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Case Report

Persistent Hyperparathyroidism due to Parathyroid Adenoma after Initial Parathyroidectomy

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Abstract:

Persistent hyperparathyroidism (HPT) is defined as the development of hypercalcemia within 6 months of the first parathyroid operation, whereas hypercalcemia presenting after an interval of 6 months is termed recurrent HPT.

A 43year old woman with persistent parathyroid adenoma with bilateral nephrocalcinosis following left lower parathyroidectomy. Initially, she was referred to a urologist for lower abdominal pain and urinary symptoms. Upon further evaluation, she was diagnosed with bilateral nephrocalcinosis, secondary to hypercalcemia caused by a left lower parathyroid adenoma.

She underwent a left lower parathyroidectomy. Despite initial improvements, the patient's PTH levels remained elevated during postoperative follow-up, indicating persistent hyperparathyroidism. Further imaging and biochemical investigations were performed, leading to the decision for a second surgery. A re-exploration of the neck was performed, during which the hyperfunctioning parathyroid tissue was identified and excised. Postoperatively, her PTH and calcium levels normalized. In this case the intra operative PTH level decreases more than 50% , and also frozen section biopsy showed positive for parathyroid tissue . There has been no post operative hypocalcemia is developed. Though PTH level initially within normal range but in post operative follow up 2 months after 2nd operation her S. PTH level was raised but normal calcium level.

Keywords*: Persistent hyperparathyroidism, parathyroid adenoma, primary hyperparathyroidism*

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Introduction:

Primary hyperparathyroidism causes one or more of the four parathyroid glands to secrete excessive amounts of parathyroid hormone (PTH). In most of the cases, parathyroid adenoma is the cause[1].

Other causes of elevated serum PTH, such as mild secondary hyperparathyroidism from renal insufficiency, renal calcium leak, gastrointestinal disorders, vitamin D deficiency, and other rare conditions, must also be considered[2].

A detailed family history is required to screen for familial disease. Patients with familial hypocalciuric hypercalcemia (FHH) typically have mild, asymptomatic elevations in serum calcium, hypocalciuria and normal to mildly elevated PTH levels. In contrast, those with MEN1 usually develop primary hyper-parathyroidism before age 30 and are more prone to persistent or recurrent disease[3].

A benign tumor, parathyroid adenoma is typically sporadic and more prevalent in women than in men (3:1). Although it can happen at any age, most cases happen in the 50s and 60s. Patients usually have high serum calcium and parathyroid hormone levels as indicators of primary hyper-parathyroidism[4].

The primary clinical manifestations of persistent hyperparathyroidism (PHPT) affect the skeleton and kidneys. Key symptoms include bone pain, skeletal deformities, and an increased risk of fractures at various skeletal sites. In rare cases, PHPT may first present as rickets or osteomalacia, often accompanied by short stature[5].

The parathyroid gland or glands can be removed to treat primary hyper-parathyroidism. Prior to surgical progression, patients should have their serum calcium, parathormone, and bone density monitored[6].

Parathyroid surgery is the only curative treatment for PHPT, with a success rate of 95-97% in experienced hands. However, persistent or recurrent PHPT occurs in 2.5-10% of cases.[7] A larger risk of post-operative hypocalcaemia and recurrent laryngeal nerve damage (OR 0.33) is linked to wider cervical dissection[8].

Patient profile:

A 43 year old woman with persistent parathyroid adenoma with bilateral nephrocalcinosis who underwent left lower parathyroidectomy on 1/12/2022. Initially the patient was referred to urologist due to pain in the lower abdomen and increase frequency and urgency of micturition. She was diagnosed as a bilateral nephrocalcinosis due to parathyroid adenoma on left side.

Investigations:

Before operation her **Serum-parathormone** level was 836.9 pg/ml (reference range 10-65 pg/ml), **serum calcium**14.1 mg/dl (reference range 8.5-10.5 mg/dl).

parathyroid scintigraphy reveals scan positive for parathyroid adenoma/ hyperplasia (left lower).

