

abdominal aortic calcification (AAC) is a strong predictor of future cardiovascular events and all-cause mortality. Multi-detector computed tomography provides a reliable and accurate method for the detection of abdominal aortic calcification. The aim of this study was to investigate the prevalence of AAC in patients with psoriasis. Adult psoriasis patients (n=69) and controls (n=80) were recruited from the Dermatology and Rheumatology clinics at 3 academic hospitals in Johannesburg, South Africa. Controls were matched for gender, ethnicity and body mass index (BMI). Non-contrast abdominal CT imaging was performed on patients and controls. The images were then assessed for presence and location (supra-coeliac, suprarenal, supra-renal, proximal infra-renal, aortic bifurcation) of AAC. Patients had a mean age and disease duration of 53.3 ± 14.5 years and 18.9 ± 13.3 years, respectively. There was a significantly higher prevalence of smoking, hypertension and type 2 diabetes in patients compared to controls (56.5% vs 25.0%, $P < 0.005$; 72.5% vs 55.0%, $P < 0.005$; 24.6% vs 3.80%, $P < 0.0005$, respectively). Furthermore, there was a significantly higher prevalence of AAC at any site in psoriasis patients (47.8% vs 22.5%, $P < 0.005$). The aortic bifurcation was the commonest site for AAC in patients and controls, and the prevalence was significantly higher in the psoriasis group (42.0% vs 21.3%, $p < 0.005$). However, multivariable logistic regression analysis demonstrated that age, smoking and the metabolic syndrome were significantly associated with AAC ($P < 0.0001$, $P = 0.0002$, $P = 0.027$ respectively) and attenuated the relationship between psoriasis and AAC to non-significance ($P = 0.376$). This suggests the increased risk of aortic calcification in psoriasis is mediated by the high prevalence of cardiometabolic disease in this population. These data highlight the increased cardiovascular disease risk within subjects with psoriasis and the need for lifestyle modification to decrease risk factor burden.

Thyroid

THYROID DISORDERS CASE REPORTS I

Fueling the Fire: A Case of Hypokalemic Periodic Paralysis Associated with Type I Renal Tubular Acidosis and Thyrotoxicosis in Pregnancy

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Background: Hypokalemic periodic paralysis (HPP) related to thyrotoxicosis, though rare, is more often seen in Asian males. Type 1 renal tubular acidosis (T1 RTA), which can also cause HPP, is typically managed with alkali therapy and potassium supplementation, though there are no well-established guidelines for management in pregnancy. Clinical Case: A 27-year-old Puerto Rican woman, at 32 weeks gestation, presented to the hospital with sudden onset muscle weakness, and was found to have 1/5 muscle strength in her lower extremities. She had no personal or family history of similar illness. Laboratory analysis revealed hypokalemia (potassium 2.0 mmol/L, range:

3.5 – 5); non-gap metabolic acidosis (sodium 137mmol/L, range 136 – 145; chloride 113 mmol/L, range 98- 107; and bicarbonate 8 mmol/L, range 22 – 29); and an arterial pH of 7.09. Urine studies demonstrated a urine pH of 6.5 and a urine sodium of 32 mmol/L which was diagnostic of T1 RTA in the context of her metabolic derangements. She was treated emergently with potassium and bicarbonate infusions, with improvement in her symptoms. Subsequent thyroid function testing revealed: a low TSH of 0.01 uIU/ml, normal free T4 of 1.66 (range: 0.9 - 1.7) ng/dl, normal free of T3 3.7 (range: 2.0 -4.4) pg/ml and elevated total T4 of 16.5 (range: 4.5 - 11.7) ug/dl. Renal ultrasound demonstrated medullary nephrocalcinosis. She was discharged on potassium and sodium citrate tablets. At 37 weeks, the patient was readmitted for induction of labor due to pre-eclampsia, and delivered a healthy male baby. Several months later, she presented to the Endocrinology clinic with symptoms of increased frequency bowel movements, palpitations and heat intolerance, which had been ongoing since pregnancy. On review, a metabolic panel prior to pregnancy had demonstrated non-gap acidosis and mild hypokalemia. Further testing demonstrated the following: TSH < 0.01 uIU/ml, Free T4 1.71 ng/dl, Free T3 4.8 pg/ml, TSI 280%, and a thyroid uptake scan with homogenous radiotracer uptake, with a 24-hour uptake of 40%. She was started on methimazole therapy, and continued on potassium and sodium citrate tablets with clinical and biochemical improvement.

