Unilateral Exploration for Parathyroid Adenoma

Maddibande Ramachar Sreevathsa^{1,2} · Khyati Melanta¹

Received: 14 August 2016 / Accepted: 1 December 2016 / Published online: 27 December 2016
© Indian Association of Surgical Oncology 2016

Abstract Between January 2012 to 2016, 20 patients with primary hyperparathyroidism underwent surgical exploration for presumed diagnosis of parathyroid adenoma. Nineteen patients underwent ultrasonography of neck and USG was found to be accurate in localizing the adenoma in 84.2%. Seventeen patients underwent sestamibi isotope scanning and imaging correlated with operative findings in 94.1%. Combined accuracy of ultrasound and sestamibi scan which was done in 17 patients was 95%. Seventeen patients underwent unilateral exploration and there was resolution of disease in 94.1%. Three patients underwent bilateral exploration and had a success rate of 100% in the removal of offending adenoma. Fifteen minutes post excision, rapid intraoperative intact parathormone assay was sent in 14 out of 17 unilateral explorations and was found to have true positive rate of 93% and false positive rate of 7%. There was a significant difference in the operating time between unilateral (17 patients, mean operating time 1 h) and bilateral (3 patients, mean operating time 1¼ hrs) explorations. It is clear from this study; the preoperative localization of adenoma with plan for unilateral exploration with a combination of ultrasonography and sestamibi scan is extremely useful if unilateral exploration is planned for excision of parathyroid adenoma. However, the number of patients who underwent 15 min post excision intact

parathormone assay, is a small number to comment on its usefulness in predicting the success of unilateral exploration.

Keywords Primary hyperparathyroidism · Parathyroid adenoma · Minimally invasive parathyroidectomy · Unilateral exploration · Four gland exploration · Preoperative localization · Sestamibi scan · Recurrence

Introduction

Bilateral neck exploration is the gold standard in the surgical treatment of primary hyperparathyroidism including those caused by parathyroid adenoma. This surgical method of treatment was introduced by Mandel in 1925 that is, nearly 90 years ago [1]. It is also well known that in 90% of cases of primary hyperparathyroidism (PHPT) due to parathyroid adenoma, a single adenoma is found as the culprit [2, 3]. Due to this fact and with excellent preoperative imaging techniques being available for localization of adenoma, the success rate of minimally invasive or unilateral approach to management of PHPT has almost equalled in outcome, to that obtained by standard bilateral neck (four gland) exploration [4]. In addition, studies on the intraoperative intact parathyroid hormone assay obtained 15 min after removal of parathyroid adenoma have fortified the confidence of surgeons performing unilateral exploration for PHPT.

Material & Methods

Between January 2012 to 2016, case records of 20 patients screened as parathyroid adenoma were studied retrospectively. The mean age of the patient was 47.2 yrs. The sex ratio was M:F–9:11. Nineteen patients were symptomatic and one was

✉ Maddibande Ramachar Sreevathsa
chee_vaccha@yahoo.co.in

Khyati Melanta
kmelanta@gmail.com

¹ Department of General Surgery, MS Ramaiah Medical College and Hospital, Bangalore 560094, India

² Department of Surgery, MS Ramaiah Medical College and Hospital, New BEL Road, Bangalore 560054, India

Fig. 1 Sestamibi scan showing right inferior gland adenoma

asymptomatic but detected on serum calcium estimation on routine check up. Seventeen patients presented electively and three patients as emergency. Four patients had symptom-period ranging from 1 to 10 days. Fifteen patients had symptom-period ranging from 1 month to 10 years. Emergency admission for three patients was for (a) hypercalcemic encephalopathy, (b) acute kidney injury with multiple myeloma, and (c) acute severe pancreatitis. These patients with emergent presentation did not undergo sestamibi scan. All patients had estimation of serum calcium and serum parathormone. Nineteen patients had undergone ultrasonography of the neck and 17 patients, sestamibi scan (Fig 1 & 2). In one patient, chronic kidney disease was found as the cause for PHPT. Seventeen patients underwent unilateral exploration, and three patients underwent four gland exploration. In 14 patients, 15 min post excision intraoperative intact parathormone assay was done.

