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Giant parathyroid adenoma presenting with a pathological left clavicular fracture: An extremely rare case report

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ABSTRACT

INTRODUCTION: Parathyroid gland has a distinct physiologic and endocrinologic role in the body system. Primary hyperparathyroidism is the most common cause of hypercalcemia with a marked female dominance. It is characterized by hypercalcemia, hypophosphatemia and elevated parathyroid hormone. Parathyroid adenoma, parathyroid hyperplasia and parathyroid carcinoma form the differential diagnosis. Giant parathyroid adenomas are rarely symptomatic than non-giant parathyroid adenomas and parathyroid carcinoma.

CASE PRESENTATION: A 41 years old previously healthy male patient with undetectable surgical and familial history presenting with left clavicle fracture by mild trauma. He was diagnosed for primary hyperparathyroidism after the finding of multiple bony lesions and elevated serum calcium and Parathyroid hormone. Preoperative imaging aided in diagnosis of a parathyroid lesion and secondary bone resorption lesions (brown tumors). After adequate medical treatment and preparation, selective right lower parathyroidectomy was held, and the final pathology came with a giant parathyroid adenoma.

CONCLUSION: Primary hyperparathyroidism should be suspected when dealing with a hypercalcemic patient having osteolytic bony lesions. Distinguishing Parathyroid adenoma from carcinoma is a challenging and essential preoperative step in planning and surgical procedure.

1. Introduction

Since the discovery of the Parathyroid gland in 1850, its endocrine roles and pathologies have gained the attention of the previous and contemporary physicians [1]. Primary Hyperparathyroidism (PHPT) is a well-known, despite uncommon, endocrine disorder leading the causes of hypercalcemia due to autonomous functioning of 1 or more parathyroid glands. Its incidence ranges from 20 to 25 per 100,000 yearly [2]. It can be sporadic or familial (such as Multiple Endocrine Neoplasia 1 and 2A) and mostly occur in the 5–6th decade in life with female to male predominance 4:1 [3, 4)]. Many causes for PHPT exist, mostly being a solitary parathyroid adenoma (PA) (85%), while parathyroid hyperplasia (PH) (15%) and parathyroid carcinoma (PC) (<1%) account for rare causes [4]. The weight of parathyroid gland is around 60 mg when normal, 600 mg when adenomatous, and more than 3.5 g when defined as giant parathyroid adenoma (GPA) [2, 5)]. Despite it is unknown, the only defined possible etiologic factor for GPA is neck irradiation, as found among the Japanese atomic bomb survivors [2)]. With the invention of new imaging and biochemical tests, diagnosis of PA is earlier in the asymptomatic period [5]. Hypercalcemia (>10.5 mg/dL), hypophosphatemia (<2.5 mg/dL) and elevated parathyroid hormone (PTH) (>65 pg/mL) are characteristic for PHPT, and are more pronounced in cases of GPA and PC [5]. Imaging modalities such cervical U.S, Computed tomography scan, MRI and particularly Tc sestamibi scan all play a precise role in diagnosis and preoperative planning [4,5]. Selective adenoma Parathyroidectomy is the gold standard for treatment [3]. Here we present a case of a 41 years old sporadic PHPT in a previously healthy male patient who seeked medical advice for a clavicle fracture and was diagnosed for GPA. This work has been reported in line with the SCARE criteria [6].

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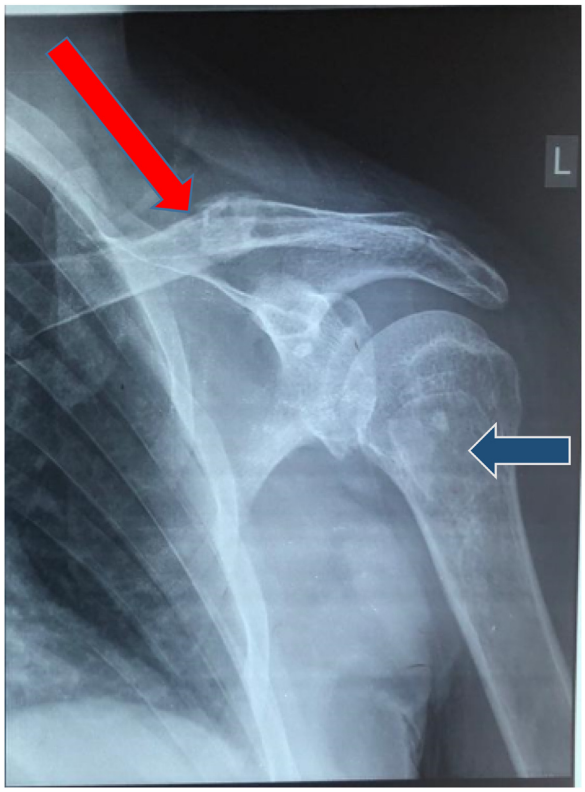

Fig. 1. Left Shoulder Xray showing the fractured clavicle (red arrow) and a humeral lesion (blue arrow).

