postoperative predictor of patients needing long term insulin management following TPIAT. This observation may identify a high risk group of patients in need of more intensive diabetes education and treatment prior to hospital discharge.

Pediatric Endocrinology

ADVANCES IN PEDIATRIC OBESITY AND CANCER

NF-κB Pathway Is Implicated in Thyroid Embryogenesis

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Background: Congenital hypothyroidism due to thyroid dysgenesis (CHTD) is the most common congenital endocrine disease with a prevalence of 1:4,000 live births. We have suggested a two-hit hypothesis to explain CHTD, combining an inherited or *de novo* variant with a post-zygotic event. This model could explain the sporadicity of the disease (99%), its ethnic predominance and the high discordance rate between monozygotic twins. Despite years of research, more than 95% of cases of CHTD remain unexplained, especially those with thyroid ectopy. This suggests that research on genes and/or pathways not previously associated with thyroid development need to be pursued. Inactivation of the NF-κB pathway can cause deficient anterior pituitary and variable immunodeficiency, or DAVID syndrome. Whether this pathway is also involved in CHTD remains to be established. **Objective:** To evaluate the implication of the NF-κB pathway during thyroid migration. **Methods:** Knock down experiments using morpholinos in a zebrafish model were carried out to investigate the roles of certain genes related to the NF-kB pathway during thyroid development. Rescue experiment was also performed to evaluate the specificity of the morpholino. The first gene to be tested was *IKBKE*, a member of the inhibitor of κB kinase (IKK) family. Thyroid location was assessed by microscopy of live larvae. **Results:** *ikbke* depletion in zebrafish caused defective aortic arch artery formation and abnormal thyroid migration. The thyroid phenotype was partially rescued by injection of human *IKBKE* RNA in *ikbke* morphants. **Conclusion:** *IKBKE* seems important for normal thyroid migration suggesting that the non-canonical NF-kB pathway might be implicated. Further studies targeting other genes in this pathway are ongoing to extend these results.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

Testosterone Therapy Reduces Inflammatory Activation of Human Monocytes in Hypogonadal Type-2 Diabetic Men as a Potential Mechanism to Improve Atherosclerosis

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Testosterone deficiency is prevalent in men with type 2 diabetes (T2D) and is associated with greatly elevated risk of cardiovascular mortality. Testosterone replacement has beneficial effects on surrogate markers and risk factors of atherosclerosis including inflammation, cholesterol and insulin resistance improving survival in men with T2D. The underlying mechanisms of this action remain poorly understood. Inflammation is a central feature to both T2D and atherosclerosis and is driven by monocyte/macrophages, placing these immune cells at the crossroads of disease pathology. The recruitment of immune cells to atherosclerosis-prone areas of the vasculature is influenced by many factors including the inflammatory status of the circulating monocytes. The present study investigates the influence of testosterone replacement on monocyte inflammatory markers in a randomised double blinded placebo controlled clinical trial. 65 men with poorly controlled diabetes (HbA1c between 53 and 80 mmol/mol) and confirmed hypogonadism via early morning [0800−1200h] total testosterone ≤12 nmol/L or calculated free testosterone ≤255 pmol/L on two occasions ≥1 week apart, with at least two symptoms of hypogonadism were included in the study. Patients were randomly assigned to either placebo or treatment (depot testosterone undecanoate, 6 weekly followed by 3 monthly intramuscular injections) for 6 months. Monocytes were isolated from whole blood collected at baseline, 3 and 6 month visits followed by gene expression of key inflammatory targets IL-1β, IL-6, IL-10, TNFα, ICAM1, TLR2, TLR4, SCARB1 and MCP1 assessed via qPCR. Pro-inflammatory targets TNFα and MCP1 were significantly reduced over time in monocytes from patients treated with testosterone between 3 and 6 months (1.39±0.39 Vs 0.68±0.09, P<0.01; 15.36±7.79 Vs 1.88±0.93, P<0.01 respectively) and TNFα at 6 months compared to the start of the study (1.00±0.00 Vs 0.68±0.09, P<0.001) when normalised to baseline. TNFα expression was also significantly reduced compared to placebo treated patient monocytes at 6 months (0.68±0.09 Vs 3.45±1.50, P<0.01). Other targets were not significantly altered over time or between treatment groups. These findings importantly indicate for the first time that testosterone influences monocyte inflammatory activation in type 2 diabetic men by altering expression of the most potent atherogenic chemokine MCP1 and potent pro-inflammatory cytokine TNFα, as a potential mechanism to protect against atherosclerotic plaque development in hypogonadism.

Adrenal

ADRENAL CASE REPORTS II

Development of Adrenocortical Carcinoma in an Adrenal Nodule After Nine Years of Size Stability on Imaging: A Case for Critical Review of Efficacy of Radiographic Size Criteria

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