CLINICAL ASPECTS OF PRIMARY HYPERPARATHYROIDISM

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ABSTRACT
We present 4 cases of primary hyperparathyroidism presenting with pathological fracture. All of them were females with age range of 26-37 years. The average time for which they remained symptomatic before diagnosis was made is 2 years. Ultrasonic abdomen showed renal calculi in all. Serum calcium was in the normal range in 2 of the cases. Serum PTH assay was elevated and Para-thyroid Scinti-scan was positive in all cases. Bilateral neck exploration was the procedure carried out on all of them. Parathyroid adenoma was the underlying cause in all the cases as confirmed on histopathology.

INTRODUCTION
Primary hyperparathyroidism (PHPT) is a condition characterized by inappropriately increased production of parathyroid hormone (PTH) caused by enlargement of one or more of the parathyroid glands. It is the most common cause of hypercalcemia. It is due to a benign parathyroid adenoma in 80% of cases and multiglandular involvement in 120% of cases. Parathyroid cancer is exceedingly rare (0.5% of all cases).1

In United States and many other developed countries, PHPT is mostly an asymptomatic disorder with hypercalcemia and raised levels of PTH.1,3 Detection of asymptomatic cases is made possible by routine check of serum calcium for any illness via automated laboratory analyzers that are widely available there.4 After successful surgical treatment, many patients thought to be asymptomatic become aware of improvement in unrecognized preoperative symptoms.4 Early symptoms include muscle weakness, polyuria, anorexia and nausea.5 Other manifestations are nephrolithiasis, bone and joint pains, osteoporosis, fracture, depression, fatigue, poor memory, vomiting, constipation, abdominal pain, peptic ulcer and pancreatitis.5,9 In developing countries including Pakistan, majority of the patients with PHPT are diagnosed in an advanced stage.7-10

The history and physical examination may provide the clue to diagnosis of PHPT, however, elevated PTH levels in the setting of hypercalcemia establish the diagnosis.7 Although measuring the concentration of ionized calcium rather than the total calcium provides added accuracy, one may alternatively use the total serum calcium concentration corrected for the patient’s albumin concentration.11

As familial hypocalciuric hypercalcemia can also present with raised levels of PTH, it can be distinguished from typical PHPT by (i) family history, (ii) onset of hypercalcemia early in life, (iii) exceedingly low urinary calcium excretion, and (iv) a specific gene abnormality.1

This study would provide us with an insight into the subject and help us to diagnose and treat more patients at an early stage when it is asymptomatic or only mildly symptomatic as late presentations can be terrible.

CASE REPORTS
We present four cases of primary hyperparathyroidism presenting at Hayatabad Medical Complex and Khyber Teaching Hospital during the years 2005 and 2006 respectively.

Demographic details of all 4 cases are presented in Table 1.

It was found that in all 4 cases, pathological fracture was the main presenting complaint. Two of them had a history of multiple fractures. One of the two had become bedridden due to fractures. Bodyaches and pains were the earliest symptoms experienced by all the 4. The average time for which they remained symptomatic before diagnosis was made is 2 years. One of the patients had left mandibular swelling (Fig-1), giving cystic appearance on x-rays. Family history was insignificant in all the 4 patients. Neck
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swelling was palpable in one having history of multiple fractures and the swelling moved up and down with swallowing. Left inferior parathyroid gland was involved in 3 of them. Ultrasound abdomen showed renal calculi in all of them but were small in size and for 2 of them it was an incidental finding.

The average age was found out to be 32 years. All 4 of the patients were females.

Serum calcium was in the normal range in 2 of the cases (Table-1).

Bilateral neck exploration was the procedure carried out on all of them. All the patients fared well after surgery except that one of them developed transient hypocalcemia and tetany that was treated by calcium and vitamin D supplements. Parathyroid adenoma was the underlying cause in all the cases as confirmed on histopathology.

DISCUSSION

Although PHPT can occur at any age, it is rare below the age of 50 years. Bhatti A et al and Biyabani S et al in their studies based in Pakistan have shown that most of the patients were below 40 years of age. Similarly all the patients in our study were below 40 years of age.