Conclusion: Thyrotoxicosis can augment hypokalemia in T1 RTA, and can increase the risk of HPP. Our patient had biochemical evidence of RTA prior to pregnancy, though without episodes of HPP, and we believe that her hyperthyroidism, triggered by pregnancy, may have been the additional insult that precipitated her paralysis. This is the first reported case of HPP related to co-existing thyrotoxicosis and T1 RTA in a pregnant individual.

Reference:1. Tu ML, Fang YW, Leu JG, Tsai MH. An atypical presentation of high potassium renal secretion rate in a patient with thyrotoxic periodic paralysis: a case report. *BMC Nephrol.* 2018;19(1):160. Published 2018 Jul 4. doi:10.1186/s12882-018-0971-9

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH THROUGHOUT THE LIFESPAN

Role of Phosphorylated Gonadotropin-Regulated Testicular RNA Helicase (GRTH/DDX25) in the Regulation of Germ Cell Specific MRNAs in Chromatoid Bodies During Spermiogenesis

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Gonadotropin-regulated testicular RNA helicase (GRTH/DDX 25) is a member of the DEAD-box family of RNA helicases which play an essential role in spermatogenesis. There are two species of GRTH, the 56 kDa non-phospho and 61 kDa phospho forms. Our early studies revealed a missense mutation (R²⁴²H) of GRTH in the Japanese azoospermic men which resulted in the lack of phospho-GRTH

(pGRTH) in *in vitro* studies. GRTH knock-in (KI) mice with insertion of the human mutant GRTH gene show loss of the cytoplasmic 61 KDa phospho-species with preservation of the non-phospho nuclear form. KI mice are sterile, lack elongated spermatids and spermatozoa with arrest at step 8 of round spermatids (RS) which contain chromatoid bodies (CB) markedly reduced in size. CB is a non-membranous, cytoplasmic organelle present adjacent to the nucleus of RS, where mRNAs bound to GRTH transported from nucleus to cytoplasmic sites are temporarily stored, translationally repressed for later transport to polyribosomes for translation at specific stages of spermiogenesis. Owing to the specific function of CBs and importance of pGRTH in spermatid elongation, CBs isolated from germ cells of WT and GRTH KI mice were used for subsequent experiments. CBs isolated from GRTH KI mice are smaller, highly condensed and lack the nuage texture of CBs in WT mice. We observed the absence of pGRTH in CB of round spermatids of GRTH KI mice. Also, MVH protein (recognized CB marker protein) was decreased in the CB of GRTH KI mice. Expression of genes related to spermatid regulation, chromatin compaction, remodeling (TP1 and 2, PRM1 and 2, GRTH, TSSK6, HMG2, GCNF, RNF8, TDRD 1, 6, 7 and 9) analyzed by qPCR were markedly reduced in the CB of GRTH KI mice compared to WT. No change was observed in the expression of bromodomain mRNAs and protein, indicating that pGRTH does not participate in the translational regulation of this protein class at the level of this organelle. Notably, mRNAs of TP2, PRM2 and GRTH which associated with GRTH protein were co-localized with MVH protein in the CB. This indicated the relevance of GRTH as a binder/transport protein of key chromatin remodelers for ensuring their mRNA repression/stability within the CB. In addition, GRTH binding to genes essential for spermatid development and regulation (TP1 and 2, PRM1 and 2, GRTH, TSSK6, RNF8 and GCNF) were also found to be markedly decreased in the CB KI mice. These results demonstrate the importance of pGRTH in the maintenance of biochemical composition/structure of the CB and role in spermatid regulation, chromatin compaction, spermatid development and completion of spermatogenesis.

