Diagnosis and management of a giant cystic parathyroid adenoma: the largest reported to date

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ABSTRACT

Background: About 1-5% of all anterior cystic neck masses account for parathyroid cysts, which can be functional and nonfunctional. Functional cyst or cystic parathyroid adenoma is a very rare tumor which causes primary hyperparathyroidism and relatively hypercalcemia. Here, we present a giant cystic parathyroid adenoma which is the largest reported to date in the literature.

Case Presentation: Our patient presented with a right-sided neck mass and manifesting symptoms, which developed recently, such as itching, fatigue, proximal muscle weakness, and polyuria. In this case, the high calcium level had not been taken into account when evaluating the patient; the possibility of parathyroid adenoma had not been suspected; and repeated aspirations had been performed. After parathyroidectomy, the patient developed postoperative hyperparathyroidism as a complication.

Conclusion: Even though cystic parathyroid adenoma is a rare diagnosis, it should be considered in differential diagnosis, and parathyroid hormone of the aspirated fluid from the neck mass should be measured.

Keywords: primary hyperparathyroidism, giant cystic parathyroid adenoma, persistent hyperparathyroidism, case report, neck mass, surgery.

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Background

About 1-5% of all anterior cystic neck masses account for parathyroid cysts, which are divided into functional and nonfunctional. Only a small number of all are functional, which can cause primary hyperparathyroidism (PHPT) [1]. Fewer than 400 cases of parathyroid cysts have been reported [2] since the first parathyroid cyst description published by Sandstrom in1880 [3]. PHPT is the non-physiological overproduction of the parathyroid hormone (PTH) and is the third most common endocrine disorder after diabetes and thyroid diseases, and the most common cause of hypercalcemia [4]. It is generally caused by solitary parathyroid adenoma (80%-90%), multigland hyperplasia (10%-15%), double adenomas or carcinoma (1%-4%) [5]. A normal parathyroid gland weighs approximately 50-70 mg. Parathyroid adenomas (PTAs) weighing more than 3.5 g are defined as giant adenomas [6]. Cystic PTAs are rare and account for 1%-2% of PHPT cases [7], which are mostly located in the neck, although around 10% are found in the mediastinum [8]. Up until 2016, 25 cases of adenomas weighing over 30 g had been reported in the literature [9]. The largest PTA (mediastinal) reported to date weighed 145 g in a 63-year-old female [10]. Here, we present a 49-year-old male with a non-ectopic giant cystic PTA, weighing 205 g, which to the best of our knowledge is the largest giant parathyroid adenoma (GPTA) reported.

Case Presentation

A 49-year-old male was admitted to our surgery department with a right-sided neck mass, which initially was noticed 2 years ago and since then, four times with no workup done, it has been aspirated but recurrently enlarged after each. Symptoms mostly appeared 6 months ago, which include fatigue, irritability, appetite loss, cough worsening lying down, proximal muscle weakness, polyuria, and itching on the nose and feet. There were no significant signs of osteoporosis or nephrolithiasis. Otherwise the medical history of the patient was unremarkable and there was not any familial medical condition. On physical examination, the patient was awake and alert; vital signs were within the normal range; but a 10*5, soft, nontender mass was felt at right side of the neck (Figure 1); also, firm, painful wheals on the nose and left foot were suggesting calcinosis cutis.

Figure 1. *Picture showing the right-sided neck mass.*

Biochemical investigations and serology laboratory tests confirmed euthyroidism with thyroid-stimulating hormone, free thyroxine, and free triiodothyronine levels of 1.085 uIU/ml (normal range: 0.35-4.94), 0.95 ng/dl (normal range: 0.7-1.48), and 2.97 pg/ml (normal range: 1.71-3.71), respectively. He was found to have hypercalcemia and elevated parathyroid hormone with serum calcium of 13.2 mg/dl (normal range: 8.4-10.2) and intact parathormone of 964.6 pg/ml (normal range: 15-68.3). In renal function tests, the estimated glomerular filtration rate was high (107.31), 24-hour urine calcium was low (12.1 mg/dl) (normal range: 100-300), volume of urine was critical (4840 ml), and creatinine was in the normal range (0.77 mg/dl) (normal range: 0.72-1.25). In complete blood count, neutrophil level of 13.78 10^3/µl (normal range: 1.8-6.98) and lymphocyte level of 1.46 10^3/µl (normal range: 1.26-3.35) were noted. Liver lab findings were normal. In imaging investigations, chest X-ray showed severe tracheal deviation (Figure 2). An ultrasound of his neck showed a 100*80*77 mm cystic lesion with a few septa next to the right thyroid lobe compressing it and pushing vascular structures to the lateral; a 6 mm solid nodule was detected in the thyroid left lobe. On computed tomography scan, a cystic structure at fourth cervical level prolonged to the entry of thorax, 73*68 mm at its largest axial plane, pushing the right common carotid artery and jugular vein to lateral, right thyroid gland to anteromedial, and trachea to the left was reported (Figure 3). A parathyroid sestamibi

