

Clinical evaluation, diagnosis, and management of primary hyperparathyroidism: A retrospective analysis of 152 patients

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ABSTRACT

Objective: Primary hyperparathyroidism is a common endocrine disease with autonomic production of parathormone from one or more of the parathyroid glands. PTx is recommended for patients who meet the criteria for surgical treatment in the guidelines. The purpose of the present study was to evaluate the clinical and biomarker characteristics of patients with PHPT who underwent PTx in the light of policies.

Material and Methods: The present study was conducted with 152 patients that were followed in our clinic between 2015 and 2022. The patients' data were obtained retrospectively from patient files and electronic records. Demographic characteristics, laboratory findings, and surgical and pathology reports were collected. In PHPT, PTx was performed in line with surgical indications according to the surgical guideline.

Results: Most of the patients were diagnosed in the asymptomatic stage. Scintigraphy localized 76.3% of parathyroid adenomas, which were consistent with USI. Histopathologically, parathyroid adenoma was 94.0%, and parathyroid hyperplasia was 5.9% (n=9). Transient hypocalcemia was the most common postoperative problem. More rarely, there were Hungry Bone Syndrome, transient hoarseness, and permanent vocal cord paralysis.

Conclusion: Serum calcium and neck imaging have recently been performed with increasing frequency. This approach enables PHPT patients to be detected at an asymptomatic stage. The compatibility of scintigraphy and USI in predicting parathyroid adenoma localization is very successful for correct topographic localization.

Keywords: Primary hyperparathyroidism, clinical presentation of hyperparathyroidism, Parathyroidectomy.

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INTRODUCTION

Primary Hyperparathyroidism (PHPT) is a disease characterized by hypercalcemia, low phosphorus, and high or inappropriately normal parathormone levels (1). Although a single parathyroid adenoma is present in 80% of such patients, hyperplasia accounts for 10-15%, multiple adenomas for 5%, and parathyroid cancer for <1% of cases (2).

The prevalence of PHPT varies between 0.4% and 3.1% (3). The diagnosis is made based on the clinical presentation at the age of 40 and usually at the asymptomatic stage.

Parathyroidectomy (PTx) is the curative approach in PHPT. PTx is recommended for those who meet the surgical treatment criteria in the guidelines. Techniques have been proposed in recent years for the protection of musculoskeletal and other systems and for lowering serum calcium for patients for whom surgery is impossible (4).

The purpose of the present paper was to evaluate the clinical and biomarker characteristics of patients who underwent PTx for PHPT in our clinic in the light of guidelines.

MATERIAL and METHODS

The present study was conducted on 152 patients that were followed up in our general surgery, endocrinology, and internal diseases clinics between 2015 and 2022. The patients' data were obtained retrospectively from patient files and electronic records in the study. Demographic characteristics, laboratory findings, and surgical and pathology reports were collected. Also, the patients' preoperative biochemical, ultrasonographic, and scintigraphy reports such as parathyroid hormone, calcium, phosphorus, creatine, albumin, 25-OH vitamin D, and 24-hour urine calcium levels were obtained. The study was conducted following the ethical rules with the decision of the Private Medicana International Samsun Hospital Clinical Research Ethics Committee on 28/06/2022 with the number 12.

The patients who had a biochemical and clinical diagnosis of primary hyperparathyroidism, those who had parathyroid adenoma localized by neck ultrasonography (Image 1) and/or parathyroid scintigraphy (Image 2), and patients who underwent PTx after the diagnosis of parathyroid adenoma were included in the study. Those who had secondary and tertiary hyperparathyroidism, malignancy, malabsorption, pregnant women, and patients under 18 years of age were excluded from the study.

PTx corrects the underlying abnormality in symptomatic PHPT. In conclusion, Parathyroidectomy improves bone mass, decreases bone turnover, and improves fracture-free survival. There is an improvement in clinical symptoms (5-6). In asymptomatic PHPT, on the other hand, PTx was performed in line with surgical indications according to the surgical guideline (6) (Table 1). PTx was conducted in the presence of only one of these criteria.

