

## Rare And Demanding: Parathyroid Adenoma Localization, Surgery And Outcome. Self Experience With 8 Cases

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### ABSTRACT

**Objectives:** We report our experience with parathyroid adenoma localization and surgical removal

**Patients and methods:** Between June 2017 and June 2019, we had operated 8 cases of parathyroid adenoma. Three patients were males and 5 patients were females. Age ranged from 26 year old to 72 year old with average of 42 year old.

**Results:** preoperative localization was achieved in 7 patients (87%) and intraoperative localization in one case (13%). Seven cases (87%) were sporadic while one case was part of MEN2a. Single adenoma was found in 6 patients (75%) and two adenomas in two patients (25%). The adenomas were located in the neck in 7 patients ( 87%) and in the anterior mediastinum in one patient ( 13%). Surgical removal of the adenomas was done without difficulties in all the cases through a neck incision in 7 cases and midline sternotomy in one patient. All the patients had resolution of symptoms within the follow up period.

**Conclusion:** parathyroid surgery is one of the challenging procedures, but with adequate localization and technique, the outcome can be excellent for the patient.

**Keywords:** Multiple Endocrine Neoplasia -Parathyroid Adenoma- Parathyroid hormone - Sestamibi scan.

### نادرة ومتطلبية: عقد الغدد جار الدرقية، تحديد الموقع، الجراحة والنتائج. خبرة شخصية في ثمان حالات

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### الخلاصة

**الاهداف:** لتوثيق خبرتنا الشخصية في التعامل مع عقد الغدد جار الدرقية من حيث تحديد الموقع، التداخل الجراحي والنتائج.  
**المواد والأساليب:** ما بين حزيران ٢٠١٧ وحزيران ٢٠١٩، قمنا بإجراء عمليات رفع عقد الغدد جار الدرقية لثمان مرضى، ثلاثة من الذكور وخمس من الإناث، تراوحت اعمارهم بين ٢٦ و٧٢ عاما بمعدل ٤٢ عاما  
**النتائج:** تم تحديد موقع العقد قبل التداخل الجراحي في سبعة مرضى (٨٧%) فيما تم تحديد الموقع داخل العملية في مريض واحد (١٣%). سبعة مرضة كانت حالاتهم فردية (٨٧%) في حين كانت جزءا من متلازمة MEN2a في مريض واحد (١٣%).  
في ستة مرضى (٧٥%) وجدنا عقدة واحدة بينما وجدنا عقدتين اثنتين في مريضين (٢٥%).  
كانت العقد موجودة في الرقبة في سبعة مرضى (٨٧%) في حين كانت موجودة في الصدر خلف عظم القص في مريض واحد (١٣%). تم استئصال العقد في جميع المرضى بدون صعوبات عن طريق جروح في الرقبة في سبعة مرضى وفتح صدر في مريض واحد. تحسن جميع المرضى بعد العملية خلال فترة المتابعة.  
**الاستنتاجات:** التداخلات الجراحية في الغدد جار الدرقية تمثل تحديا حقيقيا للجراح ، ولكن باتباع الطرق السليمة لتحديد الموقع قبل العملية وتوفر المهارة الجراحية اللازمة تكون النتائج ممتازة للمريض.

**الكلمات الرئيسية:** متلازمة الاورام الهرمونية، عقد الغدد جار الدرقية، هرمون الغدة جار الدرقية، فحص سيستامبيبي.

## INTRODUCTION

The parathyroid glands are endocrine glands that are situated in the neck in close relation to the posterior surface of the thyroid gland. Usually they are four in number divided into 2 superior glands located close to the upper part of the thyroid and 2 inferior glands that are more variable in anatomical position due to the longer pathway in embryological life<sup>1</sup>

The glands secrete parathyroid hormone which is crucial in calcium homeostasis by increasing reabsorption of calcium in the kidneys, intestinal absorption of calcium and release of calcium from bones. The main regulator for parathyroid hormone (PTH) secretion is the calcium level in the blood, where decrease in serum calcium will stimulate PTH release while a rise in the level will inhibit the secretion by negative feedback. Increase in serum PTH can be primary due to parathyroid gland adenoma, hyperplasia or less commonly carcinoma, or it can be secondary to low levels of serum calcium as in cases of renal failure, and the term tertiary hyperparathyroidism describes hyperplasia of the parathyroid glands in long standing secondary hyperparathyroidism.<sup>1,2</sup>

