A (p.A401D), in exon 9, was found in heterozygous state in a female patient with isolated GH deficiency and intellectual disability. The variant was absent in the databases and predicted as deleterious or disease-causing. The variant was absent in the mother and stepsister and the father was not available for testing. The c.1430_1431delCCinsTG allelic variant (p.P477L) was found in heterozygous state in a patient with septo-optic dysplasia, GH, TSH and ACTH deficiencies. It was absent in the databases and was predicted as deleterious or disease causing. The Human Splicing Finder predicted exonic splicing enhancer breakdown leading to the loss of 93 nucleotides. Normal mother is heterozygous carrier suggesting incomplete penetrance. **Conclusion**: Heterozygous variants in *CDH2* were found in 2% of a cohort of Brazilian patients with congenital hypopituitarism and none in homozygous or compound heterozygous state. Further *CDH2* analyses in unrelated patients from different ethnic backgrounds are needed to establish the role *CDH2* variants in the etiology of congenital hypopituitarism.

Cardiovascular Endocrinology

PATHOPHYSIOLOGY OF CARDIOMETABOLIC DISEASE

Impaired Vascular Relaxation and Altered eNOS Regulation in Boys with Hypospadias

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SUN-551

Background: Sex hormones influence vascular function. Whether boys with hypospadias who have insufficient androgen exposure during the masculinisation programming window have altered vascular function is unknown. **Objective:** To investigate whether vascular function is impaired in boys with hypospadias and to explore the putative role of eNOS. **Methods:** Peripheral arteries from excess foreskin tissue obtained from boys undergoing hypospadias repair (cases) or circumcision (controls) were used. Vascular function was assessed by myography. mRNA expression was measured by qPCR in vascular smooth muscle cells (VSMCs). Nitric oxide (NO) was measured by DAF fluorescence assay and peroxynitrite levels measured via ELISA. **Results:** 23 boys with hypospadias and 34 age-matched controls were studied. There were 18 (52%) cases of distal, 7 (22%) of midshaft and 9 (26%) of proximal hypospadias and none of them had biochemical evidence of hypogonadism or a variant in *AR*. Clinical cardiometabolic parameters were similar between groups. Endothelium-dependent relaxation to acetylcholine (ACh) and endothelium-independent relaxation to sodium nitroprusside (SNP) were reduced in arteries from cases vs controls (Emax %U46619: 72.4 vs 1.2, p<0.0001 and Emax %U46619: (42.7 vs 11.8, p<0.01 respectively). Incubation with the NO synthase inhibitor, L-NAME (1x10-5 M) worsened endothelial-dependent relaxation in controls (Emax % U46619: 76.8 vs 1.2, p<0.0001) but had no effect in cases (Emax % U46619:60.6 vs 72.4, p=0.3). Testosterone (1x10-7 M) ameliorated vascular relaxation (p<0.05), whereas17[[Unsupported Character - Symbol Font 𝝱]];-estradiol stimulation (1x10-9 M) did not. In cultured VSMCs, mRNA expression of *eNOS* and *iNOS* was reduced whereas that of *nNOS* was increased in cases versus controls. Nitric oxide production was reduced in cases (5 fold, p<0.01), as was peroxynitrite production (0.5 fold, p<0.05). Testosterone increased expression of *eNOS* in VSMCs. There was no difference in mRNA expression of the *AR* and *GPRC6A* but cases had increased expression of *ESR1* (2.71 fold), *ESR2* (2.63 fold) and *GPR30* (2.86 fold) (p<0.05). **Conclusion:** Arteries in eugonadal boys with hypospadias show vascular dysfunction which involves impaired NOS/NO regulation effects that are ameliorated with testosterone but not oestrogen. These processes may predispose to long-term cardiovascular disease.

Neuroendocrinology and Pituitary

CASE REPORTS IN UNUSUAL PATHOLOGIES IN THE PITUITARY

Pituitary Macroadenoma Treated with Peptide Receptor Radionuclide Therapy in a Patient with Common Variable Immunodeficiency - Case Report

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SUN-274

Background: Nonfunctional adenomas comprise 25-35% of all pituitary tumors, 70-90% of these are gonadatroph cell adenomas. While 'silent' adenoma is the most common type of pituitary macroadenoma. The incidence of silent adenomas is estimated at 22/100000. Common Variable Immune Deficiency (CVID) is the most common primary immune disorder which is associated with neoplasia, mostly of the lymphatic or digestive system. We present probably the first case report of gonadotropinoma in a patient with CVID, treated with PRRT.

Clinical Case:

A 45-year-old man has been a patient at the Endocrinology Clinic for 12 years. Aged 33 years, he was diagnosed with a common variable immunodeficiency. The human immunoglobulin treatment was included. He also suffered from severe, spreading headaches. MRI of the head was performed. A 45mm tumor was found in the sella turcica, spreading to the sphenoid sinus. The tumor was slipped into the epidural reservois and both cavernous sinuses, causing compression of the internal carotid arteries and compressed the optic chiasm. Laboratory tests were as follows: TSH 2.18uIU/ml, LH 4.26mIU/ml, FSH 9.76 mIU/ml, ACTH 25.88pg/ml, PRL 18.34 ng/ml, HGH 3.9uU/ml, normal plasma and urine osmolality. So, the silent pituitary macroadenoma was diagnosed. Endoscopic transsphenoidal incomplete tumor resection was performed. The operation was complicated by massive parenchymal bleeding. Histopatological examination confirmed presence of pituitary adenoma, and immunohistochemical positive staining also of FSH (+), subunit alpha (+), TSH (+/-). A Ki67 proliferation

