

Management of hyperparathyroidism: A five year surgical experience

Ameer Afzal, Tooba Mahmud Gauhar, Waqas Tariq Butt, Ali Azim Khawaja, Khawaja Muhammad Azim
East Surgical Ward, Department of Surgery, Mayo Hospital and King Edward Medical University, Lahore.

Abstract

Objective: To summarize the management of hyperparathyroidism at a tertiary care hospital in Lahore, so that the disease characteristics specific to our population could be identified. Also to determine if focused parathyroidectomy was successful without intra operative localization studies.

Methods: Retrospective analysis was conducted on all cases of hyperparathyroidism, managed at the East Surgical Ward, Mayo Hospital, Lahore, during a five year period (2005-2009).

Results: Thirty-two cases of primary hyperparathyroidism and 3 cases of secondary hyperparathyroidism were managed at the East Surgical Ward from 2004-2009. For primary hyperparathyroidism the mean age of presentation was 40.78 ± 15.42 years and the mean duration of symptoms was 33.96 ± 27.29 months. Advanced musculoskeletal symptoms were the most common presenting feature followed by gastrointestinal complaints and recurrent renal stones. Unilateral neck exploration and excision of adenoma was carried out successfully in all cases where the results of ultrasound neck and technetium-99m sestamibi scan were concordant. Bilateral neck exploration was performed in all other cases. Decreased serum calcium level was achieved post operatively in all cases and no residual disease or recurrence was encountered on follow up.

Conclusion: Patients of hyperparathyroidism in our country, tend to present late after the development of complications. Pre operative localization studies like ultrasound neck and sestamibi scan have enabled us to carry out directed exploration rather than bilateral neck exploration in every case. Accurate pre operative assessment and safe surgery offers cure to all patients with primary hyperparathyroidism.

Keywords: Primary hyperparathyroidism, Secondary hyperparathyroidism, Lahore (JPMA 61: 1194; 2011).

Introduction

Primary hyperparathyroidism [pHPT] is the most frequently encountered cause of hypercalcaemia in the outpatient department.¹ The hypercalcaemia and hypophosphataemia seen in this condition is caused by the inappropriate excess secretion of parathyroid hormone (PTH).² Majority of the cases of primary hyperparathyroidism are caused by a single benign parathyroid adenoma. Few cases are due to hyperplasia or multiple adenomas and carcinoma is seen only in 1-2% of the cases.^{1,3}

Western data indicates that most patients with primary hyperparathyroidism are either asymptomatic or present with mild symptoms as the condition is increasingly being diagnosed on routine biochemical testing and PTH assay.³⁻⁶ However studies from Asian countries like India, China, Hong Kong and Malaysia show that most patients with primary hyperparathyroidism still present with classical symptoms of the disease and accompanying bone and renal complications.⁷⁻¹¹

Surgery is indicated for all patients with symptomatic primary hyperparathyroidism and selected asymptomatic patients (according to the NIH Consensus Conference 2002).⁵ In recent years, with the advances in pre operative localization studies such as ultrasound neck and technetium-99m sestamibi imaging and advent of intra operative rapid PTH assays the emphasis has shifted from bilateral neck exploration to unilateral exploration and focused parathyroidectomy.^{12,13} However the treatment of choice for primary or secondary hyperplasia remains bilateral neck exploration with subtotal or total parathyroidectomy with auto transplantation.^{1,14}

Parathyroid surgery is safe if carried out by an experienced surgeon and is successful in 95-99% of the cases with very low complication rates.^{5,14} It is associated with improved health related quality of life.¹⁵

Little data is available on the epidemiology and characteristics of parathyroid disease from Pakistan. Our objective to carry out this study was to help identify the disease characteristics specific to our population and to determine whether focused cervical exploration is successful when intra operative PTH or gamma probe is not used but pre operative localization studies have been carried out.

Patients and Methods

A retrospective analysis of patients presenting with hyperparathyroidism during five years (2004-2009) in East Surgical Ward, Mayo Hospital Lahore was made.

All the 35 cases were reviewed; the age, sex, presenting symptoms, duration of symptoms, preoperative calcium, phosphate, alkaline phosphatase and parathyroid hormone (PTH) levels were noted. Pre operative localization studies including ultrasound neck and technetium-99m sestamibi imaging had been carried out in all cases, the results of which were analyzed and compared. In addition all radiological evidence was reviewed. All laboratory investigations had been carried out from Shaukat Khanum Cancer Hospital laboratory for uniformity. The ultrasound neck was also done by a single experienced radiologist in all cases.

