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Research Article

Unusual Case of Occult Solitary Parathyroid Adenoma : A Case Report

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Abstract

Parathyroid adenoma is a rare but well described clinical entity. Here we report an occult inferior solitary parathyroid adenoma in a 56 yrs old male patient who presented to us with complaints of low back pain over past sixteen years, pain over right leg and right hand over six months and intermittent swallowing difficulty over past 1 month.

Keywords: Parathyroid Adenoma; Ozone Therapy; Serum

Case Report

A 56 years old gentleman presented to us with history of low back pain over past sixteen years, right leg and right hand pain over past six months, intermittent difficulty in swallowing over past 1 month.

Patient had received ozone therapy for lumbar disc prolapse in the past.

Patient

On Clinical examination, there was no visible swelling in the neck.

On video laryngoscopic examination, there was incidentally detected tiny vallecular cyst.

Following specific investigations were done

- Dexa Scan
- Serum calcium profile
- Serum Vitamin D
- Serum Vitamin B12
- Serum PTH (Serum Paratharmone).

Dexa scan revealed Osteoporosis T score 3.3.

Serum calcium levels revealed hypercalcemia (Serum Calcium: 13.5 mg/dl).

Serum phosphorus revealed hypophosphatemia (serum phosphorous: 2.4 mg/dl).

Serum Vitamin D deficiency (Sr Vitamin D -21 ng/ml).

Serum alkaline phosphatase level within normal range (101 IU/L).

Serum Parathormone (Serum PTH) revealed hyperparathyroidism. (Serum PTH: 613.4 pg/ml).

Subsequently case was further investigated with following specific investigations

- **Ultrasonography of Neck:** Revealed Well defined heterogenoulsy hypoechoic lesion ~1.4x1.0x2.2 cm lesion in the inferior aspect of the left lobe thyroid gland with moderate internal vascularity (Figure 1)

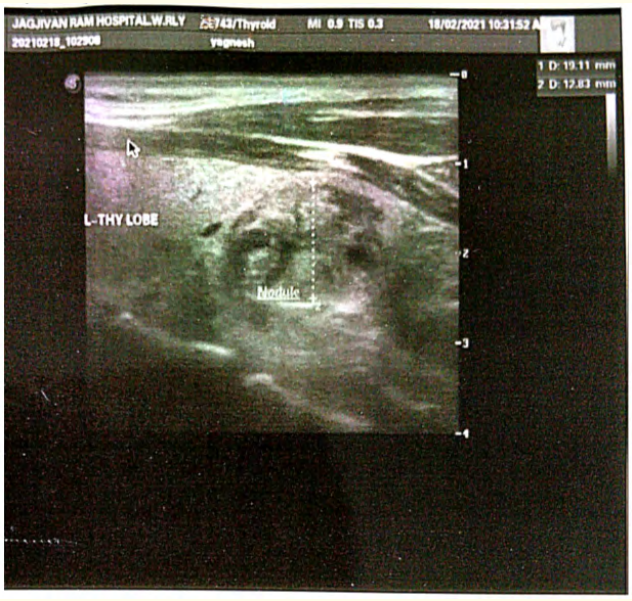

Figure 1: USG Neck: Well defined heterogenoulsy hypoechoic lesion ~1.4x1.0x2.2 cm lesion in the inferior aspect of the left lobe thyroid gland with moderate internal vascularity.

