

Bone mineral density in hypoparathyroidism: Not a useful tool (a case in point)

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ABSTRACT

Hypoparathyroidism is a rare condition associating autoimmune, genetic, post-operative (most frequent) or idiopathic causes. Low calcium causes neuromuscular irritability of chronic or acute type like muscle cramp, paresthesia, tingling, cardiac rhythm anomalies, seizures, etc. Despite calcium and active vitamin D replacement, acute complications are frequently seen and generally a reduced quality of life is registered since pathogenic medication like parathormone drug substitution is not currently available in daily practice. Other complications are due to overtreatment with calcium and vitamin D like kidney stones and associated urinary infections and hypercalciuria while increased calcium-phosphor product causes calcifilaxia of different locations causing complications like skin necrosis, brain calcifications with seizures, etc. We introduce a case of hypoparathyroidism in association with other co-morbidities and a brief discussion around the case related to bone mineral density anomalies or usefulness in general panel of investigations in this particular topic. This is a 43-year old non-smoking male coming from non-endemic area that had a small lesion of skin necrosis at left hand. He has autoimmune thyroiditis and on admission low values of calcium and PTH 2 pg/ml (normal 15-65 pg/ml) are consistent for the diagnosis of hypoparathyroidism, probably of autoimmune cause. Central DXA shows high BMD at each site. He was offered calcium and vitamin D replacements with a mild clinical improvement. This case of autoimmune hypoparathyroidism associated with Hashimoto's thyroiditis highlights the idea of high DXA-BMD due to cortical and trabecular effects of PTH deficiency.

Keywords: skin necrosis, hypoparathyroidism, bone mineral density, thyroid nodule, thyroiditis

Abbreviations

BMD = bone mineral density

DXA = dual-energy X-ray absorptiometry

PTH = parathormone

TSH = thyroid stimulating hormone

TBS = trabecular bone score

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INTRODUCTION

Hypoparathyroidism is a rare condition associating low calcium and parathormone levels of different causes like autoimmune, genetic, post-operative (most frequent) or idiopathic (1,2). Low calcium causes neuromuscular irritability of chronic or acute type like muscle cramp, paresthesia, tingling, cardiac rhythm anomalies, seizures etc. (1,2). Despite calcium and active vitamin D replacement, acute complications are frequently seen and generally a reduced quality of life is registered since pathogenic medication like parathormone drug substitution is not currently available in daily practice (3). Parathormone represents the key player of mineral metabolism and its role is related to adequate synthesis and actions of vitamin D, too (4,5). Other complications are due to overtreatment with calcium and vitamin D like kidney stones and associated urinary infections and hypercalciuria while increased calcium-phosphor product causes calcifilaxia of different locations causing complications like skin necrosis, brain calcifications with seizures etc. (1,2,3).

AIM

We introduce a case of hypoparathyroidism in association with other co-morbidities and a brief discussion around the case related to bone mineral density anomalies or usefulness in general panel of investigations in this particular topic.

METHOD

This is a case presentation. The patient agreed for the introduction of his medical records.

CASE DATA

Admission

This is a 43-year old non-smoking male coming from non-endemic area that had a small lesion of skin necrosis at left hand (at the level of this 4th finger). After remission he was referred for an endocrine assessment because the patient had a history of autoimmune hypothyroidism. Also he experienced acral paresthesia of different intensities since last several months and a value of low serum calcium has been detected.

Assessments

On admission the general and endocrine clinical evaluation was not significant. The blood assays were done and revealed a very low value of total calcium of 5.09 mg/dl (normal levels between 8.5 and 10.2 mg/dl) as well as ionic calculated calcium of 2.1 mg/dl (normal values between 3.9 and 4.9 mg/dl); normal total serum proteins of 7.55 mg/dl (normal limits of 6.5-8.7 mg/dl), high serum phosphorus of 6.2 mg/dl (normal between 2.5 and 4.5 mg/dl). In addition to these aspects the subject had normal renal and hepatic function, hemoglobin, serum magnesium (1.5 mg/dl, normal between 1.6 and 2.4 mg/dl). 25-hydroxivitamin D was of 38 ng/ml (normal level is more than

