

Trichrome staining). The post burn scars formed in 11 β -HSD1 knockout mice demonstrated different skin elastic properties compared to those formed in wildtype mice. In wildtype mice application of scaffolds loaded with inactive glucocorticoid (prednisone) significantly impacted wound healing demonstrating the feasibility of using enzyme substrates to improve wound outcomes.

The findings demonstrate the importance of skin 11 β -HSD1 in wound healing and scarring after burn injury and indicate ways in which excessive scarring might be prevented.

Neuroendocrinology and Pituitary PITUITARY AND NEUROENDOCRINE CLINICAL TRIALS AND STUDIES

Lower Oxytocin Levels Are Associated with Lower Bone Mineral Density and Less Favorable Hip Geometry in Hypopituitary Men

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Introduction: Hypopituitary patients are at risk for bone loss. Oxytocin (OT) and vasopressin (VP) are hypothalamic-posterior pituitary hormones with opposing actions on bone (anabolic and catabolic, respectively). Whether OT and/or VP contribute to impaired bone homeostasis in hypopituitarism is unknown.

Hypothesis: We hypothesized that lower plasma OT and higher VP levels would be associated with lower bone mineral density (BMD) and less favorable hip geometry and estimated strength in men with hypopituitarism.

Design: We performed a cross-sectional study of 37 men with hypopituitarism ages 20–60 (mean \pm SEM 45.8 \pm 1.9) years: 20 with anterior pituitary deficiencies only (APD) and 17 with central diabetes insipidus (CDI; marker of posterior pituitary dysfunction), of similar age, body mass index and number of adeno/hypophyseal deficiencies, on stable hormone replacement. Main outcome measures were fasting plasma OT and VP levels, and dual X-ray absorptiometry-derived BMD (lumbar spine, total hip, femoral neck, distal radius and subtotal body) and hip structural analysis (HSA; cortical thickness, section modulus, and buckling ratio at narrow neck, intertrochanteric region and femoral shaft). All analyses were adjusted for multiple comparisons using Holm-Bonferroni correction.

Results: Mean BMD Z-scores were lower at all sites and all HSA parameters at the intertrochanteric region as well as

cortical thickness at the femoral shaft were less favorable in those participants who had fasting OT levels below the median than in those with higher levels ($P\leq 0.022$). There were no differences in any bone variables at any skeletal site in those with fasting VP levels below vs. above the median ($P\geq 0.232$). Lower fasting OT levels were positively associated with (1) lower BMD Z-scores at the lumbar spine, femoral neck, total hip and subtotal body ($P\leq 0.02$) and (2) less favorable hip geometry and strength variables (lower cortical thickness, lower section modulus and higher buckling ratio) at the intertrochanteric region in CDI ($P\leq 0.018$), but not APD participants ($P\geq 0.458$ and $P\geq 0.429$, respectively). The associations between OT and bone variables remained significant after adjusting for key determinants of BMD including lean body mass and IGF-1 levels. There were no relationships between plasma VP levels and bone variables in CDI or ADP groups ($P\geq 0.173$).

Conclusions: OT, but not VP levels, are positively associated with BMD at multiple sites as well as favorable hip geometry and estimated strength in men with hypopituitarism and CDI. Future studies will be important to determine whether OT could be used therapeutically to optimize bone health in patients with hypopituitarism.

Adrenal

ADRENAL - HYPERTENSION

Pheochromocytoma and Paraganglioma: An Emerging Cause of Secondary Osteoporosis

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Context: Many endocrine diseases are known to cause secondary osteoporosis, which is potentially reversible by treatment of the underlying disease itself. Pheochromocytoma (PHEO) and paraganglioma (PGL) (PHEO and PGL: PPGLs) are the rare catecholamine-producing neuroendocrine tumors, which are associated with low bone mineral density (BMD). However, PPGLs have not been recognized as a cause of secondary osteoporosis. Indeed, even the prevalence of osteoporotic fracture in patients with PPGLs is currently unknown. Furthermore, whether surgical resection contributes to the improvement of BMD has never been addressed. **Objective:** This study was designed to evaluate 1) whether PPGLs increase the risk of vertebral fracture (VF), which is the most common type of osteoporotic fracture and 2) whether surgical resection of PPGLs contributes to the improvement of BMD. **Design and Settings:** A retrospective cross-sectional study in a single referral center. **Participants:** Among 443 patients with adrenal tumor (AT), we included 62 patients with histologically confirmed PPGLs and 61 patients with non-functional AT. **Intervention:** The prevalence of VF was examined in 49 out of 62 patients with PPGLs and 61 patients with non-functional AT. In 23 out of 62 patients with PPGLs, BMD was evaluated at baseline and after

surgery. **Results:** PPGLs had a higher prevalence of VF (43% [21/49]) than non-functional AT (16% [10/61]; $p = 0.002$). PPGLs were an independent risk factor for VF after adjusting for age and sex (odds ratio, 4.47; 95% confidence interval, 1.76–11.3; $p = 0.001$). In PPGLs, BMD expressed as Z score at the lumbar spine was significantly improved at follow-up (before -0.5 ± 1.0 , after -0.2 ± 0.9 ; $p = 0.005$). **Conclusion:** This study demonstrates that PPGLs are an independent risk factor for VF and that their surgical resection contributes to the improvement of BMD in the trabecular bone. These observations support the notion that PPGLs are an emerging cause of secondary osteoporosis.

