International Journal of Surgery 9 (2011) 339–342

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.theijs.com

Original Research

Radio-guided excision of parathyroid lesions in patients who had previous neck surgeries: A safe and easy technique for re-operative parathyroid surgery

Serkan Sarı [a], Yeşim Erbil [a,*], Feyzullah Ersöz [a], Aydemir Olmez [a], Artür Salmaslıoğlu [b], Işık Adalet [c], Nese Colak [d], Selçuk Özarmağan [a]

[a] *Department of General Surgery, Istanbul Medical Faculty, Istanbul University, Çapa, İstanbul, Turkey*
[b] *Department of Radiology, Istanbul Medical Faculty, Istanbul University, Çapa, İstanbul, Turkey*
[c] *Department of Nuclear Medicine, Istanbul Medical Faculty, Istanbul University, Çapa, İstanbul, Turkey*
[d] *Department of Endocrinology, Istanbul Medical Faculty, Istanbul University, Çapa, İstanbul, Turkey*

ARTICLE INFO

Article history:
Received 12 October 2010
Received in revised form
30 January 2011
Accepted 14 February 2011
Available online 22 February 2011

Keywords:
Primary hyperparathyroidism
Radio-guided excision
Radio-guided surgery

ABSTRACT

Background: Several methods have been recommended to detect parathyroid lesions in patients who have previously undergone neck surgeries, including radio-guided surgery or intraoperative ultrasounds. In this study, we aimed to investigate whether the radio-guided excision of pathologic parathyroid lesions allowed us to find affected lesions in patients who had previously undergone neck operations.
Methods: This prospective study included 18 patients with primary hyperparathyroidism who had previously undergone neck surgeries. The pathologic parathyroid lesions were localized by ultrasonography, and a radiotracer was injected directly into the lesions.
Results: Careful dissections were carried out by following the area of maximum radioactivity until the lesions were identified and excised. Eighteen parathyroid adenomas were removed in 18 patients. The median count from each lesion was significantly higher than the values measured from the adjacent tissues and the lesion beds (12550/20 s, 370/20 s, and 35/20 s, respectively; $p < 0.001$).
Conclusion: Radio-guided excision of parathyroid lesions can be performed safely for re-operative parathyroid surgery.

1. Background

Primary hyperparathyroidism (pHPT) is the most common cause of hypercalcemia. The surgical treatment of pHPT involves removal of abnormally enlarged parathyroid gland(s). Bilateral neck exploration is the gold standard approach for the treatment of pHPT.[1,2] Bilateral exploration has a 95% success rate without localizing studies when performed by experienced endocrine surgeons. Most authors agree that preoperative imaging studies are helpful in the recurrent or re-operative setting. The purpose of all preoperative imaging is to facilitate operative planning. Imaging modalities should never be used to establish the diagnosis of pHPT.[1–3]

Re-operation on the neck is technically more demanding than an initial surgical procedure because of the presence of scar tissue and distorted anatomy following the initial procedure. Even if a pathologic parathyroid lesion is identified by preoperative or intraoperative imaging studies, difficult techniques are required to operate on patients who have previously undergone neck surgery.[4–6]

Various strategies have been developed to make the surgical excision of cervical masses easier, including the use of intraoperative US, wire-guided excision, or intraoperative, ultrasound-guided dye injection.[7–9] We previously described the preoperative injection of a radiotracer under ultrasound guidance and subsequent radio-guided excision of metastatic lymph node(s).[10]

2. Aim of the study

In the present study, we aimed to investigate whether radio-guided excision of pathologic parathyroid lesions allowed us to find affected lesions in patients with neck compartments that had previously undergone surgery.

3. Patients and methods

3.1. Patients

This prospective study included 18 patients with primary hyperparathyroidism who had previously undergone neck surgery

* Corresponding author. Tel.: +1 212 4142000; fax: +1 212 5331781.
E-mail address: yerbil2003@yahoo.com (Y. Erbil).