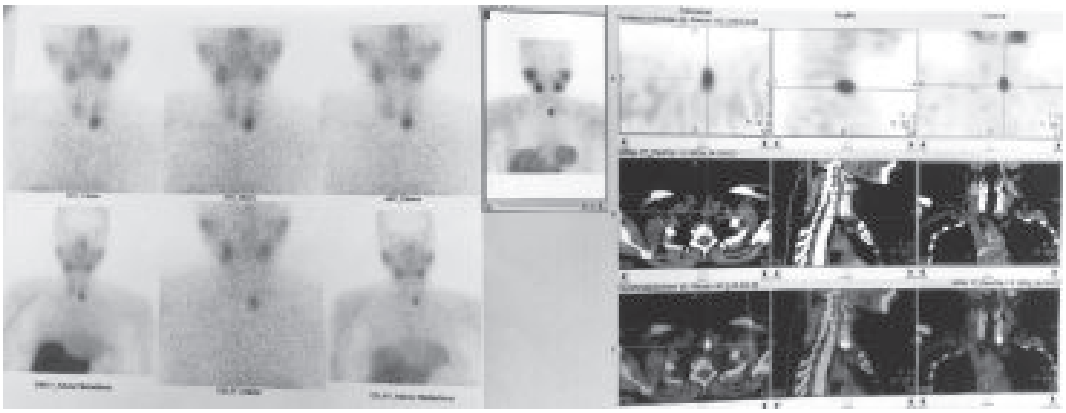

Fig.-1: Parathyroid scintigraphy showing parathyroid adenoma / hyperplasia in left lower part

These findings were concerning for a single parathyroid adenoma of left inferior gland. The patient underwent a parathyroidectomy on left lower part with the utilization of intraoperative PTH monitoring. (table I)

Her parathormone representing more than 50 % drop from the initial value(pre incision) which gives false impression.

Her histopathological report reveals reactive lymphadenitis .no parathyroid gland is seen. Post operative PTH and calcium levels during outpatient follow up were raised. As her biochemical report was raised, she required second surgery for persisting adenoma . For these reason she again admitted to BSMMU. Repeat laboratory Investigations were obtained (Table II)

Table I

Results of intraoperative PTH levels

	S PTH (pg/ml)	Reference range (pg/ml)
Pre incision	1352	10-65
1 hr after incision	565.3	10-65
After operation	237.8	10-65

Table II

Result of biochemical blood test

Blood parameter	Case	Normal range
S. calcium	2.9 mmol/L	2- 2.6 mmol/L
S. PTH	1060 pg/ml	10- 65pg / ml
S. inorganic phosphate	2.1 mg /dl	2.4 – 5.1 mg /dl
Vitamin D	8.79ng/ml	20-50 ng/ml
S. phosphate	2.3 mg/dl	2.5-5 mg/dl
Urine calcium in 24 hr	5.4 mg / day	100-300 mg/day
Phosphate urine in 24 hr	195.6 mg/dl	300-1000 mg / dl

Pre operative workup with an **ultrasonogram of neck** reveals hypervascular nodule at Lt parathyroid location, nodule size = 0.8×1.24×1.9 cm

HRCT scan of neck reveals suggestive of parathyroid adenoma at lower pole region of left lobe of thyroid with mild superior mediastinal extension.

Parathyroid scintigraphy shows scan positive for parathyroid adenoma / hyperplasia. Thyroid gland is normal in size and position. Focal area of increase radiotraced concentration is seen in the lower pole of left thyroid bed with homogenous radiotracer concentration in rest of thyroid gland.

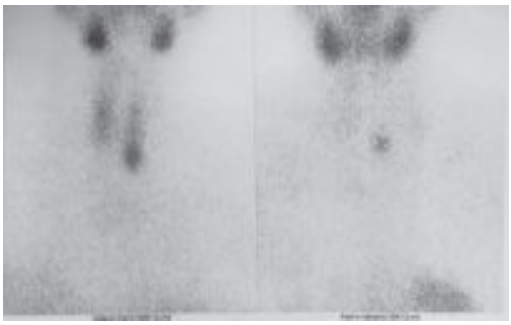

Fig 2: parathyroid scintigraphy showing parathyroid adenoma near lower pole of left thyroid gland .

Intervention:

In department of Otolaryngology -Head and Neck surgery, BSMMU,she underwent surgical excision of left lower parathyroid gland.

Table III

Pre, Per, Post operative parathyroid hormone, s-calcium level :

		S. PTH	S. Calcium
Pre operative		1060 pg/ml	3.62 mmol/l
Per operative	-Before incision	977.8	
	-After excision of medial and lateral part	604.4 pg/ml	
	-after excision of inferior and central part	95.7 pg/ml	
	-After surgery	41.2 pg/ml	
Post operative	1st Post operative day	3.68 pg/ml	2.41 mmol/l
	2nd post operative day		2.27 mmol/L

Frozen section biopsy:

1. Tissue from medial to lower pole of Left thyroid lobe: Tissue positive for parathyroid gland
2. Tissue from lateral to lower pole of left thyroid lobe: soft tissue containing small lymph node
3. Tissue from inferior to lower pole of left thyroid lobe: tissue positive for parathyroid gland
4. Tissue from central compartment: fatty tissue, small lymph node

Post operatively she exhibited no sign or symptoms of hypocalcemia and was deemed safe for discharge.

