



## Atypical Presentations of Primary Hyperparathyroidism

Authors

P.M. Prasanna Kumar<sup>1</sup>, Rajanala Madhu<sup>2</sup>, T.J. Prasanna Kumar<sup>3</sup>

<sup>1</sup>General Surgery Department, NRI General Hospital, Mangalagiri, Guntur District

Andhra Pradesh, 522503, India

Email: [anjiiam4u@gmail.com](mailto:anjiiam4u@gmail.com)

### Abstract

Primary hyper parathyroidism [PHPT] is a common endocrine disorder associated with increased serum calcium due to over secretion of Parathormone [PTH]. The early presentations of patients with PHPT were dominated by those with Osteitis fibrosa cystica [OFC], Brown tumors of the long bones and associated subperiosteal bone resorption, distal tapering of the clavicles and the classical 'salt and pepper' erosions of the skull were typical findings. Over 80% of patients had associated renal stones, significant neuromuscular dysfunction and muscle weakness. This led to the traditional mnemonic of 'bones, stones, abdominal groans, and psychiatric overtones'. Symptoms usually include neuromuscular weakness, fatigue, decreased concentration, and memory loss. Patients can also be presented with muscle and joint pains, peptic ulcers. The current pattern of clinical presentation of PHPT shifts from the classical symptomatic form to the asymptomatic form that the majority of the patients are now identified incidentally on routine biochemical investigations. In our institute there were 3 cases presented atypically with symptoms not related to PHPT although not suspected initially complete investigative workup revealed a solitary parathyroid adenomas with co existing PHPT.

**Keywords:** Primary Hyperparathyroidism, Parathormone, Osteitis Fibrosa Cystica, Hyperparathyroidism jaw tumor syndrome, Parathyroid adenoma.

### Introduction

Primary hyperparathyroidism [PHPT] is a common endocrine disorder associated with increased serum calcium due to over secretion of Parathormone [PTH]<sup>[1]</sup>. PHPT prevalence is approximately 0.5%, while it shows no gender predisposition. PHPT occurs at any age group, affects 1 in 500 in females and 1 in 2000 males. It is most commonly seen in people over the age of 50 years and post menopausal woman, where as in 12-28 years is less than 5%<sup>[2],[3]</sup>.

The early presentations of patients with PHPT were dominated by those with osteitis fibrosa

cystica. Brown tumors of the long bones and associated subperiosteal bone resorption, distal tapering of the clavicles and the classical 'salt and pepper' erosions of the skull were typical findings<sup>[4]</sup>. Over 80% of patients had associated renal stones, significant neuromuscular dysfunction and muscle weakness. This led to the traditional mnemonic of 'bones, stones, abdominal groans, and psychiatric overtones'<sup>[3][4]</sup>.

The underlying etiology of PHPT is most commonly caused by a solitary Parathyroid adenoma accounting for approximately 80% of cases. However in a small number of (2-4%) there

are double adenomas. Parathyroid hyperplasia is caused by an increase of parenchymal mass within all the parathyroid glands, and it accounts for 4-15% of cases. It may occur in a sporadic fashion or it can be familial (MEN type 1 or type 2A, hyperparathyroidism -jaw tumor syndrome (HPT-JT) in nature<sup>[1][5]</sup>. The incidence of acute pancreatitis associated with hyperparathyroidism is less than 10%, and the incidence of hyperparathyroidism associated with a Brown tumor is less than 5%<sup>[5]</sup>.

Known risk factors for primary hyperparathyroidism include abnormalities of the PRAD1, MEN1, and HRPT2 genes that encode for cyclin D1, Menin, and Parafibromin, respectively, and radiation exposure to the neck, especially during childhood<sup>[6]</sup>.

Although a common reason for developing PHPT, are parathyroid adenomas may rarely present clinically with palpable neck mass <10%, with raised serum calcium, Parathormone, nephrolithiasis, nephrocalcinosis occur <20%<sup>[5]</sup>.

Symptoms usually include neuromuscular weakness, fatigue, decreased concentration, and memory loss. Patients can also be presented with muscle and joint pains, peptic ulcers<sup>[4]</sup>.

The current presentation of PHPT shifts from the classical symptomatic form to the asymptomatic and unusual form that the majority of the patients are now identified incidentally on routine biochemical investigations.