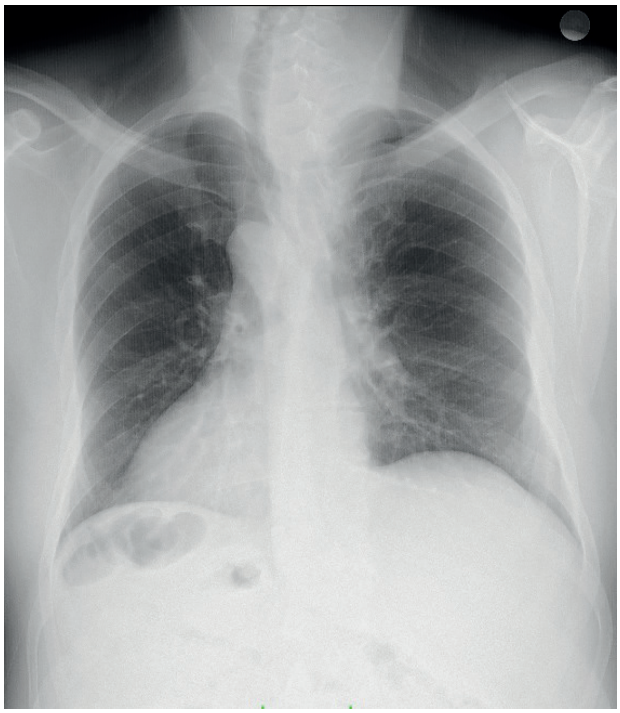

Figure 2. *X-ray showing severe trachea deviation to the left.*

Figure 3. *Computed tomography scan showing a giant right-sided cystic structure in the neck pushing the trachea to the left.*

scan was not feasible. Following preoperative workup and surgical planning, the patient underwent surgery. After general anesthesia, an extended collar incision was made up to the right submandibular angle. An approximately 10 cm giant cystic mass (Figure 4), filling the right anterior cervical triangle, was adherent to the surrounding tissue. Intraoperative fine needle aspiration was performed and the fluid was sent to the laboratory, which reported a PTH level of 2,500 pg/ml. The cyst was separated from the surrounding tissue. Superior to the lesion, the facial branch of the internal jugular vein was ligated and cut. Two tissue samples around 1 cm from the inferior to the lesion were resected and sent to frozen pathology, which reported back lymph nodes. The mass was excised while protecting the strap muscles medially and jugular vein anteriorly.

Figure 4. *Intraoperative picture of the giant cystic mass excised from the neck.*

Due to the suspicion of whether it originated from the thyroid, right thyroid lobectomy was done, and recurrent and superior laryngeal nerves were protected. Parathyroid glands were not seen on the right side. After controlling the bleeding and the drain put in, the layers were closed according to the physiological anatomy. The patient did not develop any complications and was discharged on the second postoperative day. The postoperative first day laboratory results showed a decrease in PTH and serum calcium levels (6 pg/mL and 10.6 mg/dL, respectively). The final histopathology reported a 12*7*6 cm, 205 g cystic parathyroid adenoma (Figures 5 and 6). On post-operative day 9, the patient came back for checkup and removal of the sutures (Figure 7). His laboratory results revealed a "postoperative primary hyperparathyroidism"; the PTH level was 144.7 pg/ml; and serum calcium level was 8.6 mg/dl; the wheals on the nose and left foot had disappeared as other symptoms.

