Primary Hyperparathyroidism – A surgical review of 12 cases

Freda A. Meah, FRACS
Associate Professor
*T.T. Tan, MRCP(UK)
Lecturer
Abdullah Taha, FRCS
Lecturer
*B.A.K. Khalid, FRACP, PhD
Professor of Medicine and Dean

*Department of Surgery and *Medicine, Universiti Kebangsaan Malaysia*

Summary

Twelve cases of primary hyperparathyroidism operated by the Universiti Kebangsaan Malaysia Surgical Team from 1978 to 1989 were reviewed. There was a preponderance of Indian females in this series. The majority of the cases presented late and with complications. Renal calculi and bone disease were the commonest complications noted. Of the 12 patients, 9 had single parathyroid adenoma of which 4 were ectopically located, and 2 had hyperplasia of the parathyroids. These were all successfully operated. The remaining patient had 2 failed neck explorations. Failure at initial exploration was due to ectopic location of the glands. Meticulous surgical technique, knowledge of the anatomical variations of location of the parathyroid glands and availability of frozen section facility are essential for successful outcome.

Key words: Primary hyperparathyroidism, Parathyroid surgery.

Introduction

Primary hyperparathyroidism is one of the two commonest causes of hypercalcemia in hospital populations. In the community at large it is the commonest cause of raised serum calcium.[1,2] With the advent of multichannel analysers, recognition of asymptomatic hypercalcaemia and primary hyperparathyroidism has increased.[2,3] The treatment for primary hyperparathyroidism remains surgical. Despite the introduction of newer and more sophisticated imaging techniques[4-6] neck exploration in a previously unoperated patient by an experienced surgeon provides the best way of locating the adenoma. For the past 11 years, 12 cases of primary hyperparathyroidism were referred from the Universiti Kebangsaan Malaysia (UKM) endocrinology unit and operated upon in the UKM surgical unit. This paper reviews the results of the surgery.

Materials and Methods

Case records of 12 patients with primary hyperparathyroidism referred for neck exploration from the Endocrinology Unit of UKM over a period of 11 years (1978 to 1989) were reviewed retrospectively. The diagnosis of primary hyperparathyroidism was based on (1) clinical, biochemical and radiological (in some patients) features consistent with primary hyperparathyroidism, (2) raised immunoreactive parathyroid hormone (iPTH) (when this assay became available in the UKM Endocrinology Unit), and (3) absence of other known causes of hypercalcemia.

Serum calcium, phospate, alkaline phosphates and albumin were measured using Technicon Multi-channel Analyser (Terrytown, N.Y.). Hypercalcemia is defined as total serum calcium level (corrected for albumin) of greater than 2.63 mmol/L. Total corrected calcium (mmol/L) = measured calcium (mmol/L) + 0.02 x (40-serum albumin in g/L). Serum iPTH were assayed using Incstar PTH-Mid-molecule radioimmunoassay kit (Incstar corporation, Minnesota, USA).

Results

The race, sex and age distribution data of patients at presentation are shown in Table 1. Of the 12 patients reviewed. 9 (75%) were female of which 5 were Indians. The majority of the patients (83.5%) presented between the age of 30 to 60 years. The youngest and the oldest patients were 12 and 61 years old respectively. The laboratory data of the patients at presentation are shown in Table 2. The mean serum calcium level was 3.34 mmol/L (range 2.94 – 4.10 mmol/L. Only one patient had serum calcium level greater than 4.0 mmol/L. Of the 7 patients with normal serum creatinine 4 had low serum phosphate concentration. All patients (where data were available) had raised alkaline phosphatase but only 7 patients were symptomatic (Table 3).

All the patients had symptoms of hypercalcemia and/or complications of primary hyperparathyroidism (Table 3). Polyuria, lethargy, epigastric pain and constipation were the commonest hypercalcemia symptoms in that order. Renal calculi (75%) and clinical bone disease (50.8%) were the commonest complications noted. Interestingly, in 3 of the patients, the parathyroid adenoma was clinically palpable.

Table 1
Age, Race and Sex Distribution of the 12 Patients with Primary Hyperparathyroidism

Age (yr)	No. of Patients	Race	Male	Female	Total
10 – 19	1	Chinese	1	2	3
20 – 29	0	Indian	–	5	5
30 – 39	3	Malay	2	1	3
40 – 49	4	Others	–	1	1
50 – 59	3				
60 – 70	1				
Total	**12**		**3**	**9**	**12**

Table 2
Laboratory data of the 12 patients with primary hyperparathyroidism

Patient	SERUM CONCENTRATIONS				
	Calcium (mmol/L)	Phosphate (mmpl/L)	Alk. Phos (U/L)	Creatinine (umol/L)	*PTH (pmol/L)
1	3.30	0.63	N.A.	N.A.	N.A.
2	3.00	1.10	> 350	70	100.6
3	3.73	1.03	N.A.	67	N.A.
4	3.00	0.70	150	98	N.A.
5	4.10	N.A.	> 350	138	N.A.
6.	3.10	1.00	> 350	96	N.A.
7	3.75	1.02	> 350	212	> 2500
8	3.08	0.94	139	142	N.A.
9	3.74	0.57	137	128	N.A.
10	3.10	0.80	154	89	N.A.
11	2.94	0.74	118	101	N.A.
12	3.30	0.68	143	93	437
Normal Range	2.13–2.63	0.88–1.58	30–115	62–124	29–85

