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Case report
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Seven-year follow-up in a case of primary hyperparathyroidism using quantitative ultrasound and dual X-ray absorptiometry.

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Abstract: We have previously reported a case of a 36-year-old woman who was diagnosed with primary hyperparathyroidism following initial skeletal abnormalities in the hand phalanges and calcaneus revealed by quantitative ultrasound (QUS). Successful parathyroid adenoma surgery resulted in progressive increase of bone mineral density and QUS parameters within 6 months, 1 year and 2 years of follow-up. Now, 5 years after the last measurement and at the onset of her menopause, the study was repeated. It has shown further increase in some ultrasonic and densitometric parameters but decrease in others. This discrepancy could be associated with the early influence of perimenopause on trabecular bone. Based on the current report one can conclude that peripheral QUS used on the hand phalanges and calcaneus is a useful tool for the diagnosis and monitoring of skeletal alterations due to parathyroid dysfunction. Moreover, it can detect early changes associated with perimenopause.

Keywords: Primary hyperparathyroidism, quantitative ultrasound, bone densitometry, perimenopause

1 Introduction

Primary hyperparathyroidism (PHPT) is a generalized disease caused by the parathyroid hormone (PTH) producing parathyroid adenoma. PTH secreted excessively in an autonomous manner increases bone resorption, causing osteoporosis and fractures. The majority of affected individuals are older women, although some of them might be asymptomatic. Hypercalcemia is incidentally discovered when serum calcium is measured as a

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screening test. Parathyroid surgery remains to be the most efficacious method of PHPT therapy [1]. Quantitative ultrasound (QUS) is a widely accepted method for the diagnosis of skeletal status in postmenopausal osteoporosis and different metabolic bone diseases [2]. There are several studies on QUS measurements in patients with PHPT [3, 4].

We have previously reported a case of a 36-year-old woman who was diagnosed with PHPT following initial skeletal abnormalities revealed by QUS at the hand phalanges and calcaneus. The QUS results were confirmed by dual-energy X-ray absorptiometry (DXA) measurements in the lumbar spine, proximal femur and forearm. She had typical alterations in hormonal and calcium/phosphate results. Successful parathyroid adenoma surgery resulted in progressive increase in bone mineral density (BMD) and QUS parameters within 6 months, 1 year and 2 years of follow-up [4].

2 Case report

Presently, 7.5 years after the initial skeletal assessment and 7 years following parathyroidectomy, a subsequent follow-up was carried out. The patient is now 43 years old; she does not suffer from any symptoms, and her menstrual cycles are regular. Her laboratory results - serum calcium 4.8 mEq/l (normal range 4.04−5.1), serum phosphate 0.84 mmol/l (normal range 0.81−1.45), urinary calcium 4.56 mEq/24h (normal range <15), PTH 27.3 pg/ml (normal range 12 − 72), total alkaline phosphatase (AP) 103 U/l (normal range < 240) - support complete normalization of calcium metabolism. Her hormonal results showed increased gonadotropin levels, LH 54.5 mIU/l and FSH 120 mIU/l, suggesting the onset of menopause, and mild hyperprolactinaemia 28 ng/ml (normal range 1.9−25). She was submitted for magnetic resonance (MR) of the pituitary gland in order to exclude the presence of pituitary adenoma, possible in the case of primary hyperparathyroidism (as Multiple Endocrine Neoplasia type 1 - MEN-1). No evidence for pituitary adenoma was shown on the MR scan, and other pituitary hormones (growth hormone, thyroid stimulating hormone, adrenocorticotropin hormone) were in normal range. Adrenal and thyroid functions were normal too.

Current skeletal assessment showed further increase in some QUS measurements: amplitude-dependent speed of sound (Ad-SoS) at the hand phalanges and speed of sound (SOS) in the calcaneus. The value of broadband ultrasound attenuation (BUA) declined in comparison to the last measurement, and stiffness index (SI) remained the same, although they were still higher than baseline results (Table 1). Ultrasonic results were associated by similar increases in some BMD results (femoral neck, trochanter major and 1/3 radius) assessed by DXA. The results obtained from the lumbar spine, ultradistal radius and Ward's triangle revealed slight decreases of BMD in comparison to the results obtained 5 years earlier, but they were higher than the results at onset before parathyroidectomy (Table 2). The differences between current and baseline measurements are shown in Tables 1 and 2 according to least significant change (LSC).

Table 1 Results of QUS measurements in patient with primary hyperparathyroidism before and after parathyroid adenoma surgery. Presentation of the differences between values according to least significant change .

