

**PARATHYROID ADENOMA CAUSING HYPERPARATHYROIDISM WITH COMPLICATIONS OF MULTIPLE FRACTURES, BROWN'S TUMOUR, RENAL CALCULI & HYDRONEPHROSIS.****RADHAKRISHNAN PAULRAJ , HANNIEYA ELMO PAUL AND SANDHYA SADAN PALANDE**

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**ABSTRACT**

Primary Hyperparathyroidism can be present with various complications when diagnosed in a later stage of the disease. Radiological investigations, such as USG of the neck, Technetium 99m MIBI Scintigraphy, Magnetic Resonant Imaging (MRI), Computer Tomography (CT) scans, and X-rays of the cortical and cancellous bones, can be of great aid in screening the disease. The Tc99m MIBI Scintigraphy is a newer imaging modality to view any foci of increased vascularity and retention of traces of Tc99m<sup>1,10</sup>. CT scan and MRI provide the location of the gland, and any enlargement, and may also reveal any ectopic parathyroid glands. In addition to radiological imaging, histopathological pictures -microscopy and macroscopic, in correlation with biochemical values of Parathyroid Hormone, serum Calcium, serum Magnesium, serum Phosphorus and Alkaline Phosphatase can confirm the diagnosis<sup>1</sup>.

In this study we describe a case of Parathyroid adenoma, presenting as Primary Hyperparathyroidism in a middle-aged woman with complaints of myalgia, multiple swellings over the limbs, inability to stand upright from a sitting posture, and inability to walk. Investigations revealed multiple pathological fractures over the limbs, Brown's tumour, renal calculi and hydronephrosis. Her sign and symptoms are typical of a Primary Hyperparathyroidism and its complications. As she is a symptomatic case of Primary Hyperparathyroidism, surgical removal of the parathyroid adenoma was required to control the parathyroid hormone levels, and to prevent further complications. Studies have shown that removal of the parathyroid adenoma, causing the elevated hormone levels. will cause a reversion of the brown tumour.



## KEY WORDS

Hormones, Tumour, Parathyroid, Serum Calcium

## INTRODUCTION

A middle aged, 42 year old, woman came with the complaints of difficulty in standing upright and walking for the past 2 years. Her symptoms initially presented with difficulty in standing upright and walking in the year of 2009, when she was diagnosed in the neighbouring hospitals as having a parathyroid adenoma, with primary hyperparathyroidism. After a couple of months of treatment at the hospital for control of the hormone levels, she regained the ability to stand upright and walk. For 1 year after her discharge from the hospital, she was asymptomatic. Currently, she came to our hospital, SRM Medical College Hospital & RC, with complaints of an inability to stand upright or walk, with multiple swellings in the limbs for the past 6 months.

### **Case Report:**

On examination, multiple swellings of the right upper limb, left lower limb, and left clavicle were present, being tender. Minor restriction of movement was present in association with the swellings. Further investigations of the limb swellings showed that there were multiple old fractures of the clavicle, radius and femur (subtrochanteric); the latter presenting with the attitude of the left thigh in an externally rotated position.

Her reflexes, tone and power were normal. However, she was unable to bear weight over both her lower limbs. Her lower limb muscles appeared decreased in muscle bulk. On examination of the neck, a swelling was present on left side of the neck, in the region of the thyroid, occupying more predominantly in the left inferior pole of the gland. The swelling was not warm or tender, and moved along with the thyroid gland. No other obvious swellings were present in the region of the neck.

Various Biochemical analyses were done to check the levels of the serum electrolytes, and parathyroid hormone levels. On March 14, 2011 the Biochemical test results showed increased levels of serum calcium levels of 13.3 mmol/L, Parathyroid hormone level of 1805.7 pg/mL, alkaline phosphate levels of 2185 U/L, and serum phosphate of 2.4 mmol/L. These values show an increase in the serum calcium levels, and more than a five-fold increase in the parathyroid hormone levels, and an increase in the alkaline phosphatase. This leads to the possibilities of primary hyperparathyroidism, maybe due to a benign parathyroid adenoma, or parathyroid carcinoma.

Radiological investigations were done to know the exact location of the tumour, and any ectopic locations of the parathyroid gland, or other loci of focus of increased activity of parathyroid hormone. Technetium 99m MIBI parathyroid Scan (scintigraphy) that was taken on June 25, 2009, revealed a parathyroid adenoma in the region of the lower pole of the left lobe of the thyroid. Reports describe the scan as a focus of mild hypervascularity with focal retention of tracer in delayed images suggesting Parathyroid adenoma of lower pole of the left lobe of the thyroid gland. Along with an abnormal focus of tracer concentration in the lower end of the right femur suggest the probability of Brown Tumour. (Appendix 1)

The Technitium 99m MIBI (2-methoxy isobutyl isonitrile) will accumulate in the parathyroid glands, showing a peak in 4-6 minutes. This Technitium 99m MIBI is metabolized in the mitochondria of the cells, and in this case of parathyroid adenoma, there is an increase number of mitochondria which will take up the Tc-99m MIBI, and be visualized on delayed images<sup>1</sup>.



