



PARATHYROID ADENOMA: AN INDIAN SCENARIO AND REVIEW

Oncology

Prof Dr Subbiah Shanmugam

Mch, Centre for Oncology, Kilpauk Medical College, Chennai

Dr K Bharathiraja* Centre for Oncology, Kilpauk Medical College, Chennai *Corresponding Author

ABSTRACT

Parathyroid adenoma is part of a spectrum of parathyroid disorder that includes parathyroid hyperplasia, parathyroid adenoma, and parathyroid carcinoma. Primary hyperparathyroidism is usually related to a benign adenoma of the parathyroid gland. Surgical excision is the primary management with a dramatic response. We report about six patients we treated recently. Based on our experience, we discuss the nature and presentation of this disease and available therapeutic modalities in this review.

KEYWORDS

Introduction:

The parathyroid glands are two pairs of glands usually positioned behind the left and right lobes of the thyroid. Normal parathyroid glands are mainly composed of chief cells which are the secretory, granule-rich cells responsible for Parathyroid Hormone (PTH) release. Parathyroid adenomas are benign neoplasms composed usually of chief cells but may also be rarely derived from oncocytic or transitional oncocytic cells. Hyperparathyroidism is divided into primary, secondary, and tertiary hyperparathyroidism. Patients typically present with evidence of primary hyperparathyroidism with elevated serum calcium levels and elevated serum parathyroid hormone levels. Eighty to eighty-five percent of primary hyperparathyroidism is caused by parathyroid adenoma followed by parathyroid hyperplasia (15%) and parathyroid carcinoma.

Demographics:

It is the third most common endocrine disorder affecting 0.3% of the general population, 1%–3% of postmenopausal women and a total population incidence of 21.6 per 100,000 person-years. Female gender is known to impart a higher risk for the development of parathyroid adenomas and hyperparathyroidism; in fact, the prevalence in women has been found to be twice that found in men. In Indian series, females were commonly affected (1.7: 1, F: M). In our cases 4 out of 6 were females and all of them are below 40 years of age. Our observations are in agreement with other Indian series where a mean age of fewer than 40 years has been reported. Whereas patients from developed nations are diagnosed in the fifth and sixth decades.

Clinical presentation

Primary hyperparathyroidism in India remains symptomatic disorder, affects comparatively younger patients whereas in western countries it is mostly asymptomatic and affects older patients. One of our cases, 32 years old female presented with pathological fracture lower femur and another patient a young female presented with a lytic lesion in femur and ilium with severe pain. One patient presented with osteitis fibrosacystica, swelling in the scapula, core biopsy showed giant cell tumour of scapula for which he was undergone partial scapulectomy. After 3 years he presented with multiple lytic lesion in the rib and biopsy shows a brown tumour. Another female presented with hypercalcemia and renal stone. Other two patients were having asymptomatic hypercalcemia.

One of the reasons for early presentation in India could be associated with vitamin D deficiency, which has been shown by Indian series Kochupillai et al., and SK Mishra et al., Worldwide, the presentation of PHPT has changed from symptomatic to an asymptomatic disease. In India, however, an asymptomatic presentation is virtually unheard of. Data from SGPGIMS, India revealed fractures in 57% of the patients, brown tumours in 49%, and 27% of patients were crippled (due to multiple fractures). Skeletal manifestations account for the most of the morbidity associated with this disease. In our patients, mostly they presented with bone disease. Bhansali et al., have observed figures from another premier institute in India where 67% had bone disease, 48% had fractures, 21% had stone disease, 23% had psychiatric symptoms and 15% had peptic ulcer.

Evaluation and diagnostic work up:

Biochemical evaluation:

Hypercalcemia is the most common presentation in about 85% of cases, which is like most of the west. Elevated serum calcium and parathyroid hormone (PTH) is the characteristic of this condition. In our cases, the mean calcium level is 12 ± 2 and PTH is mostly above 600. When evaluating a patient with hypercalcemia, the diagnostic workup includes tests to differentiate between PTH- and non-PTH-mediated causes of elevated calcium. Evaluation should begin with measurement of PTH by second- or third-generation immunoassay along with phosphorus, alkaline phosphatase, 25(OH)D, creatinine, estimated glomerular filtration rate (eGFR), and albumin. Additionally, a 24-hour urine collection for calcium, creatinine, and creatinine clearance should be considered in patients with overt nephrolithiasis or nephrocalcinosis. If the urine calcium is > 400 mg/24 h, a renal stone risk profile is indicated because nephrolithiasis is one of the most common complications of PHPT. At SGPGIMS India, the patients had a mean serum calcium levels of 12.3 ± 1.4 (range 10.8–15 mg %), serum alkaline phosphatase (ALP) 1544.3 ± 2077 IU/L (range 177–7240 IU/L), and serum Vitamin D levels of 13.6 ± 6.3 (range 6.2–25 ng/mL).

