PRIMARY HYPERPARATHYROIDISM AT THE SINGAPORE GENERAL HOSPITAL

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SYNOPSIS

A retrospective study was carried out on 15 patients with Primary Hyperparathyroidism treated by the authors at the Singapore General Hospital from 1974 to 1982.

Their ages ranged from 18 to 68 years (mean 40.9y). There were 10 female and 5 male patients. Five patients presented with bone disease, 5 with renal stones, 2 with lethargy, polyuria and polydipsia, 2 with hypertension and 1 with symptoms in the gastrointestinal tract. Six patients had both bone and renal stone disease.

All patients had elevated serum calcium levels ranging from 10.5 to 13.6 mg % (mean 12.6mg%). Phosphate levels ranged from 1.6 to 12.6 mg% and was of no discriminatory value. Serum alkaline phosphatase was raised in 12 patients and was related to the presence of bone disease. Serum albumin ranged from 2.6 to 5.0 g/dl (mean 4.1 g/dl) and was below 4.0 g/dl in 8 patients.

At surgery, 14 patients had an adenoma while 1 had a parathyroid carcinoma.

The unusual feature found in this study was the presence in 6 patients of both bone disease and renal stone disease from primary hyperparathyroidism.

INTRODUCTION

The bone changes of Primary Hyperparathyroidism were first described by von Recklinghausen (1891). Askanazy (1904) first noted the association of a tumour in the neck with osteitis fibrosa cystica but it was not until 1925 that the first parathyroidectomy was performed in Vienna (Mandl, 1926). The association of hyperparathroidism with renal stones was recognised in 1932 (Cope et al, 1957) and hypertension (Hellstrom, Birke and Edvall, 1958) since that time.

Bone disease was the predominant presenting feature earlier in the century which has given way to calculous disease of the urinary tract (1-3). More recently, several studies indicated a growing recognition that Primary Hyperparathyroidism exists frequently as a seemingly mild condition lacking the florid renal and skeletal manifestations of past cases due to the availability of accurate and inexpensive measurement of serum calcium (4-6).

The purpose of this paper is to present our experience in Singapore General Hospital.

PATIENTS AND METHODS

A retrospective study was carried out on patients presenting to the authors with primary hyperparathyroidism at the Singapore General Hospital over an 8 year period (August 1974 to March 1982). The mode of presentation and results of various investigations were analysed. Their investigations included: (1) serum — calcium, phosphate, alkaline phosphate, urea, electrolytes and albumin, (2) Xrays of hands, thorax, skull, intravenous pyelogram and parathyroid arteriogram. Serum parathyroid hormone assay was not available.

The diagnosis of primary hyperparathyroidism was based on the following criteria: (1) histological evidence (after parathyroidectomy); (2) clinical features consistent with the disease with no other cause of hypercalcaemia found.

RESULTS

In the 8 year period under study, there were 15 patients with primary hyperparathyroidism treated by the authors.

Clinical and Biochemical Features

1. Age and Sex

Ages of the 15 patients ranged from 18 to 68 years (mean 40.9y). Their age distribution is shown in Table I. The largest number of patients were in the 20-29 age group. There were 10 females and 5 males.

TABLE I
DISTRIBUTION OF PATIENTS BY AGE* AND SEX

Age	Males	Females	Both Sexes
20	0	1	1
20 — 29	2	2	4
30 — 39	2	1	3
40 — 49	1	2	3
50 — 59	0	2	2
60 — 69	0	2	2
Total	5	10	15

*Age at diagnosis of Primary Hyperparathyroidism

2. Mode of Presentation and Symptoms

The majority of patients presented with symptoms due to urinary calculi or bone disease (Table II). Two patients presented with hypertension. Two patients had hypercalcaemic symptoms of lethargy, polyuria and polydipsia. Only 1 patient had a gastrointestinal complaint of constipation. None of our patients had psychiatric or acute hypercalcaemic symptoms of confusion and vomitting. Two patients had a palpable parathyroid gland in the neck.