2. Case presentation

This is a case of 41 years old previously healthy male patient with unremarkable previous surgical or family history presented to ER for a left nondisplaced clavicular fracture after a mild fall down from his height that was diagnosed on standard Xray (Fig. 1). Patient has been examined by an orthopedic and was given pain killers and shoulder immobilizer arm sling. Due to repeated pain on his left shoulder, a CT scan for left clavicle was performed one month later showing the presence of multiple osteolytic bone lesions at the level of the scapula, humerus and acromial bone. A large well delineated mass was seen on the right thoracic inlet extended posterior to and separated from the right thyroid gland, esophagus and trachea measuring 4.5 × 2.7 × 2.4 cm (Fig. 2). Cervical and thorax MRI of was performed for further details showing more bones affected like the vertebras L1 and T12 suggestive of metastatic bone disease of unknown primary tumor with normal tendinous and muscular systems, left humeral head lesion (Fig. 3) and right lower cervical mass same described by CT scan, with no local invasion (Fig. 4A–C). Fine Needle Aspirate was taken from the right retro thyroidal mass showing tumoral cellular proliferation of endocrinoid aspect. Biopsy from the left clavicular bony lesion was performed noting a brown tumor. A Tc99 m Sestamibi scintigraphy (Fig. 5) showed a large right hyperfunctioning parathyroid adenoma, and no ectopic lesions. Full labs were ordered marking a high Ca = 13.9 mg/dL (Normal: 8.5–10.5 mg/dL) and PTH = 1388 pg/mL (Normal: 25–65 pg/mL), an insufficient Vit D of 15.2 ng/mL (Normal: >30 ng/mL), and normal thyroid function tests. Patient was diagnosed with primary hyperparathyroidism due to a giant palpable right lower pole parathyroid adenoma. He received intravenous fluids and diuretics to relief his near threatening hypercalcemia then followed on oral loops diuretic (Lasix 20 mg once daily) and vitamin D (cholecalceferol 10,000 IU daily). CT scan Abdomen and pelvis was obtained to search for any associated endocrine anomaly showed normal parameters. After having a serum calcium of 11.6 mg/dL and perfectly consulting his endocrinologist and surgeon,

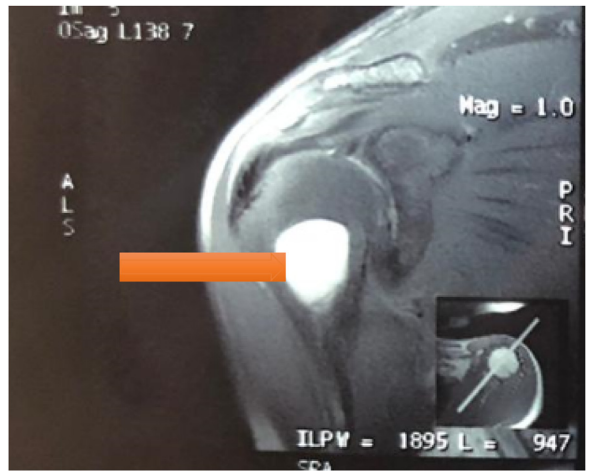

Fig. 3. Left shoulder MRI detailing the humeral lesion (orange arrow).

