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Radioguided parathyroidectomy: Initial results of Hacettepe experience

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ABSTRACT

In 85-90% of the cases primary parathyroidism is caused by a single adenoma. In experienced hands the success of the standard parathyroidectomy is 95%. Recently, radioguided parathyroidectomy offers an alternative to standard parathyroidectomy. The sensitivity of the sestamibi scintigraphy is 90%for single adenomas. In Hacettepe University Hospitals sestamibi scintigraphy is performed successfully. In 2001, the arrival of a hand held gamma probe to our hospital enabled us to perform radioguided surgery. Here, we describe first nine cases treated by radioguided parathyroidectomy. In all of the cases the pathological parathyroid tissue could be localized. In eight of nine cases preoperative sestamibi scan localized the parathyroid tissue. As a result of our study, one can say that radioguided surgery facilitates recurrent and difficult cases. It's obvious that the intraoperative use of gamma probe can decrease the incidence of recurrent nerve damage. For these reasons, radioguided surgery may be appropriate for selected cases. [Turk J Cancer 2007;37(4):137-142]

KEY WORDS: Radioguided parathyroidectomy, retrospective, minimally invasive

INTRODUCTION

Primary hyperparathyroidism is caused by a single adenoma in 85-90% of the cases. The classic operation for hyperparathyroidism involves exploration of all parathyroid glands and identification of the pathological one. The success of operation depends on the surgeon, his knowledge of the anatomy and the variations of the localization of the parathyroid glands. An experienced surgeon can identify the diseased gland in 95% of cases at the first operation.

Non invasive localization studies such as ultrasonography, computerized tomography, magnetic resonance imaging and scintigraphy are complimentary to each other and each has its own limitations (1). The accuracy of the sestamibi scan in detecting single adenoma is 90%. When these techniques fail to localize the adenoma, invasive techniques such as selective venous sampling, angiography and fine needle aspiration biopsy may be necessary.

Minimally invasive thyroidectomy is first described by Tiblin et al. (2). They explored only one side of the neck and if they identified a pathological and a normal parathyroid gland on that side of the neck they ended the operation.

The use of the sestamibi scintigraphy for localization of parathyroid adenomas offered the surgeons a new alternative to the classical operation for parathyroidectomy. Sestamibi is a monovalent lipophilic cation which accumulates in the mitochondria. The substance accumulates in metabolically active parathyroid adenoma and the other suppressed parathyroid glands are not visualized (3).

In 1996, Irwin et al. (4) used preoperative sestamibi scintigraphy to detect the adenoma and they used the results to explore only one side of the neck. Same year Norman (3,5) used for the first time intraoperative gamma probe to guide the dissection. In their first series of 15 patients they could successfully identify the adenoma in 14 patients and show the parathyroid hyperplasia which could not have been diagnosed preoperatively in one patient.

Goldstein et al. (6) showed in a prospective study of 40 patients that the operation time and hospital stay are shorter and operation and hospital costs are less in patients operated by minimally invasive method with preoperative scintigraphy as the localization study than the patients operated with classical method (6). Controversies to this opinion exist in the literature (7).

Here we report our first 9 patient experiences with radioguided parathyroidectomy.

MATERIALS AND METHODS

The charts of first nine patients operated with radioactive guidance for parathyroid adenoma in our department were examined retrospectively.

The diagnosis of hyperparathyroidism was established by elevated serum calcium and intact parathormone levels.

Technique

Preoperative localization

We used the technique described by Norman (5) as most of the studies in the literature. After the intravenous administration of 99m Tc labeled sestamibi, early and late scans were performed at 15^{th} and 60^{th} minutes. During scanning process the patient was given the same position as the operation and anteroposterior and lateral oblique images were taken. The images were evaluated by the nuclear medicine doctor and the surgeon. If an adenoma was seen the patient was taken to the operating room within two and a half hour.

Operation

After the routine positioning and preparation of the operative field radioactive counts were taken (Neoprobe 2000, Neoprobe Cooperation, Dublin) from four quadrants; the projections of upper and lower thyroid lobes on both sides. Following a bilateral cervical incision, skin flaps were elevated in craniocaudal direction. The strap muscles were divided at the midline and radioactive counts were repeated from both sides. Dissection was started from the side with the higher count. After the removal of the parathyroid tissue, ex-vivo counts were obtained and the specimen was sent for frozen section. Exploration was continued until the identification of all four parathyroid glands. A final radioactive count was performed and the operation was finalized.

RESULTS

Among 9 patients 7 were female and 2 were male. Median age of patients was 45.9. The frozen section results of the patients are shown in table 1.

The frozen section diagnosis was parathyroid adenoma in 5 cases, hyperplasia in one and intrathyroidal adenoma in one patient. In two patients although gross appearance resembled to an adenoma frozen section could only demonstrate parathyroid tissue. As detection of the normal parathyroid tissue on the edge of the adenoma is essential to diagnose parathyroid adenoma histologically and this diagnosis cannot always be established in frozen sections, gross appearance of parathyroid adenoma together with histological diagnosis of parathyroid tissue was sufficient for the diagnosis of the parathyroid adenoma.

