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# A Rare Case of Primary Hyperparathyroidism Caused by a Giant Solitary Parathyroid Adenoma

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Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
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**Conflict of interest:** None declared

**Patient:** Female, 73  
**Final Diagnosis:** Primary hyperparathyroidism  
**Symptoms:** Bone fractures • nephrolithiasis • palpable mass • weakness  
**Medication:** —  
**Clinical Procedure:** Operation  
**Specialty:** Surgery

**Objective:** Rare disease  
**Background:** Solitary parathyroid adenomas are the leading cause of primary hyperparathyroidism in 0% to 85% of cases. Diagnosis of parathyroid adenoma is based on typical clinical presentation of hypercalcemia, biochemical profile, and modern imaging studies. The purpose of this article is to present the diagnostic and therapeutic approach used for a 73-year-old female patient with a giant parathyroid adenoma measuring 5×2.5×2.5 cm and weighing 30 grams.

**Case Report:** A 73-year-old female was referred to the outpatient clinic of our Surgical Department with the diagnosis of primary hyperparathyroidism. The patient suffered from typical symptoms of hypercalcemia such as weakness, bone disease, and recurrent nephrolithiasis; she had a painless cervical mass for 5 months. Primary hyperparathyroidism was confirmed based on the patient's biochemical profile, which showed increased levels of serum calcium and parathyroid hormone. SestaMIBI scintigraphy with <sup>99m</sup>Tc and cervical ultrasonography revealed a large nodule at the inferior pole of the right lobe of the thyroid gland. Intraoperatively, a giant parathyroid adenoma was found and excised. Additionally, levels of intact parathyroid hormone (IOiPTH) were determined intraoperatively and a 95% reduction was found, 20 minutes after the removal of the adenoma.

**Conclusions:** This is an extremely rare case of a giant solitary parathyroid adenoma. Diagnosis of a giant hyperfunctioning solitary parathyroid adenomas was based on clinical presentation, biochemical profile, and imaging studies. Selective treatment was based on surgical excision combined with IOiPTH levels measurement.

**MeSH Keywords:** Adenoma • Hyperparathyroidism • Parathyroid Neoplasms

**Full-text PDF:** <https://www.amjcaserep.com/abstract/index/idArt/911452>

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## Background

Prevalence of primary hyperparathyroidism is approximately 1–7 per 1000 in the general population, affecting predominantly postmenopausal women. The leading cause of primary hyperparathyroidism is the solitary parathyroid adenoma in 80% to 85% of cases [1–3]. Secondary causes include parathyroid hyperplasia (10% to 15% of cases), multiple adenomas (5% of cases) and rarely parathyroid cancer (<1% to 5% of cases) [1,2]. Primary hyperparathyroidism shows a similar incidence for males and females before the age of 45 years; however, it presents a clear female predominance with ratio 3: 1 around the seventh decade of life [4–6].

Usually, parathyroid adenomas are small in size and weigh less than 1 gram [2]. Rarely adenomas can become rather large and weigh more than 3.5 grams. Those adenomas are characterized as “giant” [7].

Hyperparathyroidism is suspected when characteristic clinical signs and symptoms are present, such as neuromuscular weakness, bone disease, recurrent nephrolithiasis, and psychiatric disorders [8,9]. The diagnosis is based on elevated levels of serum calcium and parathyroid hormone (PTH). Moreover, modern imaging techniques, such as cervical ultrasonography (US), sestaMIBI scintigraphy and magnetic resonance imaging (MRI), are routinely used for the localization of the adenoma.

Treatment of choice is the excision of the adenoma. Minimal invasive parathyroidectomy (MIP) in combination with intraoperative measurement of intact parathyroid hormone (IOiPTH) levels is the optimal surgical approach [4].

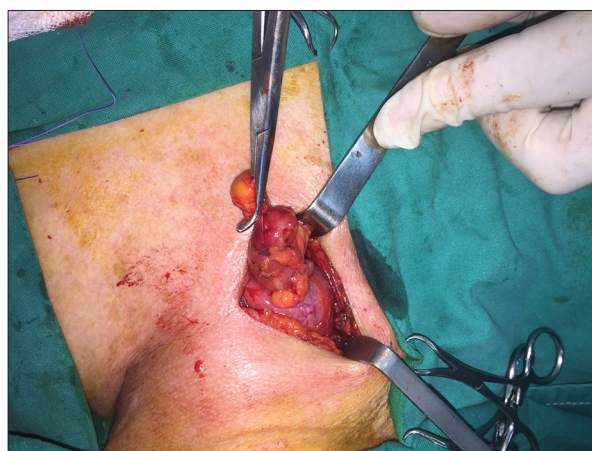
## Case Report

A 73-year-old female patient was referred to our Surgical Department due to a palpable painless mass on her neck noticed for the last 5 months. The patient also suffered from fatigue and recurrent pain in the left ankle for the last 3 months. Her past medical history revealed recurrent nephrolithiasis treated with ESWL (extracorporeal shock wave lithotripsy) 7 years ago.