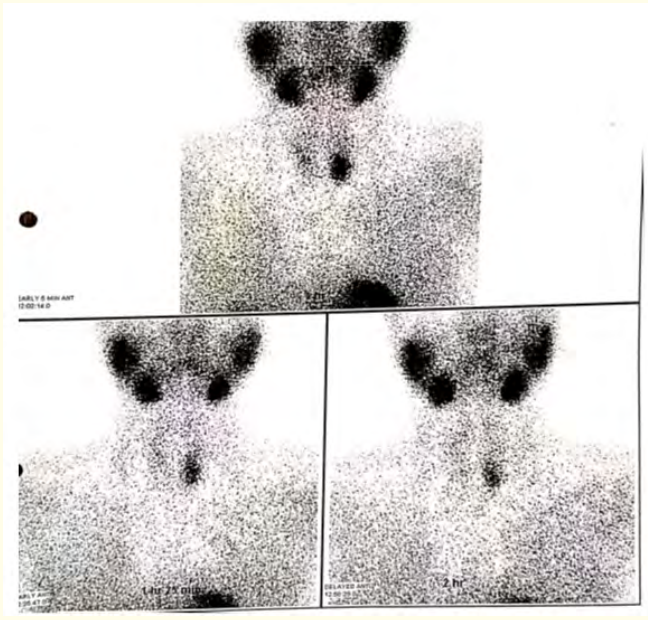

Figure 2: Scintigraphic evidence of MIBG avid lesion close to the Left lobe of thyroid suggestive of parthyroid adenoma , delayed image at 2hours post injection shows te persistence of tracer concentration in the left side of neck close to the inferior pole of the left thyroid lobe with normal washout of tracer from the left and right lobes of thyroid gland.

- **Techniciam 99 scan:** Revealed evidence of MIBI avid lesion close to lower lobe of thyroid suggestive of parathyroid adenoma. No evidence of ectopic thyroid tissue elsewhere
- Serum prolactin
- Serum Growth Hormone
- Serum insulin like growth factor 1
- Contrast enhanced Computerised tomography of Neck for the site and extent of the tumour (Figure 3).

Serum prolactin, Serum Growth Hormone and Serum insulin like growth factor 1 levels were within normal limits.

Subsequently the Patient underwent excision of parathyroid adenoma [Figure 4]. Sample for serum Parathormone levels collected prior surgery.

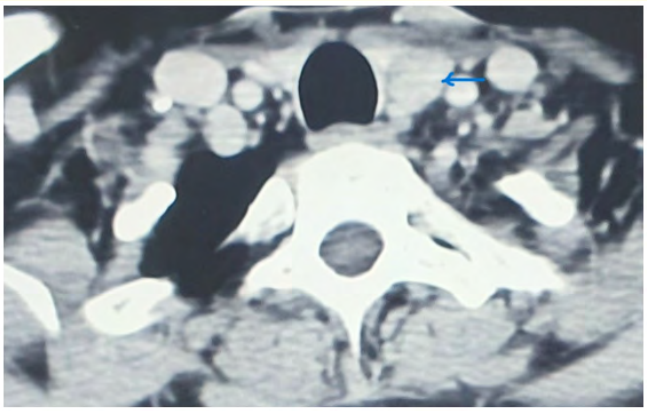

Figure 3: Contrast enhanced computerized tomography image Axial cut slice thickness 5 mm - Arrow depicting parthyroid adenoma.

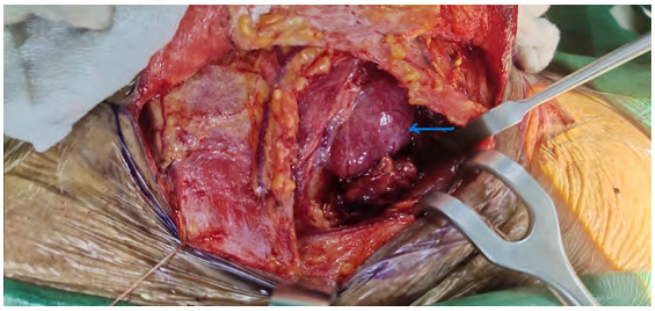

Figure 4: Intraoperative photo depicting parathyroid adenoma depicted by an arrow.

Intraoperative Finding revealed parathyroid adenoma at lower pole of thyroid lobe.

Post excision blood samples were collected for serum parathormone (PTH) at 5 minutes, 10 minutes and 15 minutes intervals which revealed rapid drop in PTH levels.