N.A. = Not available **PTH assay was available only in 1989*

Table 3
Clinical presentations of 12 cases of primary hyperparathyroidism

Presentations	No. of Patients
Lethargy	4
Palpable parathyroid nodule	3
Metabolic bone disease	7
Pathological fracture of femur	1
Gastritis	3
Constipation	3
Pancreatitis	1
Renal calculi	7
Nephrocalcinosis	1
Polyuria	6
Pre-renal failure (dehydration)	1
Recurrent Urinary tract infection	2

The operative and histological findings are shown in Table 4. No attempt was made for localising the prathyroid glands preoperatively. All explorations were performed with frozen section facilities available except for the first. Of the 12 patients, 9 were successful on the first exploration, the remaining patients (No: 1, 2 and 6) underwent 2 neck explorations. In patient 1, a benign thyroid cyst was removed durintg the first exploration and he subsequently had a parathyroid adenoma located on the cervical thymus which was removed. The second patient underwent 2 unsuccessful operations. She is still hypercalcaemic with active bone disease and is currently managed with oral phosphate. Patient 6 had a previous exploration elsewhere. She was referred to us for re-exploration and a parathyroid adenoma was removed at the right para-oesophageal region.

Table 4
Surgical and histolical data of the 12 patients with primary hyperparathyroidism

Patient No.	No. of Operations	Operative Findings
1	2	1) Benign thyroid cyst 2) PTH Adenoma (cervical thymus)
2	2	Failed Explorations
3	1	Palpable nodule (Intrathyroid PTH adenoma)
4	1	Palpable nodule (PTH adenoma-right lower)
5	1	Palpable nodule (PTH adenoma-right lower)
6	2	1) Done elsewhere 2) PTH adenoma (right paraoesophageal)
7	1	PTH hyperplasia (recurred)
8	1	PTH hyperplasia
9	1	PTH adenoma-right lower
10	1	PTH adenoma (Left retrolaryngeal)
11	1	PTH adenoma (Right paraesophageal)
12	1	PTH adenoma - right lower

In both patients with hyperplasia three and a half glands were removed. Patient 7 unfortunately had recurrence of his hyperparathyroidism. A re-exploration was not considered because of severe ischaemic heart disease with heart failure despite having had a coronary artery bypass surgery.

Six of the patients were immediately normocalcaemic following surgery. Four patients had transient hypocalcaemia lasting between 2 weeks to 2 months. They subsequently became normocalcaemic. One patient had persistent hypocalcaemia.

Discussion

In contradistinction to a previous local report[7], there was a female preponderance of 3:1 in this series. This is similar to one of the authors' previous experience[8] and other reports[2,9]. The reason for the difference between these two local series is not clear. It is unlikely to be due to difference in patient populations seen in these two hospitals. In both the series the number of patients reviewed are small therefore the difference may be spurious. However, the age distribution amongst our patients and the late presentations, as evidenced by high prevalence of bone disease, are similar to that of Goh et. al.[7]. The importance of early recognition needs emphasis. In countries where multichannel analysers are widely used, measurement of serum calcium is routinely done, late presentation with multitudes of complication is rare and the incidence of asymptomatic primary hyperparathyroidism has increased[2,3]. Despite multichannel analysers being used in our hospital since 1975, early detection of hyperparathyroidism has not been the practice. This could be due to technical, laboratory or interpretative problems or the lack of clinical awareness of this condition.

It is rare for parathyroid adenoma to be clinically palpable, but in our series. 3 of the patients had parathyroid adenoma palpable in the neck. This further suggests that our patients presented late.

The surgeon performing parathyroid surgery must be well versed with the causes and presentations of hypercalcaemia. A thorough knowledge of the embryology and anatomic variations of location of parathyroid glands in addition to the availability of an experienced intraoperative pathologist is essential[11,12]. Pre-operative joint management with the endocrine colleagues is desirable especially in cases with complications. Post-operative hypocalcemia due to i) 'hungry bone syndrome' 2) hypomagnesaemia and/or 3) hypoparathyroidism can be severe and prolonged[13].

The pathology found in our patients are: adenoma in 9 patients (81.8%) and hyperplasia in two (18.2%). This is consistent with those of larger series[14,15]. The commonest location of the adenoma was the right lower position. There were 4 patients (36.4%) who had adenoma located in abnormal positions: 2 were in the paraesophageal, 1 in the retrolaryngeal area and 1 on the thyro-thymic tract. This shows that abnormally located parathyroid adenomas are fairly common.

Several imaging techniques have been used to pre-operatively localise the parathyroid glands. High resolution sonography and computed tomography (CT) and thallium-technetium substraction (TTS) scanning are the commonest methods employed[4-6,16]. The efficiency of these methods are highly operator and instrument dependent. The accumulated series for TTS scanning had a sensitivity rate of 82%, an accuracy of 78%, a positive predictive value of 94%nd a false-negative rate of 18%[5]. The reported accuracy for high resolution CT and sonography are between 50% – 77% and 69% – 78% respectively[4].

No elaborate pre-operative localising techniques need to be done when exploring the neck for the first time. However, the availability of an accurate imaging system would be a useful adjunct especially in those where the risk of prolonged anaesthesia is considerable. If a second neck exploration is being contemplated selective venous sampling proves to be the most useful modality for pre-operative localisation[5].

In conclusion, we would like to stress the importance of recognising the vague and variable presentations of hypercalcemia and an increased awareness of primary hyperparathyroism in the population. It is possible that this condition is being under-diagnosed as shown by the late presentations and the small number of patients in both our series and Goh et al[7]. Surgery is curative for this condition and should not be delayed. This may help to avoid getting the complications of prolonged hypercalcaemia and hyperparathyroidism.

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