

Parathyroidectomy for primary hyperparathyroidism: The results of a single institution

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Abstract

Aim: Primary hyperparathyroidism (PHPT) is a clinical entity characterized by an excess synthesis of parathormone due to one or more autonomic parathyroid gland. The present study aims to evaluate the outcomes of parathyroidectomies performed due to PHPT.

Material and Methods: The results of 52 parathyroidectomies performed due to PHPT between September 2014 and October 2018 were retrospectively evaluated for demographic, clinical, imaging and pathologic characteristics.

Results: Fifty-two patients with primary hyperparathyroidism were included in the study. The mean age of the patients was 50 ± 14.5 years. Forty-three (82.9%) patients were female and 9 (17.4%) were male. The most common complaints at admission were generalized muscle and bone pain in 13 patients (15.3%). In 2 patients (3.8%) osteoporosis and another 2 (3.8%) patients, nephrolithiasis was identified. Thirty-five (67.3%) patients had no complaints. The mean preoperative calcium level was 11.21 ± 0.88 mg/dl. Mean preoperative phosphate level was 2.58 ± 0.72 mg/dl. Mean preoperative parathormone level was 278.65 ± 317.67 pg/ml. Technetium 99m-sestamibi scintigraphy was obtained for 41 patients. Cervical ultrasonography was performed in 43 patients. The surgical localization of the parathyroid adenoma showed that the accuracy of ultrasonography was 60.4% whereas the accuracy of Technetium 99m-sestamibi scintigraphy was 80.4%. Three of the 12 (25%) patients with no localization in ultrasonography had parathyroid hyperplasia as the pathologic diagnosis. There were two patients in whom ultrasonography and scintigraphy could not localize the pathologic parathyroid tissue and all of them (100%) were found to have parathyroid hyperplasia as the pathologic evaluation. Pathologic evaluation of the surgical specimens showed that there was adenoma in 40 patients (76.9%), hyperplasia in 5 (9.6%), normal parathyroid tissue in 5 (9.6%), tumor with undetermined biologic potential in 1 patient (1.9%) and adenomatous parathyroid tissue in 1 patient (1.9%). In fifteen patients (28.8%) concomitant total thyroidectomy, right lobectomy in 7 patients (13.4%) and left lobectomy in 4 patients (7.6%) were performed.

Conclusion: Parathyroid adenoma can be localized in places other than the expected locations; despite the advances in imaging technologies. Surgeons experience and accurate localization before the operation are important for a successful parathyroid operation. If scintigraphy and ultrasonography cannot localize the pathologic parathyroid tissue, hyperplasia should be suspected.

Keywords: Parathyroidectomy; primary hyperparathyroidism; hypercalcemia; parathormone.

INTRODUCTION

Primary hyperparathyroidism (PHPT) is a clinical entity characterized by an excess synthesis of parathormone due to one or more autonomic parathyroid gland. The symptoms are related to hypercalcemia that is the result of hyperparathyroidism (1,2). PHPT is the third most common endocrine disorder and the most frequent reason for outpatient admissions due to hypercalcemia (3). Eighty to eighty-five percent of the cases with PHPT have solitary adenoma, 4-5% have double adenoma and 10-15% have parathyroid hyperplasia and less than 1%

of the cases have parathyroid carcinoma (3).

The result of hyperparathyroidism is hypercalcemia, hypophosphatemia and bone resorption. As a result of these changes renal, musculoskeletal and neuropsychiatric systems are affected and specific symptoms evolve. The only curative treatment option of PHPT is parathyroidectomy. However, 80% of the patients at the time of diagnosis is asymptomatic, therefore the surgical treatment of the patients is controversial. The imaging tests that are used are bilateral cervical ultrasonography and dual-phase Technetium 99m-Sestamibi. In necessary

Received: 11.10.2019 **Accepted:** 21.10.2019 **Available online:** 23.10.2019

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cases computerized tomography, magnetic resonance imaging can be used (4).

The present study aims to evaluate the outcomes of parathyroidectomies performed due to PHPT in light of current literature.

MATERIAL and METHODS

Selection of the patients

The results of 52 parathyroidectomies performed due to PHPT between September 2014 and October 2018 were retrospectively evaluated in the present study. None of the patients were excluded.

Acquisition of the data

The patient database was evaluated for demographic data, the complaints at admission, preoperative and postoperative 24th-hour calcium, phosphorus and parathormone levels. Localization of the adenoma all patients received bilateral cervical ultrasonography and dual-phase Technetium 99m-Sestamibi scintigraphy. Adenoma localization data, the type of operation, thyroid and parathyroid morphology in the operation, postoperative thyroid and parathyroid pathologic evaluation, perioperative frozen section results and the postoperative complications were evaluated.

The patients with scintigraphy and ultrasonography that were performed in another center; the patient files were evaluated and the necessary data for the imaging studies were obtained. Furthermore, the patient data-base was evaluated as a cross check for any imaging studies performed in our institution for these patients. There were 4 patients with no data regarding the localization studies, yet parathyroidectomy was performed and these patients were included in the pathologic evaluation section of the study.