An Ultrasonography of the thyroid region was done on March 25, 2011. The reports describe a well defined smooth, margined, ovoid, and hypoechoic lesion with a moderate flow. The diameters being 28 x 22 x 13 mm, situated in inferior to the left thyroid gland with no signs of cystic or calcific changes within the lesion. (Appendix 2)

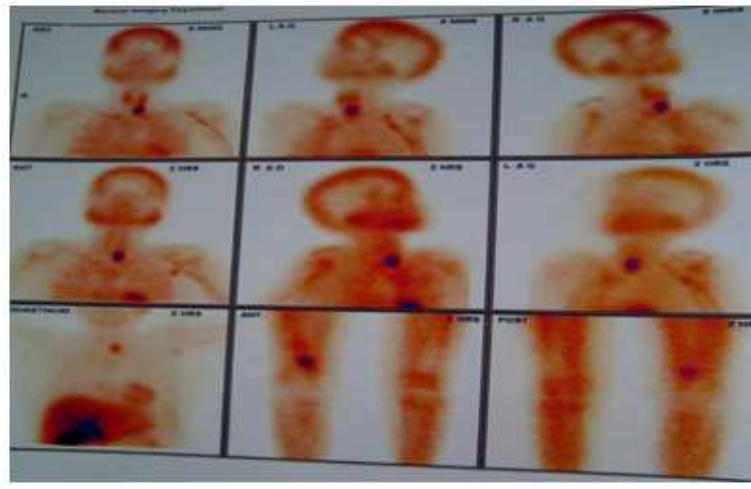
Incidentally, to rule out other complications of Hyperparathyroidism, a Intravenous Urogram was taken on June 18, 2009. The Urogram shows bilateral hydronephrosis along with bilateral renal calculi. However, the patient did not have any complaint regarding any alteration in her urinary output or micturition difficulties. (Appendix 3)

X-rays were taken for the multiple swellings in the left clavicle, left lower limb (tibia), and right upper limb (ulna) at the junction of the middle 2/3 and lateral 1/3, for the past 1 year. Her swellings are associated with pain tenderness, and restriction of movements of all the limbs. X-ray of the left clavicle shows a fracture of the middle 2/3 and lateral 1/3 on March 14, 2011. X-rays of the left femur and the right tibia, dated March 15 2011, show translucent lesions. Whereas, the x-rays of the pelvis with the left femur shows multiple, old, subtrochanteric fracture (Appendix 4). Currently, she has a fracture of the left humerus from a history of using her arm to help her move to a different position on the bed. Her X-ray shows displaced fracture of the proximal 2/3 and distal 1/3 of the humerus April 11, 2011. (Appendix 5)

Surgical removal of the parathyroid was done on March 12, 2011. The adenoma was situated below the left inferior pole of the thyroid. The size of the tumour is approximately 4 X 4cms in dimension. Along with this, a lymph node tissue was taken for microscopic and macroscopic examination.

Histopathological examination reveals the tumour to be 3 x 2 x 1 cm, the outer surface being grey-white in colour with attached fascias. The Cut surface is homogeneously tan in colour with a firm consistency, and encapsulated. Microscopic picture shows an encapsulated neoplasm composed of sheets of chief cells and nodules of water clear cells with occasional intervening oxyphil cells. The cells are uniform, with round nuclei, and well defined borders of cytoplasm. There is no evidence of mitoses, and capsule remains intact. The lymph nodal tissue macroscopically was 1 x 0.3 x 0.2 cm in dimension; the microscopic picture shows two lymph nodes with reactive changes.

Post operatively the patient were given Calcium gluconate 8.4g/24hrs slow infusion as well as magnesium sulphate 1g iv slow infusion, since calcium levels dropped to 5.8mg/dl on April 20<sup>th</sup> 2011(post-operative day 8). Now the patient has regained her calcium levels to the normal range, and the patient is regularly on calcium supplement tablets. Her Parathyroid levels have decreased to 138.0 pg/mL, Vitamin D (25 – OH) levels are 23.2 ng/mL, and calcium levels are 9.1 mg/dL.



**Appendix 1**  
***Technetium 99m MIBI Parathyroid Scan (scintigraphy) June 25, 2009.***



**Appendix 2**  
***Ultrasonography of the thyroid region. March 25, 2011***



**Appendix 3**  
***Intravenous Urogram June 18, 2009***



**Appendix 4**  
***X-ray left clavicle March 14, 2011.***



***b) X-rays of the left femur and the right tibia dated March 15 2011***



**Appendix 5**  
***X-ray left humerus April 11, 2011***

## DISCUSSION

The parathyroid gland produces parathyroid hormone (PTH), which has a function of controlling the levels of calcium, phosphorus, alkaline phosphatase, magnesium, and vitamin D levels within the blood and bone<sup>2</sup>. When calcium levels are low, the body responds by increasing the production of parathyroid hormone<sup>3</sup>. This increase in parathyroid hormone causes more calcium to be taken from the bone and more calcium to be reabsorbed by the intestines and kidney<sup>3</sup>. When the calcium level returns to normal, parathyroid hormone production slows down.