Parathyroid adenomas are the most common cause of primary hyperparathyroidism, accounting for about 80-85% of the causes, while adenoma of two glands occurs in 4-5%, and in about 10% of the cases 4 glands hyperplasia is the main pathology. Parathyroid carcinoma occurs in less than 1%. The age range for developing adenoma is between 50 and 70 year old with females being affected about 3 times than males.<sup>2,3</sup>

Hyperparathyroidism will lead to hypercalcaemia, which can be asymptomatic or may cause bone pain, fatigue, renal stones, psychological upset, abdominal cramps and constipation.<sup>1</sup>

Once hyperparathyroidism is confirmed by laboratory investigations, the next step should be imaging of the glands to determine the cause. Ultrasonography is usually the initial investigation. An adenoma is characteristically homogeneously hypo echoic compared to the thyroid tissue and usually a feeding vessel will be seen entering the adenoma in Doppler ultrasonography. The adenoma is usually separated from the thyroid capsule.<sup>4,5</sup>

The gold standard for preoperative parathyroid adenoma localization is with technetium-99m (99mTc) Sestamibi scan. It can also be combined with single photon emission computed tomography (SPECT) imaging to increase the accuracy in localization.<sup>6,7</sup> CT and MRI are also used in preoperative localization. Four-dimensional CT and MRI may have a more beneficial role in localizing ectopic glands<sup>8</sup>

Since a single parathyroid adenoma is responsible for 80-85% of cases of primary hyperparathyroidism, a selective parathyroidectomy is now the surgical procedure of choice, historically, surgeons used to remove all the 4 glands.<sup>9,10</sup>

## MATERIALS AND METHODS

Between June 2017 and June 2019, we had operated 8 cases of parathyroid adenoma. Three patients were males and 5 patients were females. Age ranged from 26 year old to 72 year old with average of 42 year old.

## PRESENTATION

Seven of the 8 patients had symptomatic hypercalcaemia, with fatigue and generalized body aches as the main symptom (87%), renal stones (75%) and psychological upset mainly in form of depression in 50%. Chronic abdominal pain rather than urological was found in 37%.

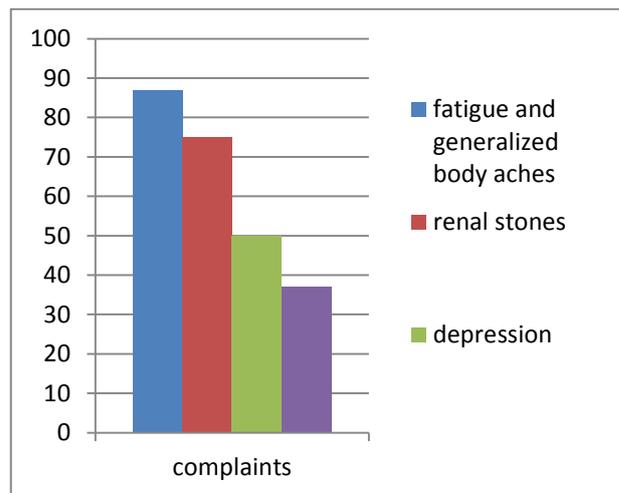


Figure 1: complaints of the patients with hypercalcaemia

In one patient the only presentation was a high parathyroid hormone level with multiple bony lesions misdiagnosed to have metastatic deposits in the vertebrae and bony pelvis. (Figure2)