In many developed countries it is rare to have overt symptoms in cases of PHPT and majority of the cases (80%) diagnosed are asymptomatic. Although the incidence of nephrolithiasis has reduced much over time, it still remains the most common manifestation (15-20% of cases) of PHPT.

However Pakistani studies including ours suggest that late presentations are still common here with hyperparathyroid bone disease and renal stones being the commonest first presentation. Biyabani S and Talati J in their study have demonstrated that 35% of their patients with primary hyperparathyroidism had renal stone disease, 32.4% had bone disease alone and 27% had both bone disease and renal stones. While the number of patients with neither bone disease nor stones was estimated to be only 5.4%. Routine testing of serum calcium can help us to detect cases of primary HPT early in a big way.

It is important to remember that patients with primary HPT occasionally have normal serum calcium levels and some have even persistently normal serum calcium levels. In these patients diagnosis is made by obtaining serum PTH levels. However in patients with persistently normal serum calcium levels having elevated serum PTH, all the known causes of secondary HPT including vitamin D deficiency should be ruled out (25-hydroxyvitamin D levels should be >20 ng/mL). Bhatti A et al used serum PTH and alkaline phosphatase levels to differentiate between PHPT and osteomalacia. Levels of both these indicators fall rapidly after vitamin D therapy in osteomalacia but remain high in PHPT.

Parathyroidectomy is the mainstay of treatment. There is a consensus that surgery should

### PATIENTS DEMOGRAPHIC DATA

<table>
<thead>
<tr>
<th>S. No</th>
<th>Age</th>
<th>Sex</th>
<th>Duration of symptoms before diagnosis</th>
<th>Serum Calcium mg/dl</th>
<th>Serum alkaline Phosphatase mg/dl</th>
<th>Serum PTH assay pg/ml</th>
<th>Tc99m bone scan conclusion</th>
<th>Parathyroid Scinti-scan</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>37</td>
<td>F</td>
<td>22 months</td>
<td>12.5</td>
<td>1007</td>
<td>557</td>
<td>metabolic bone disease/HPT</td>
<td>Positive</td>
</tr>
<tr>
<td>2</td>
<td>35</td>
<td>F</td>
<td>26 months</td>
<td>11.5</td>
<td>880</td>
<td>462</td>
<td>metabolic bone disease/HPT</td>
<td>Positive</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>F</td>
<td>12 months</td>
<td>9.1</td>
<td>485</td>
<td>999</td>
<td>metastases</td>
<td>Positive</td>
</tr>
<tr>
<td>4</td>
<td>26</td>
<td>F</td>
<td>36 months</td>
<td>8.52</td>
<td>1505</td>
<td>1636</td>
<td>metastases</td>
<td>Positive</td>
</tr>
</tbody>
</table>

* After correction for hypoalbuminemia (adding 0.8 per dl to the total serum calcium value for every 1 gm/dl below a serum albumin conc. of 4 gm/dl).
be undertaken on all symptomatic patients. Surgery is also advised for asymptomatic patients who meet one of the following criteria: Serum calcium > 1 mg/dl above the upper limit of normal, marked hypercalcuria (> 400mg/dl) or reduction in creatinine clearance by more than 30% below age and sex matched reference values, markedly reduced bone density (T-score < -2.5) at any site and age less than 50 years.1,2 The asymptomatic patients who are to be followed without surgery should undergo serum calcium estimation on 6 monthly basis. Bone densitometry should be repeated annually at three sites, the lumbar spine, hip and distal radius. Such patients are asked to maintain adequate hydration, avoid thiazide diuretics and prolonged immobilization, while dietary calcium intake up to 1000 mg/day may be taken.1,2

With the exception of familial hypocalcaemic hyperparathyroidism, most experts feel that parathyroid surgery is indicated when PHPT presents in the context of a familial syndrome like in multiple endocrine neoplasia (MEN)1 and MEN2A. The guidelines for asymptomatic PHPT are thus not directly applicable to these special situations.1

REFERENCES


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