Primary hyperparathyroidism is caused by swelling of one or more of the parathyroid glands. This leads to the release of too much parathyroid hormone, which raises the level of calcium in the blood. The term "hyperparathyroidism" generally refers to primary hyperparathyroidism<sup>3</sup>. The incidence is more in females than in males over the age of 40 years<sup>4</sup>. Radiation of head and neck also increases the risk of hyperparathyroidism<sup>5</sup>.

Parathyroid adenoma is a benign tumour of the parathyroid gland which causes hyperparathyroidism. They are usually asymptomatic but can be diagnosed earlier with screening techniques<sup>1</sup>. However, untreated Primary Hyperparathyroidism can lead to complications involving the bones, renal system, and the Central Nervous System (CNS). Osteoporosis, Osteitis fibrosa cystica, Osteomalacia, and Arthritis are some of the bone diseases which are likely to occur in long-standing increase in parathyroid levels<sup>6</sup>. As Parathyroid hormone levels and Calcium levels are interrelated, increased parathyroid levels causes an increase in the calcium levels in the blood<sup>7</sup>; from the osteoclastic activity in the bone which enhances the minerals, such as calcium to be released into the blood-stream. Replacement of calcified structure to fibrous tissue ultimately causes loss of bone mass

and pathological fractures<sup>8</sup>. The areas of bone mass loss form "brown tumours", which are cyst-like lesions (appearing brown in colour)<sup>9</sup>. Studies have shown that these brown tumours will decrease when PTH levels and calcium levels are maintained<sup>10</sup>.

Increased Parathyroid Hormone levels also play an important role in renal functions. As parathyroid hormone (PTH) influences the calcium, and Vitamin D, prolonged exposure to elevated PTH levels causes abnormalities in renal function<sup>5</sup>. The usual presentation is patients with multiple Renal Calculi (from the hypocalcaemia)<sup>11</sup> and Renal Failure (in the later stages)<sup>12</sup>. Reduced renal clearance of the calcium, and elevated levels of calcium in the renal tubules favour the formation of renal calculi (usually medullary renal calculi are common)<sup>13</sup>. This patient had multiple renal calculi and hydronephrosis- rooting from the mechanical obstruction by the renal calculi, which accounts for the distension of the renal pelvis calyces<sup>14</sup>.

Other Psychiatric complications such as moans, depression, anxiety, psychosis, delirium, etc are entities that were not established in this patient<sup>5</sup>. Gastric and Pancreatic complications are also found in Primary Hyperparathyroidism, such as peptic ulcer disease, indigestion, constipation, and acute pancreatitis<sup>15</sup>; however, this patient did not provide any such history pertaining to this.

Controlling parathyroid levels prevents the complications that debilitate patients<sup>1</sup>. Therefore, early screening of the disease, monitoring and effective control methods are possible preventive measures for the complications, such as the ones observed in this patient and other symptomatic patients. In this scenario, surgical removal of the parathyroid gland was needed, as the cause for the primary hyperparathyroidism rested on the benign Parathyroid adenoma, and the patient was symptomatic with complications, such as Osteitis fibrosa cystica<sup>16</sup>. Criteria for surgical intervention vary from symptomatic and asymptomatic patients. Symptomatic

patients presenting with bone disease, renal impairment, and/or neuromuscular complaints, are possible candidates for surgical intervention<sup>1</sup>. Whereas Asymptomatic patients must satisfy the guidelines for surgical intervention: serum calcium levels should be greater than

Routine check-ups for these patients diagnosed with parathyroid adenoma, even after the removal of the adenoma is a requirement. Initially, controlling calcium and parathyroid hormone levels is apt for reducing the complications and brings the patient to a stable state. Beyond maintaining calcium levels, the patient needs to be screened periodically to rule out any ectopic sites of parathyroid tumour, and to rule out any malignancy using the Tc-99m Sestamibi uptake scan<sup>18</sup>. Parathyroid carcinoma is rare, however, it is not unlikely that patients

1.0mg/dL above the upper limit, less than the age of 50 years, bone density T scores less than -2.5 at any given site, and abnormal serum creatinine level<sup>1</sup>. It is better to find the best treatment option for asymptomatic patients besides surgery<sup>17</sup>.

are misdiagnosed or diagnosed early for the carcinoma. Parathyroid carcinomas usually have multisystem involvement similar to the parathyroid adenoma complications that we have seen in this patient (Renal system, Bony complications)<sup>1</sup>. In adjacent to the complications that can present in a similar fashion, values of parathyroid hormone, serum calcium, alkaline phosphatase levels can be drastically increased<sup>1</sup>. This patient, however, shows only benign changes in the histopathological examination of the tumour specimen.

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