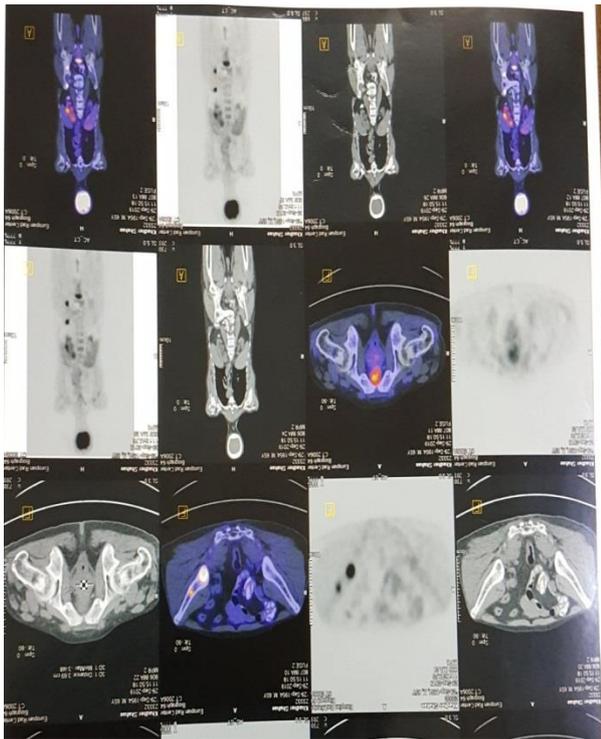


Figure2 : PET scan showing multiple osteolytic lesions involving multiple vertebrae and bony pelvis

Two of our patients presented with pathological fractures before diagnoses (Figure3).



Figure 3: pathological fracture in a 26 year old patient

## WORK UP AND LOCALISATION

After laboratory confirmation of the elevated PTH, Sestamibi scan was done (outside Iraq) in 4 patients preoperatively (50%) (Figure 4).

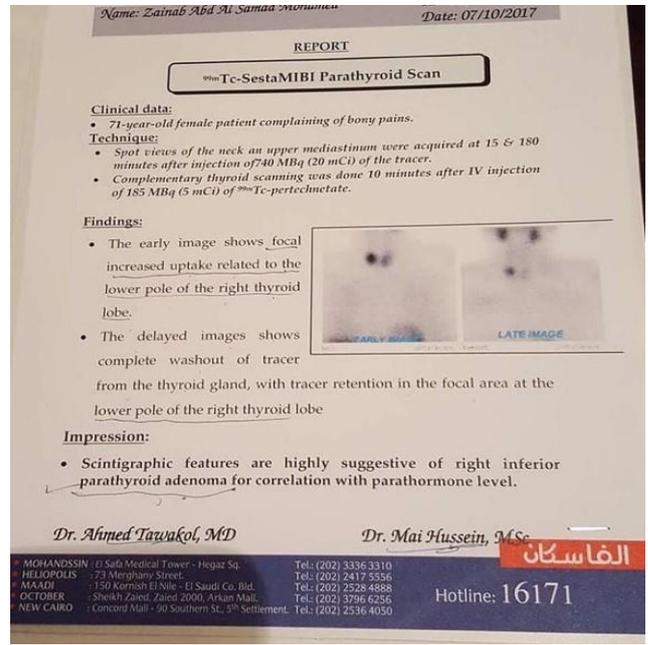


Figure 4: Sestamibi scan for pre-operative localization of the adenoma

In 2 patients, preoperative localization was achieved by MRI and CT scan, and by ultrasonography only in one patient (figure5), and in one patient intraoperative localization was done.

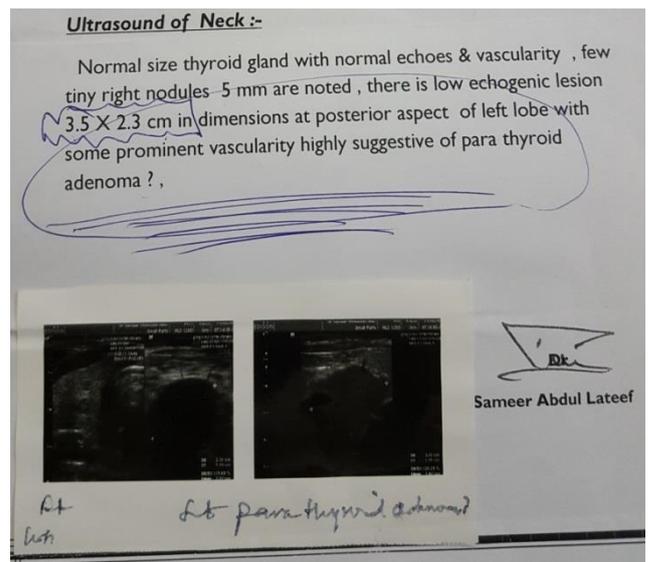


Figure 5: pre-operative localization by ultrasonography

In 7 patients the adenomas were located in the neck and were related to the inferior border of the thyroid gland, in one patient the adenoma was confirmed by CT scan to be located in the anterior mediastinum (Figure6)