Statistical analyses

The continuous variables are expressed as mean and standard deviation. The categorical variables are expressed as the number of patients and percentage of the study population. The dependent and independent variables were compared using student t test. Any p value less than 0.05 was considered as statistically significant. All statistical analyses were performed on Statistical Program for Social Sciences software version 20 (SPSS v20, IBM,USA).

RESULTS

The Patient Demographic Data

Fifty-two patients with primary hyperparathyroidism were included in the study. The mean age of the patients was 50 ± 14.5 years. Forty-three (82.9%) patients were female and 9 (17.4%) were male. The most common complaints at admission were generalized muscle and bone pain in 13 patients (15.3%). In 2 patients (3.8%) osteoporosis and another 2 (3.8%) patients nephrolithiasis. Thirty-five (67.3%) patients had no complaints. The mean preoperative calcium level was 11.21 ± 0.88 mg/dl. Mean

preoperative phosphate level was 2.58 ± 0.72 mg/ dl. Mean preoperative parathormone level was 278.65 ± 317.67 pg/ml. Preoperative and postoperative laboratory values were summarized in Table 1. The postoperative calcium and parathormone levels were significantly lower when compared to operative levels ($p < 0.001$). The postoperative phosphate levels were significantly higher when compared to the preoperative levels ($p < 0.001$).

Table 1. Laboratory variables of the patients

Laboratory values (normal range)	Preoperative values	Postoperative values	P-value*
Calcium: (8.4-10.2 mg/dl)	11.21 ± 0.88	9.2 ± 0.73	<0.001
Phosphate: (2.7-4.3 mg/dl)	2.58 ± 0.72	3.22 ± 0.93	<0.001
Parathormone: (14-72 pg/ml)	278.65 ± 317.67	27.04 ± 28.42	<0.001

*All values are expressed as mean±standard deviation.

*Student t test was used for evaluation of distribution of the dependent according to the independent variables.

The results of Imaging studies

Technetium 99m-sestamibi scintigraphy was obtained for 41 patients. In only three of the 41 patients (7.4%), scintigraphy was not successful in localizing the parathyroid adenoma. Two of these three patients (66.6%) were diagnosed to have parathyroid hyperplasia in the pathologic evaluation. Cervical ultrasonography was performed in 43 patients and parathyroid adenoma could not be localized in 12 patients (27.9%). Three of the 12 (25%) patients with no localization in ultrasonography had parathyroid hyperplasia as the pathologic diagnosis. There are two patients in whom ultrasonography and scintigraphy could not localize the pathologic parathyroid tissue and all of them (100%) were found to have parathyroid hyperplasia as the pathologic evaluation. Therefore, imaging studies seems to give an idea about the pathologic diagnosis in the patients.

The surgical localization of the parathyroid adenoma showed that the accuracy of ultrasonography was 60.4% whereas the accuracy of Technetium 99m-Sestamibi scintigraphy was 80.4%. The most frequent site of the ultrasonographic location of the parathyroid adenoma was left lobe inferior pole in 14 patients (26.9%), whereas the left lobe upper pole was never reported. The most frequent technetium 99m-Sestamibi scintigraphic localization was left lobe lower pole in 14 patients (41.4%), furthermore, in a patient with previous total thyroidectomy for papillary thyroid carcinoma technetium 99m-Sestamibi showed a midline localization of the parathyroid adenoma in the cervical region.

The results of pathologic evaluation

Frozen section pathologic evaluation was performed in 16 (30.7%). In 51 patients (98%) there was a solitary adenoma, in one patient bilateral inferior double adenoma was observed. Pathologic evaluation of the surgical specimens showed that there was adenoma in 40 patients

(76.9%), hyperplasia in 5 (9.6%), normal parathyroid tissue in 5 (9.6%), tumor with undetermined biologic potential in 1 patient (1.9%) and adenomatous parathyroid tissue in 1 patient (1.9%). In fifteen patients (28.8%) concomitant total thyroidectomy, right lobectomy in 7 patients (13.4%) and left lobectomy in 4 patients (7.6%) were performed. In 2 patients (3.8%) parathormone and calcium levels did not decrease following the parathyroidectomy operation. The imaging showed that the pathologic adenoma persisted in these patients and they were re-operated for adenoma excision.

DISCUSSION

Primary hyperparathyroidism is the most frequent etiology of the incidental hypercalcemia in the patients. The incidence in the general population is reported to be 0.7%. The incidence is 2% in the postmenopausal women and its incidence in the female are 3 times the male patients (5). Its incidence increases with age and it reaches a peak after 50 years of age (6). In the present study, there was 43 female (82.6%) patients whereas 9 (17.4%) were male. Mean age of the patients were 50 ± 14.5 years. In our study female to male ratio was 5 and the mean age was consistent with the current literature.

