-MIBI SPECT and US scan. In our case, a decreasing radioactive uptake was observed in the cystic nodule, which was less helpful for preoperative diagnosis.

In <sup>99m</sup>Tc-MIBI SPECT-negative PHPT patients, the FNA manipulation was reported to be a feasible method for differentiation from cystic thyroid or parathyroid lesions. Cystic fluid of ETPA with higher level of PTH and parathyroid adenoma cells can be obtained by FNA. However, the safety of FNA for complete assessment of cystic ETPA needs further studies since FNA biopsy may cause some risks of needle tract seeding, tissue fibrosis, rupture of cystic ETPA.<sup>[11,12]</sup> Sudden cystic degeneration of ETPA resulted in neck mass and hoarseness, which has considerably affected the quality of life. Patient would rather first choose surgical operation than extra invasive FNA manipulation. Besides, the reduction in patient fees is another factor.

Enucleation of solitary cystic intrathyroidal nodule should be performed to excise total ETPA as early as possible to preserve thyroid functions and reduce compressive damage. During thyroid surgery, cystic fluid from incidentally ruptured ETPA should be cleared away to reduce the release of PTH into the blood circulation. Besides, cystic fluid should be collected for assay of PTH. Intraoperative and postoperative pathological examinations should be conducted for conclusive diagnosis. Parathyroid exploration should only be done on homolateral region as it easily damages blood supply of parathyroid and recurrent laryngeal nerve.

So far, cystic ETPA is exceedingly rare with about 7 cases previously reported, but this case is the 1st from China. In this case, it is interesting and unusual to first report acute compression of laryngeal recurrent nerve and trachea, the patient's most advanced age and the largest volume of the cyst particularly in a developing country such as China. Besides, the FNA was not performed to reduce invasive preoperative manipulations and patient fees in accordance with patient's request.

There are some profound lessons in our report. Diagnostic pitfalls, including unusual symptoms, inconclusive imaging manifestation, and unidentified gross specimen, may lead to the misdiagnosis. The importance of assay of cystic fluid is neglected. The rupture of cystic ETPA may increase the risk of hyperparathyroidism.

### Author contributions

Resources: Zhiqiang Ma, Jianchun Yu, Jianguo Chen.

**Table 1**

Changes shown before surgery, 3 days after surgery, and about 1 month after surgery.

Items	Normal range	Before surgery	3 Days after surgery	About 1 month after surgery
Serum-free calcium (mmol/L)	1.08–1.28	1.43	1.15	1.16
PTH (pg/mL)	12.0–68.0	210.4	26.9	55.1
Thyroid enlargement	Negative	Second-degree	Negative	Negative
Hoarseness	Negative	Positive	Mildly improved	Negative
Trachea compression	Negative	Positive	Negative	Negative
T3, T4, TSH	Normal	Normal	Normal	Normal

TSH = thyroid stimulating hormone.

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