1743-9191/$ – see front matter
doi:10.1016/j.ijsu.2011.02.008

at the Department of General Surgery, Istanbul Medical Faculty, between June 2007 and June 2010. All patients included in this study had undergone previous neck surgeries. The causes of pHPT were solitary parathyroid adenoma, persistent HPT, and recurrent HPT.

Persistent HPT was defined as the persistence of hypercalcemia due to hyperparathyroidism within 6 months following the initial operation. Recurrent HPT was diagnosed by the reappearance of hypercalcemia after 6 months of normocalcemia. The diagnosis of pHPT was based on biochemical tests. Ultrasonography (US) and scintigraphy (MIBI) were routinely used for preoperative localization in all patients. The assessment of parathormone (PTH) levels in suspicious lesions, which was sampled via US-guided, fine-needle aspiration, was carried out by confirming the presence of parathyroid tissue. Parathyroid operations were performed by the same surgeons in all patients.

In all patients, indirect laryngoscopic examinations were used to evaluate vocal cord motility both before and after surgery. In cases of dysphonia with vocal cord injury, indirect laryngoscopies were performed 1 month and 6 months later. Persistent nerve palsy was defined as persistent dysfunction and clinical dysphonia that lasted for 12 months postoperatively.

In all patients, serum calcium and PTH levels were measured pre- and postoperatively. Serum calcium concentrations were adjusted for serum albumin. The normal ranges of biochemical parameters were defined as 8.5–10.5 mg/dl for serum calcium and 10–65 pg/ml for serum PTH. The study plan was reviewed and approved by our institutional ethical committee, and informed consent was obtained for all patients.

3.2. Radio-guided parathyroid adenoma localization

Prior to the operations, parathyroid lesions were localized by US with a high frequency, 10 MHz transducer. Parathyroid, fine-needle aspiration and PTH assays have been used to discriminate other tissues from pathologic parathyroid glands. In the current study, a 20-gauge needle was placed into the center of the lesion under US, and ^{99m}Tc-labelled rhenium colloid was injected directly into the pathologic parathyroid lesion. The radiotracer was prepared before the procedure (on the morning of the operation), and a single 0.2 mL aliquot was drawn into a syringe containing 20 MBq of ^{99m}Tc rhenium colloid as a radiotracer. We preferred to use Tc-99m in our study because of its lower radioactive emission and shorter half-life. The risk of radiation exposure to the patient and the surgeon is negligible with intraoperative administration of 0.5 mCi Tc-99m. The injection of the radiotracer was performed by an experienced radiologist in the Radiology Department.

3.3. Radio-guided parathyroid excision

An intraoperative, hand-held gamma probe (Navigator, Surgical γ-probe, Auto suture, France) was used to detect tumor foci. An incision was made at the previous neck incision. Superior and inferior subplatysmal flaps were created in a standard fashion, and the neck was scanned with the probe to localize the area of maximal radioactivity. This allowed us to make the incision directly over the lesion. The radioactive area was identified with a γ-probe, and the 'hot spot' was shown to correspond to the area of maximum radioactivity. A mean count was calculated by taking three measurements from each region, with each of the counts recorded for 20 s. Careful dissections were carried out by following the areas of maximum radioactivity until the pathologic parathyroid lesions were identified and excised. After the lesions were removed, radioactivity was measured in the lesion beds to confirm the success of the operation. The intraoperative measurements of count rates were obtained from pathologic parathyroid lesions, adjacent tissues and background activity (Figs. 1 and 2). The weights of all parathyroid adenomas that were removed were recorded.

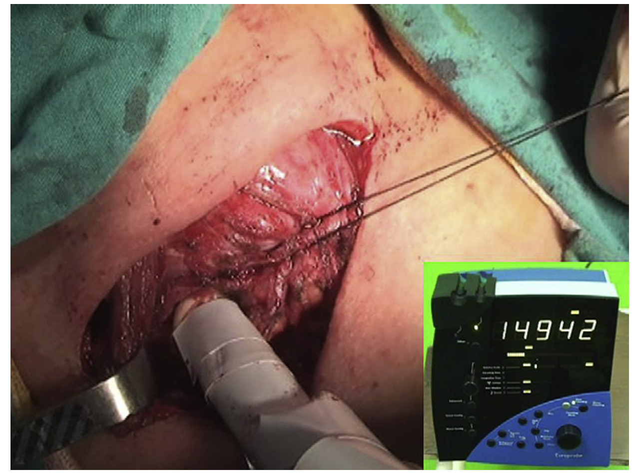

Fig. 1. The area of maximum radioactivity.