Her initial blood examination revealed hypercalcemia ( $\text{Ca}^{+2}$ =14.5 mg/dL) and mild hypophosphatemia ( $\text{P}$ =2.4 mg/dL). These results led us to measure the levels of serum PTH, which was remarkably elevated (1629 pg/mL), therefore, the diagnosis of primary hyperparathyroidism was established. Thyroid hormones and tumor markers were normal. The patient suffered also from anemia (Hematocrit=29%) and elevated levels of C-reactive protein (CRP) and ferritin. Cervical US revealed a hypochoic nodule at the inferior pole of the right lobe of the



**Figure 1.** Parathyroid adenoma after excision.



**Figure 2.** Minimally invasive parathyroidectomy.

**Table. 1.** Intra-operative PTH levels.

PTH level (pg/mL)	Time after excision
1415	0 min
739	10 min
57	20 min

IOiPTH levels were measured immediately after the removal of the adenoma, 10 minutes after excision, and 20 minutes later.

thyroid gland. SestaMIBI scintigraphy with  $^{99\text{m}}\text{Tc}$  revealed a hyper functioning right lower parathyroid gland.

The patient underwent a MIP and a giant parathyroid adenoma was found at the inferior pole of the right lobe of the thyroid gland and was excised (Figures 1, 2). Its dimensions were 5×2.5×2.5 cm and it weighed 30 grams. IOiPTH levels were measured and revealed a gradual reduction after the removal of the adenoma. The values were 1415 pg/mL immediately after excision, 739 pg/mL 10 minutes after excision, and 57 pg/mL 20 minutes later (Table 1).

Histological examination confirmed the diagnosis of a parathyroid adenoma with no signs of malignancy. Hungry bone syndrome presented immediately after operation. The patient presented low levels of serum calcium ( $\text{Ca}^{+2}=8.2$  mg/dL) and the next postoperative day ( $\text{Ca}^{+2}=7.8$  mg/dL) and expressed mild symptoms of tetania. The syndrome was initially treated with intravenous calcium in the first postoperative day and oral calcium and vitamin A for a week after operation. Postoperative PTH levels, serum calcium, and serum phosphate were normal 10 days after the operation and 6 months later. Patient's symptoms were also resolved after successful treatment.

## Discussion

In most cases of primary hyperparathyroidism due to solitary parathyroid adenoma, the adenoma is usually small in size and weighs less than 1 gram [2]. Very few cases have been reported in the literature in which the adenoma weighed more than 3.5 grams. These adenomas are usually referred as "giant". The presence of a huge adenoma such as our patient's that weighed 30 grams is very rare and it is questionable whether such a huge adenoma has ever been reported [7].

Primary hyperparathyroidism presents with a variety of symptoms such as neuromuscular weakness, fatigue, bone disease, recurrent nephrolithiasis and nephrocalcinosis, psychiatric disorders, decreased concentration and memory loss, nausea, vomiting, constipation and bradycardia [8–12]. During the last decades, patients have presented with profound symptoms of severe hypercalcemia and bone disease. Moreover, dehydration has led many patients to hypercalcemic crisis, a condition related to sudden increase of serum calcium levels that causes abdominal pain, nausea, vomiting, constipation, as well as cardiac and renal impairment [12]. Nevertheless, the increased use of biochemical screening tests contributed to incidental identification of patients with slightly elevated serum calcium levels and milder symptoms [6]. On the other hand, a palpable parathyroid adenoma is very rare. In our case, apart from clinical findings depending on the serum calcium levels, a palpable mass was obvious on the patient's neck. Cases of palpable parathyroid adenoma are extremely rare in the published literature.

Biochemical findings showing high levels of serum calcium and increased levels of PTH are essential for the diagnosis.