#### **Gestational primary hyperparathyroidism [GPHT]**

GPHT is a rare condition with fewer than 200 cases reported<sup>[8]</sup>. A 26 year old woman with 32 weeks of gestation presented with complaints of acute onset of pain in upper abdomen radiating to back and thoracic region and vomiting. There was no history of prior neck irradiation, neck surgery and radioisotope administration. She had neither suffered from renal calculus disease nor been incidentally diagnosed with in the past. On examination, her findings were consistent with that of acute pancreatitis with tachycardia and abdominal tenderness which was maximal in the

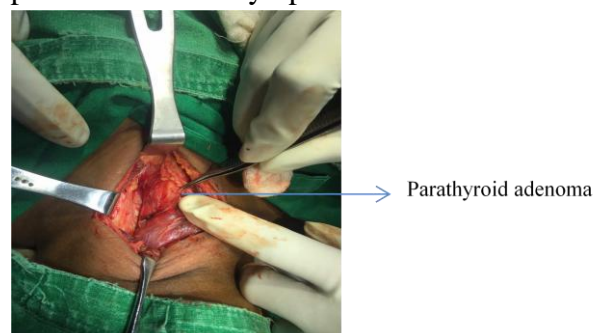
epigastric region, fundal height corresponding to 34 weeks of gestation.

#### **a. Investigations**

On Ultrasound [US] of abdomen reveals bulky, heterogenous echotexture of pancreas, mild hepatomegaly & minimal ascites. MRCP features are suggestive of acute interstitial pancreatitis. Serum calcium levels are 16.4 mg/dl, Serum intact PTH 265.9 pg/ml. On US of neck – well defined mixed echogenic lesion posteroinferior to left lobe of thyroid – probably parathyroid adenoma. Parathyroid Tc99M-Sestamibi scan: Well defined parathyroid adenoma in the region of the lower pole on the left side of the thyroid gland. No evidence of ectopic parathyroid tissue was found.

#### **b. Treatment**

After thorough discussion of risks, benefits, and to prevent the maternal and fetal complications of hypercalcaemia we have done left inferior Parathyroidectomy. HPE report – the tumor cells exhibit perivesicular as well as trabecular growths pattern. There is moderate pleomorphism in cells and plenty of giant cells scattered among the tumor cells. There are two populations of chief cells and oxyphilic cells, there is fat infiltrating into stroma, all are suggestive of parathyroidadenoma. Postoperative period was uneventful for the patient, with decline in calcium (9.5 mg/dl), while her (PTH) levels returned within normal limits approximately 8 h after surgery. She was discharged on the 6th day, while at 36 week she a delivered a healthy female child with no complications. 3 month follow up she reported no further symptoms.



**Fig. 1** shows excision of left parathyroid adenoma through left thyroid incision.

### Hyperparathyroidism jaw tumor [HPT-JT] Syndrome

The presence of excessive parathyroid hormone over stimulates osteoclast which, in turn, leads to an increase in bone turnover with bone resorption predominating over bone formation, resulting in the rarefaction of bone<sup>[9]</sup>. The changes in bone are substantial with the cortical thickness decreasing and cortical porosity increasing, along with the occurrence of cystic and fibrous nodule formation known as 'Brown tumors'. Osteoclasts and blood pigments accumulate and line the cysts, imparting a reddish-brown hue. This designation as a tumour is a misnomer as it is not a true neoplasm. The marrow may be replaced by vascularized fibrous tissue and osteoclast-like giant cells. There may be multiple brown tumours that may arise in the pelvis, ribs, clavicles, spine, and extremities<sup>[5] [9]</sup>.

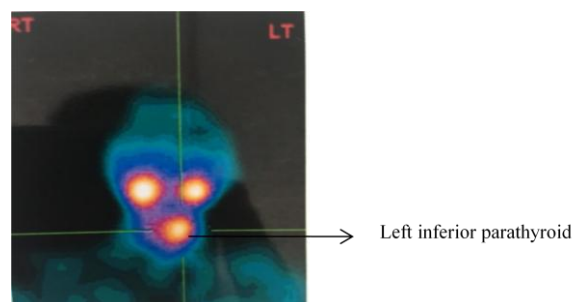
A 29 year old female presented with a complaints of a painless swelling on the left side of her jaw since 2 years, which appeared insidiously and gradually increased to its current size of 4x4 cm. there was no history of prior neck irradiation, neck surgery, and radio isotope administration. On examination, there was a globular, painless, non-pulsatile swelling of 4x4 cm in size situated over the ramus of left side of mandible. The swelling is hard in consistency and fixed to underlying mandible, not visible intra orally. There were no signs of inflammation, sinus formation in the skin. Neck examination revealed no abnormal findings or lymphadenopathy.