4. Results

4.1. Patients

The mean age of the patients was 44.5 ± 14 years (range: 17–61 years). The female/male ratio was 2.6/1 (n = 13/5). Of the 18 patients, 14 were previously operated on for thyroid disease, and 4 patients received previous operations for pHPT. Of these 4 patients, 2 had persistent HPT and 2 had recurrent HPT. The indications for thyroidectomy were nodular goiter (n = 9), papillary carcinoma (n = 3), and Graves' disease (n = 2). Normal parathyroid glands were removed in the patients with persistent HPT, but pathologic parathyroid glands of the patients with recurrent HPT were left in place during the initial surgery.

4.2. Operations

A total of 18 pathologic parathyroid lesions from 18 patients were injected with a radiotracer. All of the injected lesions were detected in the area of maximum radioactivity. During the operation, all of the injected pathologic parathyroid glands were excised.

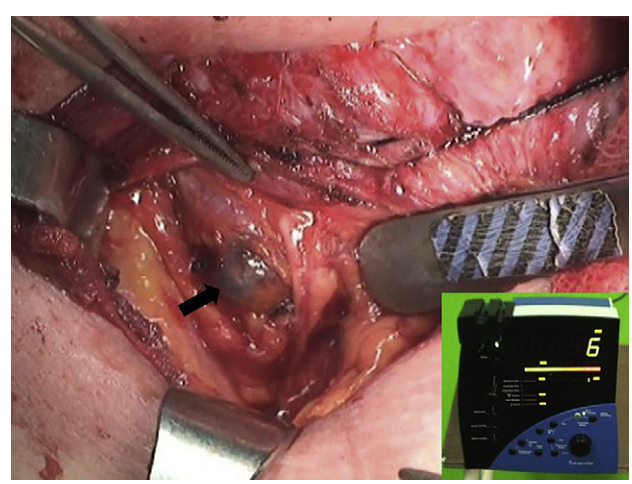

Fig. 2. Parathyroid adenoma (black arrow) and the count of background activity.

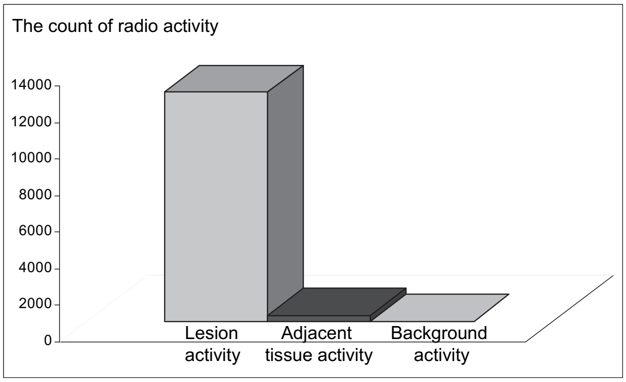

Fig. 3. Lesion, adjacent tissue and backgraound activity.

The median radioactive counts from a lesion were significantly higher than the values measured from the adjacent tissues or the lesion beds (background activity) (12550 counts/20 s, 370 counts/20 s, and 35 counts/20 s, respectively; $p < 0.001$) (Fig. 3). There were no complications related to the injections. Two patients had preoperative, unilateral vocal cord paralysis due to previous operations. Persistent and transient vocal cord paralyses were not encountered in connection with the radio-guided excision of parathyroid lesions.

