Hyperparathyroidism revisited — Old wine in new bottles!

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ABSTRACT

Aim: Hyperparathyroidism (HPT) is a condition that occurs due to exacerbated activity of the parathyroid glands. According to the etiology it may be primary, secondary or tertiary hyperparathyroidism (pHPT, sHPT, tHPT). This is a study done to document and evaluate the presentations of primary and secondary HPT, with the associated complications and the approach to management in these patients, at our hospital. Materials and Methods: Twenty-one patients with HPT were encountered at Sri Ramachandra Medical College and Research Institute between January 2000 and January 2010. Operative notes, histopathology files, and medical records were used for the retrospective analysis of the patients with HPT. Parathormone, calcium, and phosphate levels were estimated on all the patients, to determine the primary or secondary etiology of this endocrine abnormality. Furthermore, these patients were subjected to ultrasonography (USG) of the neck and Technetium (99mTc) scan of the neck to identify the parathyroid gland. Results: This study revealed that about 76, 19, and 5% of the patients suffered from pHPT, sHPT, and tHPT, respectively, with a female preponderance (62%). The neoplasm in all patients with pHPT was parathyroid adenoma. The patients presented with renal, bony, and menstrual abnormalities. Cases with sHPT had a 15 – 20 year history of chronic kidney disease and they subsequently developed bony abnormalities. Even as all the patients with pHPT were managed with parathyroidectomy, individuals with sHPT were treated conservatively. Postoperative features of hypocalcemia were noted in only one patient. Conclusion: This study re-emphasizes that pHPT is more common and is often due to an adenoma. Recent advances in parathormone sampling operatively and minimal access surgery, along with accurate and prompt clinical diagnosis, is necessary for the cure of these patients presenting with obscure abdominal, bony, and renal ailments.

Key words: Females, hyperparathyroidism, parathyroid adenoma, parathyroidectomy

INTRODUCTION

Hyperparathyroidism (HPT) is one of the most important causes of calcium and phosphate metabolic disorders. It is a condition that occurs due to an increased activity of the parathyroid gland arising from either an intrinsic or extrinsic cause.[1] An intrinsic change in the parathyroid gland culminating in the overproduction of the parathyroid hormone (PTH) is termed as primary hyperparathyroidism (pHPT), while an extrinsic cause leading to the lowering of serum calcium level with subsequent hyperfunctioning of the parathyroid glands results in secondary hyperparathyroidism (sHPT). The most common cause of pHPT and sHPT is a parathyroid adenoma and chronic renal insufficiency, respectively. About 0.5 – 4% of the patients diagnosed with pHPT have parathyroid carcinoma.[2] This endocrine abnormality produces vague and variable bony, renal, menstrual, nervous, and abdominal symptoms in the patients, which is often ignored, and hence results in a delayed diagnosis. The imaging studies to identify the abnormal parathyroid gland are ultrasonography (USG) of neck and Technetium (99mTc) scan of neck. Nuclear imaging successfully detects persistent or recurrent
HPT. The gold standard treatment for these conditions is parathyroidectomy.

This study has been conducted to analyze the presentations of primary and secondary HPT and its associated complications. We have also aimed at evaluating the approach to the management of these patients.

**Materials and Methods**

This was a retrospective study conducted at Sri Ramachandra Medical College and Research Institute (SRMC and RI) between January 2000 and January 2010. In this period of ten years, among the patients with calcium and phosphate metabolic disorders, twenty-one patients were identified with hyperparathyroidism by perusal of the case files, operative notes, and histopathology reports. The patient details studied included serum levels of parathormone, calcium, and phosphate levels. Ultrasonography of the neck and a Technetium (99mTc) scan of neck were performed to identify the abnormal parathyroid gland. No workup was performed on the osteoporotic profile, urine calcium or creatinine clearances of these patients. In sixteen patients with pHPT and one patient with tHPT, parathyroidectomy was performed. Intraoperative PTH was not conducted on the patients. However, all the parathyroidectomy cases were followed up for two weeks postoperatively.

**Results**

The demographics in the present study highlight that about 76%, 19%, and 5% of the patients suffered from pHPT, sHPT, and tHPT, respectively. The prevalence of this disease was 62% in females, which indicated that they were more prone to develop HPT. About 77% of the females belonged to the age group of 20 – 50 years [Figure 1], and the maximum clustering was noted in the fourth decade, which accounted to about 62%. The neoplasm identified in all our patients with pHPT was parathyroid adenoma [Figure 2]. Details of the USG and Technetium (99mTc) scans of the neck were not available for all cases, and hence, the details could not be analyzed.

On evaluating the clinical presentation, the patients mainly had renal, bony or menstrual abnormalities at presentation [Table 1]. Symptoms in all of them included the involvement of two or more of these systems. An interesting case of an asymptomatic pHPT was also noted. A twenty-five-year-old, asymptomatic female patient was suspected to have an underlying silent parathyroid lesion causing HPT, when her eleven-month-old child, presenting with convulsions, was diagnosed with hypoparathyroidism. Screening revealed a parathyroid adenoma for which a parathyroidectomy was performed on her.