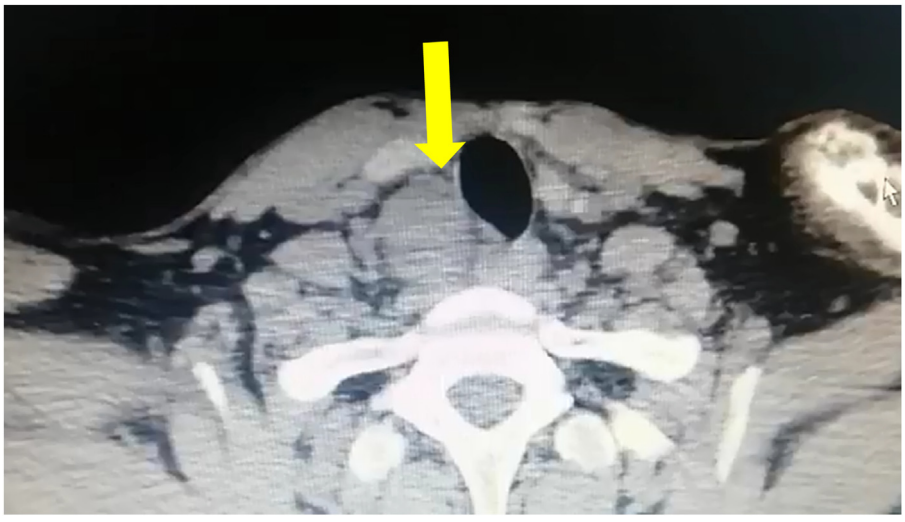

Fig. 2. Cervical CT scan with IV contrast marking the right parathyroidal lesion (yellow arrow).

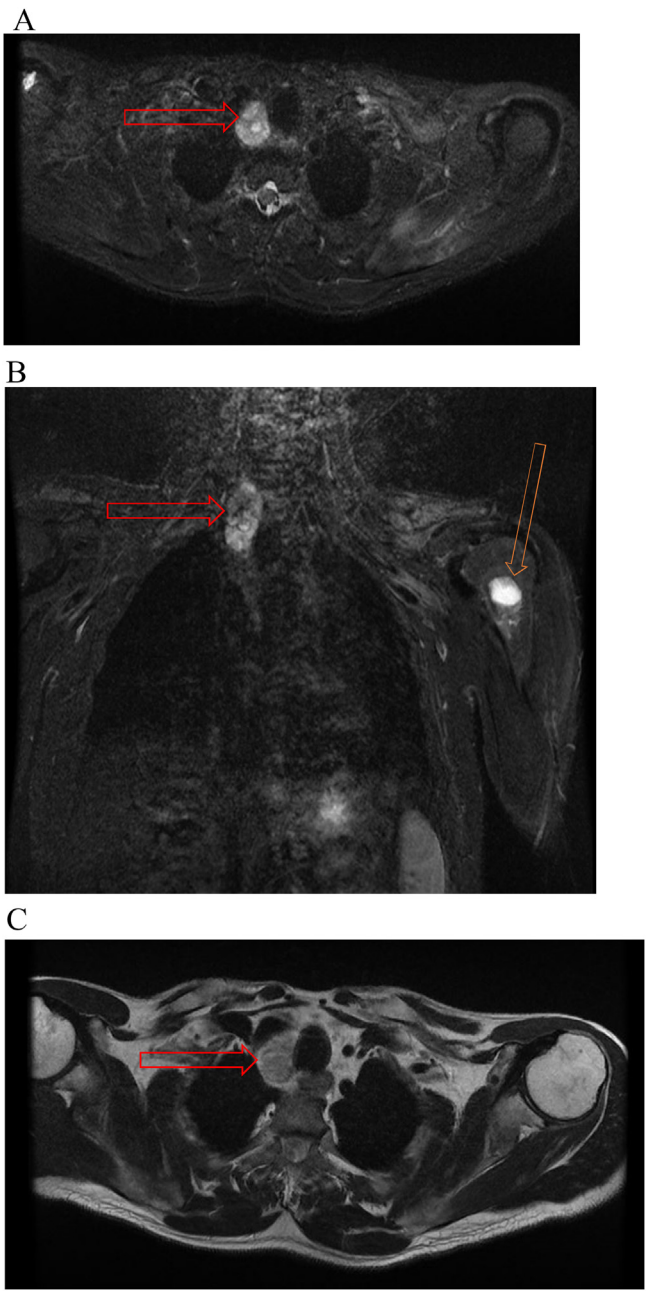

Fig. 4. A. Coronal MRI T2 showing the right lower parathyroid adenoma (red arrow).
B. Frontal MRI T2 View showing the right inferior Parathyroid Gland (red arrow) and the left humeral lesion (orange arrow).
C: Coronal MRI T1 Mode showing the right inferior parathyroid gland (red Arrow)

