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

Angela K. Lucas-Herald, MRCPCH[1], Rheure Alves-Lopes, PhD[1], Laura Haddow, Bsc Hons[1], Stuart O'Toole, MD-FRCS[2], Martyn Flett, FRCS[2], S Basith Amjad, MD[2], Boma Lee, FRCS[2], Mairi Steven, FRCS[2], Augusto C. Montezano, PhD[1], S Faisal Ahmed, MBChB,MD,FRCPCH[2], Rhian Touyz, FRCP[1].
[1]University of Glasgow, Glasgow, United Kingdom, [2]Royal Hospital for Children, Glasgow, United Kingdom.

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

Dorota Brodowska-Kania, PhD[1], Marek Saracyn, PhD[1], Maciej Kolodziej, MD[1], Lukasz Kowalski, MD[1], Grzegorz Kaminski, Professor[2].
[1]Military Institut of Medicine, Warsaw, Poland, Warsaw, Poland, [2]Military Institut of Medicine, Warsaw, Poland.

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