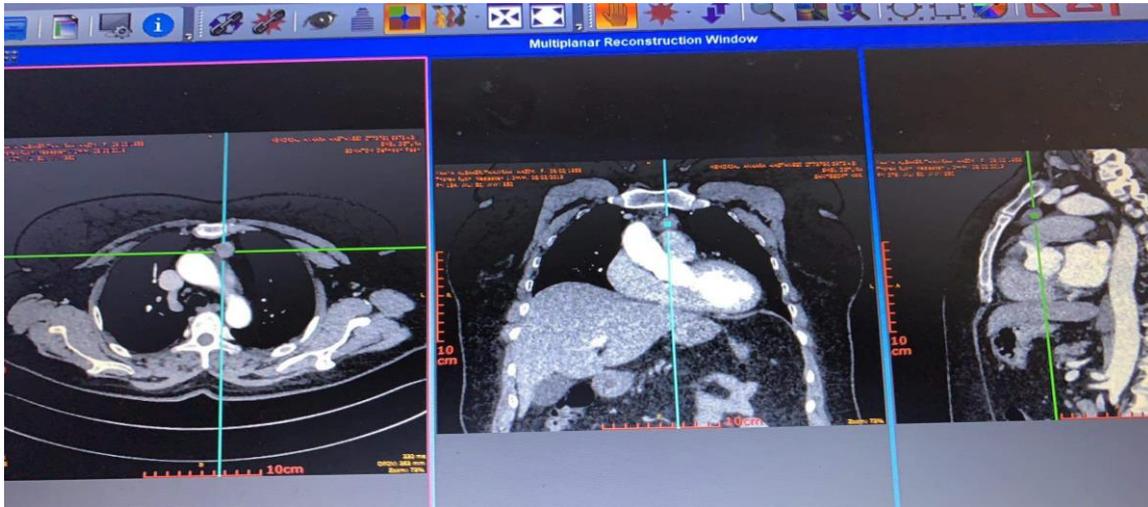


Figure 6: CT scan showing the adenoma located in the anterior mediastinum near the manubrium sterni

Single adenoma was found in seven patients (87%) and two adenomas in one patient (13%). In all patients, work up to exclude familial syndromes, namely multiple endocrine neoplasia (MEN) 1 and 2a was done including abdominal CT to exclude pancreatic and adrenal masses and neck CT to exclude medullary thyroid cancer, in one patient there was an adrenal mass and a thyroid mass, and work up revealed pheochromocytoma and medullary thyroid cancer (MEN2a) (figure7).

**OPERATIVE FINDINGS**

Depending on the preoperative localization, a neck collar incision was used in 7 patients, Single adenoma was found in 5 of them and two adenomas in 2 patients (Figures 7and 8)

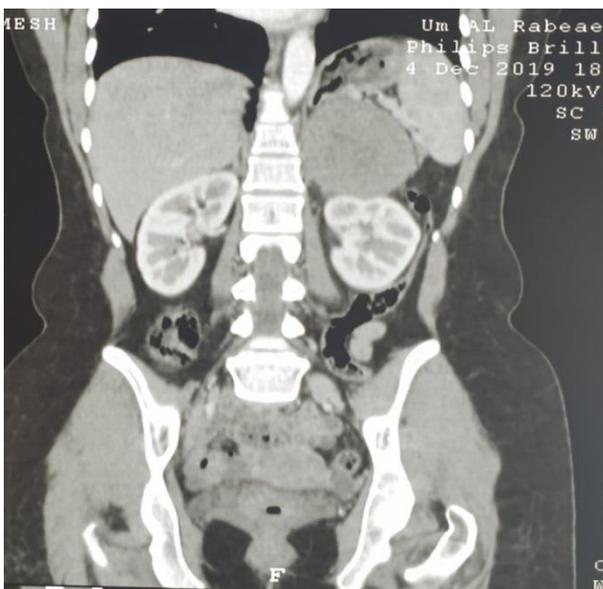


Figure 7: pheochromocytoma found in one of the patients (together with a medullary thyroid cancer MEN2a)