TABLE II
MODE OF PRESENTATION OF PRIMARY HYPERPARATHYROIDISM

Symptoms	No. of Cases
Renal (stones or nephrocalcinosis)	5
Bone disease	5
Hypertension	2
Hypercalcaemia	2
Gastrointestinal	1

3. Laboratory Investigations

The serum calcium level before treatment was elevated in all patients ranging from 10.5 to 13.6 mg% (Normal 8.4—10.4), mean was 12.3 mg%. Higher levels of serum calcium were noted in patients with bone disease (Fig 1).

The serum phosphate level ranged from 1.6 to 12.6 mg%, thereby making it of little value as a diagnostic index.

Elevated levels of serum alkaline phosphatase were found in 12 patients; the majority were noted in patients with bone changes (Fig 2). Twelve patients had serum chloride levels of 102 mEq/L or above.

A chloride over phosphate ratio of greater than 30 (described as suggestive of primary hyperparathyroidism) was noted in 14 out of the 15 patients.

The serum albumin ranged from 2.6 to 5.0 g/dl with a mean value of 4.1 g/dl. Eight patients had a serum albumin of 3.8 g/dl or less (Normal range 3.8 to 5.0 g/dl).

Raiological Features

1. Routine Xrays

Eleven patients had evidence of urinary stones on either plain Xray or intravenous pyelography.

Nine patients had osteitis fibrosa cystica.

Six patients had radiological evidence of both urinary stone and bone disease.

Other radiological features in patients with bone disease included generalised osteoporosis, phalangeal subperiosteal resorption, terminal phalangeal resorption, skull moth eaten appearance, and stress fractures.

2. Arteriography

Parathyroid arteriograms were done in 8 patients and they were found to be useful in locating the involved gland preoperatively in 4 patients.

Operative Findings

1. Pathologic Findings

At operation, the inferior glands were noted to be most involved (Table III). Two patients had tumours localised to the upper mediastinum.

TABLE III
DISTRIBUTION OF TUMOURS

	No. of Cases	
	Left	Right
Superior	1	2
Inferior	4	6
Mediastinum	2	

2. Histological Findings

Fourteen patients had adenomas (all singular) while 1 patient had a low grade carcinoma removed from the mediastinum. There were no cases of parathyroid hyperplasia in this series.

3. Post-operative Serum Calcium

Postoperatively 6 patients became normocalcaemic. Seven patients developed prolonged hypocalcaemia requiring treatment. Two patients remained hypercalcaemic requiring a second operation to remove the offending gland situated in the mediastinum.