The surgery, in all 35 cases was carried out by a single experienced surgeon. Where pre operative localization studies were concordant, excision of the localized gland was carried out. In cases of failed localization, hyperplasia and secondary hyperparathyroidism, bilateral neck exploration was done. Intra operative monitoring of PTH or gamma probe was not used and parathyroid gland was identified based on the pre operative localization and the gross appearance per operatively. In a single case of parathyroid carcinoma ipsilateral thyroid lobectomy was also done. Similarly in case of mediastinal adenomatous gland thymectomy had to be simultaneously carried out. One patient had concurrent secondary thyrotoxicosis with primary hyperparathyroidism, subtotal thyroidectomy was done in addition to the excision of the adenomatous parathyroid gland.

Recurrent laryngeal nerve function was documented by observing the mobility of vocal cords in each case after the procedure. Post operatively patients were kept under observation in the ward and serum calcium levels were monitored at 12, 24 and 36 hours. All data was analyzed through SPSS version 17.0.

Results

Out of the 35 cases of hyperparathyroidism reviewed, 32 cases were of primary hyperparathyroidism and only 3 cases of secondary hyperparathyroidism due to chronic renal failure. The mean age at presentation of patients with primary hyper parathyroidism was 40.78±15.42 years (range 13-70 years). There was 28 (87.5%) females and 4 (12.5%) males. Twenty-eight (87.5%) patients with primary hyperparathyroidism presented with generalized body aches and pains, 8 (25%) patients had radiological evidence of fracture of one or more long bones, 3 (9.4%) presented with bony swelling which on biopsy was found to be reparative granuloma. Gastrointestinal symptoms such as epigastric pain, and constipation were present in 6 (18.8%) patients. Four (12.5%) patients had recurrent renal stones. Only one

(3.1%) patient had symptoms of depression in addition to musculoskeletal complaints. The mean duration of symptoms before presentation was 33.96 ± 27.29 months (range 1-120 months). Concurrent disease was present in three patients. One had hyperthyroidism and the other two were hypertensives.

Preoperative parathyroid hormone assays was markedly elevated in all patients of primary hyperparathyroidism with a mean of 1408.62 ± 1044.51 pg/mL (normal 11-67). Serum alkaline phosphatase levels were also elevated in all patients. Serum phosphate was decreased in all patients. Hypercalcaemia was detected in 25 (78.12%) patients and the rest were normocalcemic. The normal serum calcium levels were taken as 8.5-10.5mg/dL, alkaline phosphate 40-125U/L and phosphate 2.48-4.34mg/dL.

Adenoma was found to be the cause of primary hyperparathyroidism in 30 (93.8%) cases whereas hyperplasia and carcinoma constituted only one case each (3.1%). The most common per operative localization of the adenoma was right inferior 48.4% (15 cases) followed by left inferior 35.5% (11 cases). Left superior gland was involved in 9.7% (3 cases). Right superior and mediastinal glands were involved in one case each.

Ultrasound neck and technetium-99m sestamibi scan was carried out preoperatively in every patient. With concordant results of both tests the pre operative localization was accurate in 100% cases. Excision of the gland localized by pre operative imaging studies was successfully done in 27 (84.4%) cases. Bilateral neck exploration had to be done in 5 (15.6%) cases where it was deemed necessary to visualise all four glands per operatively. Post operatively there was a gradual decline in the serum calcium levels and development of tetany in all cases. No residual hyperparathyroidism or recurrence was reported on follow up for a year.

All three cases of secondary hyperparathyroidism were due to long standing chronic renal failure and the patients were on dialysis. They all presented with severe bone pain that had failed to respond to medical treatment. The patients had markedly deranged renal function with normal calcium, increased phosphate and PTH levels were persistently above 800pg/mL. Bilateral neck exploration and subtotal parathyroidectomy was carried out in all cases with successful decline in the PTH levels and improvement in symptoms post operatively. Damage to the recurrent laryngeal nerve was not seen in any of the cases.

Discussion

Surgical department of Mayo Hospital Lahore is

one of the busiest in the whole of Punjab with patients presenting from far and wide, so we can presume that our data represents the characteristics of parathyroid disease in this region of our country.