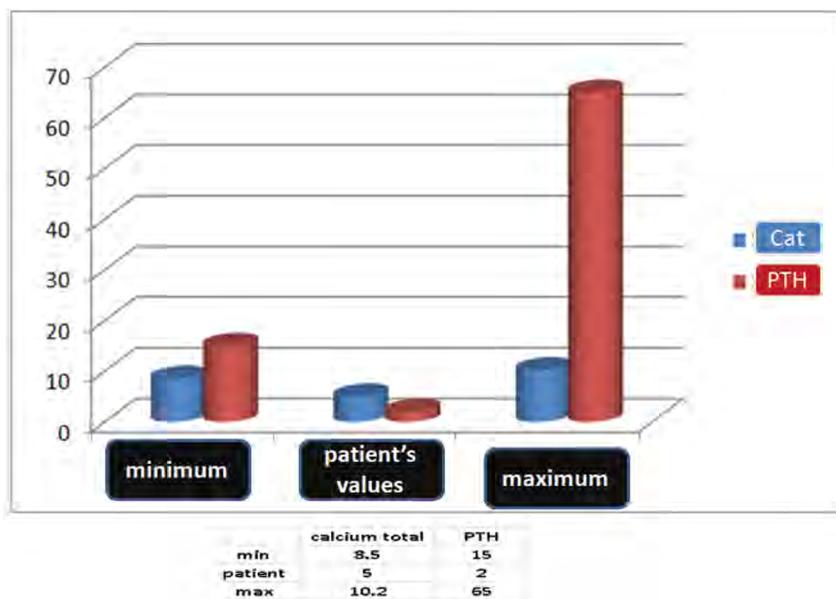


FIGURE 1. Total serum calcium and PTH levels on a 43-year old patient with hypoparathyroidism; normal levels are displayed within the chart

30 ng/ml) and PTH (parathormone) was of 2.15 pg/ml (normal between 15 and 65 pg/ml) (Figure 1).

The values of PTH remained low when the assays were repeated. The blood bone turnover markers showed CrossLaps (marker of bone resorption) of 0.23 ng/ml (normal between 0.158 and 0.442 ng/ml), and osteocalcin, respective total alkaline phosphatase (markers of bone formation) of 8.25 ng/ml (normal ranges between 14 and 42 ng/ml), respective 53 U/l (normal less than 108 U/l). TSH (thyroid stimulating hormone) was of 3 µU/ml (normal between 0.5 and 4.5 µU/ml). Anti-thyroperoxidase antibodies of 417 U/ml confirmed the diagnosis of Hashimoto's thyroiditis (normal levels less than 35 UI/ml) with normal values of anti-thyroglobulin antibodies of 30-70 UI/ml).

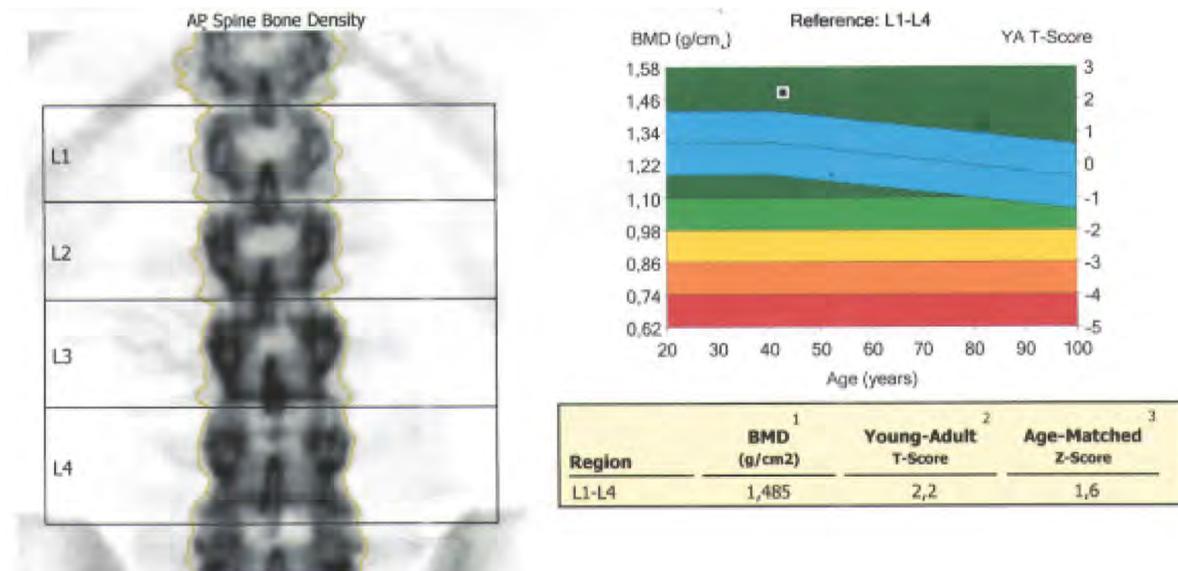
Thyroid ultrasound pointed out hypoechoic pattern and a thyroid hypo-echogenous nodule of