Of the 18 patients who were operated on for hyperparathyroidism, 6 (33%) had ectopic parathyroid glands. Ectopic glands were observed in the thymus ($n = 2$), tracheoesophageal groove ($n = 2$), carotid sheath ($n = 1$), and paraesophageal space ($n = 1$). All patients with persistent and recurrent HPT had ectopic parathyroid glands. The mean adenoma weight was 937 ± 618 mg (range = 150–2300 mg). Parathyroid adenomas were identified on pathologic examination in all patients.

During follow-up, postoperative sixth-month blood tests revealed that all patients were normocalcemic, and PTH concentrations were found within normal ranges. Pre- and postoperative details are shown in Table 1.

5. Discussion

The causes for which patients required re-operative surgery for pHPT can be divided into three groups: (1) persistent pHPT, (2) recurrent pHPT, and (3) patients who underwent a previous thyroid surgery and subsequently developed pHPT. Following initial resection, approximately 1–6% of patients develop persistent or recurrent pHPT. Persistent pHPT is much more commonly observed than recurrent pHPT (80–90% and 10–20%, respectively). Persistent or recurrent pHPT is, for the most part, caused by the inexperience of the surgeon. Supernumerary and ectopic parathyroid tissues are present in as many as 50% of these patients.[4–6]

Thyroidectomy is one of the most frequent operations performed for patients with multinodular goiters in iodine-deficient regions.[11,12] Although the incidence of the patients who have undergone previous thyroid surgeries and who subsequently develop pHPT is not known, we are frequently confronted with these patients in our region, where this condition is endemic.

Re-operation in the neck is approached cautiously, given the increased risk of dissection in scarred tissues, particularly to the recurrent laryngeal nerve and to the parathyroid glands, and it is difficult to estimate the location and functional status of the parathyroid glands. According to the experiences of different surgeons, RLN palsy and hypoparathyroidism rates vary from 0 to 14% in these patients.[13–15]

If re-operative, parathyroid surgery is required, the parathyroid remnant should be located with imaging techniques; however, there are difficulties with these imaging techniques, including anatomic distortion and dense adhesions that continue in the patients who have previously undergone neck surgery.[4–6]

Several additional methods have been recommended to detect parathyroid lesions, including radio-guided surgery after the injection of a radiotracer and intraoperative ultrasound.[4,5,16,17] There are, however, some pitfalls associated with the use of these methods. Gamma probe detection of radiolabeled sestamibi has been used to guide cervical dissection in re-operative parathyroid surgery[16,17]; however, this technique has not gained widespread acceptance. In patients with negative sestamibi scans, the gamma probe may not be useful. Some authors have also discouraged the use of sestamibi scans in such patients because the existence of thyroid nodules with MIBI uptake usually worsens the performance of the scan, unless the nodules are found at ectopic locations.[18]

The other method that is frequently used to perform secondary operations on the thyroid is intraoperative US; however, this method can make it difficult to recognize parathyroid lesions with extensive scarring. It is necessary to dissect the scarred field to

Table 1
Characteristics of the patients scheduled for radio-guided excision of pathologic parathyroid lesion.

No	Sex, Age, Pathology	Preop Ca level (mg/dl)	Preop PTH level (pg/ml)	MIBI	US	Operative finding	Postop 6 mo. Ca level (mg/dl)	Postop 6 mo. PTH level (pg/ml)
1	F, 54, perHPT	12.4	480	left side	right side	right side (E)	8	44
2	F, 32, perHPT	11.4	1150	left side	left side	left side (E)	9	54
3	F, 45, recHPT	13.4	279	left side	left side	left side (E)	9	25
4	F, 81, recHPT	11.9	550	right side	right side	right side (E)	9	25
5	M, 17, pHPT#	14	379	right side	right side	right side	8	47
6	F, 38, pHPT#	12.6	1200	right side	right side	right side	8	65
7	M, 29, pHPT#	13.5	780	left side	left side	left side	8	70
8	F, 51, pHPT#	11.9	554	right side	right side	right side	9	44
9	F, 36, pHPT#	12	1290	left side	left side	left side	9.3	32
10	F, 60, pHPT#	13	470	right side	right side	right side (E)	8.8	45
11	F, 59, pHPT#	12.9	245	right side	right side	right side	9.2	35
12	M, 39, pHPT#	12.5	580	left side	left side	left side (E)	9.3	30
13	F, 21, pHPT#	11.4	365	right side	right side	right side	8.6	40
14	M, 55, pHPT#	13.6	400	left side	left side	left side	8.5	55
15	F, 48, pHPT#	15.5	800	right side	right side	right side	8	47
16	F, 55, pHPT#	13	554	right side	right side	right side	9	17
17	M, 44, pHPT#	12	980	left side	left side	left side	9	27
18	F, 57, pHPT#	12	670	left side	left side	left side	9	35

