



BIOCHEMICAL WITH NORMAL PARATHYROID HORMONE : A CASE REPORT

Endocrinology

Shikhil Puzhakkal Associate Consultant, Dept of Endocrine surgery, Baby Memorial Hospital.

Farhana Chathoth Kannoli Consultant, Dept of Pathology, Baby Memorial Hospital.

Anoop Kumar Consultant Dept of Critical care, Baby Memorial Hospital.

Pradeep Puthen Veetil* Senior Consultant, Dept Of Endocrine Surgery, Baby Memorial Hospital.
*Corresponding Author

ABSTRACT

Normo-hormonal primary hyperparathyroidism (NPHPT) is an uncommon condition which has been increasing in last decade. This milder biochemical entity remains incompletely understood due to lack of long term health outcomes regarding management. NPHPT poses two challenges to the surgeon, first is when to operate and second is the use of intra-operative parathyroid hormone assay to predict the success of surgery. Here we present a 53 year old lady who came with low back ache of more than 2 years duration. It is found to have elevated calcium levels and on further evaluation found to have high normal parathyroid hormone levels in two occasions. Pre operative localization studies were done by suspecting normo-hormonal hyperparathyroidism which showed concordant lesions in both ultrasound neck and Sestamibi scan. She underwent focused parathyroidectomy with intra-operative parathyroid hormone levels which dropped in to less than 30pg/ml. Postoperative calcium was within normal limits and she was symptomatically better. In patients with symptoms of hypercalcemia, elevated calcium levels and high normal intact parathyroid hormone levels should be considered as inappropriate and should lead to the suspicion of normo-hormonal hyperparathyroidism. Intra operative parathyroid hormone levels below 30pg/ml can be utilized as an indicator of successful operation in normo-hormonal hyperparathyroidism. In symptomatic hypercalcemic patients, even if the parathyroid hormones are high normal, a further investigation should be done to locate the parathyroid adenoma and surgery is the best cure.

KEYWORDS

Normo-hormonal Hyperparathyroidism, Parathyroid hormone, Hypercalcemia, Intra operative parathyroid hormone Assay

INTRODUCTION

Primary hyperparathyroidism is a common endocrine problem whereas normo-hormonal primary hyperparathyroidism (NPHPT) is less known. NPHPT is diagnosed by symptomatic hypercalcemia with high normal parathyroid hormone levels. Incidence of this condition has been increasing in last decade. This milder biochemical entity remains incompletely understood due to a lack of long term health outcomes regarding management. NPHPT poses two queries to the surgeon, first is when to operate and second is the use of intra operative parathyroid hormone assay to predict the success of surgery.

Case Description:

We present a 53 year old lady who is diabetic on oral hypoglycemic agents, came with low back ache of more than two years duration. Symptoms were progressive and persistent in nature despite any treatment. She also had arthralgia, fatigue and on further examination found to have proximal myopathy. She was moderately built and nourished and no neuro-cutaneous markers were seen. Her neck and abdominal examinations were unremarkable. All other systems were normal. Biochemically she had hypercalcemia (corrected calcium – 11.9 mg/dl) (Normal range 8.5-10.0 mg/dl) and hypophosphatemia of 2.5 mg/dl (Normal range 3.0-4.5 mg/dl). Her vitamin D was normal and parathyroid hormone levels (PTH) were high normal (64 pg/ml and 61 pg/ml) (Normal range -15-65 pg/ml) in two different occasions with normal creatinine levels (Table 1). Her parathyroid hormone related peptide (PTHrP) was in normal range 10 pg/ml (Normal range 11-20 pg/ml). As she had symptomatic hypercalcemia with high normal PTH, normohormonal hyperparathyroidism (NPHPT) was suspected and proceeded with localization studies. Ultrasound of neck was done which showed 27x14x6 mm well circumscribed hypoechoic solid lesion corresponding to left inferior parathyroid lesion.

Parathyroid scintigraphy (Sestamibi) also showed possibility of left inferior parathyroid lesion (Figure 1). As she had concordant imaging, focused parathyroidectomy was planned with intra operative parathyroid hormone (IOPTH) assay. Intra operatively she had normal left inferior parathyroid gland. There was a descended left superior parathyroid lesion of size 27x14x10mm with antero-medially placed left recurrent laryngeal nerve. Left superior parathyroid lesion was excised and sent for histopathology examination (HPE). IOPTH after 20 minutes of excision was done which dropped to 12pg/ml from baseline of 64pg/ml. Post operative period day one calcium was 9.1mg/dl. Immediate post operative day she felt better and had no

symptoms of hypocalcemia. Her histopathology reported as parathyroid adenoma (Figure 2). She was on follow up for last 6 months and she was asymptomatic and her calcium was within normal limits.