The specimen was sent for histopathology examination which confirmed benign parathyroid adenoma (Figure 5).

The patient had uneventful recovery post operatively over 2 years of follow up.

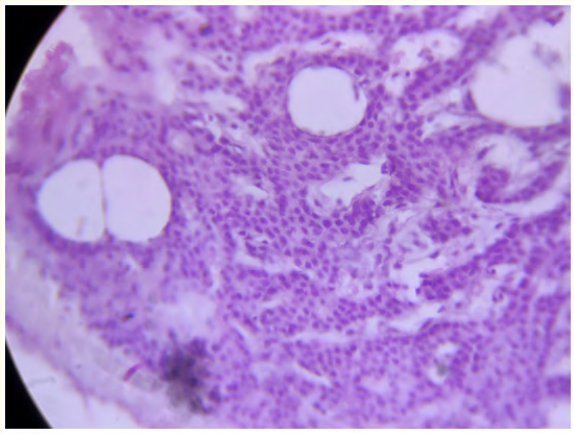

Figure 5: Photomicrograph of histopathological slide of tumour suggestive of benign parathyroid adenoma [H & E stain, Magnification 20X].

Discussion

Parathyroid adenoma is a benign tumor of parathyroid gland, which leads to primary hyperparathyroidism.

There are four parathyroid glands located on the posterior surface of the thyroid in the neck. In order to maintain calcium metabolism, the parathyroid glands secrete parathyroid hormone (PTH) which stimulates the bones to release calcium and the kidneys to reabsorb it from the urine into the blood, thereby increasing its serum level. The parathyroid gland when secrets excess parathormone (PTH), then leads to elevation in the serum calcium levels resulting into hypercalcemia.

The Incidence of primary hyperparathyroidism is more common in female gender compared to male gender and ratio of female to male prepondence is 3:1 [1].

If symptomatic, the patient experience pain in joints, bones muscles urinary calculi depression, mood changes, the classic pentad of painful bones, abdominal groans, psychic moans, and fatigue overtones.

Brown's tumor is a bone lesion that arises in settings of excess osteoclast activity, such as hyperparathyroidism. They are a form of osteitis fibrosa cystica. It is not a neoplasm, but rather simply a mass. It most commonly affects the maxilla and mandible, though any bone may be affected. Brown tumors are radiolucent on x-ray [1].

The weight of parathyroid adenoma varies between 70 mg to 1 g, but some sporadic cases of tumors were reported to be more than 30 g. Parathyroid tumor weighing more than 3.5 grams is referred to as" giant tumor" and adenoma weight has a direct relation with serum calcium and PTH levels and indirect relation with serum phosphate levels. A transient hypocalcemia and lower mean serum calcium level on day 3-4 post operation is commonly seen in cases of larger parathyroid adenomas. Ectopic parathyroid gland scan be located at the aortopulmonary window, so for better recognition [2]. In the present case the weight of parathyroid adenoma was around 915miligrams.

Effect of calcium metabolism and bone: The parathyroid gland secretes parathyroid hormone (PTH), a polypeptide, in response to low calcium levels detected in the blood. PTH facilitates the synthesis of active vitamin D and calcitriol (1,25-dihydroxycholecalciferol) in the kidneys. In conjunction with calcitriol, PTH regulates calcium and phosphate. PTH effects are present in the bones, kidneys, and small intestines. As serum calcium levels drop, the secretion of PTH by the parathyroid gland increases. Increased calcium levels in the serum serve as a negative-feedback loop signaling the parathyroid glands to stop the release of PTH [1].

In the bones, PTH stimulates the release of calcium in an indirect process through osteoclasts which ultimately leads to resorption of the bones. However, before osteoclast activity, PTH directly stimulates osteoblasts which increases their expression of RANKL, a receptor activator for nuclear factor kappa-B ligand, allowing for the differentiation of osteoblasts into osteocytes.

