

# Ectopic Parathyroid Adenoma - The Hidden Culprit

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## Abstract

Primary Hyperparathyroidism is known to present with protean manifestations leading to misdiagnosis in the initial stages of the disease. Inability to locate the adenoma in an ectopic parathyroid gland may further delay the diagnosis of these cases. Aberrant migration during development may lead to intrathyroidal or other ectopic locations of parathyroid glands. This may lead to their misdiagnosis as a thyroid nodule or failure to locate parathyroids during surgery. Similarity in cytological picture between thyroids and parathyroids may further complicate diagnosis by fine needle aspiration cytology. Nuclear imaging scintigraphy accurately localizes the tumor in 90% of cases and simplifies the surgical management. We encountered three such cases with the parathyroid gland adenomas in ectopic locations in which pre-operative nuclear imaging played a major role. ©

## INTRODUCTION

Primary Hyperparathyroidism often presents with unusual clinical manifestations and ectopically located Parathyroid gland adenomas. Inability to locate the adenoma in an ectopic parathyroid gland may delay the diagnosis of these cases.<sup>1</sup> Intrathyroidal or other ectopic locations of parathyroid glands are uncommonly encountered which presents as a diagnostic dilemma.<sup>2</sup> Cytological similarity between thyroid and parathyroid gland may further add to this diagnostic problem. Nuclear imaging scintigraphy accurately localizes the tumor in 90% of cases<sup>2</sup> and simplifies the surgical management. We encountered three cases of parathyroid gland adenomas in ectopic locations which presented with diagnostic problems. Pre-operative nuclear imaging helped in localizing the culprit lesion and in directing the surgeon to the affected gland.

## CLINICAL DATA

### Case 1

A 21 years lady presented with the complaints of pain in the low back and hip joint area associated with a limp while walking for two years duration. She gave history suggestive of proximal muscle weakness in the lower limbs. She denied having sustained any trauma or fracture to her back or hips. In the past, she was suspected to have tuberculosis of the hip joint for which she was treated with anti-tubercular treatment

for 1½ years with no improvement in her symptoms. On clinical evaluation, she had painful proximal myopathy and bony tenderness in the lumbar region. Investigations revealed serum calcium 9 mg/dl, corrected for serum albumin, (normal 8.8 to 10.5 mg/dl), serum phosphorus 3.0 mg/dl (normal 3.0 to 4.5mg/dl) and s. alkaline phosphatase 1562 IU/l (normal 30 to 120 IU/l). After supplementing vitamin D (Calcitriol 0.25 mcg twice daily) for 1 week, repeat serum calcium was 11.2 mg/dl and simultaneous intact PTH was 1544 pg/ml (normal 10 to 65 pg/ml). Other investigations revealed normal complete blood count and renal parameters.

Skeletal survey revealed diffuse areas of lysis and sclerosis in the skull, lytic area in the 3<sup>rd</sup> metacarpal and middle phalanx of the 5<sup>th</sup> finger. Imaging by Sestamibi scan revealed an area of increased uptake in the upper pole of right thyroid with retention of the tracer in the delayed images and Brown tumor in the left shoulder region. Diagnosis of primary hyperparathyroidism due to right superior parathyroid adenoma was made and surgical exploration was planned. Visible tumor was not seen on the surface of right thyroid lobe. However, due to strong suspicion in view of biochemical parameters and Tc99m sestamibi scan report, further exploration was done to locate parathyroid adenoma. With high index of suspicion, the right thyroid lobe was explored for an intrathyroidal parathyroid adenoma. The tumor was located within the right thyroid lobe parenchyma and right hemithyroidectomy was performed. Grossly, the tumor was seen to be well-circumscribed within the thyroid tissue (Fig. 1). Histopathological examination showed characteristic parathyroid adenomatous tumor with water clear cells embedded within the thyroid tissue (Fig. 2). Post-operatively, the patient showed