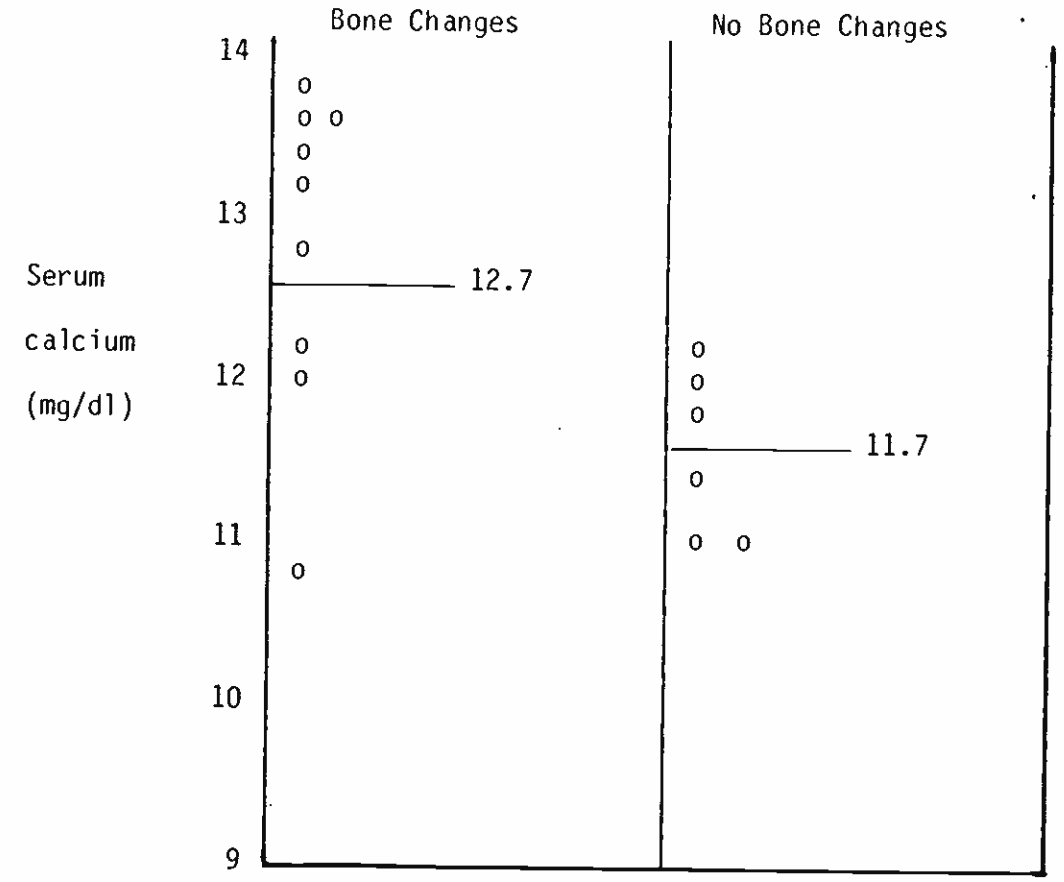

FIGURE 1
Serum Calcium in Patients with Bone and no Bone Changes (Mean for each group indicated)

