Brief Communication

Primary hyperparathyroidism in India: A cocktail of contemporary and classical presentations: Lesson from 47 cases

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ABSTRACT

Primary hyperparathyroidism (PHPT) is now the contemporary form of previously existing classical disease, which is increasingly diagnosed due to hypercalcemia with asymptomatic form predominant in developed countries, whereas symptomatic form predominant in developing countries. So, we highlighted important subtle features of PHPT, problems in diagnosis in day to day practice in patients with PHPT at our center.

Key words: Contemporary presentations, primary hyperparathyridosim, adenoma

Introduction

Primary hyperparathyroidism (PHPT) is the disease characterized by hypercalcemia due to the autonomous production of parathyroid hormone (PTH). PHPT can present as adenoma (85%), hyperplasia (14%) or carcinoma (1%) with 1% of the adult population and its incidence increases to 2% after the age of 55 years.[1] Subsequently, the clinical entity of asymptomatic form has become more frequent.

PHPT is now the contemporary form of previously existing classical disease, which is increasingly diagnosed due to hypercalcemia found in routine biochemical screening as frequently reviewed in Western literature. But, Indian physician still encounters a mixture of classical and contemporary PHPT due to the multifactorial reasons. So, we tried to highlight important subtle features of PHPT, problems in diagnosis in day-to-day practice and to frame out most practical, cost-effective and rapid protocol for the diagnosis.

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Materials and Methods

A retrospective, review of clinical, biochemical and histopathological data of all 47 patients with PHPT between January 2008 and June 2012 at our institution was undertaken. PHPT was based on the following criteria: (1) Persistent elevation of serum calcium above the upper limit of normal; (2) increased circulating intact PTH; and (3) histological evidence of parathyroid adenoma or hyperplasia. Serum calcium and phosphorus levels were measured by ion-specific electrode and phosphomolydate ultraviolet method, respectively. Serum intact PTH levels and 25(OH) vitamin D levels were measured using Radioimmunoassay (Diasorin, MN, USA). Intraoperative intact PTH level was measured at 10 min by the same assay and in some cases the result was available after 2 h.

Results

The mean age and the duration of the disease were 43 years (9-78 years) and 5.5 years (3 months to 8 years), respectively. Female to male ratio was 2.1:1. The most

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common presenting features were bone pains (86%), fatigue (96%) and abdominal pain (27%). The other manifestations were nephrolithiasis (49%) fracture (40.4%) and pancreatitis (27%). Rare presentations were behavioral disturbances, seizures, encephalopathy, arrhythmias, myopathy, oliguria, intractable constipation and paraparesis. Few patients were also misdiagnosed as rheumatoid arthritis, sciatica and lumbar spondylosis. Conversely, only few patients had brown tumors and pepper-pot skull as shown in Figure 1. Subperiosteal erosion was only found in 12%.

The mean corrected serum calcium, phosphorus, PTH and vitamin D level were 12.69 mg/dl, 2.55 mg/dl, 807.87 IU/l and 26.89 ng/dl, respectively. Sestamibi scan diagnosed parathyroid adenoma in all not in but four cases as per Figure 2. Hyperplasia was noted in three cases, ectopic parathyroid adenoma in one and carcinoma in one and atypical in one. PHT was accompanied with Multiple endocrine neoplasia-1 in one patient and pregnancy in another case.

Discussion

In our study, females were commonly affected (2.1:1, F:M). Most of the patients were less than 45 years of age, whereas patients from developed nations are diagnosed in the 5th and 6th decades.[1]

The presentation of PHPT has changed from a symptomatic to an asymptomatic disease globally.[2] There are striking discrepancies around the world with respect to incidence, symptoms and complications of PHPT. In India, PHPT is still an uncommonly diagnosed, overtly symptomatic disease of bones, stones and abdominal groans and psychic moans.[3-5] The differences are highlighted in Tables 1 and 2. Bone disease was the most common mode of presentation seen in 53% patients followed by the renal stones 26%. This is less than previously reported from India.[2] Even the symptomatic disease is picked up late after a series of management for fractures and renal stones by the orthopedic surgeons and the urologist.