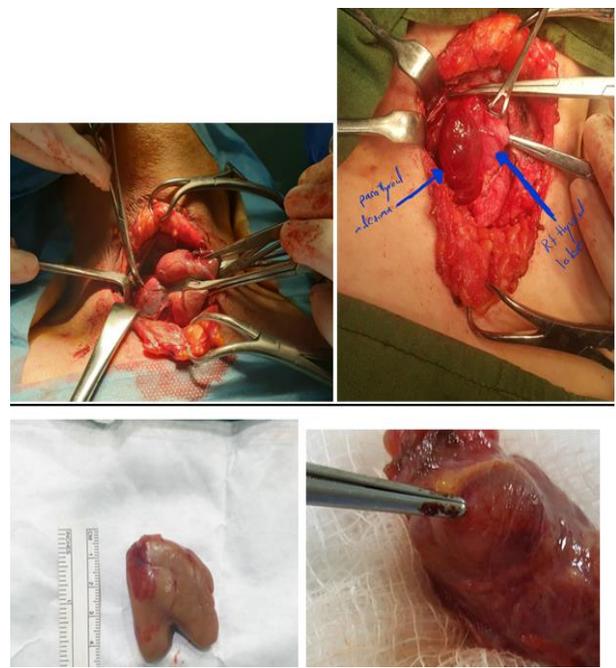


Figure 7: A single parathyroid adenoma was found in 75% of the patients



Figure 8: Two adenomas found in 25% of the patients

In one patient in whom the adenoma was located in the anterior mediastinum, a midline sternotomy was used for removal. (Figure 9)

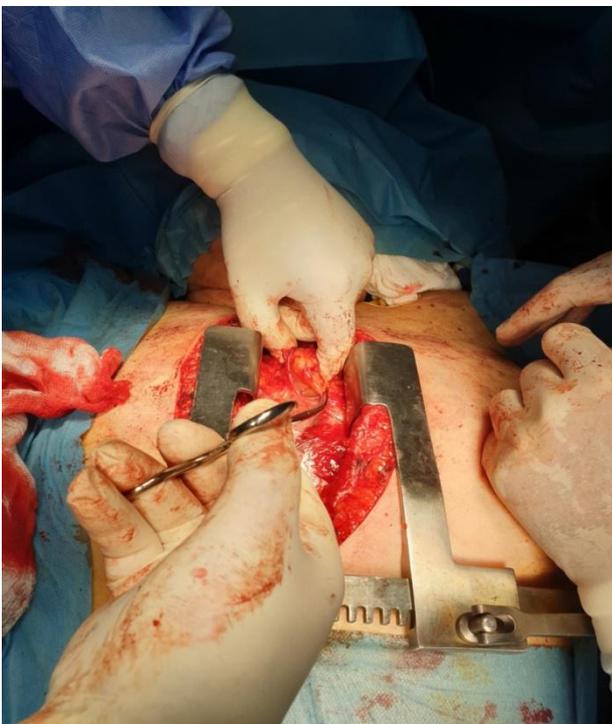


Figure 9: A midline sternotomy for removal of the parathyroid adenoma

Surgical removal of the adenomas was done without difficulties in all the cases including one patient in whom pre-operative imaging studies could not find the pathology, during exploration an adenoma of 12 mm was found in the usual position and was removed.

A blood sample was taken in all the cases before and 10 minutes after the excision of the adenoma to confirm the drop in parathyroid hormone level which was observed significantly ( 62-93%) in all the cases (Figure 10)