Localization Strategies:

Preoperative imaging localization of parathyroid adenomas has traditionally been considered unnecessary in the context of bilateral neck exploration. Preoperative localizing imaging is mandatory, however if unilateral neck exploration or minimally invasive methods are being planned. In fact, failure to successfully and unequivocally localize a parathyroid adenoma preoperatively by imaging is a major contraindication to unilateral or minimally invasive surgery. Neck ultrasound (USG) has been reported to localize the adenoma in 65–77% of patients. Methylisobutylisonitrile (MIBI) scan positivity has been reported in 86.9–100%. Contrast-enhanced computerized tomography (CECT) of the neck has a sensitivity ranging from 65% to 93.5% in localizing parathyroid adenoma. These are all data derived from Indian publications which are same as western literature. USG Neck was done for 4 cases and MIBG scan for 2 cases. MIBG scan is done also to rule out an extra parathyroid disease.

Management:

Surgical management: The mainstay of therapy for parathyroid adenomatous disease is surgical removal. Bilateral neck exploration is still technically considered the gold-standard surgical treatment for primary hyperparathyroidism. A unilateral neck exploration can be performed if the preoperative imaging is successful in localizing a solitary adenoma to one side of the neck. We have done 4 cases of parathyroidectomy cases by unilateral exploration after successful preoperative localisation. There was no recurrent hyperparathyroidism observed in our cases. Limited data are available on the surgical approach to PHPT in most of the literature from India. The approach has ranged from bilateral conventional neck exploration and unilateral neck exploration to focused parathyroidectomy. Unilateral focused open exploration has been generally performed only in those patients who have concordant USG and MIBI findings. Recurrent PHPT has ranged from zero to 4.16% and persistent PHPT

between zero and 2.7%.

Non-surgical management:

For asymptomatic hypercalcemia, observation may be an option. Patients with asymptomatic hyperparathyroidism, detected serendipitously by biochemical serum testing, should also be treated surgically if they meet one of the following criteria set out by the National Institute of Health (NIH): age less than 50 years, serum calcium level 1 mg/dl above the upper limit of being normal, 24-hour urine calcium excretion greater than 400 mg, 30% reduction in creatinine clearance, and osteoporosis as defined by a T score below -2.5 at any one of three sites (lumbar spine, hip, distal third of radius). We kept one asymptomatic patient aged more than 60 years under observation with regular follow up.

The use of estrogen replacement or raloxifene in postmenopausal women with primary hyperparathyroidism has demonstrated only small favourable effects on serum calcium levels and bone density. bisphosphonates have been shown to significantly increase bone mineral density without much change in either serum calcium or PTH levels. We kept one patient under hormonal therapy.

Conclusion:

In conclusion, parathyroid adenoma is rare and associated with elevated calcium and PTH levels. In Indian scenario, they presented comparatively symptomatic and early presentation mainly as bone disease. Preoperative localisation is important for surgical decision. Surgical management is parathyroidectomy with curative intention.

