Adipose Tissue, Appetite, and Obesity

CNS, INFLAMMATORY, AND THERMOGENIC INFLUENCES OF BODY WEIGHT

Identification of a Novel Transcriptional Regulator of Metabolic Disease in Circulating and Central Myeloid Cells

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Derangement in systemic metabolic homeostasis is tightly associated with widespread activation of resident and circulating immune cells, a phenomenon known as 'metaflammation'. Numerous studies have explored the role of tissue resident and circulating macrophages in contributing to metaflammation, obesity, and their sequelae; however, there is a dearth of information regarding targetable transcriptional regulators of the genesis and persistence of metabolic disease. Here, we identify myeloid Krüppel-like factor 2 (KLF2) as a novel regulator of metabolic disease. Previous reports demonstrate that KLF2 serves as a critical regulator of myeloid cell quiescence and is downregulated in numerous acute and chronic inflammatory states. Specifically in the context of chronic metaflammation, we note that KLF2 expression is decreased in circulating immune cells of obese patients and in adipose tissue macrophages of high fat diet (HFD) fed mice, which is consistent with the hypothesis that KLF2 regulates metaflammation. To explore this further, we utilized mice with myeloid cell-specific deletion of KLF2 (K2KO) which exhibit accelerated obesity and insulin resistance. K2KO mice have widespread central (i.e. CNS) and peripheral metaflammation both in the basal and HFD-stimulated states. To discern whether the effect of myeloid deletion of KLF2 on metabolism is due to deletion in microglia in the feeding centers of the hypothalamus or in peripheral immune cells, bone marrow chimeras with head shielding were created. 50% reconstitution of circulating immune cells with K2KO cells in wildtype (WT) mice was sufficient to maintain the metabolic disease phenotype, while mice with K2KO microglia + WT circulating cells had only slightly improved outcomes compared to K2KO mice. Conversely, ablation of microglia in K2KO mice using PLX5622 formulated in HFD also successfully attenuated the aberrant feeding behavior, weight gain, and glucose dyshomeostasis seen in K2KO mice. Together, these data demonstrate a role for loss of KLF2 in hematopoietic and CNS resident cells in causing metabolic disease. Given that myeloid KLF2 expression decreases under metabolic stress in WT mice and humans, we sought to explore whether maintenance of KLF2 expression in these cells would be protective against diet-induced metabolic disease. Indeed, mice with myeloid-specific overexpression of KLF2 demonstrated a markedly improved metabolic phenotype when challenged with HFD, providing evidence that targeting KLF2 expression in myeloid cells may prove to be a therapeutic option against metaflammation.

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OBESITY TREATMENT: GUT HORMONES, DRUG THERAPY, BARIATRIC SURGERY AND DIET

Anthropometric Parameters, Body Fat Percentage and Metabolic Profile in Sarcopenic Women with Recommendation for Bariatric Surgery

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INTRODUCTION: Sarcopenia (SARC) is a musculoskeletal disorder that predisposes several complications, including metabolic ones. Obesity also provides higher risk for metabolic complications, however, there is lack of evidences regarding the association of obesity with SARC on metabolic parameters in non-elderly individuals. **OBJECTIVE:** To evaluate anthropometric parameters, body fat percentage (BFP) and metabolic parameters in women with and without SARC preceding Bariatric Surgery (BS). **METHODS:** A cross-sectional study involving 60 obese women in the outpatient care in a public Brazilian University Hospital between March to September 2018. Body composition was given by bio-impedance (inbody-370), multifrequency (5, 50, 250Hz) with 12 hours fasting, dominant Handgrip Strength (HS) was evaluated by Jamar dynamometer (3 measurements; 30 sec interval). Were also evaluated fasting blood glucose, HbA1c, homeostatic model assessment-insulin resistance (HOMA-IR), total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides and high-sensitive C-reactive protein (hs-CRP). SARC was defined by the association of a low muscle mass index (weight-adjusted appendicular skeletal muscle mass: ASMM/weight x 100%) and decreased HS, using as cutoff points the smallest quintile for each variable. Data were expressed as mean ± standard deviation and independent t-test was used for comparison between groups. Statistics were made by SPSS software, 20th version (IBM Corp., Armonk, NY). **RESULTS:** The mean age, weight, body mass index and BFP of sarcopenic and non-sarcopenic women were: 40.75 ± 11 x 39.23 ± 8.92 years old (p=0.665), 102.93 ± 9.58 x 109.19 ± 14.25 Kg (p=0.237), 44.88 ± 2.7 x 42.24 ± 4.79 Kg/m^2 and 54.12 ± 1.11 x 51.44 ± 3.43% (p=0.052), respectively. Regarding the laboratory parameters of women with and without SARC: fasting blood glucose 89.25 ±

14.48 x 98.40 ± 27.48 mg/dL (p=0.359), HbA1c 5.83 ± 0.33 x 6.21 ± 1.18% (p=0.185), HOMA-IR 3.61 ± 1.28 x 5.31 ± 4.74 (p=0.160), TC 170.87 ± 39.36 x 180.82 ± 34.51 mg/dL, LDL 94.67 ± 26.63 x 105.60 ± 30.85 mg/dL, HDL 53.37 ± 18.50 x 50.84 ± 10.32 mg/dL, triglycerides 114.12 ± 38.84 x 127.30 ± 75.04 mg/dL and hs-CRP 8.51 ± 6.50 x 7.51 ±6.52 mg/L (p=0.792). **CONCLUSION:** Women with SARC and recommendation for BS when compared to women without SARC had similar anthropometric, metabolic and BFP parameters.