Neck US was performed with a high-resolution device (The Philips Affiniti 70 Ultrasound, Philips North America Corporation 3000 Minuteman Road M/S 109 Andover, MA 01810, USA) equipped with an eL 18-4 MHz broadband linear array probe. In our clinic, scintigraphy-negative parathyroid adenomas were localized with Washout Parathormone (FNA-PTH) if the neck USI result was suspicious for a parathyroid lesion. Right after the aspiration, the aspirates and the syringe are washed with 1 mL saline and the parathyroid hormone is measured in this way. Parathyroid hormone (cut-off level, 10-65 pg/mL) was examined with an electrochemiluminescence immunological assay kit (ECLIA) (Abbott, IL, USA). Washout PTH/ serum PTH ≥ 2 were considered positive.

Statistics: Statistical analysis was made with the SPSS 20.0 (NY, USA). The continuous variables were expressed as mean \pm standard deviation or median according to the distribution of the data. The variables with statistically significant effects were included in the regression analysis and $P < 0.05$ was considered statistically significant.

RESULTS

Eighty patients were included in the study, 40 in the study group and 40 in the control group. Of these patients, 47 The present study was conducted with 152 patients who were followed up in our endocrinology and general surgery clinic 102 of these patients were female and 50 were male. The mean age of the patients was 51.3 ± 6.8 years. The clinical and biochemical characteristics of the patients were compatible with primary hyperparathyroidism, and most were asymptomatic. Clinical findings were mostly non-specific (weakness, fatigue), muscle, joint, bone pain, and gastrointestinal complaints, and skeletal involvement were rare. The prevalence of renal complications was greatly reduced.

The biochemical and hormonal values of the patients who were included in the study were as follows; serum Ca level 10.9 ± 0.8 (10.5-13.7) mg / dL, serum P 2.2 ± 0.3 (1.7-4.1) mg/dL, serum 25-OH Vitamin D 28.4 ± 2.4 (22-56) ng/mL, serum PTH 123 ± 42 (92-167) pg/mL, and 24-hour urinary Ca excretion 288 ± 44 (124-456) mg/day. Also, serum creatine was 0.87 ± 0.6 (0.79-1.32) mg/mL and albumin was 4.5 ± 0.4 (3.3-5.2) g/dL.

Scintigraphy (99mTc-Sestamibi+Single-Photon Emission Computed Tomography) localized 76.3% (n=116) of the parathyroid adenomas, consistent with USI results. Scintigraphy was negative, and US-suspected parathyroid adenoma was 23.6% (n=36). These cases were diagnosed and localized with the Washout Parathormone Method. The laboratory characteristics of the patients are given in **Table 1**.

When the surgery and tissue pathology reports were evaluated in the present study, parathyroid adenoma was 94.0% (n=143), parathyroid hyperplasia was 5.9% (n=9), and transient hypocalcemia was the most common postoperative problem. More rarely, there were Hungry Bone Syndrome, temporary hoarseness, and permanent vocal cord paralysis. These findings are given in **Table 2**.

Table 1: Biochemical markers and imaging characteristics of the patients

Parameters	
Creatine, mg/mL	0.87 ± 0.6 (0.79-1.32)
Albumin, g/dL	4.5 ± 0.4 (3.3-5.2)
Ca, mg/dL	10.9 ± 0.8 (10.5-13.7)
P, mg/dL	2.2 ± 0.3 (1.7-4.1)
25-OH-Vit D3, ng/mL	28.4 ± 2.4 (22-56)
PTH, pg /mL	123 ± 42 (92-167)
Ca ⁺⁺ excretion in 24-hour urine, mg/day	288 ± 44 (124-456)
Localization Methods:	
1) Scintigraphy (⁹⁹ mTc-Sestamibi+Single-Photon Emission Computed Tomography), USI-consistent parathyroid lesion, n (%)	76.3% (116)
2) Scintigraphy negative, USI-suspected parathyroid lesion (with Washout Parathormone Method), n (%)	23.6% (36)

Data are expressed as mean \pm SD, median, and n (%).

Table 2: Postoperative complications and histopathology reports

Parameters	
Numbness, contractions, and cramps, n (%)	124 (% 81,5)
Transient hypocalcemia, n (%)	42 (%27,6)
Hungry Bone Syndrome, n (%)	6 (%3,9)
Transient hoarseness, n (%)	4 (%2,6)
Permanent hoarseness (Vocal Cord Paralysis), n (%)	2 (%1,3)
Tissue histopathology:	
1) Parathyroid adenoma, n (%)	%94,0 (n=143)
2) Parathyroid hyperplasia, n (%)	%5,9 (n=9)
3) Parathyroid cancer, n (%)	0

Data are expressed as n (%).