		After parathyroidectomy						
	Before	6 m	1 yr	2 yr	7 yr	Δ_{0-7}	Δ_{2-7}	LSC
Phalanges								
Ad-SoS (m/s)	1876	1912	1933	1913	1993	+117	+80	34
Calcaneus								
SOS (m/s)	1482	1513	1530	1526	1539	+57	+13	15
BUA (dB/MHz)	90	94	84	98	92	+2	−6	11
SI (%)	55	66	65	72	72	+17	0	5

Δ_{0-7} - difference between the results at 7-yr follow-up and at the onset (before parathyroidectomy)
Δ_{2-7} - difference between the results at 7-yr follow-up and at 2-yr after parathyroidectomy
LSC - least significant change

Table 2 Results of QUS measurements in patient with primary hyperparathyroidism before and after parathyroid adenoma surgery. Presentation of the differences between values according to least significant change .

	After parathyroidectomy							
	Before	6 m	1 yr	2 yr	7 yr	Δ_{0-7}	Δ_{2-7}	LSC
Lumbar spine BMD (g/cm^2)								
L2-L4	0.728	1.055	0.990	1.047	0.899	+0.171	−0.148	0.018
Forearm BMD (g/cm^2)								
1/3 radius	0.306	0.353	0.349	0.360	0.415	+0.109	+0.055	0.054
Ultradistal radius	0.232	0.234	0.268	0.246	0.244	+0.012	−0.002	0.014
Proximal femur BMD (g/cm^2)								
Femoral neck	0.636	0.815	0.872	0.885	0.891	+0.255	+0.006	0.022
Trochanter major	0.524	0.697	0.762	0.754	0.766	+0.242	+0.012	0.037
Ward's triangle	0.488	0.723	0.778	0.735	0.715	+0.227	−0.020	0.039

Δ_{0-7} - difference between the results at 7-yr follow-up and at the onset (before parathyroidectomy)
Δ_{2-7} - difference between the results at 7-yr follow-up and at 2-yr after parathyroidectomy
LSC - least significant change

3 Discussion

We report a case of a 43-year-old woman in whom severe skeletal abnormalities due to PHPT resolved following the parathyroid adenoma surgery. Skeletal abnormalities were recognized early by peripheral QUS examination, and we had reported rapid postsurgical increases in the results of QUS examination at the hand phalanges and calcaneus and in the BMD of this patient when she was previously premenopausal [4]. Nowadays, she is at the onset of her premature menopause, so this implied that we should study her again, before menopause could blur the results.

The current examination showed further increase (significant according to LSC) in

Ad-SoS at the hand phalanges. There was a rather stable level of Ad-SoS within 2 years following the parathyroidectomy, but the current result is clearly higher than the previous ones were (increase of more than 2 LSC). SOS in the calcaneus increased too, but only the difference between present and baseline measurements was significant, since the difference between the present and the last measurement (5 years ago) was not. Our results of greater response of SOS in the phalanges than in the calcaneus are similar to those reported by other authors [3]. The BUA value decreased (not significant according to LSC) in comparison to the last measurement, and SI remained the same, although they both were higher than baseline results. Similarly, there was increase in BMD results (significant according to LSC) within femoral neck, trochanter major and 1/3 radius, reflecting cortical bone assessed by DXA. But these differences were not significant, except for the 1/3 radius when compared to the last examination 5 years ago. The results obtained within the sites of skeleton with predominance of trabecular bone revealed slight decrease of BMD in comparison to the results obtained 5 years earlier (significant according to LSC for lumbar spine), but they were higher than the results obtained before the parathyroidectomy (significant for lumbar spine and Ward's triangle).

The discrepancies between results reported could be due to the onset of the menopause (shown by hormonal analyses - elevated FSH) in our patient. The decrease of BMD within the trabecular bone occurs in an early stage of menopausal bone loss, contrary to increased cortical bone loss in PHPT.

The QUS method is a useful, relatively cheap, non-invasive one and it utilizes portable devices. It was validated in various hormonal disorders such as menopause, primary hyperparathyroidism, acromegaly or metabolic bone diseases [2, 5–7]. Moreover, QUS is suitable both for monitoring of the antiresorptive therapy and for the prediction of fracture occurrences. This method is able to effectively discriminate between fractured and non-fractured subjects, osteoporotic and non-osteoporotic ones, and to identify different types of non-traumatic fractures as well [8–10].

In conclusions, based on the current report, one can conclude that peripheral QUS of the hand phalanges and calcaneus is a useful tool for the diagnosis and monitoring of skeletal alterations due to parathyroid dysfunction. Moreover, it could detect early changes associated with perimenopause.

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