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Received : 7.7.2006; Revised : 20.10.2006;

Re-Revised : 22.3.2007; Accepted : 10.4.2007



Fig. 1 : Gross specimen (cut Section) of resected right lobe of thyroid gland showing intrathyroidal Parathyroid Adenoma

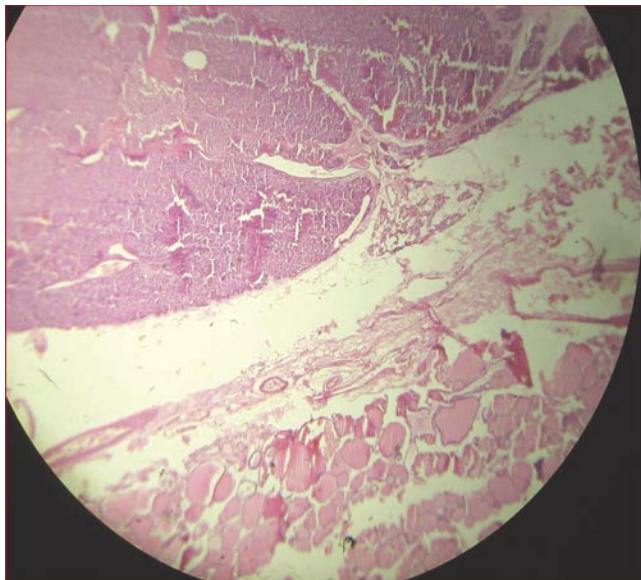


Fig. 2 : Photomicrograph of the resected thyroid lobe showing characteristic parathyroid adenomatous tumor embedded within the thyroid tissue. (Intrathyroidal parathyroid adenoma)

evidence of incipient hypoparathyroidism with positive Trousseau's sign. She was managed with calcium and vitamin D3 supplementation and followed up for recovery. On follow up, her serum alkaline phosphatase and serum calcium declined to normal limit. Serum intact PTH level on follow up was 55 pg/ml.

#### Case 2

A 26 years lady presented with the complaints of generalized bone pains associated with difficulty in walking of 1 year duration. There was no history of repeated fractures, pain abdomen or urinary symptoms. There was no significant past or family history. On clinical evaluation, she had painful proximal myopathy and diffuse bone tenderness. Investigations showed

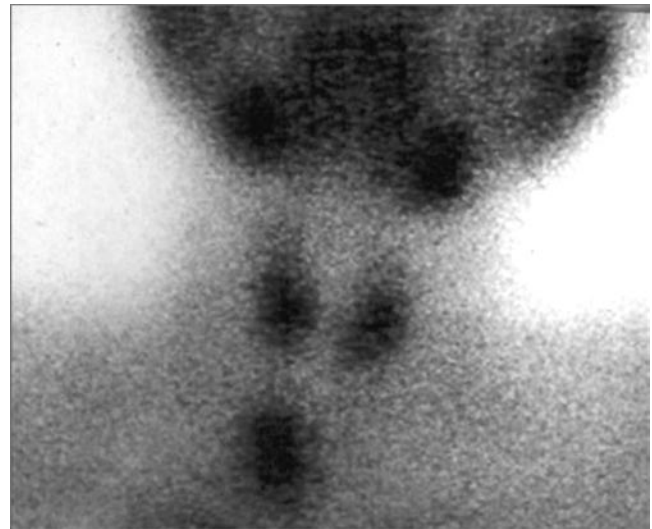


Fig. 3 : Imaging by Technetium 99m Sestamibi scan showing an area of increased uptake in the superior mediastinum

corrected serum calcium 11 mg/dl (normal 8.8 to 10.5 mg/dl), serum phosphorus 3.8 mg/dl, s. alkaline phosphatase 1604 IU/l and simultaneous intact PTH was 1624 pg/ml. Other investigations revealed normal complete blood count and renal parameters.