DISCUSSION

Hyperparathyroidism is recently detected incidentally during routine blood tests in general. Normocalcemic and/or asymptomatic PHPT forms are detected more frequently than clinical PHPT forms (6-7). Clinical findings are often nonspecific or asymptomatic (7). In the present study, the clinical presentation was asymptomatic, nonspecific findings were dominant, and skeletal system involvement was prominent. Nonspecific hypocalcemia findings after surgery were mostly numbness, spasms, and cramps. Most parathyroid lesions were localized in the same topographic location with scintigraphy and neck USI results. With this combination, the success rate of positivity was determined to be 100%.

The predominant presentation was generally reported as an asymptomatic disease in previous studies. The prevalence of asymptomatic disease was found to be 47-84% (8). Bone pain, polyuria, kidney stone disease, and fatigue were reported as the most common classical symptoms in clinical PHPT (9-10). It has been reported in recent studies that the fracture rate decreased significantly (11). In the present study, the presentation was most frequently asymptomatic and incidental. Clinically, weakness, musculoskeletal pain, gastrointestinal system findings, kidney stones, and urinary system findings were detected. In the present study, nonspecific symptoms were the most common finding. In this context, PHPT must be excluded in patients with fatigue, skeletal findings, and muscle and bone pain. No fracture cases were detected in the present study.

Abnormal bone densitometry was reported at a rate of 36-50% in bone densitometry studies (12-13) and 18.4% abnormal bone densitometry was detected in the present study. Kidney stones and kidney involvement is an important complication of PHPT. In previous studies, the prevalence of clinically overt stone disease decreased to 7-20% in the Western population (14). The known risk factor for kidney stones is hypercalciuria (15). In the present study, it was found that the prevalence of stone disease was 4.6%. Recently, the frequency of kidney stones and bone involvement has decreased significantly, as serum calcium and neck US examinations have become widespread, greatly facilitating the diagnosis of PHPT at an early stage.

The association of hypercalcemia, low phosphorus, and high or inappropriate normal parathormone levels are biomarkers compatible with PHPT (16). It is seen in Table 2 that calcium, phosphorus, parathormone, 25 OH-Vit D3, and urinary calcium excretion levels are compatible with PHPT.

These biomarkers appear to show moderate deviations from normal reference ranges. This finding is explained by the more frequent monitoring of serum calcium and the more frequent evaluation of cases with neck USI.

Preoperative imaging of parathyroid lesions has excellent benefits during surgery. Generally, 99mTc-sestamibi scintigraphy, ultrasound, and computed tomography are used in imaging. The sensitivity of USI was 76-87% with a positive predictive value of 93-97%, and its diagnostic accuracy was 88% (17-18). Also, 99mTc-sestamibi scintigraphy is known to be very sensitive (90%) with high accuracy (97.2%) in PHPT. In the presence of scintigraphy and ultrasonographic imaging compatibility, the positive predictive value for the correct topographic location was reported as 97% (17). In the present study, topographic localization compatible with scintigraphy (99mTc-Sestamibi+Single-Photon Emission Computed Tomography) and neck USI were 76.3%. If scintigraphy and neck US were in topographic compatibility, it was found that the lesion was 100% parathyroid adenoma. Scintigraphy was negative, and neck USI-suspected parathyroid lesion was 23.6%. Accurate topographic localization of these lesions was achieved with the Washout Parathormone Method.

PTx has a very low complication rate (<1-3%). Patients usually have a single adenoma (~85%). Parathyroid hyperplasia is detected in ~14% of patients (19). In the present study, the complication (vocal cord paralysis) rate was found to be 1.3%. Transient findings were more often related to low calcium. Parathyroid adenoma was found in 94% and parathyroid hyperplasia in 5.9% in the histopathological evaluation of the patients.

Limitations: The most important limitation of our study is that it is a single-center and retrospective study.

CONCLUSION

Serum calcium and neck imaging are performed with increasing frequency recently in our country. Also, nonspecific symptoms are being investigated in more detail with the increasing number of endocrinologists and experienced clinicians. In this context, PHPT is usually detected at an asymptomatic stage. PHPT must be considered in patients with nonspecific symptoms. Topographic compatibility in scintigraphy and USI clearly shows the localization of parathyroid lesions. PTx in treatment is curative in experienced hands.

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Ethical approval: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and/or with the Helsinki Declaration of 1964 and later versions. This study was approved by Private Medicana International Samsun Hospital, Ethics Committee on June 28, 2022, with the number 12

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