F, female; *M*, male; *perHPT*, persistent hyperparathyroidism; *recHPT*, recurrent hyperparathyroidism; *pHPT#*, patients having undergone previous thyroid surgery who subsequently develop primary hyperparathyroidism; *(E)*, ectopic localization.

properly visualize the lesion. The parathyroid lesion usually cannot be visualized until the scar tissue is removed because of the dense areas of scar tissue.[4–6]

We previously described a series in which preoperative ultrasound was used to inject radioactive material directly into affected lymph nodes. In this series, ^{99m}Tc was injected directly into the center of the suspicious lesion using US guidance. The dissections were performed following the area of maximum radioactivity until the metastatic lymph nodes were identified and excised.[10] Interestingly, this method has never been described in re-operative parathyroid surgery. The use of a gamma probe enabled us to find the relevant area. The gamma count decreased with distance from the affected area, which made it possible to safely and easily target and remove the injected parathyroid lesion within the scarred tissue. This technique also depends on the use of US as a guidance system.

Tumor foci were easily identified as being independent of the parathyroid gland due to the capability of the parathyroid gland to trap the radiotracer and because the radiotracer was injected directly into the lesion. This technique requires preliminary identification of a pathologic parathyroid gland by PTH measurement in a fine-needle aspirate washout. Our direct injection technique can only be performed for lesions that are visible by US. Small parathyroid lesions or glands with ectopic localizations are not easily detected. Therefore, the overall success rate of the technique may be decreased, and the need to localize the parathyroid lesion by US may be a disadvantage.

Sippel et al.[9] reported the use of intraoperative, US-guided dye injection into metastatic lymph nodes, which facilitated their identification. In some cases, it can be difficult to recognize the metastatic lymph nodes that are marked with blue dye, especially within areas of extensive scarring. With the blue dye technique, scar tissue must be dissected to visualize the lymph nodes that are marked with blue dye. An injected node usually appears dark blue, but lymph nodes usually cannot be visualized because of the dense scar tissue surrounding it. Reaching the lymph node requires a difficult dissection. In our technique, we also had to dissect the scar tissue. The use of gamma probe guidance enabled us to quickly and easily find the relevant area in which the greatest radioactive signal was observed. Radioactive counts decreased as distance from the relevant area increased. Therefore, the affected lymph nodes within the scar tissues were removed safely and easily. The blue dye technique also depends on the use of US; however, the blue dye method has never been described in re-operative parathyroid surgery.

6. Conclusion

Ultrasonography and sestamibi scintigraphy are useful in re-operations for pHPT. The purpose of all preoperative imaging is to facilitate operative planning; however, these imaging modalities are insufficient for solving problems with intraoperative techniques. Although there are some pitfalls, radio-guided excision of parathyroid lesions can be performed safely during re-operative parathyroid surgeries.

Conflicts of interest

None declared.

Sources of funding

None declared.

Ethical approval

Local ethical group of Istanbul Medical Faculty 2009/1640.

Author contribution

Serkan Sarı data analysis, writing.
Yeşim Erbil study design, data analysis, writing.
Feyzullah Ersöz data collections, data analysis.
Aydemir Olmez data collections, data analysis.
Artür Salmaslıoğlu data analysis.
Işık Adalet data analysis, critical revision.
Nese Colak data analysis, writing.
Selçuk Özarmağan critical revision.