Before the incision, gamma counts at the lesion side were significantly higher than the opposite side (Table 2) (Wilcoxon test, p=0.028). The difference between two sides disappeared after the removal of the pathological parathyroid tissue (Wilcoxon test, p=0.593) (Table 3).

Preoperative scintigraphy localized the diseased gland successfully in 8 patients while preoperative ultrasonography localized six (McNemar test, p=0.5, not significant).

A total of 17 tissue samples were sent for frozen section and the diagnosis are shown in table 4. The ex-vivo gamma counts were low for non parathyroid tissues and higher for parathyroid glands. Normal parathyroid gland had lower counts than diseased glands and hyperplasia had higher counts than adenomas (Table 5). P value of

Table 1
Frozen section diagnosis of the patients

	n	%
Adenoma	5	55.56
Hyperplasia	1	11.11
Parathyroid tissue	2	22.22
Intrathyroidal adenoma	1	11.11
Total	9	100.00

Table 2
Descriptive statistics of percutaneous gamma counts of the lesion and the opposite sides

	Mean	SD	Median	Min.	Max.
Lesion site	458.7	119.9	405	365	694
Opposite side	392.7	93.6	355	305	563

Table 3
Descriptive statistics of intraoperative gamma counts after the excision

	Mean	SD	Median	Min.	Max.
Right	294.0	95.6	250	220	450
Left	301.6	88.1	250	220	413

Table 4
Distribution of the excised specimens according to the frozen section

Frozen section result	n	%
Lymph node	1	5.88
Parathyroid	4	23.53
Parathyroid adenoma	5	29.41
Parathyroid hyperplasia	3	17.65
Thyroid nodule	1	5.88
Fatty tissue	1	5.88
Fatty tissue/cyst	1	5.88
Intrathyroidal adenoma	1	5.88
Total	**17**	**100.00**

non parametric trend test for the gradual change in gamma counts from non parathyroid tissues to hyperplasia was found to be lower than 0.001 (Spearman test).

To ratio of ex-vivo gamma counts to the background counts was examined for each type of tissue. In 82.4% of the adenomas or hyperplasia the ex-vivo count over background count ratio was over 20%. In 77.8% of the non adenoma/hyperplasia lesions this ratio was below 20%. The probability of a lesion with ex-vivo/background count grater than 20% to be an adenoma/hyperplasia was 85%. For the lesions with ex-vivo/background count lower than 20%, the probability of not being an adenoma/hyperplasia was 77.8% (negative predictive value).

In 61.5% of parathyroid tissue excised the ratio of ex-vivo/background count was under 20%, but all of the excised non parathyroid tissues had an ex-vivo/background count ratio under 20%. So the probability of a lesion with ex-vivo/background count ratio over 20% was 100%.

DISCUSSION

The traditional therapy of the primary hyperparathyroidism is bilateral exploration of the neck. The minimally invasive radioguided hyperparathyroidectomy offers an alternative to this concept.

Minimally invasive parathyroid surgery has some advantages over classical operation: most patients can be operated with local anesthesia, the patient can be discharged the same day, the operation time is shorter, the patient feels less pain and the cosmetic result is better and this technique is less costly (8,9).

Table 5
Descriptive statistics of ex-vivo gamma counts according to the lesion type

Ex-vivo gamma counts	Mean	SD	Median	Min.	Max.
Hyperplasia	486.3	112.0	550	357	552
Adenoma	183.5	135.7	177	35	365
Parathyroid tissue	39.3	34.2	37	6	77
Other*	8.5	9.7	7	0	20

*Fatty tissue/lymph node/cyst/thyroid nodule

The sensitivity and specificity of sestamibi scintigraphy depends on the pathology. Shen et al. (10) found the sensitivity to be 71% for single adenomas, 44% for multiple adenomas and 0% for hyperplasia.

In a series of 35 patients Sullivan et al. (11) could localize 34 adenomas using preoperative scintigraphy and 33 adenomas with intraoperative gamma probe. In two patients the gamma probe localized erroneously thyroid adenomas (false positive).

Kumar et al. (12), in a series of 29 patients, could localize successfully parathyroid adenomas in all patients.

Norman et al. (13) reported 17 patients whose first operation failed. All the patients had positive sestamibi scintigraphy and all the adenomas were excised with the aid of the intraoperative gamma probe.

We do not routinely order a preoperative scintigraphy or ultrasonography for primary hyperparathyroidism. These tests were only ordered for the patients enrolled in the study. In this study although we used intraoperative gamma probe, we did not perform a minimally invasive parathyroidectomy. After the excision of the adenoma the operation was continued until the visualisation of all parathyroid glands. This technique is similar to that described by Angelos (14) in his article in which he reports his first experiences with radioguided parathyroidectomy.