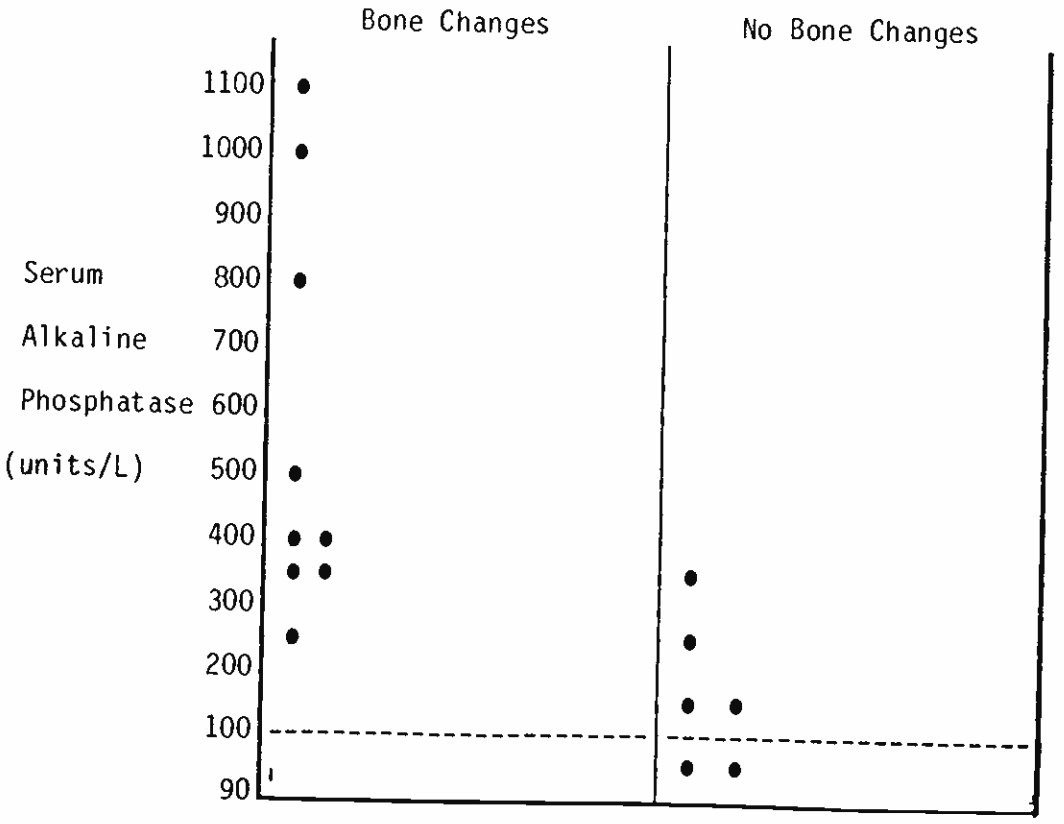

FIGURE 2
Serum Alkaline Phosphatase in Patients with Bone and no Bone Changes

DISCUSSION

Primary hyperparathyroidism is a disease with a peak incidence in the fifth decade (7). Women are affected approximately twice as often as men (7) and our series agrees with these reports. The mode of presentation has shifted from bone disease earlier in the century to that of renal tract calculi. In our series, we had about equal numbers of patients presenting with one mode or the other. None of our 15 patients were diagnosed as a result of hypercalcemia found incidentally as part of a multiphasic health screening at the Singapore General Hospital.

In our study, the serum calcium was the most important diagnostic test exceeding 10.4 mgm % (Normal range 8.4 — 10.4 mgm %) in every case. There have been reports of patients with primary hyperparathyroidism having normal serum calciums at one time or another (8). Repeated calcium estimations are therefore necessary in all patients suspected of having this condition. Lloyd (9) in 1968 reported higher levels of calcium in patients with overt bone disease. We were able to confirm this relationship in this study.

Elevated levels of serum alkaline phosphatase are reported in patients with and without radiological evidence of bone disease, although the proportion of those with an elevated level is greater in patients with bone changes (8). In our patients, we also noticed this association. In addition we noticed higher levels of serum alkaline phosphatase in patients with bone changes as compared to those without bone changes. The plasma chloride may be useful in the differential diagnosis of patients with hypercalcaemia as parathyroid hormone acts on renal tubules to promote bicarbonate loss resulting in hyperchloraemic acidosis in primary hyperparathyroidism. Hypercalcaemia due to other causes promotes potassium and chloride loss. Serum chloride levels above 102 mEq/L have been found in hyperparathyroidism and below this level in patients with hypercalcaemia due to other causes (10). The chloride to phosphate ratio in patients with hyperparathyroidism is usually greater than 30 while in those with hypercalcemia from other causes it is less than 30 (11). We find this to be a reliable index as 14 out of 15 of our patients do have ratios above 30. Serum radioimmunoassay of parathyroid hormone was introduced by Berson et al (1963) (12). Although early reports suggested that all patients with hyperparathyroidism had elevated levels, it was not so in the experience of others (1). Our patients did not have the benefit of parathyroid hormone radioimmunoassay as it was not available here at that time. Even in its absence we felt that a diagnosis of primary hyperparathyroidism could be confidently made in our cases, perhaps due to the advanced nature of the disease at presentation.

Arteriography was found by Seldinger (13) to be useful in locating the involved glands pre-operatively but we were only able to do so in 50% of our patients. The lower parathyroids were involved most frequently (14) as we found in our series. Adenomas predominate in most series (14) with carcinoma being the least common. Cope's series (15) of 250 cases contained 34 patients with hyperplasia and 14 patients with parathyroid carcinoma. Most groups report initial operative success rate of 90% (14, 16). In our series, we find 2 patients remaining hypercalcaemic after operation due to the fact that their tumours were in the mediastinum requiring a second operation to make them normocalcaemic. Although several studies have emphasised an apparent increased incidence of primary hyperparathyroidism found on routine biochemical screening, we still find this endocrine condition to be uncommon here. Out of almost 5000 estimations of serum calcium done in multiphasic screening at the Singapore General Hospital in the last 6 years, no cases of asymptomatic hyperparathyroidism have been diagnosed this way.

Our series is unusual in having 6 patients who have involvement of both the urinary tract and the skeletal system. We are unable to explain this feature found in our study. We think it is unlikely to be solely due to the advanced state of the disease at presentation as historical descriptions of hyperparathyroidism (17) have tended to describe a presentation with only one of the 2 systems rather than both.

The advanced state at presentation in our patients may be the explanation for our serum albumin findings. Recent studies have shown that in hypercalcemia, a low serum albumin strongly suggests underlying malignant disease (18). A serum albumin of 4.05 g/dl was suggested as a highly discriminatory cut-off point (19) indicating hyperparathyroidism only if the serum albumin was above that value. Our study shows that a low serum albumin is compatible with primary hyperparathyroidism.

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