In 80% of the cases with PHPT, there are no symptoms and hypercalcemia is found incidentally. Fatigue, myopathy and muscular atrophy can also be observed (5,6). Since 1970, together with more rapid determination of calcium levels, more incidental cases are being diagnosed (7). Currently, patients diagnosed with PHPT are usually incidental and no classical symptoms can be observed. The incidence of asymptomatic PHPT ranges between 72.7% to 95% cases, asymptomatic PHPT is the most frequent clinical form of PHPT (8,9). In the present study, 35 patients (67.3%) had no symptoms related to hyperparathyroidism and hypercalcemia. In 13 (15.3%) patients, there were generalized muscular, joint and bone pain. The asymptomatic PHPT incidence was slightly lower in general literature. We believe that most of the non-specific symptoms such as fatigue, constipation, depression and muscular pain are being missed in these patients and these patients are considered as asymptomatic.

A decade ago bilateral cervical exploration was the curative treatment option with a success rate of 95-98%. One of the most important factors in the success of the surgery was reported to be the experience of the endocrine surgeon (10). However, this was associated with prolonged operative times and risk of injury to certain structures during the procedure. The advancements in the imaging techniques enabled focused minimal invasive surgical alternatives. Bilateral cervical ultrasonography, technetium 99m sestamibi scintigraphy, 4-dimensional parathyroid computerized tomography, and magnetic resonance imaging are the imaging alternatives for localization of the parathyroid adenoma. Gamma probe can be used in the intraoperative setting for parathyroid localization and this procedure requires radionuclide

injection 45 minutes before the operation. Technetium 99m sestamibi scintigraphy is a very accurate technique with 80-90% sensitivity in patients with solitary adenoma. Ultrasonography, when performed by experienced hands, has 70-80% sensitivity for determination of parathyroid adenoma. Combination of scintigraphy and ultrasonography has a 90-95% of sensitivity in determination of solitary adenoma (11). In the present study sensitivity of ultrasonography was 72.1% whereas it was 92.6% in technetium 99m sestamibi scintigraphy. Our results seem to be compatible with the literature. Successful localization of the parathyroid pathology is mandatory for a minimally invasive approach. Accuracy of ultrasonography and scintigraphy in our study was 60.4 and 80.4 %, respectively. In the present study, scintigraphy is the most useful technique for the localization of the parathyroid pathologies. We have not used a gamma probe in any of our patients. We used frozen section pathologic analysis in 16 patients (30.7%). However, we believe that the experience of the surgeon in determining pathologic parathyroid tissue is still a very important issue despite the developments in imaging techniques.

One finding in the study that is also worth mentioning is the fact that parathyroid hyperplasia could be predicted before the operation. According to our result, 25% of the patients that could not be localized on ultrasonography had parathyroid hyperplasia. On the other hand 66.6% of the patients that could not be localized in scintigraphy had parathyroid hyperplasia. Hundred percent of the patients that could not be localized in both imaging techniques had parathyroid hyperplasia. We have only seen McHenry et al (12) pointing out this phenomenon in their study involving 549 patients that underwent parathyroidectomy. In their study they found that parathyroid hyperplasia could not be determined in scintigraphy, ultrasonography or both techniques in 92%, 91% and 96% of the patients, respectively (12). We only have 5 patients with parathyroid hyperplasia in our study therefore we will have more accurate results as the number of the patients increase. However, our results seem to be in accord with the study performed by McHenry et al. We also believe that hyperplasia should be suspected in any patient with negative scintigraphic localization or in cases whom both of the imaging techniques fail to localize the pathologic parathyroid tissue.

The only curative option for PHPT is parathyroidectomy. In a successful operation, drop in the postoperative 10th-minute parathormone level following excision of the pathologic parathyroid gland to less than 50% of the preoperative levels is mandatory (13). In the present study due to technical problems postoperative 24thhour parathormone levels were studied and a more than 50% drop was observed in 50 patients (96.1%). In two patients (3.9%) there was no drop in the parathormone levels and these patients were re-operated and the pathologic parathyroid gland was resected. The malignancy rate in parathyroidectomy specimens was reported to be 6-11%. Dirican et al (14) have evaluated 53 patients and

micropapillary carcinoma rate was reported to be 7.5%. Furthermore, concomitant thyroid pathologies were reported to range between 60-76% (15,16). In the present study, 5 (9.6%) patients had malignant thyroid pathologies including papillary thyroid carcinoma in 4 patients and follicular neoplasia in 1 patient. Twenty-one patients (40.3%) had a benign multinodular goiter. Our results are consistent with the current literature.

CONCLUSION

In conclusion, the parathyroid adenoma can be localized in places other than the expected locations; despite the advances in imaging technologies. Combining scintigraphy and ultrasonography gives a better localization for the adenoma and enables minimally invasive surgery. Gamma probe should be used until the surgical team gains enough experience. Indications for surgery in asymptomatic cases are young age (<50), moderate to severe hypercalcemia, renal disease, osteoporosis or presence of bone fractures. Surgeons' experience and accurate localization before the operation are important for a successful parathyroid operation. However, if both ultrasonography and scintigraphy fail to localize the parathyroid pathology, hyperplasia should be suspected. In these cases, advanced imaging options and a thorough surgical exploration is mandated.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: This study was approved by the Institutional Ethics Committee and conducted in compliance with the ethical principles according to the Declaration of Helsinki.

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