index was 1%. After 12 months endoscopic reoperation was performed. The extent of operation was larger but not total. After 12 month the tumor mass increased (50x50x45mm). Imaging of somatostatin receptors by SPECT-CT was performed. It showed a heterogeneous radiolabel accumulation in the pituitary tumor. In 2010, 2 doses of 200mCi 90-Y-DOTATATE were administered with good effect. Tumor size was reduced to 20x23x25mm. The patient has had no headache for that
time. Since 2011 he has also been treated with octreotide30 mg/month, with good therapy tolerance.
Conclusion:
This is probably the first description of a 12-year history of complicated but successful treatment of pituitary silent macroadenoma. It was also probably the first use of PRRT in the pituitary tumor with excellent effect. The patient remains in a very good condition, without neurological symptoms and no disorders of pituitary function.

Adrenal

ADRENAL - CORTISOL EXCESS AND DEFICIENCIES

The Diagnostic Value of DHEAS in Subtyping Patients with Cushing Syndrome

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MON-188

The diagnostic value of DHEAS in subtyping patients with Cushing Syndrome
Objective: Serum dehydroepiandrosterone sulfate (DHEAS) can be used to assess the integrity of the hypothalamic-pituitary-adrenal (HPA) axis. The aim of this study was to evaluate the clinical value of DHEAS in differentiating adrenal Cushing syndrome (ACS) from Cushing' disease (CD). **Methods:** We recruited 100 patients with Cushing syndrome, 36 with CD and 64 with ACS. 72 sex-, age- and BMI-matched nonfunctional adrenal adenomas (NFAAs) were served as controls. Clinical and laboratory data were collected. DHEAS levels were measured and DHEAS ratio was calculated by dividing the measured DHEAS by the lower limit of the respective reference range (age- and sex-matched). **Results:** 1) No significant differences in age, sex, or BMI were detected among the NFAAs, ACS and CD groups. **C**ompared to NFAAs group, ACS patients had lower plasma ACTH levels [1.11(1.11,1.74) vs 5.0 ± 2.9 pmol/L, P<0.01], lower DHEAS levels (24.00 ± 20.72 vs 189.05 ± 82.03 ug/dL, P < 0.01) and lower DHEAS ratio [0.58(0.27,0.98) vs 5.34 ± 3.0]; Plasma ACTH (22.12 ± 14.22 pmol/L), DHEAS (309.4 ± 201.1 ug/dL) and DHEAS ratio (10.51 ± 7.65) in CD patients were significantly higher compared to those in NFAAs and ACS patients (all P<0.01). 2) In ACS patients, there were 53 patients with suppressed ACTH level of <2.0 pmol/L, 11 patients without plasma ACTH suppression (≥2.0pmol/L). Compared to NFAAs, lower DHEAS and DHEAS ratio were detected in these two groups, and no significant differences were found in the DHEAS [15(15, 23.5) vs 23.8 ± 14.4 ug/dL, P=0.86] and DHEAS ratio [0.58(0.27, 0.80) vs 1.0(0.25,2.09) ug/dL, P=0.40] between the two groups. 3) ROC analysis showed that the area under the curve (AUC) of plasma ACTH, serum DHEAS and DHEAS ratio in diagnosing 0.954, 0.997 and 0.990 respectively. The optimal cut-off values for DHEAS and its ratio were 79.1ug/dL, and 2.09, respectively. The diagnostic sensitivity and specificity of plasma ACTH (<2.0pmol/L) were 84.1 and 100%, those of DHEAS were 97.5% and 100%, and those of DHEAS ratio were 95% and 100%, respectively. **Conclusions:** Patients with different subtype of Cushing syndrome showed distinctive DHEAS levels and DHEAS ratio. DHEAS and DHEAS ratio are useful in differential diagnosis of Cushing syndrome. Especially, when the plasma ACTH level is not conclusive. The measurement of DHEAS may offer a supplementary test to diagnosis ACS from CD.
Keywords: Adrenal Cushing syndrome; Cushing disease; Adrenocorticotropic hormone; Dehydroepiandrosterone sulfate

Pediatric Endocrinology

PEDIATRIC OBESITY, THYROID, AND CANCER

Serum Concentrations of FT4 and TSH in the First Six Months of L-Thyroxine Treatment in Infants with Congenital Hypothyroidism: Target Attainment Rates Should Be Improved

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MON-102

Levo-Thyroxine (L-T4) is the medication of choice for treating congenital hypothyroidism (CH). Adequate L-T4 treatment is essential for early neurodevelopment in affected patients. Both under- and overtreatment with L-T4 were associated with long-term adverse neurological outcomes. Based on clinical experience, initial L-T4 dosing does not always result in optimal TSH and FT4 concentrations in all CH patients. The purposes of this study were 1) to quantify FT4 and TSH target attainment rates (TAR) in the first six months of L-T4 treatment in infants with CH, 2) to compare characteristics of patients with FT4 concentrations "OUT of" *versus* "IN" the target range at first time of monitoring.
A multicenter retrospective analysis was conducted in infants born between 1995 and 2018. TSH and FT4 TARs were defined according to the most recent guidelines of the European Society for Paediatric Endocrinology (ESPE), as the percentage of concentrations "in" and "in the upper half" of the corresponding laboratory age-specific reference range for TSH and FT4, respectively.
We analyzed a total of 208 TSH and 186 FT4 serum concentrations from 60 patients during the first 6 months