Discussion

Parathyroid cysts are difficult to diagnose and are challenging in management due to the rarity and close localization to other neck structures, such as thyroid. Measurement of the PTH in the aspirated fluid from the

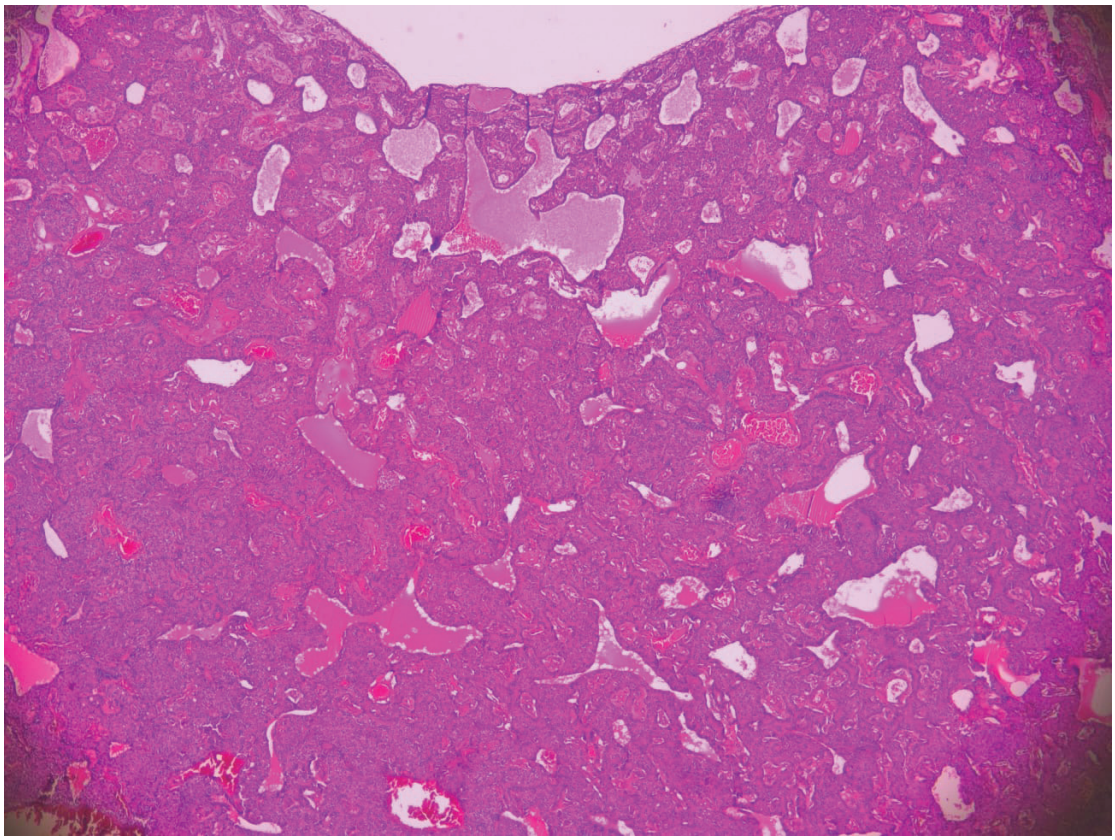

Figure 5. *Cystic parathyroid adenoma. H&E*40. Cells with small round monomorphic nucleus and wide oncocytic cytoplasma showing no remarkable atypia and mitosis; some of them palisading in perivascular area and majority of them making a nest structure.*