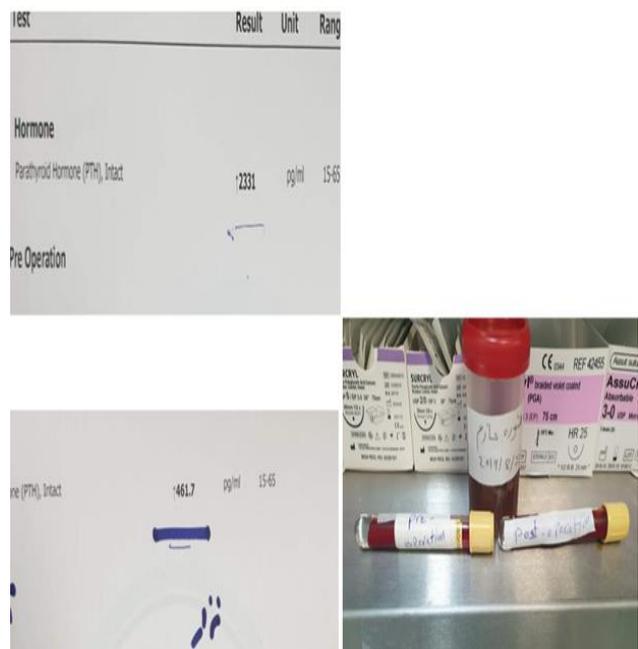


Figure10: laboratory confirmation of the drop in PTH level after excision of the adenoma was done in all cases

We had one case of MEN2b, The patient was prepared and surgical removal of the adrenal mass was performed 1<sup>st</sup> to be followed later on by total thyroidectomy and excision of the adenoma in one session.

All the patients had a smooth postoperative course and were discharged 24 hours after the operations.

**OUTCOME AND FOLLOW UP**

The histopathological reports of all the patients confirmed the diagnoses of parathyroid adenoma(Figure 11)

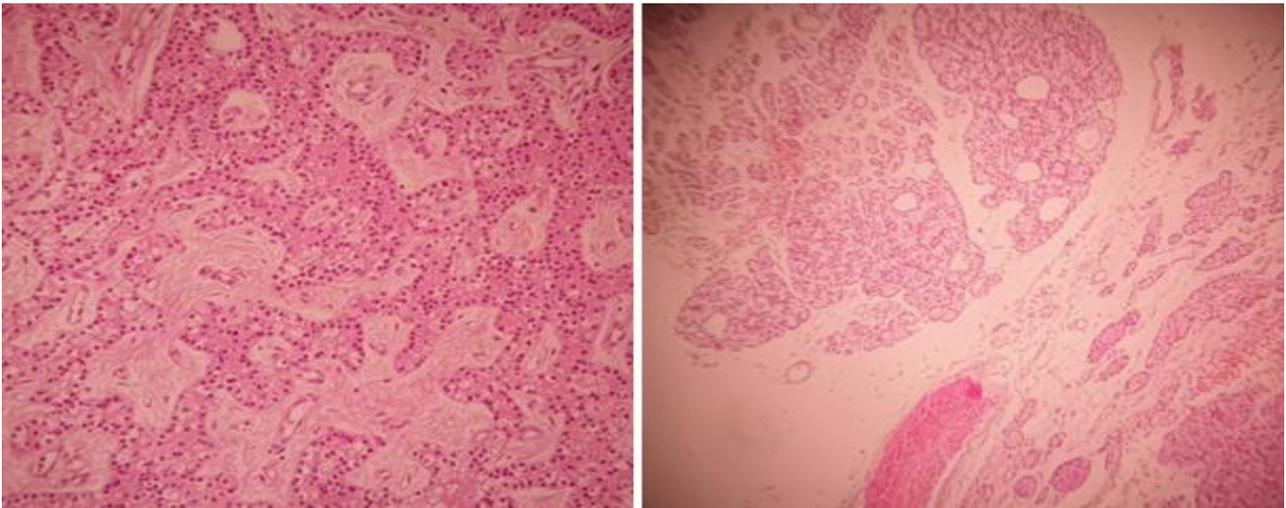


Figure 11: Histological appearance of the adenoma

We followed our patients for a period ranging from 1-3 years, with regular visits and investigations. All the patients had resolution of symptoms within the follow up period. All had normal parathyroid hormone levels, two patients developed hypocalcaemia that required oral supplementations, and one patient had hoarseness of voice because of unilateral recurrent laryngeal nerve injury documented by laryngoscopy that required 10 months for complete recovery.