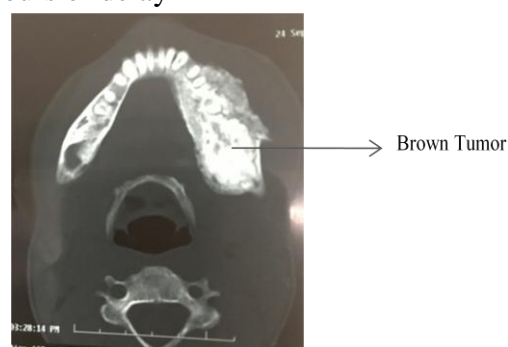
**Fig. 2** swelling present on the left side of mandible

### a. Investigations

Initially suspected as a case of osteolytic bony lesion, but after biopsy of mandibular swelling showed presence osteoclastic giant cells indicating of a brown tumor. Serum calcium levels are 15.8mg/dl, serum PTH 235 pg/ml. US of neck showed well defined hypoechoic lesion with small cystic areas noted superior to left lobe of thyroid. Parathyroid Tc99M-Sestamibi scan: persistent tracer uptake in the inferior pole of posterior aspect of left lobe of thyroid even on 2 hours of delay suggestive of parathyroid adenoma. CT study shows a lytic lesion of 3.4cm x 3.4 cm in the body and ramus of mandible, Focal areas of calcifications, ossifications are seen. cortical break is seen with no extra osseous soft tissue component, features suggestive of brown tumor.



**Fig. 3** Parathyroid Tc99M-Sestamibi scans: persistent tracer uptake in the inferior pole of posterior aspect of left lobe of thyroid even on 2 hours of delay

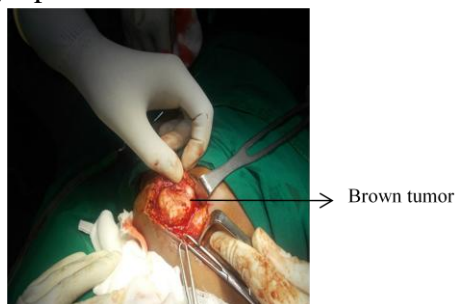


**Fig 4** CT scan showing a brown tumor in left side of mandible.

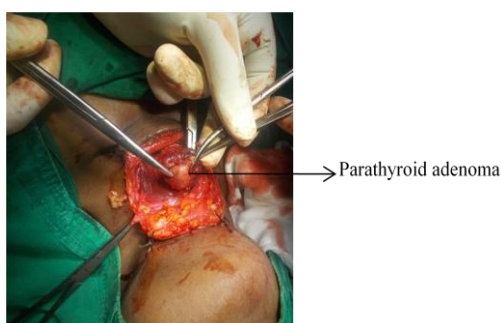
### b. Treatment

Patient was electively posted for left Parathyroidectomy with segmental mandible excision. The excised specimen was sent for pathologic examination, which was indeed

significant for a parathyroid adenoma. Postoperatively period was uneventful for the patient, with a decline in calcium 9.5 mg/dL, while her parathormone (PHT) levels returned within normal limits approximately 8 h after surgery. She was discharged on the seventh day, while at 3 month follow up she reported no further symptoms.



**Fig 5** Segmental excision of Brown tumor



**Fig 6.** Left parathyroidectomy

#### **Pathologic fractures associated with PHPT.**

A 37 year old male patient initially presented to casualty department with injuries occurred due to accidental fall from a riding bike. The patient complains of sharp and sustained pain in the left arm and left leg. Physical and local examination revealed that the patient had fractures of the left femur and left humerus to find the presence of lyric lesions changes in both left arm and left thigh. It no longer seemed tenable that the patient's fractures were exclusively the result of trauma, but were more plausibly pathologic in nature.

#### **a. Investigations**

Laboratory tests revealed serum calcium of 13.2 mg/dl, serum PTH of 863 pg/ml. Ultra sound of neck reveals a well defined iso to hpoechoic ovoid lesion of 3x2 cm noted posterior to left lobe

of thyroid with very minimal internal vascularity feature suggestive of left parathyroid adenoma. Parathyroid Tc99m-Sestamibi scan: Well defined parathyroid adenoma in the region of the lower pole on the left side of the thyroid gland. No evidence of ectopic parathyroid tissue was found.



**Fig 7** X rays shows fractures of left shaft of femur and left proximal humerus with lytic lesions.

#### **b. Treatment**

The patient was electively posted for Left parathyroidectomy, after the excision of left parathyroid gland the intra operative Intact Parathyroid hormone level showed 157pg/ml. Post operative day one his calcium levels returned to normal limits of 8.6 mg/dl. HPE showed predominantly exhibiting small acinar growth pattern with cystic change and acidophilic material in the cystic spaces suggestive of parathyroid adenoma. After post operative day 5 he underwent Open reduction and internal fixation with nailing for proximal left humerus and Intra medullary nailing with interlocking of shaft of left femur. Post operative period is uneventful with good recovery and he was discharged on day 10. For one month follow up he reported no further symptoms.



**Fig 8** Post operative intra medullary with interlocking of left femur and open reduction and internal fixation of left humerus.