Skeletal survey revealed areas of lysis and sclerosis in the skull and lytic areas in the metacarpals. Imaging by Sestamibi scan revealed an area of increased uptake in the area of superior mediastinum with retention of the tracer in the delayed images (Fig. 3).

Diagnosis of primary hyperparathyroidism due to ectopic parathyroid adenoma (mediastinal) was made and surgical exploration was planned. The tumor was located in the superior mediastinum and was resected. Grossly, the tumor was seen to be well-circumscribed. Histopathological examination confirmed parathyroid adenoma. On post-operative follow up, the serum intact PTH was 48 pg/ml and serum alkaline phosphatase and serum calcium declined to normal limit.

#### Case 3

A 52 years lady presented with the complaints of a bony swelling over right forearm, generalized bone pains associated with difficulty in walking of two year duration. There was no history of repeated fractures, pain abdomen, urinary symptoms, fever or significant weight loss. There was no significant past or family history. On clinical evaluation, she had a hard bony swelling involving her right ulna, painful proximal myopathy and bone tenderness. Other systemic examination was normal. Investigations revealed corrected serum calcium 13 mg/dl (normal 8.8 to 10.5 mg/dl), serum phosphorus 3.4 mg/dl, s. alkaline phosphatase 550 IU/l and simultaneous intact PTH was 1564 pg/ml. Other investigations revealed normal complete blood count and renal parameters. Skeletal survey revealed an area of expansile lysis in the right ulna and left 3<sup>rd</sup> rib. There were areas of subperiosteal erosion noted in the 2<sup>nd</sup>

metacarpal. Imaging by Sestamibi scan revealed an area of increased uptake in the area of superior mediastinum with retention of the tracer in the delayed images.

She was diagnosed as a case of primary hyperparathyroidism due to ectopic parathyroid adenoma (mediastinal). Intraoperatively, the tumor was located in the superior mediastinum and was resected. Histopathological examination confirmed parathyroid adenoma. On post-operative follow up, her serum alkaline phosphatase and serum calcium normalized and serum PTH was 52 pg/ml.

## DISCUSSION

Primary hyperparathyroidism is a common endocrine condition causing metabolic bone disease characterized by hypercalcemia and diffuse bone resorption. A large number of cases are usually asymptomatic and are detected incidentally with hypercalcaemia.<sup>1</sup> In the clinically manifest disease, it is known to present with subtle and protean manifestations, leading to misdiagnosis in the early stages of the disease, as seen in one of our patients. Excess PTH leads to involvement of skeletal system and the kidneys in majority of cases. Skeletal involvement is mainly as a result of increased bone resorption leading to characteristic manifestations like osteitis fibrosa cystica (OFC), subperiosteal resorption of distal phalanges, bone cysts and 'brown tumors'. Renal involvement is seen in more than 15% of cases of primary hyperparathyroidism and is mainly due to hypercalciuria leading to nephrocalcinosis and nephrolithiasis (renal stones).<sup>1</sup>

Diagnosis of primary hyperparathyroidism in a clinically suspected case is suggested by hypercalcemia, hypophosphatemia, raised levels of bone specific alkaline phosphatase and raised intact parathyroid hormone (PTH) levels. Anterior neck mass may occasionally be palpable in a case of parathyroid tumor.

The superior and the inferior parathyroid glands originate from the 4<sup>th</sup> and the 3<sup>rd</sup> branchial pouches respectively and migrate caudally to occupy their normal positions in relation to the thyroid gland. Any aberrancy during this descent may lead to ectopic locations of these glands. They may be located in posterior mediastinum behind the cervical esophagus, retrosternally in the anterior mediastinum, within the thymus (intrathymic), in the tracheo-esophageal groove or unusually within the thyroid parenchyma (intrathyroidal).<sup>1</sup>

