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AbstractBook

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BONE EVALUATION IN A FEMALE WITH HYPERCALCITONINEMIA DIAGNOSED WITH DOUBLE INCIDENTALOMA

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Objective: Adrenal incidentaloma opposite to pituitary incidentaloma associates in third of the cases autonomous cortisol secretion that is less manifested as clear Cushing syndrome; however, long terms effects might be reflected in bone and cardiometabolic features. Opposite to adrenal, pituitary incidentaloma is not correlated with hormonal anomalies that might impair bone, unless mild hyperprolactinemia. We aim to introduce a female diagnosed with hyper-calcitoninemia and double incidentaloma with considerations on bone status.

Methods: Case report.

Results: A 66-year-old female was admitted 2 y ago for accidental detection of high calcitonin at evaluation as outpatient for multinodular goiter. She associated arterial hypertension, ischemic cardiac disease, dyslipidemia and episodes of headache (menopause by the age of 53). Her medical records showed normal thyroid function: TSH=1.3 µUI/mL (N:0.5-4.5), calcitonin of 4 times upper limit, negative thyroid autoimmunity. A medullary thyroid carcinoma (MTC) was suspected; she also had an abdominal ultrasound done and a right adrenal tumor of 2 cm was identified and confirmed at CT. Also, due to persistent headache, imaging of the head was performed and found a pituitary incidentaloma of 0.6 cm. Pituitary hormones were negative, so was adrenal profile, except for partial inhibition of plasma morning cortisol of 2.2 µg/dL (N<1.8) after low dose dexamethasone test, thus a possible autonomous cortisol secretion was confirmed. She was referred for thyroidectomy; pathological report did not confirm MTC. Preoperatory bone assessments showed normal bone formation marker osteocalcin=25 ng/mL (N:15-46) and a mild suppression of bone resorption marker CrossLaps=0.3 ng/mL (N: 0.33-0.782) with normal PTH=36 pg/mL (N: 15-65). DXA showed osteopenia: lumbar L1-4 BMD(g/cm^2)=1.004, T-score(SD)=-1.5, Z-score(SD)=-0.3; total hip BMD(g/cm^2)=0.933, T-score(SD)=-0.6, Z-score(SD)=0.3; femoral neck BMD(g/cm2)=0.859, T-score(SD)=-1.3, Z-score (SD)=-0.1. She continued with vitamin D supplements. She was reassessed recently amid pandemic and identified with mild vitamin D deficiency (25OHD=22.6 ng/mL) with an incidental vertebral fracture and osteoporosis at DXA, requiring antiresorptive medication: DXA: lumbar L1-4 BMD(g/cm^2)=0.9, T-score(SD)=-2.5, Z-score(SD)=-1.2.

Conclusion: This case highlights not necessarily the single effect of aging in terms of BMD, but, yet, additional causes: hypercalcitoninemia is less likely to affect the bone, but persistent cortisol excess, even mild, should be considered; also, the role of COVID-19 pandemic and associated restrictions might impair outdoor exercise which is a boost for bone formation.

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SPONTANEOUS AND INDUCED NEUTROPHIL EXTRACELLULAR TRAPS FORMATION IN OSTEOARTHRITIS PATIENTS

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Objective: Evaluation of peripheral blood neutrophils ability to generate NET spontaneously and after induction in vitro in osteoarthritis (OA).

Methods: The research was carried out in agreement with the WMA Declaration of Helsinki principles. Neutrophils were isolated with one-step centrifugation procedure using double-layer ficoll-amidotrizoate density gradient with density of upper and lower layers 1080 kg/m^3 and 1090 kg/m^3, respectively. The cell types in the resulting fractions were identified histochemically, and the extent of cell activation was assessed using common nitro-blue tetrazolium test. Generation of NETs was stimulated by phorbol-12-myristate-13-acetate (PMA). The shape and size of NETs were assessed using fluorescence microscopy with SYBR green [1].

Results: 23 patients with verified OA (6 males and 17 females, mean age 5.4 y, mean disease duration 12.5 y). 30 healthy volunteers were enrolled as a reference group. OA patients were in clinical remission at the inclusion timepoint. Indicators of the yield of isolated cells, purity of cell fractions, viability and nonspecific activation of neutrophils in the control group were comparable to those of the same name in healthy individuals. Mean contamination fraction of neutrophils both in the reference group and in the OA patients in did not exceeded 3%. Spontaneous and induced NET formation by isolated neutrophils in patients with OA during exacerbation is significantly higher than in OA in remission and in the reference group ($p<0.05$). The growth rate of

spontaneous NET formation was 149.1%, induced NET formation - 39.8%. The growth rate of spontaneous NET formation is 3.8 times higher than the induced NET formation.