Results

Mean age of patients was 47.2 years. The sex ratio was M:F–9:11. 84.2% patients (16) had adenoma in the inferior gland and in 15.7% (3 patients), the superior gland was involved. One patient had two adenomas, which was a case of tertiary hyperparathyroidism. Fourteen patients (73.6%) had an involvement of left parathyroid and five patients (26.3%) had involvement of right parathyroid, one being bilateral out of 20 patients. Six patients had cardiac disease not related to PHPT, four presented with current or old history of fracture of long bone, four patients with pancreatitis, two patients had renal

calculus, two presented with generalized weakness, and one with psychiatric symptoms. In 18 patients (90%), the preoperative levels of serum parathormone was more than three times the upper limit of normal and in two (10%) patients, the preoperative level was less than three times normal. In these two patients, the serum calcium was also normal, but the diagnosis was made based on a combination of ultrasonography and sestamibi scan of the neck. At the same time, the serum calcium levels did not show a direct relationship to the levels of serum parathormone when plotted on a graph (Table 1, Graph 1). In seven (35%) patients, the serum parathormone levels was more than 1000 units and in 57% of these patients, the adenoma size was 1.5 cm. Nineteen patients underwent ultrasonography of the neck and in 16 of these (84.2%), the adenoma was accurately localized. Seventeen patients underwent sestamibi scan and in 16 (94.1%) of these patients, the scan was accurate in localizing the adenoma. Combined accuracy of ultrasound and sestamibi scan which was done in seventeen patients was 95%. Seventeen patients underwent unilateral exploration and in one of these, a recurrence of disease was found. The patient was a case of tertiary hyperparathyroidism and opposite site exploration resulted in identification of a second adenoma. Hence, the cure rate of unilateral exploration was 94.1%. Three patients underwent bilateral exploration for adenoma, one of the patients having thyroid nodule, in the second, the preoperative localization not being convincing, and the third due to tertiary hyperparathyroidism. The success rate of bilateral exploration was 100%.

Fifteen minutes post excision intra operative intact parathormone assay was done in 14 patients. It had a true positivity rate of 92.8% and false positive rate of 7.2%. The false positivity was found in the case of tertiary hyperparathyroidism with the 24 h post excisional parathormone levels showing no significant reduction.

There was a significant difference in the operating time between unilateral (17 patients, mean operating time 1 h) and bilateral (3 patients, mean operating time 1¼ hrs) explorations.

Mean post operative hospital stay was 26 h with unilateral exploration and 96 h for bilateral exploration. All patients who underwent bilateral exploration developed transient

Fig. 2 Sestamibi scan showing right inferior gland adenoma

Table 1 Case records of 20 patients screened as parathyroid adenoma

Correlations		PREOPCA	PREOPPTH
PREOPCA	Pearson correlation	1	0.172
	Sig. (2-tailed)		0.468
	N	20	20
PREOPPTH	Pearson Correlation	0.172	1
	Sig. (2-tailed)	0.468	
	N	20	20

hypoparathyroidism for 1 month requiring oral calcium supplementation as compared to none in unilateral exploration.

Discussion

PHPT is familial and caused by hyperplasia of the gland in 10% of cases. But in 90%, it is caused by a single adenoma [2]. Only in 2% of cases is PHT caused by double adenoma [5, 6]. When surgery for PHT is conducted by experienced surgeons, the cure rate is 95% [7]. But in a multicenter study conducted in five hospitals across the USA and Europe, it was shown that more patients with bilateral exploration had hypocalcemia postoperatively, on an 8-year follow-up than those undergoing unilateral exploration [8, 9].

Wang and Tibblin in 1982, advocated unilateral exploration for solitary adenoma based on the premise that, the adenoma is single in 85 to 90% of cases and they can be localized accurately by investigations [10]. This approach also becomes useful when re-exploration for recurrence is done, as the opposite site is left undisturbed with clear planes [11]. The incidence of

multiglandular disease has also been shown to be less than 5% [6, 12].

In a randomized controlled trial, where 91 patients were randomized to either unilateral or bilateral exploration for primary hyperparathyroidism, it was shown that the cure rate was equal between the two, and operative time was shorter in the unilateral exploration group. There was lesser incidence of hypocalcemia in the unilateral exploration group [1]. This finding was concurrent with the findings in this study.

This focussed or minimally invasive approach to adenoma has become possible due to good and accurate preoperative imaging studies [13]. In our small number of patients, ultrasonography was successful in accurately identifying the adenoma in 84.2% and sestamibi scintigraphy in 94.1% of cases. In a relatively recent article published in 2012 from Iran, high resolution USG detected the adenoma accurately in 76.3% of cases and sestamibi scan in 78.8% of cases with sensitivity of 83.5 and 85% respectively [14]. According to a study conducted by Nasiri et al., ultrasonography images detected enlarged parathyroid glands in 76.3% of patients with sensitivity of 83.5% and positive predictive value (PPV) of 89.7%. Sestamibi scintigraphy detected adenoma in 78.8% patients with sensitivity of 85% and PPV of 91.3% [14].

The utility of rapid intraoperative parathormone assay was done in 10-min post excision of adenoma to confirm the successful removal of the offending adenoma intra-operatively, has increased confidence levels in operating surgeons practicing unilateral approach. At 10-min post excision of the gland, the peak pre excision value of parathormone should reduce by more than 50% and more than 60% at 15-min post excision assay. Additionally, frozen section biopsy of the removed gland can be undertaken with the other ipsilateral gland proving to be normal on frozen section [15, 16]. This increases the recurrence free outcome of unilateral exploration. In this retrospective study, the number of patients undergoing intact parathyroid hormone (iPTH) is too small to comment on its utility.