he was planned for right lower parathyroidectomy with a sufficient medical treatment 1 month before surgery (alendronate 30 mg/day and calcitriol 2 micro-g/day). Right lower parathyroidectomy with hemi thyroidectomy was done since the mass can't be successfully separated from the right thyroid gland, preserving the recurrent laryngeal nerve and major vessels. PTH was taken from the right internal jugular vein 10 min post excision and reached 341 pg/mL. The right lower parathyroid adenoma 5 × 2 × 3 cm weighing 30 g and thyroid gland were sent to pathology (Fig. 6A and B). Patient had an uneventful postoperative course, PTH reached 12 pg/mL 2 days after excision, patient was discharged on calcium and alfacalcidol Vit D supplements over two months for having mild asymptomatic hypocalcemia (Ca = 7.5 mg/dL). Pathology result came with a parathyroid adenoma and no signs of malignancy (Ki67 = 3%). Follow up at out clinics was done, calcium and PTH were normalized and his wound healed perfectly.

3. Discussion

Counting on the interesting physiology of Parathyroid gland, PTH raises serum calcium levels by promoting bone resorption, decreasing urinary calcium excretion and stimulating the hydroxylation of 25 hydroxycholecalciferol into 1, 25 dihydroxy cholecalciferol that in turn increase the calcium absorption from the intestine [1]. PHPT due to non-giant PA usually present with asymptomatic hypercalcemia and elevated PTH, these parameters are more pronounced and lesser symptomatic in GPA as studies showed [5]. Adults present symptoms in 20% of cases as myalgia and fatigue, bone pain, arthralgia, constipation, kidney stones and psy-

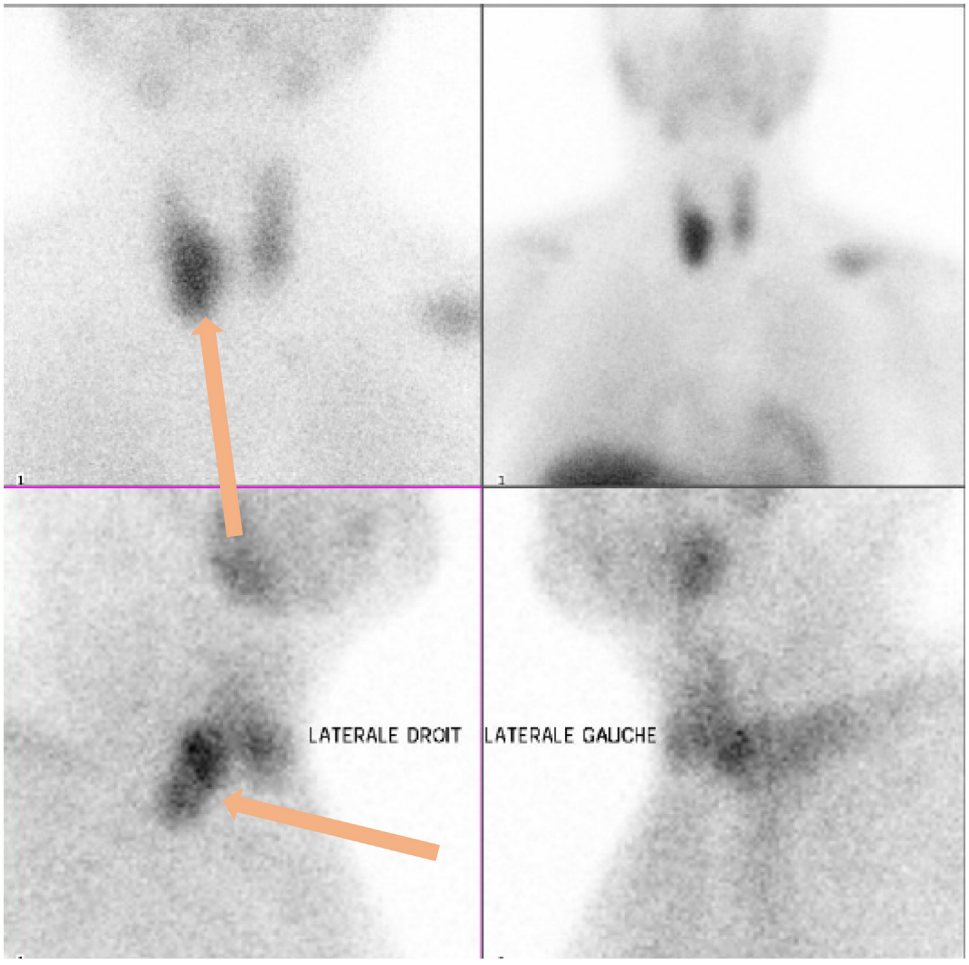

Fig. 5. 99 m Technitium sesstamibi scan with increased uptake at the right parathyroid gland (pink arrow), AP and Lateral Views.

chiatric disorders [1,7]. The weight of the encountered PA ranged from 600 mg to 110 g with Power et al. and 145 g with Cacmak et al, with most cases weighing 2–10 g [8,9]. Etiologies for parathyroid neoplasms are basically unknown, neck irradiation and chronic kidney disease are found to be risk factors [9].