All four patients with sHPT gave a 15 – 20 year history of chronic kidney disease (CKD) and had subsequently developed bone abnormalities like osteoporosis, recurrent fractures, and Brown’s tumor. A seventy-five-year-old, male patient with a 20-year history of CKD and sHPT returned with elevated calcium and PTH levels. He was
subsequently diagnosed with tHPT and USG of the neck revealed hypertrophied parathyroid glands, and the patient underwent parathyroidectomy.

Only one patient developed features of hypocalcemia like tetany, carpopedal spasm, and paresthesia on the tenth postoperative day. This was attributed to the acute dysfunctioning of the remaining parathyroid glands. The patient was promptly started on supplemental calcium and became normocalcemic in four weeks. Patients diagnosed with sHPT were managed conservatively with calcium and vitamin D3 supplements.

**Discussion**

Hyperparathyroidism is a disease characterized by an excessive secretion of PTH, which is normally regulated by a negative feedback loop. The plasma concentration of ionized calcium and phosphate inhibit the PTH production. Elevation in PTH leads to hypercalcemia, hypercalciuria, and hypophosphatemia. The incidence of HPT is maximum in older women (> 40 years), which correlates with our study.[3]

Hyperparathyroidism is classified mainly into primary, secondary, and tertiary. Primary HPT occurs due to an adenoma or hyperplasia involving all the four glands that may be a part of syndromes such as Type I and Type II of Multiple Endocrine Neoplasia (MEN), familial hypocalciuric hypercalcemia, and hyperparathyroidism–jaw tumor syndrome. Secondary HPT is typically characterized by a low level of serum calcium that occurs due to an underlying renal pathology and elevated PTH sets in to compensate for the hypocalcemia. Tertiary HPT develops with chronic hyperstimulation of the parathyroid glands. It is a state in which the glands function autonomously producing high levels of PTH and fail to normalize despite the serum calcium levels remaining within the reference range or even the elevated range. Hyperparathyroidism during pregnancy, as mentioned earlier, results in congenital hypoparathyroidism, as the calcium crosses the placental barrier and suppresses the parathyroid gland of the fetus.

The typical symptoms of HPT are classically described with the mnemonic, “painful bones, renal stones, abdominal groans, and psychic moans,” and these features were also noted in our study. The differential diagnosis of hypercalcemia includes adverse reaction to lithium, thiazide diuretic, and parenteral nutrition, familial hypocalciuric hypercalcemia, berylliosis, histoplasmosis, coccidioidomycosis, leprosy, lytic bone metastasis, multiple endocrine neoplasms, pheochromocytoma, vasoactive intestinal polypeptide hormone–producing tumor, ectopic HPT, exogenous calcium intake, and sarcoidosis.

Investigation of HPT involves estimating PTH, total serum calcium, and phosphate levels, which distinguish primary from secondary HPT. Serum albumin is estimated, as its correction becomes important in sHPT and the associated CKD. The imaging modalities commonly used in patients with pHPT include USG, Magnetic Resonance Imaging (MRI), Computed Tomography (CT), and the Sestamibi scan, which aids in localization of the abnormal gland.[4] The various methods of detection of PTH are the novel immunoradiometric assay, for detection of the fully intact molecule of PTH, and intraoperative venous sampling of PTH following excision of the hyperactive parathyroid glands. Generally a fall in the PTH concentration of more than 50% from the baseline level, 5 – 10 minutes postoperatively, suggests the absence of any residual hyperfunctioning tissue. This test has greatly reduced the postoperative failure rate of initial parathyroidectomy surgery from 6 to 1.5%.[5] and has decreased the need for performing frozen sections.[6] All excised parathyroid tissue samples are sent for histopathological examination. Ghandur-mnaymneh and Kimura[7] have clearly stated the criteria for histopathological diagnosis of the parathyroid adenoma and hyperplasia.

All the patients with pHPT in this study were managed with open parathyroidectomy. Minimal access parathyroidectomy is more advantageous as it is easier and quicker to perform, causes less pain and gives better cosmetic results.[8] Persistence of symptoms following an unsuccessful surgery is usually attributed to a missed parathyroid adenoma or due to inadequate resection of the unappreciated multigland disease.[9] In our series patients with sHPT were managed conservatively with calcium and vitamin D supplements, while tHPT patients underwent parathyroidectomy.

**Conclusion**

This study re-emphasizes the fact that pHPT is more common and is often due to an adenoma. We need a high index of suspicion in patients who repeatedly seek consultation for obscure abdominal, bony, and renal ailments. An accurate diagnosis, timely investigations, and precise surgery helps to cure these patients, who would otherwise be labeled as hypochondriacs. Secondary hyperparathyroidism treated with calcium and phosphate supplements reverses the PTH levels to normal. Recent advances in PTH sampling operatively have considerably reduced the ‘missed glands’ at surgery. Minimal access surgery is the way ahead.
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