Primary hyperparathyroidism has been found to be much more common in females than males at all ages,¹⁶ which is consistent with our data. Our mean age of presentation was less than that reported in Western studies;¹⁶ however it was slightly higher but comparable to that of other series from this part of the world.^{7,17}

Majority of patients of primary hyperparathyroidism presented with more than one symptom. Musculoskeletal complaints were at the top followed by gastrointestinal symptoms and recurrent renal stones. Same has been found in other series of primary hyperparathyroid patients.^{4,7,17} Twenty-five percent of patients in our study had evidence of fractures of long bones which is somewhat less than that reported by the Indian series.⁷ Patients in our part of the world tend to present late with a longer duration of symptoms and usually after the appearance of complications.^{7,8,17-19} This is in contrast to the developed countries where primary hyperparathyroidism is increasingly being diagnosed at an asymptomatic stage.³⁻⁶ The younger age of presentation in patients from sub continent is not clear however the severe form of disease may be related to the delay in seeking medical care and absence of routine serum calcium check for mild symptoms of fatigue and generalized body aches and pain. Only two of our patients had hypertension although increased incidence of hypertension has been reported in patients of primary hyperparathyroidism.²⁰ Normocalcaemia was seen in 21.88% of our patients. All these patients had evidence of advanced disease with markedly reduced bone density on conventional radiographs as well as on DEXA scan indicating that probably that much of the calcium from the bones had been mobilized and lost so that they were hardly maintaining normal serum levels. Normocalcaemia with advanced parathyroid disease has also been reported in other studies from the sub-continent.^{7,17} This is in contrast to many other studies where almost all patients present with hypercalcaemia.⁹ The pre operative parathyroid hormone levels were enormously raised in our series with a mean value higher than that documented by any other study in this region. Although the levels of parathyroid hormone in Indian patients have been reported to be much higher than those in patients from Western series.⁷ Adenoma is the most frequent pathology encountered in pHPT which is responsible for the increased levels of PTH.^{1,3,9}

Pre operative localization studies have changed the

trends in parathyroid surgery from bilateral neck exploration to unilateral exploration and focused parathyroidectomy. The combination of ultrasound neck and sestamibi scan has proved to be highly sensitive and specific in localizing the adenomatous gland.²¹ Various studies from different centers report successful outcome of directed parathyroid exploration with accurate localization of the adenoma pre operatively using this combination.^{4,9,12,13,22} Although intra operative PTH assay or gamma probe is often used for accurate localization of the adenomatous gland,^{3,4,12} a recent study has shown that patients with primary hyperparathyroidism having an unequivocally positive preoperative sestamibi scan can safely undergo a focused unilateral neck exploration without either intraoperative PTH monitoring or the use of a gamma probe.²³ In our study unilateral exploration with excision of the involved parathyroid gland was carried out where the results of the ultrasound neck and sestamibi scan were concordant. This was highly successful as no adenoma was missed in any of the cases. However, where the two studies failed to point out the involved gland, a bilateral neck exploration was carried out and all four glands were visualized. Due to unavailability of intra operative monitoring of PTH, gamma probe or frozen section the adenomatous parathyroid gland was identified pre operatively in these cases by the gross appearance and large size of the gland compared to the other three. In only one case where all four glands were found to be enlarged a sub total parathyroidectomy was performed and it turned out to be a case of hyperplasia.

The most common localization in our series was right inferior gland. Other studies have reported the left inferior as the most common gland involved.⁴ Post operatively the serum calcium levels were monitored which declined progressively. Patients were started on calcium supplements only after the appearance of tetany which was taken as a marker of successful removal of the hyperfunctioning gland. Calcium supplementation was tapered off to a maintenance dose as the serum calcium levels normalized. Oral calcium and vitamin D were prescribed on discharge.

In secondary hyperparathyroidism, the pre operative localization studies are not very helpful so a standard bilateral neck dissection has to be done in all cases.²⁴ The safety of parathyroid surgery in our study was in comparison with series reported from international centers.^{3,5,12,25} This can be largely attributed to the experience of the operating surgeon.

Conclusion

Patients in our country tend to present with

advanced parathyroid disease often after the appearance of complications. Pre operative localization studies like ultrasound neck and sestamibi scan have enabled us to carry out directed exploration rather than bilateral neck exploration in every case. Accurate pre operative assessment and safe surgery offers cure to all patients with primary hyperparathyroidism.