## DISCUSSION

The diagnosis of parathyroid adenoma is not always straight forward. Some patients may have the adenoma without having any manifestation especially in early stages. In most of the cases, the presentation will be that of hypercalcaemia.<sup>1-3</sup> In our patients, the main presenting symptoms were fatigue and generalized body aches, recurrent nephrolithiasis, depression and mood changes, recurrent fractures and bony lesions, abdominal colicky pain and constipation. After confirming high level of serum calcium, all patients were sent for serum PTH assessment. Some of the referred patients had normal PTH and were referred back to their physicians to look for other causes of elevated serum calcium like malignancies, drugs and other medical conditions.

In our 8 patients, there was a high PTH and the diagnoses of primary hyperparathyroidism were made. The next step was to determine the cause, we started by ultrasonography for all the patients. The reported sensitivity of ultrasonography in detection of parathyroid pathologies ranges from 16-79% in most of the literatures<sup>11</sup>, while the accuracy in detecting single lesion is 72% to 89% in most studies.<sup>11,12</sup> In our series, Ultrasonography was successful in localizing only one case with certainty (13%), in the rest of the cases, it was unable to locate the pathology. In

these cases, our next step was CT scan and MRI, which located the adenoma in another 2 patients (25%), while the reported sensitivities in most of the literatures are 35-75% and 40-85% respectively.<sup>11,12</sup>

The gold standard for preoperative parathyroid adenoma localization is with technetium-99m (99mTc) Sestamibi scan, which can also be combined with single photon emission computed tomography (SPECT) imaging to increase the accuracy in localization.<sup>6,7</sup> Four of our patients had the chance to perform the Sestamibi scan outside the country, which was able to precisely locate the adenoma in all of them (100%) including one case of ectopic parathyroid adenoma behind the sternum. A previous study have compared Sestamibi scan and ultrasonography in pre-operative localization of the adenomas found no difference between the two methods, especially when done by an expert radiologist.<sup>13</sup> We think that the rarity of parathyroid pathologies makes our radiologists more hesitated in reporting the findings with certainty.

Historically, the standard surgical approach was bilateral cervical exploration with removal of the 4 glands with a cure rate more than 90%. After that, and since a single adenoma was found to be the cause of 80-85% of cases of primary hyperparathyroidism, the approach of selective or focused parathyroidectomy emerged as the standard of care with many advantages including less post-operative hypocalcaemia, less incidence of other complications and easier and shorter operations<sup>14</sup> This approach requires an accurate pre-operative localization, but even with negative pre-operative localization, the surgeon will be able to locate the pathology intra-operatively in most of the cases, we had one case with primary hyperparathyroidism in whom imaging studies (other than Sestamibi scan) could not locate the adenoma, which was easily seen during the operation to be located behind the lower lobe of the thyroid and was easily removed.

Miami criteria says that there should be a drop in serum level of PTH of 50% and more 10 minutes after excision of the causative adenoma<sup>15</sup> We depended on that to ensure the accuracy of our procedures, blood samples were taken from all the patients immediately before and 10 minutes after surgical excision and sent for laboratory analysis which documented a drop in the level of 62-93%. This was extremely helpful especially in our patient who had a negative pre-operative localization .

The histopathological reports of all the patients confirmed the diagnoses of parathyroid adenoma, chief and oxyphilic cell type, there was no atypia or malignancy in any of the patients and the surgical excision margins were free in all of them.

After 1-3 years of follow up and regular monitoring of serum calcium and PTH level, all our patients are having improvement of their complaints and normal laboratory findings. Two patients developed hypocalcaemia that required oral supplementations, and one patient had hoarseness of voice because of unilateral recurrent laryngeal nerve injury documented by laryngoscopy that required 10 months for complete recovery.

Brown's tumor is a term used to describe the osteolytic lesions that occurs in the bones, especially ribs, clavicle and pelvis of patients with hyperparathyroidism, especially primary hyperparathyroidism<sup>16</sup>, sometimes it may be mistaken for secondary bone metastasis as in our case. Postoperatively, here was dramatic resolution of these lesions within months of follow up.

## CONCLUSION

parathyroid surgery is one of the challenging procedures, but with adequate localization and technique, the outcome can be excellent for the patient.

The ideal method of localization is the Sestamibi scan, unfortunately it is not available in our country in the meantime, other imaging studies might be of help like ultrasonography and CT scan.