Besides the biochemical laboratory tests, diagnosis of parathyroid pathology is carried out through multiple ways by radiologic imaging and biopsy. Cervical Ultrasound (CUS) imaging is accurate in detecting lesions above 1 cm and is the first modality held while suspecting parathyroid lesions [9], as well as showed higher accuracy in detecting GPA than PA [5]. 99 m Tc sesstamibi scan uses technetium 99 m isotope for localizing cells having inherent high metabolic activity as in case of parathyroid gland, showing same accuracy in detecting GPA and non-giant PA [5], and higher one when combined with CUS. Both showed minimal benefit in differentiating PA from PC [9]. Cervical Computed Tomography (CT) scan and MRI are accepted when the above modalities fail to adequately delineate the diseased parathyroid, they can assess the presence of local or distant spread when present, determine any recurrence, and are useful in cases having prior neck surgery [5,9]. CT scan showed a higher accuracy in detecting GPA than non-giant PA [5]. When PC is diagnosed postoperatively, a complete metastatic workup must be carried out through whole body CT scan, FDG-PET scan and MRI [9].

FNA biopsy is usually disliked when suspecting PC by imaging and by laboratory tests, because it is insufficient in differentiating between PA and PC and it has a risk for tumor seeding along the needle tract. However, it may be used in cases of recurrent or metastatic disease [9]. Differentiating PC than PA is a crucial preoperative step, for it determine the adequate operative procedure. PC present usually with markedly elevated serum Calcium level (>14 mg/dL), 10–15 times the normal high PTH titer, and palpable neck mass with hoarseness [9]. The maximal PTH amount stated in literature is 1220 pg/mL and was due to PC [10]. Moreover, MRI and CT scan showed to be more efficient than U.S and 99 mTc sesstamibi in differential diagnosis of PA and PC. Pathologically, PA appear to be soft, flat, rounded, and brick-red colored, while PC appear grayish and characterized histologically by vascular/capsular invasion, trabecular meshwork and mitotic figures, and fibrotic adhesions. These histologic characteristics of PC are described as Schantz/Castleman criteria for distinguishing PC from PA [9]. In the absence of these criteria besides a low ki-67 on immunohistochemistry, the lesion is suggestive for GPA [11].

Some studies showed that 1–2% of PHPT patients present with a life threatening parathyroid storm, first described in 1923, that is characterized by signs of severe hypercalcemia (>14 mg/dL) and signs of multi organ failure. This preoperative necessitate hospitalization for Intravenous fluids, loop-diuretics and bisphosphonates [10]. Selective parathyroidectomy with intraoperative PTH measuring is the gold standard in treating PHPT [3].

Skeletal osteolytic lesions, termed osteitis fibrosa cystica, rarely appear in PHPT cases, and are mistaken with bone malignancies as in the present case. These lesions may reach the axial and appendicular skeleton, are caused by overactive bone resorption, and are symptomatic in 5% of cases; causing bone pain and/or fractures [12]. Presence of such lesions besides the increased age