References

1. Kearns AE, Thompson GB. Medical and Surgical Management of Hyperparathyroidism. *Mayo Clin Proc* 2002; 77: 87-91.
2. Heath H, Hedgson SF. Primary HPT: incidence, morbidity and potential economic impact on the community. *N Engl J Med* 1980; 302: 189-93.
3. Horányi J, Szilávik R, Duffek L, Darvas K, Györke T, Lakatos P et al. Surgery of primary hyperparathyroidism. *Orv Hetil* 2006; 147: 2347-51.
4. von Breitenbuch P, Iesalnieks I, Piso P, Schlitt HJ, Agha A. Primary hyperparathyroidism: clinical symptoms, diagnostic significance and localisation--a retrospective analysis. *Zentralbl Chir* 2007; 132: 497-503.
5. Oertli D. Indications for parathyroidectomy. *Praxis (Bern 1994)* 2007; 96: 981-8.
6. Wermers RA, Khosla S, Atkinson EJ, Hodgson SF, O'Fallon WM, Melton LJ 3rd. The rise and fall of primary hyperparathyroidism: A population-based study in Rochester, Minnesota, 1965-1992. *Ann Intern Med* 1997; 126: 433-40.
7. Gopal RA, Acharya SV, Bandgar T, Menon PS, Dalvi AN, Shah NS. Clinical profile of primary hyperparathyroidism from western India: A single center experience. *J Postgrad Med* 2010; 56: 79-84.
8. Mishra SK, Agarwal G, Kar DK, Gupta SK, Mithal A, Rastad J. Unique clinical characteristics of primary hyperparathyroidism in India. *Br J Surg* 2001; 88: 708-14.
9. Yang ZQ, Zhu LW, Wang PZ. Diagnosis and surgical treatment of 48 cases of parathyroid adenoma and parathyroid carcinoma. *Zhonghua Zhong Liu Za Zhi* 2006; 28: 625-7.
10. Lo CY, Chan WF, Kung AW, Lam KY, Tam SC, Lam KS. Surgical Treatment for Primary Hyperparathyroidism in Hong Kong--Changes in Clinical Pattern Over 3 Decades. *Arch Surg* 2004; 139: 77-82.
11. Meah FA, Tan TT, Taha A, Khalid BA. Primary hyperparathyroidism--a surgical review of 12 cases. *Med J Malaysia* 1991; 46: 144-9.
12. Pellitteri PK. Directed parathyroid exploration: evolution and evaluation of this approach in a single-institution review of 346 patients. *Laryngoscope* 2003; 113: 1857-69.
13. Röösl C, Bortoluzzi L, Linder TE, Müller W. Role of minimal invasive surgery for primary and secondary hyperparathyroidism. *Laryngorhinootologie* 2009; 88: 460-4.
14. Clark OH, Duh QY. Primary hyperparathyroidism. A surgical perspective. *Endocrinol Metab Clin North Am* 1989; 18: 701-14.
15. Leong KJ, Sam RC, Garnham AW. Health-related quality of life improvement following surgical treatment of primary hyperparathyroidism in a United Kingdom population. *Surgeon* 2010; 8: 5-8.
16. Miller BS, Dimick J, Wainess R, Burney RE. Age- and sex-related incidence of surgically treated primary hyperparathyroidism. *World J Surg* 2008; 32: 795-9.
17. Bhansali A, Masoodi SR, Reddy KS, Behera A, Radotra Bd, Mittal BR, et al. Primary hyperparathyroidism in north India : A description of 52 cases. *Ann Saudi Med* 2005; 25: 29-35.
18. Ingemansson SG, Hugosson CH, Woodhouse NJ. Vitamin D deficiency and hyperparathyroidism with severe bone disease. *World J Surg* 1988; 12: 517-21.
19. Agarwal G, Mishra SK, Kar DK, Agarwal G, Mishra SK, Kar DK, et al. Recovery pattern of patients with osteitis fibrosa cystica in primary hyperparathyroidism after successful parathyroidectomy. *Surgery* 2002; 132: 1075-83.
20. Bolland MJ, Grey AB, Gamble GD, Reid IR. Association between Primary Hyperparathyroidism and Increased Body Weight: A Meta-Analysis. *J Clin Endocrinol Metabol* 2005; 90: 1525-30.
21. Lumachi F, Zucchetto P, Marzola MC, Boccagni P, Angelini F, Bui F et al.

Advantages of combined technetium-99m-Sestamibi scintigraphy and high-resolution ultrasonography in parathyroid localization: comparative study in 91 patients with primary hyperparathyroidism. *Eur J Endocrinol* 2000; 143: 755-60.

22. Piemonte M, Miani P, Bacchi G. Parathyroid surgery in primary hyperparathyroidism: an update. *Eur Arch Oto Rhino Laryngol* 1989; 246: 324-7.
23. Jacobson SR, van Heerden JA, Farley DR, Grant CS, Thompson GB, Mullan BP et al. Focused cervical exploration for primary

hyperparathyroidism without intraoperative parathyroid hormone monitoring or use of the gamma probe. *World J Surg* 2004; 28: 1127-31.

24. Lai EC, Ching AS, Leong HT. Secondary and tertiary hyperparathyroidism: role of preoperative localization. *ANZ J Surg* 2007; 77: 880-2.
25. Bumpous JM, Goldstein RL, Flynn MB. Surgical and calcium outcomes in 427 patients treated prospectively in an image-guided and intraoperative PTH (IOPTH) supplemented protocol for primary hyperparathyroidism: outcomes and opportunities. *Laryngoscope* 2009; 119: 300-6.