Bone and Mineral Metabolism
BONE AND MINERAL CASE REPORTS I
X Linked Rickets: Description of 16 Cases in the Adulthood in Argentina
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SAT-LB66
Introduction. X-linked hypophosphatemic rickets (XLH) is an inherited disorder that results from an inactivating mutation of the PHEX gene. The familiar form comprises most cases. Its incidence is 4.8 per 100000 persons (Haffner D et al., 2019). XLH is characterized by bowed or bent legs, short stature, tooth abscesses, hearing loss, joint pain and impaired mobility, which can alter quality of life.

Aim. To describe clinical characteristics, laboratory and imaging findings of XLH adult patients attending to our hospital; to evaluate physical function and impact on the quality of life; to estimate adherence to conventional treatment.

Methods. A retrospective, observational study from 16 XLH patients medical records was performed. Age, sex, BMI, age at diagnosis, number of fractures, bone deformities, corrective surgeries, biochemical and genetic profile were evaluated. Physical functionality, pain and stiffness were measured with WOMAC (Bellamy N et al., 1988) and PROMIS scale; and QOL with SF36. Adherence to treatment was assessed with the CQR questionnaire. To monitor treatment complications renal ultrasound and brain CT scan were performed.

Results. 16 patients were evaluated, 14 (88%) female, 2 (12%) male, with a mean (±) age 40.06 years (±12.4). Age at diagnosis (12%) male, with a mean:12.68 years (SD ± 18.37), BMI:28.3 kg/m² (13.07), stature:129.9 cm (± 33.9), fractures:8/16 (50%) and skeletal deformities 16/16 (100%), number of corrective surgeries required 15/16 (94%), pseudofractures 8/16 (50%) and skeletal deformities 16/16 (100%), number of corrective surgeries required 15/16 (94%), pseudofractures 8/16 (50%), kyphoscoliosis 13/16 (81%), hypophosphatemia 8/16 (50%). Laboratory: calcium 9.5 mg/dl (± 0.37), phosphatemia 4.07 mg/dl (± 0.37), FAO 2646 (± 119), PTH 0.26 (>0.05) study we found no statistical association as the p value was 0.26 (>)0.05).

Conclusion. We note that the high percentage of patients not adherent to conventional treatment leads to marked impaired physical function with important skeletal deformities, fractures and pseudofractures, bone pain and altered QOL. Early diagnosis, adequate treatment and follow-up by a multidisciplinary team will avoid complications and improve the patient’s quality of life.

Diabetes Mellitus and Glucose Metabolism
METABOLIC INTERACTIONS IN DIABETES
Violent Sensitive Preoptic Area Neurons That Express Opsin 5 Regulate Thermogenesis and Energy Metabolism
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SUN-LB125
The thermogenic potential of brown adipose tissue (BAT) is a promising therapeutic target in the treatment of obesity and metabolic disorders. The preoptic area (POA) is a region in the anterior hypothalamus responsible for autonomic thermoregulation by means of modulating BAT activity through sympathetic nerve activity (SNA). Neurons in the POA express opsin-5 (OPN5), an atypical opsin found in various extraretinal tissues and known to respond to violet wavelengths with a lambda-max of 380 nm. OPN5 has previously been shown to regulate seasonal breeding behavior in birds. Loss of OPN5 in mice have been demonstrated to impair circadian photoentrainment. We have also shown OPN5 to be required in retinal ganglion cells for in vivo entrainment of a retina circadian clock independent of the suprachiasmatic nucleus. To date, no other physiological role for mammalian OPN5 has been proposed. The same POA neurons that express OPN5 also engage the central thermoregulatory circuit that modulates BAT activity. We show that POA OPN5 neurons polysynaptically project to the BAT using a retrograde PRV-mRFP1 pseudorabies virus. Also via a genetically targeted glycoprotein-deleted rabies virus injected into the POA, we identified labeled neurons in the rostral raphe pallidus (rRPa), the lateral parabrachial nucleus (LPB), and the dorsomedial hypothalamus (DMH), all nuclei known to participate in central BAT thermoregulation. Opn5−/− mice better defend their core body temperature during acute 4°C challenge. Our results indicate this effect to be due to increased BAT thermogenesis and not heat retention or pyrexia. Furthermore, BAT thermogenesis target gene transcripts (Uncp-1, Prdm16, Pgc-1a) were elevated in these cold stressed Opn5−/− animals. To demonstrate the importance of OPN5’s violet light sensing function in cold defense, C57BL/6J mice reared from E16.5 without 380 nm light largely phenocopy Opn5−/− mice when acutely cold challenged. Furthermore, chemogenetic inhibition of POA OPN5 neurons further augments cold exposure defense and BAT activation. Indirect calorimetry studies reveal Opn5−/− mice to be hypermetabolic, consuming more food and having a higher energy expenditure than controls. Paradoxically, this increased turnover does not translate to weight-gain resistance under high fat challenge. Our
results suggest a mechanism where near-UV sensitive hypothalamic OPN5 neurons regulate BAT thermogenesis directly, proposing that the mammalian autonomic thermoregulatory apparatus is light responsive.