Clinical suspicion and laboratory findings are followed by imaging studies, which confirm the diagnosis. Cervical US is widely used to locate the pathologic gland with an approximate sensitivity and specificity of 75% and 85% respectively [13]. MRI and four-dimensional computed tomography (4D-CT) scan are routinely used to identify the cause of hyperparathyroidism

and to detect ectopic parathyroid tissue.  $^{99\text{m}}\text{Tc}$ -MIBI (sesta-MI-BI) scintigraphy utilizes the absorption of the radiotracer to detect hyperactive parathyroid tissue and has a sensitivity rate between 70% to 100% [14]. Preoperative localization of the adenoma is crucial in order to achieve the optimal surgical outcome and the combination of sestaMIBI scintigraphy and cervical US are considered the best way to delineate the anatomic correlations of an adenoma [15]. We used all these radiologic and laboratory tests in order to confirm the diagnosis and localize the adenoma. Although the adenoma was palpable, full radiologic exploration of the mass was necessary in order to define this extremely rare case of hyperparathyroidism.

The definitive treatment of primary hyperparathyroidism is the surgical resection of all pathologic parathyroid tissue. Since Dr. Felix Mandl performed the first successful parathyroidectomy in 1925, bilateral neck exploration has been the gold standard with cure rates exceeding 95% [16,17]. Excision of the pathological parathyroid tissue is achieved either through bilateral neck exploration or via MIP [18,19]. In the first method, all four parathyroid glands are recognized, and a subtotal parathyroidectomy is performed preserving part of the gland that appears normal. On the other hand, in MIP the parathyroid adenoma is excised by unilateral exploration through a small cervical incision, often under local anesthesia [18]. In this surgical procedure, the role of preoperative localization of the adenoma is of crucial importance. In our case, although the size of the adenoma was enormously large, we managed to excise it through a rather small incision, following the rules of MIP. It is not obvious whether such a huge adenoma was excised in the past using minimal invasive parathyroidectomy or not.

Preoperative localization of the adenoma followed by intraoperative quality control of the surgical excision based on intraoperative serum levels of IOiPTH became the gold standard of MIP [20]. In comparison to standard bilateral neck exploration MIP is equally effective in achieving normocalcemia. In addition MIP is associated with minimal complications, shorter hospitalization, better cosmetic outcome, and, more importantly, incidence of post-operative transient hypoparathyroidism is limited to 5% [21]. This method is widely accepted and adopted by many centers specialized in endocrine surgery. The protocol is quite strict and includes blood samples before the skin incision (preoperative baseline level) and at 10 and 20 minutes after excision of the adenoma. The 20-minute sample is taken when there is a marked but inadequate drop in 10 minutes comparing to preoperative level. According to the Miami criteria, a 50% or more reduction of IOiPTH compared to the preoperative level is indicative of the removal of the adenoma [22,23]. In our case IOiPTH at 10 minutes after excision decreased at approximately 50% of the preoperative level and became normal 20 minutes after excision. Postoperatively PTH and calcium levels must be measured as in some cases

calcium supplementation is necessary in order to avoid clinical hypocalcemia [24]. In our case, postoperative hungry bone syndrome was treated successfully. Despite the fact that giant adenomas are rare, protocols of postoperative PTH sampling and hungry bone syndrome treatment are commonly described.

Giant parathyroid adenomas are considered by several authors as a distinct clinical entity with specific genomic aberrations [6].

These adenomas occur more frequently in males and their weight correlates directly to their functionality. Nevertheless, patients remain asymptomatic for a long period that allows the adenoma to grow large prior to detection. In the literature, there are very limited case reports on the topic of non-functioning giant parathyroid adenomas [25,26]. Furthermore, giant parathyroid adenomas have features similar to parathyroid carcinomas and adenomas. In relation to small adenomas, they often present MEN1 mutations, whereas in relation to carcinomas, they usually present with parafibromin expression, gain of chromosome 5 and loss of adenomatous polyposis coli immunoreactivity [27]. They also mimic carcinomas in terms of glandular size and profound hypercalcemia. Although many researchers have questioned whether giant parathyroid adenomas possess a malignant

potential, no recurrences have been noted in literature. However, it is advisable that patients with atypical adenomas attend a close follow-up [6]. In our case, although the adenoma was extremely large, no evidence of malignancy was observed.

## Conclusions

In conclusion, this is an extremely rare case of a giant solitary parathyroid adenoma. Diagnosis of such a giant hyperfunctioning solitary parathyroid adenoma is based on clinical presentation, biochemical profile, and imaging studies. Selective treatment is based on surgical excision combined with IOPTH levels measurement.

## Department and Institution where work was done

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## Conflict of interest

None.

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