8 mm at left lobe. Anterior cervical intravenous contrast computed tomography revealed no tumor but a small thyroid nodule of 8 by 5 mm at the level of left lobe which was homogenous and well shaped. Central DXA (Dual-Energy X-Ray Absorptiometry) showed at L1-4 lumbar level a BMD (bone mineral density) value of 1.485 g/sqcm, T-score of 2.2 SD, Z-score of 1.6 SD (Figure 2).

1/3 distal radius DXA at non-dominant forearm revealed a BMD of 0.763 g/sqcm, T-score of -0.5 SD, Z-score of -0.5 SD (Figure 3). Hip DXA showed femoral neck BMD of 1.328 g/sqcm, T-score of 2 SD, Z-score of 1.9 SD, total hip BMD of 1.363 g/sqcm, T-score of 1.8 SD, Z-score of 1.6 SD (Figure 4).

Follow-up

The patient was offered oral calcium of 1-1.5 g per day in addition to calcitriol 0.5-0.75 µg per day (in case the drug was not available he switched to



Region	BMD ¹ (g/cm ²)	Young-Adult ² (%)	T-Score	Age-Matched ³ (%)	Z-Score	BMC (g)	Area (cm ²)	Width (cm)	Height (cm)
L1	1,202	104	0,3	97	-0,3	19,15	15,94	4,7	3,36
L2	1,476	119	2,0	112	1,4	24,16	16,37	4,7	3,47
L3	1,614	130	3,1	123	2,5	29,30	18,15	4,8	3,78
L4	1,594	129	3,0	121	2,3	33,85	21,24	5,2	4,10
L1-L2	1,341	112	1,2	105	0,6	43,31	32,31	4,7	6,83
L1-L3	1,439	119	1,9	112	1,3	72,61	50,46	4,8	10,61
L1-L4	1,485	122	2,2	115	1,6	106,46	71,69	4,9	14,70
L2-L3	1,549	125	2,6	118	2,0	53,46	34,52	4,8	7,25
L2-L4	1,566	126	2,7	119	2,1	87,31	55,76	4,9	11,34
L3-L4	1,603	129	3,0	122	2,4	63,15	39,38	5,0	7,88

FIGURE 2. Central lumbar L1-4 DXA on a 43-year old male with autoimmune hypoparathyroidism. High BMD is suggestive for the condition