Conclusion: We have revealed enhanced spontaneous and induced NET formation by neutrophils from OA patients, suggesting that circulating neutrophils may be primed to NETosis through immune inflammation.

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INPATIENTS WITH ACORMEGALY: TRABECULAR BONE SCORE IS ASSOCIATED WITH IMPAIRED GLUCOSE METABOLISM RATHER THAN HYPERSECRETION OF GROWTH HORMONE

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Objective: Acromegaly is associated with decreased bone structure but not BMD. Our recent study has been showing that impaired quality of cortical bone is associated with vertebral fractures (VF) regardless of acromegaly activity. Previously, trabecular bone compartment was thought to be strongest predictor of VF in growth hormone hypersecretion. Impaired glucose metabolism is common comorbidity in acromegaly, but as the risk factor for bone quality decrease in acromegaly has been not studied yet. We aimed to assess effect of glycemic compensation on DXA-derived bone parameters, such as BMD, TBS, cortical and trabecular volumetric (v)BMD, surface (s)BMD and cortical thickness (Cth) of proximal femur among patients with acromegaly.

Methods: A single-center 2-y prospective study of acromegaly patients was conducted. Each subject had L1-4 spine, femoral neck and total hip aBMD measured using DXA, and TBS measurement performed. 3D Shaper™ was used to assess proximal femur trabecular and cortical vBMD, cortical sBMD and Cth. Among all laboratory parameters, glycosylated hemoglobin (HBA1c), fasting plasma glucose (FPG), C-peptide levels and insulin resistance index in each patient was assessed. Abnormal glucose metabolism (GM) was defined as impaired glucose tolerance or diabetes according to current ADA guidelines. Follow-up periods were baseline and year 2.

Results: 70 acromegaly patients (24 males/46 females; average age 55.5 y) were included, of whom 25 and 35 had active acromegaly and abnormal GM, respectively. At baseline, subjects with abnormal GM had higher FPG, HBA1c and lower TBS in comparison to normal GM subjects ($p<0.05$). At both time points multiple regression model adjusted for IGF-1 showed HBA1c negatively associated with TBS. No significant associations between other parameters of glucose metabolism and TBS were shown at both time points.

Conclusion: This study shows in IGF-1 adjusted multiple regression model that HBA1c is negative predictor of TBS among patients with acromegaly. Based on this finding, it is likely that impairment of trabecular bone in acromegaly patients is the result of abnormal glucose metabolism rather than GH hypersecretion, as previously assumed.

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EFFECTS OF OSTEOPOROSIS DRUG TREATMENTS ON FEMUR STRENGTH USING 3D-SHAPER BASED FINITE ELEMENT ANALYSES

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Objective: To assess the effects of alendronate (AL), denosumab (DMAB), and teriparatide (TPTD) on femur strength using DXA-based 3D finite element analyses.

Methods: A cohort of 155 patients stratified by treatment, AL(N=54), DMAB(N=33), TPTD(N=31), and naïve of treatment NAIVE(N=37) were analysed. DXA scans were performed at baseline and after treatment. 3D-Shaper® software estimated 3D femur geometry and bone density distribution from the DXA scans [1]. Patient-specific finite element (FE) models were generated simulating sideways fall and femur strength (integral, cortical, trabecular) were calculated [2]. Percentage changes in aBMD and femur strength at follow-up compared to baseline were calculated and normalised to 24 months.

Results: Statistically significant($p<0.05$) increase in femoral neck aBMD were observed for DMAB(2.9%) and TPTD(1.8%) only. While total femur aBMD showed statistically significant ($p<0.001$) increase for DMAB(3.5%) and AL(1.7%) only. The changes in aBMD translated to statistically significant ($p<0.001$) increase in integral strength for DMAB(4.5%) and AL(3.7%) only. Statistically significant ($p<0.05$) increase in trabecular strength were observed for DMAB(2.8%) and AL(2.0%) only and in cortical strength for DMAB(1.9%) only. All treatment groups showed average increase in femoral aBMD and strength but were not statistically significant, while NAIVE group showed average decrease for aBMD and strength but were not statistically significant.

Conclusion: A DXA-based 3D FE analyses provided insights into effects of osteoporosis drug on femur strength that are not readily evident from aBMD measurements alone.

References:

1. Winzenrieth R, et al. Osteoporos Int 2018;29:2323