Outcome and Follow up:

We follow up the patient 2 months later,

On 3/ 4/24 =

-s. PTH = 231 .1 pg/ml (reference range = 15-65 pg/ml)

- s. calcium : 8.7 mg/dl (reference range : 8.5-10.5 mg/dl)

- USG of thyroid = cyst in right lobe of thyroid gland

(multiple tiny cystic area noted in right lobe of thyroid gland, largest one measuring about 0.2×0.2 cm)

On 25/09/24=

- iPTH = 72.1pg/ml (reference range = 11-67 pg/ml)
- s. calcium = 8.9 mg/dl (reference range = 8.5-10.5 mg/dl)

Discussion:

PHPT is a frequent endocrine disorder with a 4:1 female to male ratio and a prevalence rate of 0.1–1%[5].

Parathyroid adenoma is a surgical disease. Proper localization of parathyroid adenoma is prime importance. Preoperative localization is routinely undertaken to facilitate localized surgery and thereby increase the cure rate, decrease perioperative complications and operating time[9,10].

Non-invasive imaging methods consist of 4 dimensional CT (4D-CT), parathyroid scintigraphy with 99m technetium sestamibi (RN), ultrasound (US), and infrequently magnetic resonance imaging (MRI).[11]

When sestamibi and ultrasound results are negative or inconsistent, 4D CT should be taken into consideration as it can detect over half of the aberrant parathyroids that are overlooked by conventional imaging[11].

Consequently, to localize the lesion in such clinical situations, invasive tests are frequently required. Parathyroid venous sampling (PVS), an angiographic treatment that is most frequently performed on patients who have had prior neck surgery that resulted in scarring and obliteration of tissue planes, is the most ubiquitous invasive inquiry. These modifications result in a higher probability of surgical failure and a higher risk of recurrent laryngeal nerve injury. PVS samples the veins that drain the parathyroid glands at several locations to identify a unilateral PTH gradient[12].

The American Association of Endocrine Surgeons (AAES) states that intraoperative PTH monitoring should be performed in addition to pre-operative imaging modalities when performing targeted parathyroidectomy, with cure rates ranging from 97 to 99%[13].

A carefully planned operative procedure, often employing additional adjuncts is critical. In reoperative neck surgeries, a lateral approach is often used, involving dissection between the medial border of the ipsilateral sternocleidomastoid muscle and the lateral border of the strap muscles[14].

Intraoperative PTH level monitoring and frozen section biopsies were carried out during the index procedure. The likelihood of leaving behind hyper-functioning parathyroid tissue was reduced by assessing PTH levels before excision, five minutes after excision, ten minutes after excision, and by looking for a larger than 50% decrease in PTH from baseline and from pre-excision. The Miami and Vienna criteria, which give surgeons a quantitative threshold for finishing (or continuing) a surgery after removing a worrisome parathyroid lesion, were both satisfied by the PTH levels assessed from the index case. The Miami and Vienna criteria, at 97.3% and 92.3%, respectively, have the best overall accuracy among the available criteria[13].

Patients with persistent or recurrent 1°HPTH as well as those who develop HPTH after previous cervical surgery are far more complicated than their unexplored counterparts. Surgeons who perform reoperative procedures must have a high degree of experience to interpret discordant

preoperative imaging studies and plan for operative intervention. The surgeon often relies upon sophisticated intraoperative adjuncts to locate and resect hyperfunctioning parathyroid glands while minimizing collateral injury. Postoperative management requires experience and attentive responses to prevent and/or treat potentially life threatening complications.

In this case the intra operative PTH level decreases more than 50%, and also frozen section biopsy showed positive for parathyroid tissue . There has been no post operative hypocalcemia is developed. Though PTH level initially within normal range but in post operative follow up 2 months after 2nd operation her S. PTH level was raised but normal calcium level.

Conclusion:

This case highlights the challenges of persistent hyperparathyroidism following an initial parathyroidectomy for a parathyroid adenoma. Early recognition, accurate diagnosis, and careful surgical planning are essential to successfully manage such cases and prevent further complications.Re-exploration surgery, guided by advanced imaging and careful technique remains a viable solution for addressing residual or recurrent disease.

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