**Fig 9** Left parathyroid adenoma excision with medial retraction of thyroid gland.

### Conclusion

PHPT is a most common endocrine disorder, characterized by persistent hypercalcemia along with elevated levels of PTH<sup>[1]</sup>. Parathyroid adenomas is the leading cause, other causes are Multiple adenomas, hyperplasia, parathyroid carcinomas only in 1%, and other rare causes are isolated familial hyper parathyroidism, HPT-JBT syndrome<sup>[5]</sup>.

Patient physical examination of the cervical region is unremarkable, while the elevated levels of serum calcium account for non-specific skeletal, neurological, renal and gastrointestinal symptoms. Dehydration or fluid loss can lead to sudden increase of serum calcium, causing a rare condition known as hypercalcemic crisis; symptoms include abdominal pain, nausea, vomiting and constipation. While cardiac and renal impairment can be observed<sup>[3],[4]</sup>.

Evaluation of PTH and serum calcium plays an important role in the diagnostic management of PHPT<sup>[2]</sup>. Patient can also be presented with elevated levels of PTH with normal serum calcium known as Normal calcemic Hyperparathyroidism, which must be differentiated from secondary hyperparathyroidism. Most common causes of secondary hyper parathyroidism are Vitamin-D deficiency, Renal insufficiency, intestinal mal absorption of calcium<sup>[9]</sup>.

The imaging modalities used for PHPT are ultra sonography of neck to locate Parathyroid gland with an sensivity and specificity of 75% and 85%

respectively. MRI and Four dimensional CT scan can be used to detect ectopic thyroid tissue, while TC 99M –MIBI parathyroid scintigraphy utilizes the absorption of radiotracer from hyperactive parathyroid tissue, in order to localize abnormal parathyroid tissue<sup>[10]</sup>.

Surgery is the main stay of management in the PHPT either Parathyroidectomy, Bilateral Neck exploration [BNE], or Minimal invasive parathyroidectomy [MIP]. Pre-operative marking and localization of the target parathyroid is essential to avoid un-necessary damage to nearby tissue.

Resection of pathologic parathyroid can be confirmed with measurement of Intra operative Intact PTH which has a very short half life of 3-5 min<sup>[11]</sup>. The excision of the pathologic gland leads to rapid normalization of PTH within minutes.

Today the current pattern of previously described clinical manifestations of PHPT shifts to the asymptomatic form that the majority of the patients are now identified incidentally on routine biochemical investigations and atypically.

### Acknowledgement

Department of Pathology for their immense help in diagnosing the cases. Department of Orthopedics and Gynecology for their support in treatment.

### References

1. T. Madkhali, A. Alhefdhi, H. Chen, D. Eifenbein, Primary hyperparathyroidism, *Ulusal cerrahi dergisi* 32 (1) (2016) 58–66.
2. P. Gopinath, G.P. Sadler, R. Mihai, Persistent symptomatic improvement in the majority of patients undergoing parathyroidectomy for primary hyperparathyroidism, *Langenbeck's Archives of surgery/Deutsche Gesellschaft fur Chirurgie* 395 (7) (2010) 941–946.
3. I.M. Cordellat, Hyperparathyroidism: primary or secondary disease? *Reumatol. Clin.* 8 (5) (2012) 287–291.

4. Belezikian JP, Potts JP. Asymptomatic primary hyperparathyroidism: new issues and questions. *J Bone Miner Res* 2002;17(Suppl 2):N57–67.
5. A.R. Kunte, V.S. Dube, S.S. Balwantkar, K.K. Kulkarni, Parathyroid adenoma in a young female presenting as recurrent acute pancreatitis with a brown tumour of the mandible—a case study, *Int. J. Surg. Case Rep.* 7C (2015) 10–15.
6. Arnold A, Kim HG, Gaz RD, et al. Molecular cloning and chromosomal mapping of DNA rearranged with the parathyroid gene in a parathyroid adenomas. *J Clin Invest* 1989;83:2034–Heppner C, Kester MB, Agarwal SK, et al. Somatic mutation of the MEN 1 gene in parathyroid tumours. *Nat Genet*
7. Christensson T. Hyperparathyroidism and radiation therapy. *Ann Intern Med* 1978;89:216–7.
8. Biondi A, Persiani R, Marchese M, Cananzi F, D’Ugo D. Acute pancreatitis associated with primary hyperparathyroidism. *Updates Surg* 2011;63 (June (2)):135–8.
9. Chavassieux P, Seeman E, Delmas PD. Insights into Material and Structural Basis of Bone Fragility from Diseases Associated with Fractures: *Endo Reviews*. 2007; 28(2): 151-64.
10. Rubin MR, LiVolsi VA, Bandeira F, Caldas G, Bilezikian JP. Tc99m-Sestamibi Uptake in osteitis fibrosa cystica Simulating Metastatic Bone Disease. *J Clin Endocrinol Metab.* 2001; 86(11): 5138-4
11. L Bandeira, J. Bilezikian, Primary hyperparathyroidism, *F1000 Research* 5(2016).