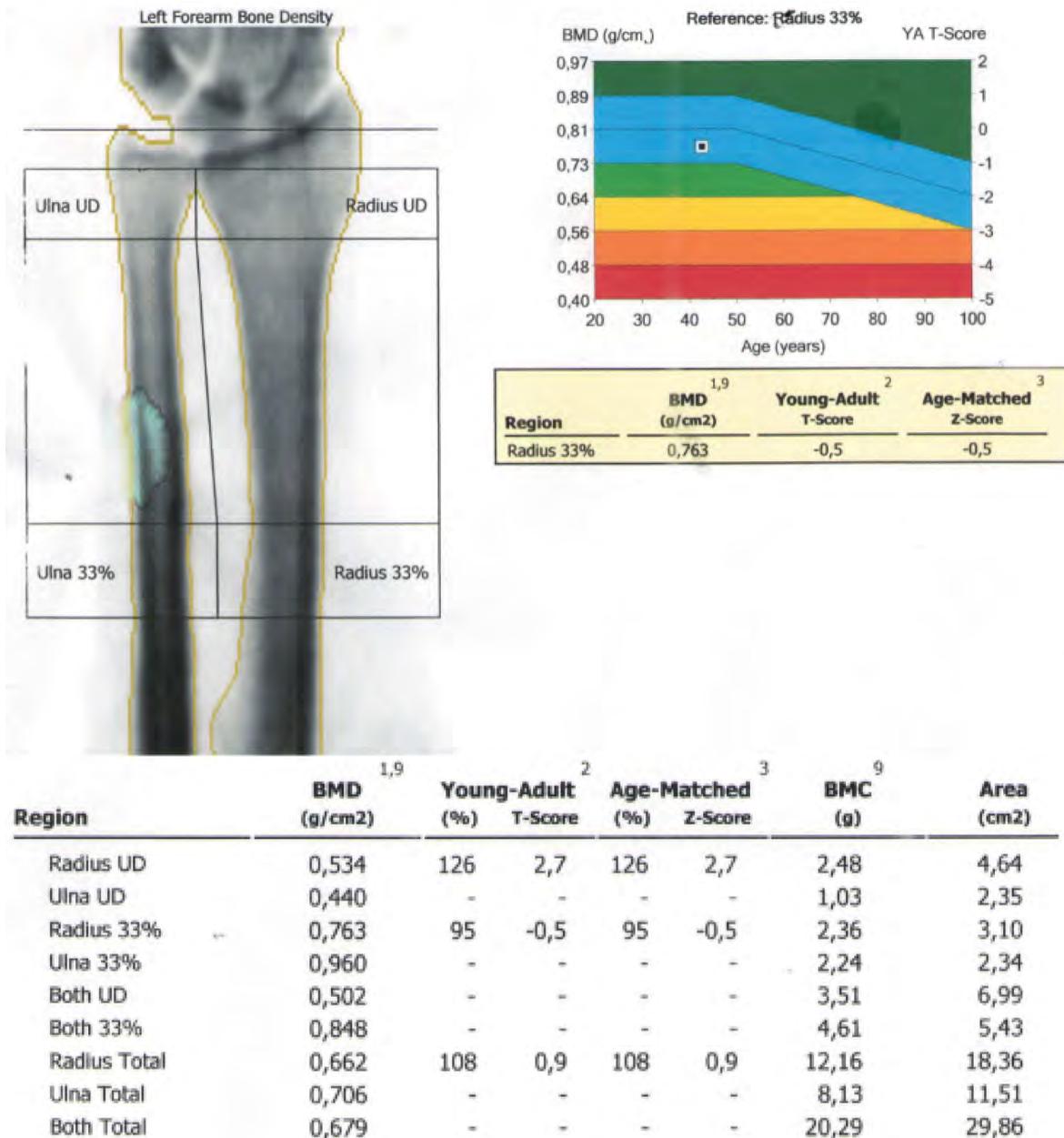


FIGURE 3. Central 1/3 distal radius on a 43-year old male with autoimmune hypoparathyroidism

1 µg alphacalcidol). He was followed for 3 more years and the values of calcium mildly increased with 1 mg/dL while the PTH levels remained extremely low. The thyroid substitution with 100 µg of daily levothyroxine was continued.

DISCUSSION

Several aspects worth to be discussed related to the present case.