Summary and Conclusion

In this retrospective study of 20 parathyroid adenomas, it was shown that unilateral approach for surgical excision of parathyroid adenoma in PHPT, based on preoperative localization by USG and sestamibi scan, had a success rate of 94.1% which compares well with the success rate of bilateral explorations as observed in the literature. It has also been shown that the mean operating time for unilateral exploration is significantly less than that taken for bilateral exploration. Hence, we recommend unilateral exploration for parathyroid adenoma in patients where the adenoma has been localised by preoperative imaging.

Graph 1 Graph showing no direct relationship between preoperative serum calcium and parathormone levels

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

References

- Bergenfels A, Lindblom P, Tibblin S, Westerdahl J (2002) Unilateral versus bilateral neck exploration for primary hyperparathyroidism: a prospective randomized controlled trial. *Ann Surg* 236(5):543–551
- Brasier AR (1994) Hyperparathyroidism and the metabolic responses to parathyroidectomy. In: Morris PJ, Malt RA (eds) *Oxford textbook of surgery*, 1st edn. Oxford Medical Publications, Oxford, pp. 755–760
- Maskey R, Panchani R, Varma T, Goyal A (2013) Primary hyperparathyroidism in India: a cocktail of contemporary and classical presentations: lesson from 47 cases. *Indian Journal of Endocrinology and Metabolism* 17(Suppl1):S209–S211. doi:10.4103/2230-8210.119574
- Purcell GP, Dirbas FM, Jeffrey R et al (1999) Parathyroid localization with high-resolution ultrasound and technetium Tc 99 m sestamibi. *Arch Surg* 134(8):824–830. doi:10.1001/archsurg.134.8.824
- Lumachi F, Zucchetta P, Marzola MC, Boccagni P, Angelini F, Bui F, D'Amico DF, Favia G (2000) Advantages of combined technetium-99 m-sestamibi scintigraphy and high-resolution ultrasonography in parathyroid localization: comparative study in 91 patients with primary hyperparathyroidism. *Eur J Endocrinol* 143:755–760
- Tezelman S, Shen W, Shaver JK et al (1993) Double parathyroid adenomas. Clinical and biochemical characteristics before and after parathyroidectomy. *Ann Surg* 218(3):300–309
- Udelsman R (2002) Six hundred fifty-six consecutive explorations for primary hyperparathyroidism. *Ann Surg* 235(5):665–672
- Tibblin S, Bizard JP, Bondeson AG, Bonjer J, Bruining HA, Meier F, Proye C, Quievreux JL, Rothmund M, Thompson NW, Uden P, Zielke A (1991) Primary hyperparathyroidism due to solitary adenoma: a comparative multicentre study of early and long term results of different surgical regimens. *Eur J Surg* 157:511–515
- Tibblin S, Bondeson AG, Ljungberg O (1982) Unilateral parathyroidectomy in hyperparathyroidism due to single adenoma. *Ann Surg* 195:245–252
- Wang CA (1985) Surgical management of primary hyperparathyroidism. *Curr Prob Surg* 22:1–50. doi:10.1016/0011-3840(85)90019-X
- Inabnet WB, Dakin GF, Haber RS, Rubino F, Diamond EJ, Gagner M (2002) Targeted parathyroidectomy in the era of intraoperative parathormone monitoring. *World J Surg* 26: 921–925. doi:10.1007/s00268-002-6619-7
- Molinari AS, Irvin GL 3rd, Deriso GT, Bott L (1996) Incidence of multiglandular disease in primary hyperparathyroidism determined by parathyroid hormone secretion. *Surgery* 120(6):934–936 discussion 6–7
- Haber RS, Kim CK, Inabnet WB (2002) Ultrasonography for pre-operative localization of enlarged parathyroid glands in primary hyperparathyroidism: comparison with 99-m-technetium sestamibi scintigraphy. *Clin Endocrinol* 57:241–249
- Nasiri S, Soroush A, Hashemi AP, Hedayat A, Donboli K, Mehrkhani F (2012) Parathyroid adenoma localization. *Med J Islam Repub Iran* 26(3):103–109
- Dillavou ED, Cohn HE (2003) Minimally invasive parathyroidectomy: 101 consecutive cases from a single surgeon. *J Am Coll Surg* 197(1):1–7. doi:10.1016/S1072-7515(03)00113-3
- Elaraj DM, Remaley AT, Simonds WF, Skarulis MC, Libutti SK, Bartlett DL et al (2002) Utility of rapid intraoperative parathyroid hormone assay to predict severe postoperative hypocalcemia after reoperation for hyperparathyroidism. *Surgery* 132(6):1028–1033. doi:10.1067/msy.2002.128480