Starting at the kidneys, PTH stimulates the production of 1alpha-hydroxylase in the proximal convoluted tubule. This enzyme, 1alpha-hydroxylase, is required to catalyze the synthesis of active vitamin D - 1,25-dihydroxycholecalciferol from the inactive form 25-hydroxycholecalciferol. Active vitamin D plays a role in calcium reabsorption in the distal convoluted tubule via calbindin-D, a cytosolic vitamin D-dependent calcium-binding protein. In the small intestine, vitamin D allows the absorption of calcium through an active transcellular pathway and a passive paracellular pathway.

Primary and secondary hyperparathyroidism

Primary hyperparathyroidism refers to an abnormality to the parathyroid gland itself, such as an adenoma or hyperplasia causing the gland to oversecrete. This is characterized by lab values that show elevated PTH levels, hypercalcemia, and hypophosphatemia. Primary hyperparathyroidism is customarily due to an adenoma, hyperplasia, or even more rare, a carcinoma. Adenomas are very sporadic and can be surgically resected. Hyperplasia can be found in cases of multiple endocrine neoplasia (MEN) types I and IIa and in an autosomal dominant condition called familial hypocalciuric hypercalcemia. In MEN type I, patients are often characterized by having tumors in the pituitary gland, parathyroid gland, and pancreas. MEN type IIa is characterized by the presence of medullary thyroid carcinoma, pheochromocytoma, and parathyroid hyperplasia. In familial hypocalciuric hypercalcemia, there is a mutation of the calcium-sensing receptor in the parathyroid gland and kidney, resulting in a higher-than-normal setpoint. This causes a lack of inhibition of PTH secretion until a higher level of serum calcium, thus resulting in increased bone resorption and hypercalcemia [1].

Secondary hyperparathyroidism refers to the compensatory over secretion of PTH in response to abnormally low calcium in the blood due to other pathological processes such as renal failure, gastrointestinal malabsorption, or simply a vitamin D deficiency. Lab values differ according to the underlying pathology. In chronic renal failure, there will be elevated PTH, but with decreased calcium and elevated phosphate. In the setting of malabsorption and vitamin D deficiency, there will be elevated PTH but decreased calcium and phosphate [1].

Tertiary hyperparathyroidism is exceedingly rare but is seen in the context of continuous PTH secretion even after a secondary hyperparathyroidism precipitating condition is resolved. Lab values will show moderately elevated PTH, normal or elevated calcium, and decreased phosphate.

Parathyroid adenoma can be associated with overexpression of the cyclin D1 gene. It is also associated with multiple endocrine neoplasia (MEN).

Genetic testing for mutations in the MEN1 gene is available for people suspected to have MEN1. A mutation in the MEN1 gene is found in about 80% to 90% of families diagnosed with MEN1. Approximately 65% of people with 2 or more tumors associated with MEN1, but no family history, will have a mutation in the MEN1 gene.

Further diagnostic evaluation for MEN 1 syndrome include:

- Serum prolactin, insulin-like growth factor 1 (IGF-1), fasting glucose, insulin, and proinsulin levels, albumin-corrected calcium level test, Serum fasting gastrin and fasting and meal stimulated pancreatic polypeptide (PP), fasting VIP, and glucagon level test
- Magnetic resonance imaging (MRI) scan of the brain to rule out pituitary adenoma
- MRI or computed tomography (CT) scan of the chest and abdomen when serum pancreatic polypeptide, and serum levels of vasoactive polypeptide are abnormal.

A specific test for parathyroid adenoma is sestamibi parathyroid scintigraphy, the sestamibi scan. This nuclear imaging technique reveals the presence and location of pathological parathyroid tissue.

4DCT is used as second line investigation to diagnose parathyroid adenoma. In addition to the three dimensional imaging of a conventional CT scan, 4DCT provides imaging on the changes of iodinated contrast enhancement overtime and present them in a video format (from plain imaging to arterial to venous and delay phases). Parathyroid adenoma would show low density on non contrast image, with peak enhancement during the arterial phase, then slowly fade away until the delay phase.