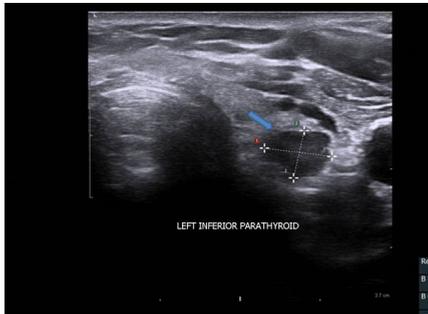


Fig 1 Ultrasound showing parathyroid Adenoma

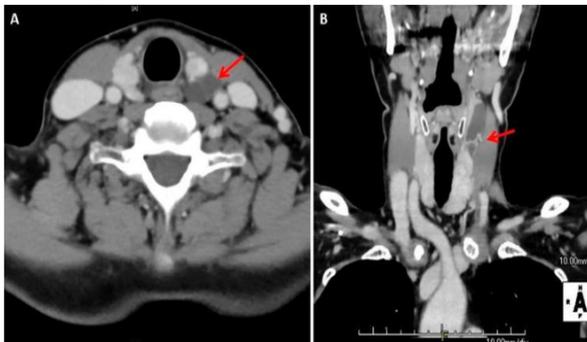


Fig 2 CT localization of parathyroid adenoma

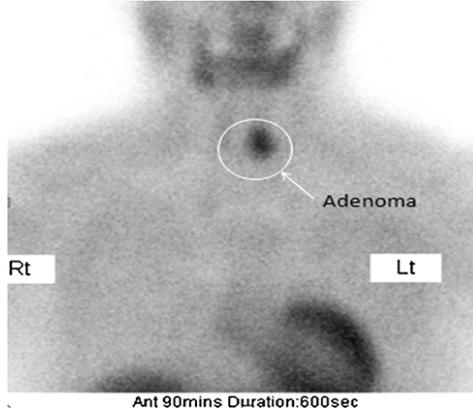


Fig 3 Sestamibi scan showing left parathyroid adenoma

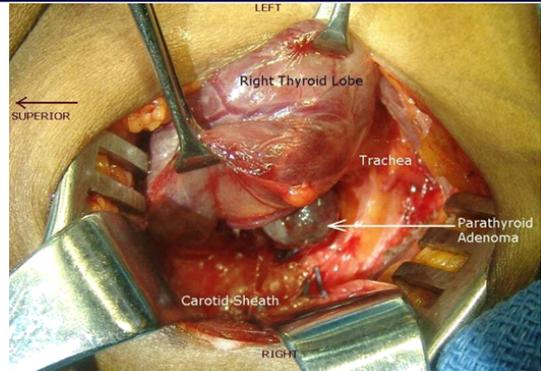


Fig 3 Intraoperative picture showing parathyroid adenoma

Bibliography:

1. MacKenzie-Feder J, Sirrs S, Anderson D, Sharif J, Khan A. Primary Hyperparathyroidism: An Overview. *Int J Endocrinol.* 2011;2011(2):1-8. doi:10.1155/2011/251410.
2. Fitzpatrick BN. Parathyroid adenoma. *Oral Surgery, Oral Med Oral Pathol.* 1969;27(5):653-658. doi:10.1016/0030-4220(69)90101-7.
3. Cadili A. The Parathyroid Adenoma. *Arch Clin Exp Surg.* 2014;3(4):240. doi:10.5455/aces.20130729035244.
4. Wieneke JA, Smith A. Parathyroid Adenoma. *Head Neck Pathol.* 2008;2(4):305-308. doi:10.1007/s12105-008-0088-8.
5. Bhansali A, Masoodi SR, Reddy KSS, et al. Primary hyperparathyroidism in north India: a description of 52 cases. *Ann Saudi Med.* 2011;25(1):29-35. <http://www.ncbi.nlm.nih.gov/pubmed/15822491>.
6. Goswami R, Mishra SK, Kochupillai N. Prevalence & potential significance of vitamin D deficiency in Asian Indians. *Indian J Med Res.* 2008;127(3):229-238. <http://www.ncbi.nlm.nih.gov/pubmed/18497436>.
7. Pradeep P V, Jayashree B, Mishra A, Mishra SK. Systematic Review of Primary Hyperparathyroidism in India: The Past, Present, and the Future Trends. *Int J Endocrinol.* 2011;2011:1-7. doi:10.1155/2011/921814.
8. Goswami R, Gupta N, Goswami D, Marwaha RK, Tandon N, Kochupillai N. Prevalence and significance of low 25-hydroxyvitamin D concentrations in healthy subjects in Delhi. *Am J Clin Nutr.* 2000;72(2):472-475. doi:10.1093/ajcn/72.2.472.
9. Barbara Austin is a Family Nurse Practitioner at Baptist Primary Care, Jacksonville F. Primary Hyperparathyroidism: A Case-based Review. *Clinician Reviews.* <https://www.mdedge.com/clinicianreviews/article/136564/endocrinology/primary-hyperparathyroidism-case-based-review/page/0/5>. Published 2017.
10. Pradeep P V, Mishra A, Agarwal G, Agarwal A, Verma AK, Mishra SK. Long-term outcome after parathyroidectomy in patients with advanced primary hyperparathyroidism and associated vitamin D deficiency. *World J Surg.* 2008;32(5):829-835. <http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L50043344%5Cnhttp://dx.doi.org/10.1007/s00268-007-9384-9%5Cnhttp://sfx.library.uu.nl/utrecht?sid=EMBASE&issn=03642313&id=doi:10.1007%2Fs00268-007-9384-9&atitle=Long-term+outcome+afte>.
11. Turner JO. Hypercalcaemia and primary hyperparathyroidism. *Medicine (Baltimore).* 2017;45(9):551-554. doi:10.1016/j.mpmed.2017.06.010.
12. Britton DC, Johnston DA, Thompson MH, Fleming LB. The outcome of treatment and changes in presentation of primary hyperparathyroidism. *Br J Surg.* 1973;60(10):782-785. doi:10.1093/carcin/bgp220.
13. Kapustin JF, Schofield DL. Hyperparathyroidism: an incidental finding. *Nurse Pract.* 2012;37(11):9-14. doi:10.1097/01.NPR.0000421433.15790.82.