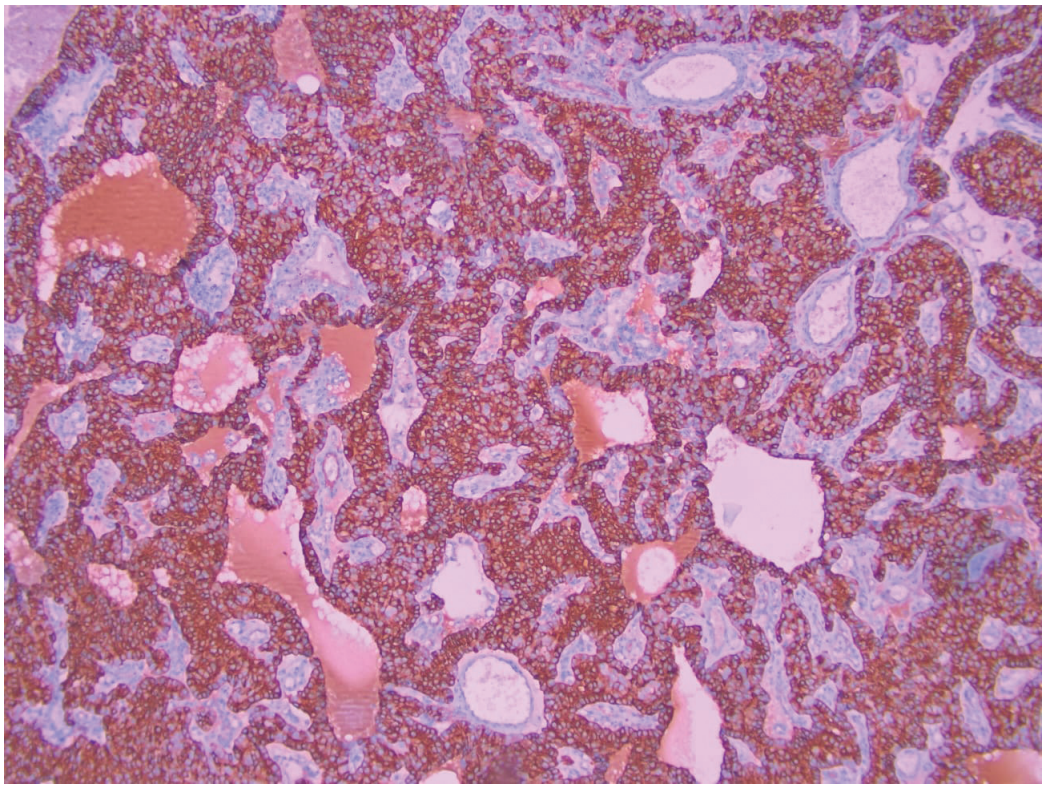

Figure 6. *Cystic parathyroid adenoma. PTH*100. Positive PTH in adenoma cells on immunohistochemical staining.*

Figure 7. *Picture showing the suture line on postoperative day 9.*

cyst is reported to be a promising method for preoperative diagnosis [11], which was not performed for our patient in the four-time fine needle aspiration during the past 2 years. Several symptoms have been reported for functional parathyroid cysts and adenomas due to hyperparathyroidism and hypercalcemia or both, generally affecting the skeletal system, renal system, and gastrointestinal system; however, GPTAs are reported to be less likely to manifest symptoms other than local symptoms in comparison to small adenomas [4,12]. In addition to the classic

symptoms, our patient presented with calcinosis cutis, despite normal renal functioning values, which adds up to the rarity of our case. Calcinosis cutis is the deposition of calcium salts in the skin and subcutaneous tissue, which cause painful itching wheals [13]. In terms of laboratory diagnostic tests, Zeren et al. [14] revealed a correlation between tumor diameter and neutrophil/lymphocyte ratio, which was noticeably high in our patient. Hungry bone syndrome, which is a prolonged hypocalcemia associated with hypocalcemia and hypomagnesaemia, is reported to develop as a post-parathyroidectomy complication with a higher prevalence in cases with GPTA and higher preoperative PTH [9], which did not develop in our case. Another issue is that after parathyroidectomy, postoperative or persistent hyperparathyroidism can occur in 8-40% of the patients; the etiology and clinical significance of this phenomenon is not understood yet. Advanced age, sex, disease severity, osteoporosis, adenoma size, multigland disease, decreased peripheral sensitivity to PTH, renal failure, and vitamin D deficiency have also been described as possible underlying causes in the development of postoperative elevated PTH levels in eucalcemic patients [15]. In our case, while the first postoperative day PTH was 6 pg/mL, on day 10 it was 144 pg/ml. We will follow-up with the patient and look for whether it is a persistent hyperparathyroidism or not.

Conclusion

In conclusion, in patients presenting with a cystic mass in the neck, parathyroid adenoma should be considered in the differential diagnosis, and if the cyst fluid is to be aspirated, PTH should be studied from this fluid.

What is new?

It is the largest cystic parathyroid adenoma reported to date in the literature and in addition to the classic parathyroid adenoma symptoms, this case presented with calcinosis cutis. After surgery the patient developed postoperative hyperparathyroidism, which is a rare complication.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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Consent for publication

Written informed consent was obtained from patient.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

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Summary of the case

1	**Patient (gender, age)**	Male, 49-year-old
2	**Final diagnosis**	Giant cystic parathyroid adenoma
3	**Symptoms**	Fatigue, irritability, appetite loss, cough worsening lying down, proximal muscle weakness, polyuria, and itching on the nose and feet
4	**Clinical procedure**	Fine needle aspiration of the cyst and cyst dissection
5	**Specialty**	General surgery