Pediatric Endocrinology

PEDIATRIC OBESITY, THYROID, AND CANCER

Prevalence and Incidence of Obesity in Children and Young Adults in Korea: The Kangwha Study

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Childhood obesity is a major global concern, arousing a variety of health problems and high social costs. The prevalence of childhood obesity has increased, but plateaued during the first decade of the 21st century in developed countries. Many previous studies reported cross-sectional data with prevalence of obesity, but researches about incidence of obesity based on longitudinal data is insufficient, especially in Korean population. In this study, we analyzed prevalence and incidence of overweight and obesity in Korean children and young adults from a prospective cohort study. We analyzed data from the Kangwha study, which is a community-based prospective cohort study began in 1986 with 6-year-old, first-grade elementary school students in Kangwha county, South Korea. The Kangwha study is a dynamic cohort, which the number of participants was expanded several times during the follow-up period. The study was started with 482 children, which expanded to total 1,223 participants. The participants were examined annually until 1997, which is 17 years of age. Four adulthood follow-up studies were performed in 1999, 2005, 2010, and 2015. The data includes a 30-year period (1986–2015), with total 16 observations conducted. We used the 2007 Korean National Growth Charts to determine cutoffs for normal weight, overweight, and obesity in children. In adulthood, Asia-Pacific classification of obesity from World Health organization (WHO) recommendation was applied to define overweight and obesity. When the children were in their first-grade of elementary school, prevalence of overweight was 1.04% and obesity was 0.62%. Prevalence of overweight and obesity increased since age 10 (fifth-grade in elementary school) (overweight 4.44%, obesity 1.18%), reaching 7.34% and 3.39% in age 12 (first-grade in middle school), and 9.5% and 5.37% in age 17 (third-grade in high school). Prevalence of overweight and obesity in girls were higher than in boys throughout childhood. Annual incidence of obesity showed small peak at entering middle

school (2.1%, age 12), and another peak at third-grade in high school (2.33%, age 17). Also, a positive correlation was found between body mass index (BMI) in younger ages and follow-up BMI. Prevalence of overweight and obesity increased since senior years of elementary school, and more prominent in girls. Detailed study design and larger population would be required for subsequent investigations.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS I

CYP24A1 Mutation Masking Malignancy Mediated Hypercalcemia

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Background: Mutations in CYP24A1, resulting in reduced conversion of 1,25(OH)₂D to its inactive metabolite 24,25-(OH)₂D₃, are rare causes of parathyroid hormone (PTH)-independent hypercalcemia. While manifestations may range from the severe idiopathic infantile hypercalcemia due to biallelic mutations, heterozygous loss-of-function mutations causing milder phenotypes are increasingly reported in adults. Elevated 1,25(OH)₂D and hypercalciuria often accompanied by a history of nephrolithiasis are characteristic. Worsening hypercalcemia, under conditions such as pregnancy or sunlight exposure that enhance 1,25(OH)₂D and 25(OH)D production, respectively, has been described in CYP24A1 mutations. We describe a patient with hypercalcemia and a history of lymphoma who was found to have elevated 25-OH-D₃ and low 24,25-(OH)₂D₃ levels, suggesting a mutation in CYP24A1. **Clinical Case:** An 80 year-old Caucasian male with history of indolent non-Hodgkin lymphoma diagnosed in 2016, well controlled after several courses of chemotherapy, was referred for recurrent hypercalcemia. Laboratory studies showed levels of 1,25(OH)₂D of 78 (18–72 pg/mL) and PTH 22 (10–65 pg/mL) with calcium ranging from 10.3 to 12.6 (8.5–10.1 mg/dL), an undetectable PTHrP, 25(OH)D level of 32.9 (30–100 ng/mL), and 24-hour urinary calcium of 378mg. He was treated with high dose prednisone for presumed 1,25(OH)₂D-mediated hypercalcemia. Despite initial good response, hypercalcemia became progressively difficult to control requiring escalating doses of steroids. Repeat 1,25(OH)₂D levels improved to 30–40 pg/mL, but subsequently rebounded to >150. Oncologic re-evaluation found low-grade follicular lymphoma in inguinal lymph nodes, which were thought to be the source of 1,25(OH)₂D overproduction. Detailed history and records review, however, revealed that onset of hypercalcemia dated back to 2006, concurrent with the development of several episodes obstructive uropathy due to stones. These events preceded the diagnosis of lymphoma by a decade, and resulted in CKD stage 4. Family history is notable for nephrolithiasis in his father and son. We suspected CYP 24A1 mutation. Vitamin D metabolite analysis demonstrated a 25-OH-D₃ of 27 (20–50 ng/mL) and 24,25-(OH)₂D₃ of 0.56 ng/mL with