Ultrasonography (US) and parathyroid scintigraphy (PS) with 99mTc-MIBI are common methods for preoperative localization of parathyroid adenomas but there discrepancies exist with regard to diagnostic accuracy. The recent The meta-analysis determined a pooled sensitivity for scintigraphy of 83% [99% confidence interval (CI) 96.358 -97.412] and for ultra-sonography of 80% [99% confidence interval (CI) 76-83], While the pooled specificity of Scintigraphy was 87% [83-91%], and that of ultrasonography was 77% [71-82%] [99% confidence interval], The pooled sensitivity of two methods are not statistically different but the pooled estimate of PS specificity is significantly higher than US specificity [3].

FNA of enlarged parathyroid glands by CT or ultrasound guidance was initially described in early 1980s. Studies have since shown FNA to be very specific in distinguishing between parathyroid and non parthyroid tissue. Cytology of FNA is less sensitive than measuring PTH levels of aspirate because follicular thyroid tumors can be misinterpreted as parathyroid tissue on FNAC.

Histopathological feature of parathyroid adenoma shows chief cells arranged in palisaded pattern around blood vessels. A rim of residual normal gland is present in approximately 50% (Fifty percent) of adenoma cells. The rim is often separated from adenoma by capsule.

Parathyroid carcinomas are rare neoplasms, accounting for less than 1 per cent (1%) of all cases of primary hyperpaartahyroidism. Most cases occur during fourth or sixth decades of life, there is no gender differences in the incidence of carcinomas, in contrast to female prepondence observed for adenomas. Very rarely, these tumours have been reported in the pediatric age group.

Most affected patients have serum calcium levels more than 14 mg/dl. Metabolic complications are considerably more common in carcinoma than in patients with adenoma.

Parathyroid carcinoma has been reported in 15% patients with HPT-JT syndrome,increased risk also been reported in patients with isolated familial HPT, but these tumors occur very rarely with MEN 1 and MEN 2A1.

As reported by Schanz and Castleman, the principal features for diagnosis of carcinoma include the presence of thick fibrus bands, mitotic activity, capsular invasion and vascular invasion. However neither mitotic activity nor trabecular growth are specific for malignancy[1]. Mitotic activity occurs in substantial portion of adenomas and hyperplesias, although the presence of abnormal mitoses is characteristic of carcinomas.

Presence of collections of neoplastic chief cells in the capsule of parathyroid neoplasms(entrapment)can not be used as criterion of malignancy, because this feature ocuurs more commonly in adenomas. However invasion of adjacent tissues, perineural psace or thyroid gland is diagnostic of carcinoma. Adenomas may be distinguished from hyperplasis by using prepoertive localization studies such as ultrasonography, Tc Sestamibi scintigraphy, operative findings, intraoperative PTH (IOPTH) assays. Most

adenomas involve a single gland, whereas enlargement of at least two glands is usually apperant on ^{99m}Tc-sestamibi scintigraphy in cases of double adenomas and hyperplasias. The presence of single, enlarged hypersecreting gland with three normal glands is virtually diagnostic of adenoma.

In the present case the parathyroid adenoma was solitary, occult and could only be discovered on detailed evaluation as patient had only chromic back ache. Upon the surgical resection of parathyroid adenoma there was instant drop in serum parathormone levels intraoperatively [3].

In this case the underlying calcium deficiency might have resulted in the excessive secretion of serum parathormone, thereby leading to parathyroid adenoma. The patient had uneventful recovery on post operative follow up of 2 years.

Conclusion

Chronic back ache could be due long standing hyperparathyroidism secondary to parathyroid aenoma and hence should be evaluated in detail to rule out underlying endocrine disorder i.e. hyper parathyroidism followed by appropriate localing tests to rule out parathyroid adenoma and subsequent surgical excision with meticulous histology and follow up with biochemical test.

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