Adrenal

ADRENAL - HYPERTENSION

Cardiovascular Risk Factors, Morbidity, and Overall Mortality in Patients with Adrenal Adenomas:

A Population-Based Study of 1,003 Patients

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Background: Benign adrenal tumors are frequently diagnosed on imaging and may pose health risks to patients regardless of functional status. Both non-functioning adrenal tumors (NFAT) and tumors with mild autonomous cortisol secretion (MACS) have been associated with

increased cardiovascular events and risk factors. However, limited data exist on the association of adrenal adenomas with cardiometabolic outcomes in the population-based setting.

Aim: 1) To determine the prevalence of cardiovascular co-morbidities and events and 2) to assess mortality in a population-based cohort of patients with adrenal adenomas.

Methods: We identified adult patients living in the community diagnosed with an adrenal tumor from 1995-2017 using a medical records linkage system. Adrenal tumors were classified as MACS if cortisol was ≥ 1.8 mcg/dL after 1 mg dexamethasone suppression test, NFAT if cortisol was < 1.8 mcg/dL, and adenoma with unknown cortisol secretion (AUCS) if dexamethasone suppression test was not performed. Cardiovascular co-morbidities and events were assessed at baseline. Patients were then followed until death, migration out of the community, or through December 31, 2018. Results were compared to age and sex matched reference subjects without adrenal tumors and adjusted for tobacco use and BMI.

Results: A total of 1,003 patients had adrenal adenomas with 136 (14%) NFAT, 86 (9%) MACS, and 781 (78%) AUCS. The median age of diagnosis was 63 years (range, 20-96) and 581 (58%) were women. At baseline, patients with adrenal adenomas were more likely to have hypertension (92% vs 81%, $p < 0.001$), overweight/obesity (89% vs 82%, $p < 0.001$), pre-diabetes/diabetes (82% vs 70%, $p < 0.001$), dyslipidemia (89% vs 82%, $p < 0.001$), and chronic kidney disease (11% vs 7%, $p = 0.004$) than age and sex matched reference subjects. Myocardial infarctions (13% vs 8%, $p < 0.001$), coronary intervention (9% vs 6%, $p = 0.007$), heart failure (12% vs 6%, $p < 0.001$), peripheral vascular disease (26% vs 15%, $p < 0.001$), and thromboembolic disease (7% vs 3%, $p < 0.001$) were more prevalent in patients with adrenal adenomas, whereas overall survival was lower compared to reference subjects (60% vs 65%, p value = 0.013). Subgroup analysis (adjusted for age, sex, BMI, and smoking) demonstrated prevalence of cardiovascular events including peripheral vascular disease was highest in those with MACS (44.7%), followed by AUCS (40.1%), and then NFAT (36.6%), although differences between groups were not significant. Overall survival was lower in patients with MACS (62%) and AUCS (59%) compared to NFAT (71%), $p < 0.001$.

Conclusions: Adrenal adenomas are associated with significantly higher prevalence of cardiovascular risk factors and morbidity at the time of diagnosis and with increased mortality during follow-up. Results are potentially related to abnormal cortisol secretion but are limited by suboptimal evaluation for hormone excess.

Adipose Tissue, Appetite, and Obesity

ADIPOSE TISSUE BIOLOGY AND OBESITY II

MED1 Is a Lipogenesis Coactivator Required for Postnatal Adipose Tissue Expansion

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Mediator is a multi-subunit transcription coactivator complex that controls gene activation by connecting enhancer-binding transcription factors (TFs) with RNA