References

1. Bergenfelz AO, Hellman P, Harrison B, Sitges-Serra A, Dralle H. European Society of endocrine surgeons. Positional statement of the European Society of endocrine surgeons (ESES) on modern techniques in pHPT surgery. *Langenbecks Arch Surg* 2009;**394**:761–4.
2. Bergenfelz A, Jansson S, Mårtensson H, Reihnér E, Wallin G, Kristoffersson A, et al. Scandinavian quality register for thyroid and parathyroid surgery: audit of surgery for primary hyperparathyroidism. *Langenbecks Arch Surg* 2007;**392**:445–51.
3. Mihai R, Simon D, Hellman P. Imaging for primary hyperparathyroidism—an evidence-based analysis. *Langenbecks Arch Surg* 2009;**394**:765–84.
4. Prescott JD, Udelsman R. Remedial operation for primary hyperparathyroidism. *World J Surg* 2009;**33**:2324–34.
5. Henry JF. Reoperation for primary hyperparathyroidism: tips and tricks. *Langenbecks Arch Surg* 2010;**395**:103–9.
6. Rodriquez JM, Tezelman S, Siperstein AE, Duh QY, Higgins C, Morita E, et al. Localization procedures in patients with persistent or recurrent hyperparathyroidism. *Arch Surg* 1994;**129**:870–5.
7. Karwowski JK, Jeffrey RB, McDougall IR, Weigel RJ. Intraoperative ultrasonography improves identification of recurrent thyroid cancer. *Surgery* 2002;**132**:924–8.
8. Triponez F, Poder L, Zarnegar R, Goldstein R, Roayaie K, Feldstein V, et al. Hook needle-guided excision of recurrent differentiated thyroid cancer in previously operated neck compartments: a safe technique for small, nonpalpablee recurrent disease. *J Clin Endocrinol Metab* 2006;**91**:4943–7.
9. Sippel RS, Elaraj DM, Poder L, Duh QY, Kebebew E, Clark OH. Localization of recurrent thyroid cancer using intraoperative ultrasound-guided dye injection. *World J Surg* 2009;**33**:434–9.
10. Tükenmez M, Erbil Y, Barbaros U, Dural C, Salmaslioglu A, Aksoy D, et al. Radio-guided nonpalpable metastatic lymph node localization in patients with recurrent thyroid cancer. *J Surg Oncol* 2007;**96**:534–8.
11. Carty SE, Cooper DS, Doherty GM, Duh QY, Kloos RT, Mandel SJ, et al. Consensus statement on the terminology and classification of central neck dissection for thyroid cancer. *Thyroid* 2009 Nov;**19**(11):1153–8.
12. Tonacchera M, Pinchera A, Vitti P. Assessment of nodular goitre. *Best Pract Res Clin Endocrinol Metab* 2010 Feb;**24**(1):51–61.
13. Chao TC, Jeng LB, Lin JD, Chen MF. Reoperative thyroid surgery. *World J Surg* 1997;**21**:644–7.
14. Thomusch O, Machens A, Sekulla C, Ukkat J, Lippert H, Gastinger I, et al. Multivariate analysis of risk factors for postoperative complications in benign goiter surgery: prospective multicenter study in Germany. *World J Surg* 2000;**24**:1335–41.
15. Rosato L, Avenia N, Bernante P, De Palma M, Gulino G, Nasi PG, et al. Complications of thyroid surgery: analysis of a multicentric study on 14,934 patients operated on in Italy over 5 years. *World J Surg* 2004;**28**:271–6.
16. Cayo A, Chen H. Radioguided reoperative parathyroidectomy for persistent primary hyperparathyroidism. *Clin Nucl Med* 2008;**33**:668–70.
17. Damrose EJ, Hoh C, Calcaterra TC. Gamma-probe localization of a parathyroid adenoma in the reoperative neck. *Am J Otolaryngol* 2000;**21**:394–7.
18. Casara D, Rubello D, Cauzzo C, Pelizzo MR. ^{99m}Tc-MIBI radioguided minimally invasive parathyroidectomy: experience with patients with normal thyroids and nodular goiters. *Thyroid* 2002;**12**:53–61.