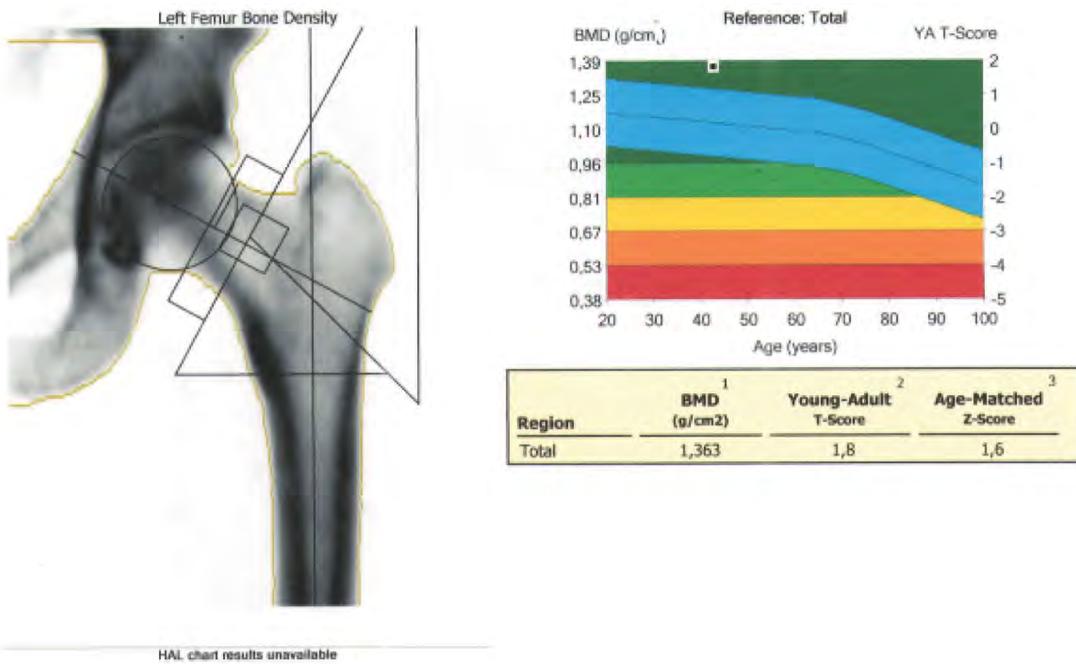
The etiology of primary hypothyroidism

This is probably an autoimmune case of hypoparathyroidism based on the co-presence of au-

toimmune chronic thyroiditis. The HLA connection is most probably involved in this adult onset type while the condition is typically a part of type 1 autoimmune polyglandular syndrome with childhood onset also associating primary chronic adrenal insufficiency and candidosis, type 1 diabetes mellitus and potentially other autoimmune disease because of the *AIRE* gene mutations (6).

Thyroid involvement and connections

In this case the patient had Hashimoto’s thyroiditis with adequately treated hypothyroidism and a small thyroid nodule which had no clinical relevance despite the fact that parathyroid glands



Region	BMD ¹ (g/cm ²)	Young-Adult ² (%) T-Score	Age-Matched ³ (%) Z-Score	BMC (g)	Area (cm ²)
Neck	1,328	124 2,0	123 1,9	7,46	5,62
Upper Neck	1,175	129 2,0	128 2,0	3,24	2,76
Lower Neck	1,475	- -	- -	4,22	2,86
Wards	1,089	113 1,0	116 1,1	3,82	3,50
Troch	1,116	120 1,7	115 1,3	22,71	20,36
Shaft	1,717	- -	- -	25,36	14,76
Total	1,363	124 1,8	121 1,6	55,53	40,74

FIGURE 4. Central hip DXA on a 43-year old male with autoimmune hypoparathyroidism

damages are positive based on a functional assessment (7). The risk of a malignancy like thyroid cancer is such a nodule is low and the mentioned co-morbidities are not correlated with the risk (8,9,10). The risk of thyroid metastasis is also low unless disseminated disease is positive (11). We perform a computed tomography of neck because of potential risk of infiltrative disorders (malignant or not) in order to induce the parathyroid glands suppression (12,13). Iatrogenic hypoparathyroidism is described in type 2 multiple endocrine neoplasia in association with other neuroendocrine neoplasia and endocrine tumors (14,15).

The patient had autoimmune chronic disorder which is more frequent in females but generally an increased prevalence is reported (16). The thyroid dysfunction is typically of hypothyroidism type but thyrotoxicosis has been reported (16,17).

BMD and PTH

PTH is situated on the mainstream of bone mass control and anomalies of PTH are directly re-

flected on BMD on patients with normal renal function or chronic renal insufficiency (18,19). A baseline evaluation of PTH is useful to appreciate the risk of primary or secondary hyperparathyroidism with DXA consequences (20,21). PTH has antagonist effects on skeleton of either anabolic or catabolic type (18). This is modulated based on time exposure (18). If PTH is low, the cortical and trabecular bone mass are high, thus DXA-BMD is increased as seen in this case, with the highest scores at lumbar spine (18,19). A TBS (trabecular bone score) evaluation was not available at that time for the patient. New data suggested, however, that TBS is normal in this condition (19). The complete panel of consequences involving low PTH at bone micro-architecture is still unclear, inclusive the risk of vertebral fractures (18). Other assessments like peripheral quantitative computed tomography at the level of radius showed that cortical is increased (19). Also, cortical volumetric BMD reveals reduced cortical porosity (19). It is still a matter of debate if the bone strength is af-

ected by trabecular changes (19). Therapy with human recombinant PTH improves bone remodeling with different responses of BMD (22,23). The therapy with PTH is not lifelong but it may be associated with an improvement of bone resistance to fractures, as well (most probably a transitory effect) (22,23).

CONCLUSION

This case of autoimmune hypoparathyroidism associated with Hashimoto's thyroiditis highlights the idea of high DXA-BMD due to cortical and trabecular effects of PTH deficiency.

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