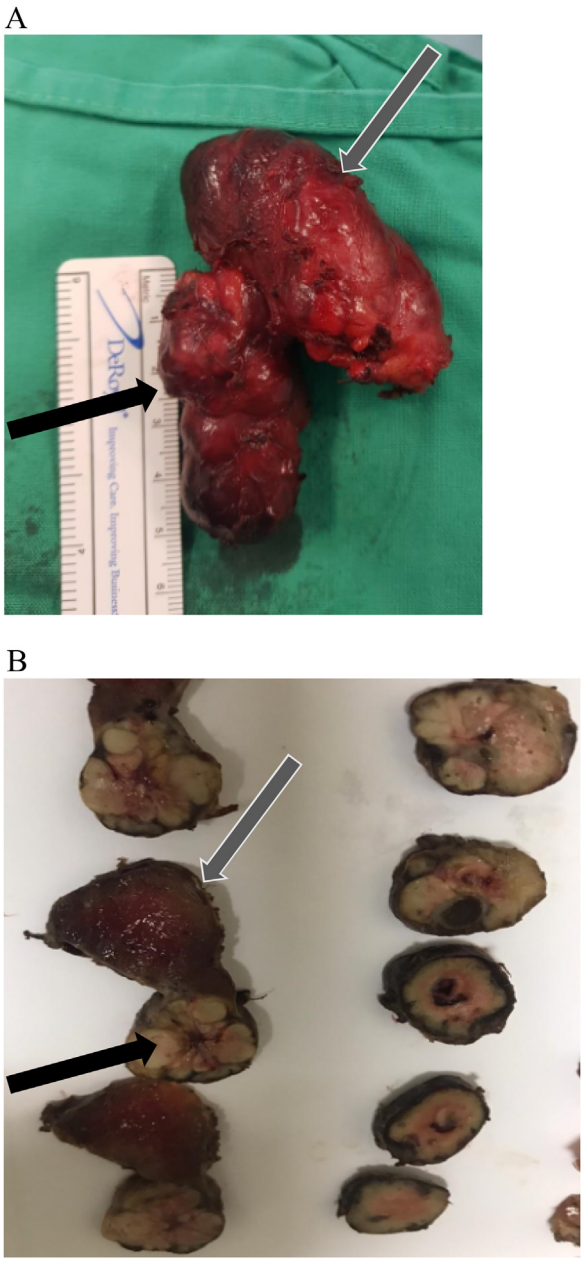

Fig. 6. A. Right Parathyroid gland specimen 5 × 2 × 3 cm (black arrow) attached to the right thyroid gland (gray arrow).
B. Transverse sectioning of the specimens in the anatomy-pathology lab, parathyroid (black arrow) and thyroid (gray arrow).

and size of parathyroid lesion, low vitamin D status and high preoperative serum Calcium and PTH increase the risk for developing postoperative hungry bone syndrome (HBS) [13]. It occurs in 13–30% in post-parathyroidectomy patients and is due to rapid remineralization of the demineralized bone lesions, and is described by a prolonged (>4 days) hypocalcemia (<7.5 mg/dL) along with neuromuscular signs and symptoms despite adequate IV calcium and Active vitamin D treatment (3). Hypophosphatemia, hypomagnesemia and suppressed PTH level are also associated [13]. This threatening postoperative complication can be managed acutely by IV calcium and active vitamin D, and can be prevented by preoperative bisphosphonates, calcitonin, and vitamin D in patients having insufficiency or deficiency, and oral calcium intake [9,13].

This case of a 41 years old male patient having multiple bone lesions that were thought to be metastatic disease with unknown primary tumor was diagnosed with PHPT with secondary brown tumors. The mass was seen well-delineated on neck MRI and CT scan. FNA biopsy was done preoperatively to rule out any metastatic disease especially after noting the osteolytic bone lesions. Adequate preoperative medical preparation to normalize the severely elevated serum calcium and to prevent the HBS postoperatively. The interesting findings in this patient are: 1) being a male (where females are 4 times more prone than males), 2) asymptomatic high serum calcium level approaching the levels seen in PC, 3) epic presentation of the previously healthy patient by a clavicle fracture, and 4) the highest seen PTH amount (1388 pg/mL) in PHPT due to GPA in English literature.

4. Conclusion

Despite the well-studied physiology of parathyroid gland and its endocrine role, PHPT can be an indolent disease that must be suspected when dealing with a hypercalcemic patient especially when associated with bone lesions. Due to advent of new diagnostic and screening criteria, PHPT becomes almost asymptomatic. Even if it is delicate and challenging, preoperative differentiation between PA and PC are crucial in any PHPT patient. Adequate preoperative medical treatment is recommended for preventing postoperative HBS for its acute life threatening complications.

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Ethical approval

The study type is exempt from ethical approval

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Writing the paper, Study Concept: Houssam Khodor Abtar, Jad J Terro, Etienne El-Helou. Data collection, Study Concept: Rayyan El Lakkis, Abbass Shibli, Mohammad Ahmad Al Raishouni, Elias El-khoury, Hammam Farhat. Supervision: Houssam Khodor Abtar.

Registration of research studies

1. Name of the registry: N/A
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Declaration of Competing Interest

This article has no conflict of interest with any parties.

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