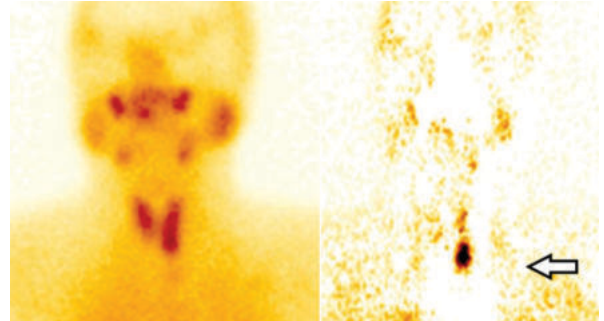


Figure 1: Sestamibi Showing Left Inferior Parathyroid Lesion

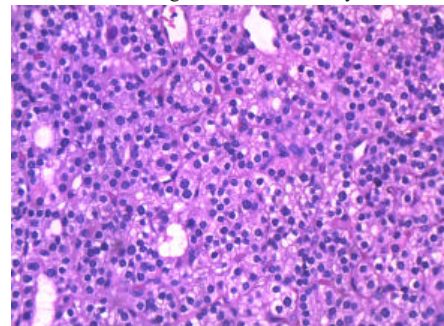


Figure 2: Microscopy Showing Abundant Chief Cells With Adipocytes - Parathyroid Adenoma

Table – 1 Laboratory Investigations

Hormones	Levels	Normal range
S. calcium(corrected)	11.9mg/dl	8.6-10 mg/dl
Parathyroid hormone (PTH)	64 pg/ml and 61 pg/ml	15-65 pg/ml
Vitamin D	31.9 ng/ml	20-50ng/ml
Alkaline phosphatase (ALP)	117 IU/ml	42-98 IU/ml

S. Creatinine	0.9 mg/dl	0.7-1.2 mg/dl
S. Phosphorous	2.5mg/dl	3.5-4.5 mg/dl
PTH related protein (PTHrP)	10pg/ml	11-20pg/ml
Intra operative parathyroid hormone (IO PTH)	12pg/ml	15-65 pg/ml
Post operative Corrected calcium DAY1	9.1 mg/dl	8.6-10 mg/dl
At 6 months corrected calcium	8.9 mg/dl	8.6-10 mg/dl

Biochemical investigations

DISCUSSION

Primary hyperparathyroidism (PHPT) can be classified in to classical, normocalcemic or normohormonal primary hyperparathyroidism (NPHPT) according to biochemical reports. Prevalence of classical PHPT is 0.23% among women and 0.08% among men (1). NPHPT is uncommon since the disease is diagnosed in its early stage. It is defined as hypercalcemia (corrected calcium of > 10.5mg/dl) and normal PTH levels less than 65pg/ml(2). Incidence of NPHPT varies in literature, recent studies showed prevalence up to 22.5% (3). In NPHPT there will be normal but non suppressed PTH levels. Wallace and colleagues suggest that these patients show a lower PTH set point. Others pointed out that pulsatile PTH secretion, PTH related peptide (PTHrP) (Both are excluded by repeating the PTH level and normal PTHrP), target tissue resistance to PTH, Post translational modification of PTH molecule as explanation for this phenomenon(4).

Clinical features of NPHPT is similar as in classical PHPT. Renal and bone involvement are more common in subset of mild PHPT as per studies(4). One of the differences with mild PHPT is that, there had been increased involvement of multi glandular disease (MGD), whereas single adenoma is common in patients with hypercalcemia and inappropriately normal PTH(4). This is pointed to the fact that, in a case of mild PHPT, bilateral neck exploration may be done or should have a low threshold for converting to bilateral neck exploration depending up on intra operative findings or IOPTH results. As per Goasguen and colleagues, mild pre operative elevation of calcium or PTH levels should warn about the risk of small adenoma and should expect intra operative difficulties(5). Because of smaller adenoma there was lower sensitivity of pre operative imaging in NPHPT patients. Over 50% has negative pre-operative nuclear localization test requiring 4-gland surgical exploration. The intra-operative drop in PTH below 30 pg/ml can be utilized as an indicator of a successful operation(6).

Parathyroidectomy should be strongly considered in NPHPT. Histopathology was in accordance with the literature. The frequency of parathyroid hyperplasia was high, but not the proportion as compared to Classical PHPT. The weight of adenoma was low (7).

CONCLUSION

Patients with elevated serum calcium levels with normal PTH levels do not eliminate Primary hyperparathyroidism. Associated low phosphorus in some cases possibly makes the diagnosis easy. In mild PHPT IOPTH below 30pg/ml can be utilized as an indicator of successful operation in NPHPT.

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