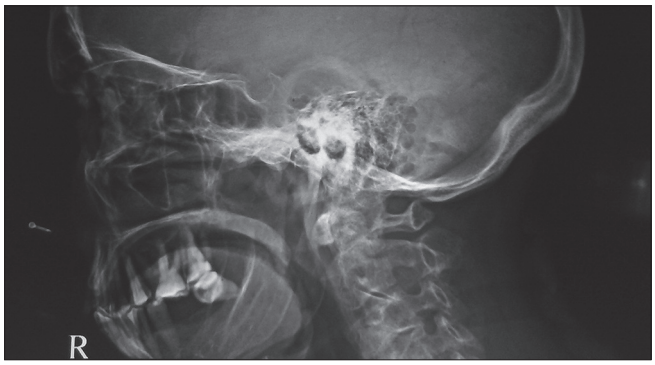

Figure 1: X-ray skull showing pepper pot appearance

There are 61 publications related to PHPT from various Indian centers containing data related to 858 PHPT patients. And the integrated data has been highlighted in Table 2. Data from Sanjay Gandhi Post Graduate Institute of Medical Sciences, India[4,5] revealed fractures in 57% of the brown tumors in 49% and 27% of patients (due to multiple fractures). Bhansali *et al*.,[6] found that 67% had bone disease, 48% had fractures, 21% had stone disease, 23% had psychiatric symptoms and 15% had peptic ulcer. Our data somewhat matches with other big institutions from India; however, features such as incidence of fractures, brown tumors and psychiatric manifestations were comparatively less and may be due to the population that our institution caters, which deals with diverse economic strata.

Table 1: Clinical manifestations of PHPT patients

Symptoms	Number of patients	% of patients affected	% of patients affected in West
Bone disease	344	77	5
Fractures	399	40.1	No record
Brown tumors	233	42	3
Renal disease	344	36	15
PMW	357	54.1	No record
Pancreatitis	302	15	Nil
Psychiatric	246	26.4	No record
Asymptomatic	246	5.6	>80

PHPT: Primary hyperparathyroidism

Table 2: Comparison of clinical manifestations of PHPT patients in India

Variable	SGPGI[4-5]	PGI[6]	KEM[3]	Our institution
Fractures	57	48	45	20.4
Brown tumors	39	-	22	04
Stones	36	21	43	49
Psychiatric	38	23	02	03
Neck mass	33	20	04	02
Pancreatitis	-	21	03	27

PHPT: Primary hyperparathyroidism, SGPGI: Sanjay Gandhi Post Graduate Institute of Medical Sciences, PGI: Post Graduate Institute of Medical Education and Research, KEM: King Edward Memorial Hospital

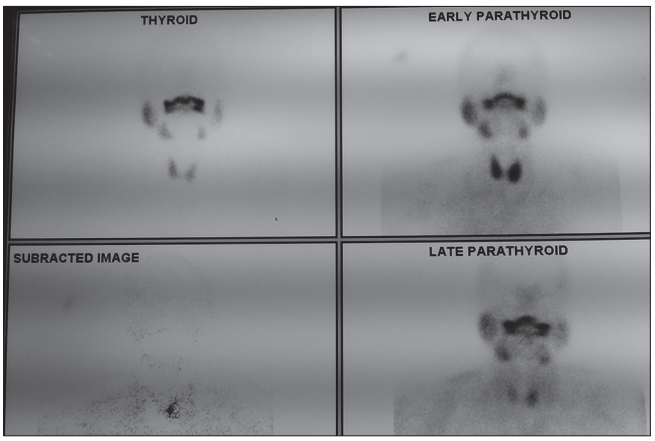

Figure 2: Sestamibi scan showing parathyroid adenoma

Table 3: Biochemical parameters of PHPT patients

Variables	SGPGI[4-5]	PGI[6]	KEM[3]	Our institution
S. calcium (mg/dl)	3.14±0.14	2.8±0.3	2.97±0.25	12.69±4.66
PTH (pg/ml)	1005.8±760.3	885.3±613.2	623±714	807.7±501.6
ALP (IU/l)	1466.5±1547.6	NA	426±549	756.5±691.7
Vitamin D (ng/ml)	11.6±8.74	NA	NA	16.89±13.26

PHPT: Primary hyperparathyroidism, SGPGI: Sanjay Gandhi Post Graduate Institute of Medical Sciences, PGI: Post Graduate Institute of Medical Education and Research, KEM: King Edward Memorial Hospital, ALP: Alkaline phosphatase, PTH: Parathyroid hormone

In the six articles with histopathology of 366 patients with PHPT, reported the prevalence of adenoma, hyperplasia and carcinoma as 89.1%, 6.56% and 4.37%, respectively.[5-10] This is higher than our study, only 6.3% of patients had hyperplasia, 6.6% had ectopic parathyroid adenoma, carcinoma and atypical presentation.

The mean PTH level was 807 ± 501.8 pg/ml, mean corrected calcium level was 12.69 ± 4.66 mg/dl and 25(OH) vitamin D levels was 16.89 ± 13.26, which were similar to other studies from India as shown in Table 3. It is speculated that Indian patients are more symptomatic due to the widely prevalent hypovitaminosis D.

Conclusion

PHT is a disease with serious complications and major morbidity. Indian physician still needs to develop a high index of suspicion because PHT escape diagnosis due to the subnormal calcium and PTH levels. So, we need to develop our own guidelines to diagnose PHT effectively in the face of economic, social, educational, awareness and availability issues.

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