acute hyperglycemia. Laboratory values were significant for glucose of 779mg/dl and sodium of 126mMol/L. Absence of ketones or acidosis ruled out DKA. Normal serum osmolality of 295 ruled out HHS. HbA1c >15% confirmed his non-compliance to insulin use. UDS was negative. Patient was admitted and started on insulin basal/bolus regimen. On the second day of hospitalisation, rapid response was called for seizure-like activity characterised by twitching of left side of face, staring into space and deviation of eyes to left upper corner. This resolved with IV lorazepam without any residual focal deficits. Glucose at the time of seizure was 425mg/dl. He was started on levetiracetam and EEG thereafter revealed no seizure-like activity. CT head and CT angiogram of the head and neck were negative. However MRI showed T2 hyperintensity and restricted diffusion with edema throughout the right occipital lobe. Neurology suspected stroke. However, extensive stroke workup for infectious, autoimmune and hypercoagulable states remained negative. Glucose control was achieved and patient was subsequently discharged on a strict insulin regimen and outpatient follow up with an endocrinologist.
Conclusion: NKH is known to manifest as seizure activity and thus, should be considered an endocrine emergency requiring prompt diabetic management. The suggested pathophysiology for seizures is prolonged hyperglycemia leading to oxidative stress and cellular edema. Furthermore, this may contribute to the unique MRI findings and should not be confused for an acute stroke.
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Bone and Mineral Metabolism

BONE DISEASE FROM BENCH TO BEDSIDE

Cultured Murine Osteoblasts Convert DHEA to Testosterone

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Androgens have complex effects on the skeleton. Besides gonadal testosterone (T), the adrenal produces the androgen precursor dehydroepiandrosterone (DHEA), using 3β- and 17β-hydroxysteroid dehydrogenases (3βHSD & 17βHSD) to convert to T in target tissues. Microarray analyses of murine calvarial osteoblasts, RT-PCR of long bone osteoblasts, and RNA-Seq of human bone biopsies confirmed that each of the enzyme families is expressed in osteoblasts, suggesting osteoblasts can generate androgens from the adrenal-derived androgen precursor DHEA. Activation of osteoblast androgen receptor (AR) signaling by DHEA was detected using an AR reporter construct, providing evidence that active androgens are generated. To understand how DHEA is converted to T, we treated murine primary osteoblasts with 100 nM and 1 μM DHEA, or vehicle control. Conditioned media were collected 1, 2, and 3 days after DHEA treatment and assayed for intermediate and active androgens by tandem mass spectrometry with two-dimensional chromatography. As DHEA was consumed, the androgen intermediates androstenediol (A5) and androstenedione (A4) were generated and subsequently converted to T. The peak concentrations of T generated by DHEA 100 nM and 1 μM were 22 and 101 pg/ml, respectively. The equilibrium dissociation constant of the AR for T is ~0.2 nM (57.7 pg/ml), indicating sufficient T production to activate AR in androgen-sensitive osteoblasts. Cultured osteoblasts preferentially converted DHEA to A5, via 17βHSD, rather than to A4, signifying that in the conversion of DHEA to T, 3βHSD is the rate-limiting step. Of the 13 17βHSD isoforms, 7 were expressed in these samples. In contrast, only a single gene isoform of Hsd3b—Hsd3b7—was abundantly expressed in mouse osteoblasts and human bone. We investigated the effects of 3βHSD7 in osteoblasts. An Hsd3b7 shRNA knocked-down mRNA and protein expression by >85%, and caused an osteoblast growth defect compared to an shRNA control. 3βHSD7 has known functions in bile acid synthesis, converting 7α-hydroxycholesterol to 7α-hydroxycholestenone (7HC). Treatment of Hsd3b7 knockdown osteoblasts with 7HC rescued the growth defect suggesting that osteoblasts might generate 7HC or a subsequent metabolite as a trophic factor. We now report an unreported function of bone as a source of T, by conversion of the adrenal androgen precursor DHEA, using 3βHSD7 as a common enzyme for androgen and bile acid synthesis, and leading to the activation of osteoblast AR signaling. These data suggest that the skeleton has evolved protective mechanisms against hypogonadal bone loss that exploits the continued production of adrenal DHEA. This concept is especially important in men with prostate cancer bone metastasis undergoing testicular-targeted therapies whereby adrenal DHEA may continue to fuel cancer growth, and in bone maturation during adrenarche before the pubertal rise in gonadal androgens.

Cardiovascular Endocrinology

ENDOCRINE HYPERTENSION AND ALDOSTERONE EXCESS

Diabetes Mellitus Is the Risk Factor of Cardiovascular and Cerebrovascular Events in Primary Aldosteronism

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The prevalence of diabetes mellitus (DM) in primary aldosteronism (PA) patients is higher than essential hypertension patients and general population. Though both DM and PA play an important role in the progression of cardiovascular and cerebrovascular (CCV) diseases, the relationship between DM and these diseases in PA patients have not been evaluated.The aim of this study was to investigate whether DM was involved in the risk of CCV events and the progression of renal disorder in PA patients. This study was conducted as a part of the Japan Primary Aldosteronism