Ectopic location of parathyroid gland is an important albeit, uncommon reason for failure to locate the gland during surgery. Pre-operative <sup>99m</sup>Tc Sestamibi scan helps in localizing the tumor accurately in almost 90% of patients.<sup>2</sup> It has a greater role in localizing ectopic glands which helps the surgeon in planning the surgical approach, as in all our cases. Ultrasonography (USG) is a convenient and economical localizing modality and has an acceptable sensitivity and specificity of 73% and

100% respectively.<sup>3</sup> In cases of recurrence of the disease or failed surgery, localization of adenoma by Sestamibi scan is mandatory.<sup>4</sup> In case of a co-existing thyroid nodule; the tracer may localize to the thyroid tissue but tends to get washed away faster. Persistence of the tracer within the thyroid suggests intrathyroidal parathyroid tumor, as was seen in case 1. Ultrasound imaging and guided fine needle aspiration cytology studies help in supplementing diagnosis in such cases. Intraoperative PTH assays can be done, and a 50% or more decline from baseline within 10 minutes of excision confirms successful surgery.<sup>5</sup>

A <sup>123</sup>I scan to delineate the thyroid gland combined with <sup>99m</sup>Tc Sestamibi scan helps in differentiating the parathyroid from thyroid tissue.

Fine needle aspiration cytology (FNAC) studies may help supplement the diagnosis in such cases. Cytology studies on FNAC of parathyroids may occasionally be confused with thyroid tissue. The cytological features of oxyphil cells and chief cells (the latter, devoid of cytoplasm) present in the parathyroid adenoma resemble Hurthle cells and lymphocytes respectively.<sup>6</sup> High PTH levels in the aspirates definitively differentiate parathyroid from thyroid tissue. However in a suspected intrathyroidal parathyroid adenoma, the patient may be subjected to hemithyroidectomy when other sites of ectopic gland have been excluded.

Primary hyperparathyroidism, with its varied manifestations and indolent course, is a condition well known to pose a diagnostic dilemma to the clinician. An ectopic location of the parathyroid gland, albeit uncommon, may further complicate the issue. Pre-operative scintigraphy helped in confirming the location of the adenoma in all these three cases and simplified their surgical management which otherwise would have been a challenging task for operating surgeon.

## REFERENCES

1. Mitlak B, Daly M, Potts JJ. Asymptomatic primary hyperparathyroidism. *J Bone Miner Res* 1991;6:S103-S110.
2. Gogas J, Kouskos E, Mantas D, Markopoulos C, Kyriaki D, Tseleni-Balafouta S, *et al.* Pre-operative Tc-99m-sestamibi scanning and intra-operative nuclear mapping: are they accurate in localizing parathyroid adenoma? *Acta Chir Belg* 2003;103:626-30.
3. Bhansali A, Masoodi SR, Bhadada S, Mittal BR, Behera A, Singh P. Ultrasonography in detection of single and multiple abnormal parathyroid glands in primary hyperparathyroidism: comparison with radionuclide scintigraphy and surgery. *Clin Endocrinol* 2006;65:340-5.
4. Thompson GB, Grant CS, Perrier ND, Harman R, Hodgson SF, Ilstrup D, *et al.* Reoperative parathyroid surgery in the era of Sestamibi scanning and intraoperative parathyroid hormone monitoring. *Arch Surg* 1999;134:699-704.
5. de la Cruz Vigo F, Ortega G, Gonzalez S, Martinez JI, Cruz Leiva J, Galvez R, *et al.* Pathologic intrathyroidal parathyroid glands. *Int Surg* 1997;82:87-90.
6. Auger M, Charbonneau M, Huttner I. Unsuspected intrathyroidal parathyroid adenoma: mimic of lymphocytic thyroiditis in fine-



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**First NORTH INDIA MEDICAL CLINICS** will be held on **29th and 30th September 2007 at JP Manor Residency, Mussoorie**. National as well as international faculty will be participating in this conference. There will be various workshops also.

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