In this study, intraoperative diagnosis of parathyroid adenoma was established by frozen section. If the gross appearance of the tissue was considered as adenoma and the frozen section confirmed the parathyroid tissue the diagnosis of parathyroid adenoma was established intraoperatively. The pathologist was not asked to differentiate between adenoma and hyperplasia. In the literature, the confirmation of the successful surgical therapy was done by intraoperative quick PTH test. The technique is quite expensive and the efficacy is subject to debate (15). The calcium levels of all patients in our study returned to normal limits at second postoperative day. Postoperative parathormone level measurements were not performed.

To our knowledge this study is the only one which evaluates the gamma count levels. Although the number of parathyroid adenomas excised is equal on both sides, the gamma counts from the left side are higher than those of the right side when these measurements were performed over the skin. This difference is not statistically significant and may be caused by the background effect of the heart. This difference was not observed in the counts performed after the incision.

The percutaneous counts were significantly higher at the lesion side which demonstrates the efficacy of the gamma probe to detect the lesion side. After the removal of the lesions the difference between the counts from left and right sides were not significant, this shows removal of the pathologic glands.

As preoperative localization study, scintigraphy could locate the diseased gland in 8 of 9 patients, whereas ultrasonographic localization was successful in 7 patients. This difference is not significant but small number of patients makes commenting difficult.

In this group of patient a total of 17 tissue samples (13 parathyroid glands) were removed. As the operation was continued until the frozen histopathological diagnosis, the diseased gland could be excised in all cases.

In the literature, the patients groups of radionuclide guided surgery are those without thyroid nodules or those who are operated for the first time. So it is hard to discuss the superiority of this technique over the classical one in all patient groups (16). In this study 3 patients have had prior neck surgery, 3 patients had thyroid nodules.

In a study performed in an endemic goiter region, 36% of hyperparathyroid patients has been found to have concomitant thyroid disease (17). The sensitivity of scintigraphy in this study was 83% and it increased to 90% with the addition of ultrasonography. In our study, scintigraphy localized the parathyroid adenoma in all patients with thyroid nodules whereas ultrasonography localized 2 of them. The parathyroid adenomas of our 3 patients with thyroid nodules were successfully detected with preoperative scintigraphy and intraoperative gamma probe.

Another discussion point in the literature is about the patients who have previous parathyroid surgery. The general opinion is to perform all available visualization techniques before the second surgery. Neumann et al. (18) could localize parathyroid tissue with sestamibi/iodine subtraction single photon scintigraphy, in 13 of 14 patients who have had total parathyroidectomy with au-

totransplantation. In a series of 11 patients by Rossi et al. (19), the sensitivity of preoperative sestamibi scintigraphy was 64% for persistent cases; the addition of intraoperative gamma probe raised this ratio to 91%. In our study, there were 4 patients with previous surgery for hyperparathyroidism. In the first one ultrasonography showed 2 probable adenomas, scintigraphy detected retention in 3 locations, the operation was ended after the removal of 3 lesions when the counts from left and right sides were equalized. In the second case the scintigraphy showed an adenoma at the inferior border of the left thyroid lobe. The parathyroid gland could not be found during the operation but as the gamma counts were higher on the left side a left thyroid lobectomy was performed, the pathology confirmed intrathyroidal parathyroid adenoma. Third patient had a near total thyroidectomy because of a papillary carcinoma; scintigraphy and ultrasonography could not locate the lesion. The operation was guided by gamma probe and the lesion was excised successfully. Our experience on the patients with persistent hyperparathyroidism is that gamma probe makes the operation easier.

According to Miller's analysis (20), the chance of localizing recurrent or persistent parathyroid adenomas by non invasive techniques is only 50%. This ratio increased with time by advancing techniques and experience of scintigraphy and ultrasonography. The use of intraoperative gamma probe increases this ration further. In our study, we did not use any invasive localization technique for recurrent or persistent hyperparathyroidism.

Murphy and Norman (21) from radioactivity counts of 129 tissue samples concluded that if the radioactivity count of excised tissue is more than 20% of total radioactivity count, the excised tissue should be parathyroid. Our results are the same. Except one case, the radioactive counts of all diseased parathyroid tissues are more than 20% of the total radioactive count. In one case the total radioactive count was 355 and ex-vivo count of the parathyroid tissue was 59 (16% of total radioactivity). Nevertheless, the radioactivity counts of non parathyroid tissues are far below than that of parathyroid tissues and there is no intersection in the statistical analysis. The low number of patients causes this case to influence the statistical results. All tissues that the counts are higher than 20% of the overall radioactivity are of parathyroid origin. If this ratio is supported in future studies, the need for frozen section and detection of intraooperative parathormone levels may be less.

CONCLUSION

According to our initial experience intraoperative use of gamma probe is useful to determine the side of the parathyroid lesion. If the ex-vivo/background gamma count ratio is over 20%, the excised tissue is definitely of parathyroid origin. The use of intraoperative gamma probe is found to be useful in localizing the pathological parathyroid tissue in recurrent cases.

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