Adrenal
ADRENAL - TUMORS
Distinct Vitamin D Receptor DNA Methylation Profiles Are Associated With the Outcome of Pediatric Patients With Adrenocortical Tumors
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SAT-LB36
Pediatric adrenocortical tumors (pACT) are rare, display complex genomic background and lack robust prognostic markers. Very recently, distinct genomic methylation profiles of pACT were associated with prognosis. The vitamin D receptor (VDR) was shown to be underexpressed in ACT, especially in carcinomas (ACC). In adult ACC, VDR inactivation by methylation was demonstrated. On the other hand, VDR activation was shown to inhibit ACC proliferation in vitro and in vivo.

Aim: To evaluate VDR DNA methylation profile and its clinical and prognostic significance in pediatric ACT.

Methods: Genomic DNA methylation from 57 pACTs [40 girls; median age: 2.1 (0.2-16.4) years] was assessed using Infinium Methylation EPIC BeadChip Array. Unsupervised hierarchical clustering analysis (Ward method, R Stats Package) was performed considering the M-values of the 49 probes targeting the whole extension of VDR gene contained in the array. Clinical, histopathological and molecular features, as well as pACT VDR mRNA levels (qPCR) and nuclear immunoreactivity (IHC) were used for association analysis.

Results: Hierarchical clustering identified three clusters of pACT. Methylated VDR-targeted probes (M-values different from 0; n=37) composed the VDR methylation profile, which differed significantly between the clusters [M-values: C1=1.77 (1.1-1.9) (low), C2=2.15 (1.7-2.7) (intermediate), and C3=2.65 (2.2-3.1) (high); p<0.0001]. The C1 cluster comprised a set of patients with favorable outcome (n=18), who were younger (p=0.035), did not present metastasis at diagnosis (IPACTR stage IV) or after surgery, nor were diagnosed with carcinomas (Wieneke criteria >>4), were not carriers of somatic Beta-catenin activating mutations, or died. Although cluster C2 patients (n=21) presented intermediary disease features, only 2 patients died and the overall outcome was positive. Instead, the C3 cluster concentrated patients (n=18) with non-localized/metastatic disease (IPACTR stages I/II vs. III/IV; p=0.004), post-surgical metastasis/recurrence (p=0.009), and patients who needed adjuvant chemotherapy (p=0.005). Moreover, C3 patients had lower overall and disease-free survival rates (log-rank: p=0.001 and p=0.014, respectively). VDR methylation was not associated with sex, clinical presentation, P53 mutations, nor with tumor VDR mRNA expression or nuclear immunoreactivity.

Conclusions: Three VDR methylation profiles were associated with distinct pACT clinical features and outcome. High VDR methylation was associated with worst outcome. Fully functioning VDR may play a beneficial role against pediatric adrenocortical tumorigenesis. This finding highlights the potential of targeting VDR as an adjuvant therapeutic target.

Reproductive Endocrinology
FEMALE REPRODUCTION: BASIC MECHANISMS
Clinical Case Series of Augmented Fertility in Females After Administration of an Amino Acid Blend That Enhances Release of Human Growth Hormone
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MON-LB003
Supplementation with adjuvant therapies, including growth hormone (hGH), is commonly used to improve fertility treatment outcomes. hGH is important for normal female fertility; low hGH has been associated with causes of infertility and impaired fertility, including polycystic ovarian syndrome (PCOS), endometriosis, diminished ovarian reserve (DOR), and advanced maternal age. A novel, low dose, orally administered amino acid blend has been previously shown in a double-blind, randomized, placebo-controlled, crossover clinical trial to produce a statistically significant increase in endogenous hGH secretion. In this clinical case series, we report outcomes in 7 women with infertility or impaired fertility and conditions associated with low hGH who administered the amino acid blend during fertility treatment (n=5) or timed intercourse/spontaneous pregnancy (n=2). Medical history included conditions associated with impaired fertility and low hGH: endometriosis (n=3), PCOS (n=2), and poor response to ovarian stimulation/history of failed in vitro fertilization (IVF) (n=3). The amino acid blend (containing 2.9 g of L-lysine, L-arginine, o xo-proline, N-acetyl-L-cysteine, L-glutamine, and schizonepeta) was administered daily on an empty stomach. Outcomes included embryo quality and success of embryo transfer (for IVF) and successful pregnancy/live births. Mean±SD age was 33±5 years (range 27-38) and BMI was 27±7 kg/m² (range 21-37). Time to pregnancy ranged from 1 week to 9 months (median 3 months) prior to egg retrieval for IVF (n=4),