Selective parathyroidectomy of the causative adenoma is the procedure of choice with less complications but we need to confirm the drop in PTH level after the excision.

## REFERENCES

1. Policeni BA, Smoker WRK, Reede DL . Anatomy and embryology of the thyroid and parathyroid glands. *Semin Ultrasound CT MR.* 2012; 33:104–114.
2. Edafe O, Collins EE, Ubhi CS, Balasubramanian SP. Current predictive models do not accurately differentiate between single and multi gland disease in primary hyperparathyroidism: a retrospective cohort study of two endocrine surgery units. *Ann R Coll Surg Engl.* 2018 Feb;100(2):140-145.
3. Mizamtsidi M, Nastos C, Mastorakos G, Dina R, Vassiliou I, Gazouli M, Palazzo F. Diagnosis, management, histology and genetics of sporadic primary hyperparathyroidism: old knowledge with new tricks. *Endocr Connect.* 2018 Feb;7(2):R56-R68.
4. Kelly HR, Hamberg LM, Hunter GJ . 4.D-CT for Preoperative Localization of Abnormal Parathyroid Glands in Patients with Hyperparathyroidism: Accuracy and Ability to Stratify Patients by Unilateral versus Bilateral Disease in Surgery-Naïve and Re-Exploration Patients. *AJNR Am J Neuroradiol.* 2014 Jan;35(1):176-81.
5. Mizamtsidi M, Nastos C, Mastorakos G, Dina R, Vassiliou I, Gazouli M, Palazzo F. Diagnosis, management, histology and genetics of sporadic primary hyperparathyroidism: old knowledge with new tricks. *Endocr Connect.* 2018 Feb;7(2):R56-R68.
6. Raruenrom Y, Theerakulpisut D, Wongsurawat N, Somboonporn C. Diagnostic accuracy of planar, SPECT, and SPECT/CT parathyroid scintigraphy protocols in patients with hyperparathyroidism. *Nucl Med Rev Cent East Eur.* 2018;21(1):20-25. [PubMed]

7. Prabhu M, Damle NA. Fluorocholine PET Imaging of Parathyroid Disease. *Indian J Endocrinol Metab.* 2018 Jul-Aug;22(4):535-541.
8. Parikh AM, Suliburk JW, Morón FE. Imaging localization and surgical approach in the management of ectopic parathyroid adenomas. *Endocr Pract.* 2018 Jun;24(6):589-598.
9. Mourad M, Buemi A, Darius T, Maiter D. Surgical options for primary hyperparathyroidism. *Ann. Endocrinol.* 2015 Oct;76(5):638-42.
10. Bilezikian JP, Cusano NE, Khan AA, Liu JM, Marcocci C, Bandeira F. Primary hyperparathyroidism. *Nat Rev Dis Primers.* 2016 May19;2:16033.
11. Ruda JM, Hollenbeak CS, Stack BC Jr. A systematic review of the diagnosis and treatment of primary hyperparathyroidism from 1995 to 2003. *Otolaryngol Head Neck Surg* 2005; 132:359–372.
12. Solorzano CC, Carneiro-Pla DM, Irvin GL 3rd. Surgeon-performed ultrasonography as the initial and only localizing study in sporadic and primary hyperparathyroidism. *J Am Coll Surg* 2006; 202:18–24.
13. Haber RS, Kim CK, Inabnet WB. Ultrasonography for preoperative localization of enlarged parathyroid glands in primary hyperparathyroidism: comparison with (99m) technetium sestamibi scintigraphy. *Clin Endocrinol.* 2002 ; 57:241–249
14. Udelsman R , LinZ , Donovan P. The superiority of minimally invasive parathyroidectomy based on 1650 consecutive patients with primary hyperparathyroidism *Ann Surg.* 2011;253:585-591
15. Mourad M, Buemi A, Darius T, Maiter D. Surgical options for primary hyperparathyroidism. *Ann. Endocrinol.* 2015 Oct;76(5):638-42.
16. Pérez-Guillermo M, Acosta-Ortega J, García-Solano J, Ramos Freixá J. Cytologic aspect of brown tumor of hyperparathyroidism. Report of a case affecting the hard palate. *Diagn Cytopathol.* 2006;34:291---4.