Adrenal

ADRENAL CASE REPORTS II

Persistent Hyperkalemia After Unilateral Adrenalectomy for Aldosteronoma

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SUN-196

Introduction

Following unilateral adrenalectomy, some patients experience persistent hyperkalemia. This has been attributed to hypoaldosteronism due to severe suppression of aldosterone synthesis in the contralateral adrenal gland. Additionally, excess aldosterone leads to glomerular hyperfiltration masking kidney dysfunction, which can then manifest after cure with CKD-related hyperkalemia.

Case Presentation

We report a case of 51-year-old male who was diagnosed with hypertension in his late 30s. He required a beta-blocker and calcium channel blocker (CCB) for 10 years, and eventually developed hypertensive nephropathy. With worsening lower extremity edema, he was switched from a CCB to an angiotensin receptor blocker. Soon afterwards, he presented with hypertensive emergency and was discovered to have significant hypokalemia (K 2.1 mmol/L), prompting work up for primary aldosteronism.

Biochemical evaluation revealed an elevated aldosterone to renin ratio of 38 [(ng/dL)/(ng/mL/hr)] and adrenal protocol CT scan revealed a 1.9 cm left adrenal nodule with benign characteristics. Adrenal vein sampling showed marked lateralization of excess aldosterone to the left adrenal gland, with proper catheter placement demonstrated in each adrenal veins (5-fold cortisol gradient bilaterally). He was started on spironolactone and 6 weeks later, underwent an uncomplicated laparoscopic left adrenalectomy. Spironolactone was discontinued

Serum K level was normal at 4.8 mmol/L immediately postoperatively. Ten hours later, his K went up to 6.6 mmol/L which was confirmed by repeat blood work, accompanied by worsened renal function (Cr 2.5 mg/dL up from a of baseline 2.0). His hyperkalemia persisted in the 5.0 – 6.0 range despite IV Calcium Gluconate, Insulin and D50. Oral potassium binders were avoided due to concerns about ileus. Upon recognition of the possibility of hypoaldosteronism, we recommended a NaHCO3 gtt, with subsequent normalization of serum K. We avoided initiating fludrocortisone in the short term, due to uncertainty about duration of hypoaldosteronism, & because he was still requiring two antihypertensive agents. Plasma aldosterone 2 wks after surgery was fully suppressed, confirming suspicion of hypoaldosteronism. He has been managed successfully with oral sodium bicarbonate tablets, remaining normokalemic at 3 weeks post-surgery.

Conclusion:

Here we present a case of persistent hyperkalemia following resection of a signficantly biochemically active and long-standing aldosteronoma, which was successfully managed with sodium bicarbonate. We attribute the post-operative hyperkalemia in this patient to a combination of hypoaldosteronism due to deep suppression of the mineralocorticoid

production of the contralateral adrenal, as well as unmasking of more severe kidney dysfunction than was he previously thought to have once aldosterone excess was withdrawn.

Thyroid

THYROID DISORDERS CASE REPORTS I

Graves' Disease Induced Renal Tubular Acidosis

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SUN-512

Thyroid gland can affect kidney function in different ways. Thyroxine as a master hormone of metabolism and growth works in many cellular levels include the renal tubules.

We present a 34-year-old Emirati gentleman who presented with multiple episodes of hypokalemic periodic paralysis. Blood test revealed thyrotoxic state, with highly positive serology for thyroid peroxidase, anti-thyroglobulin and thyrotropin receptor antibodies. Thyroid uptake scan confirmed homogenous diffuse uptake consistent with toxic diffuse goitre [Graves' disease]. In view of recent fracture, bone profile and DXA scan were done. Investigations revealed vitamin D deficiency and below expected for age bone mass density.

The patient was started on symptomatic treatment with propranolol, IV and oral potassium along with IVF hydration. Routine blood work during admission showed a persistent normal anion Gap metabolic acidosis, serum bicarb 15 mmol/l. 24 hours urine electrolytes revealed normal potassium, sodium, high magnesium, low calcium and PH levels. Biochemical lab results suggested type 1 renal tubular acidosis. As the patient had hypokalaemia, high urine magnesium and low urine calcium and limbs weakness, Gitleman Syndrome was considered in the differential diagnosis. Whole Exome Sequencing (CentoXome GOLD®) was sent which came back negative. The following gene panels were studied: Renal tubular acidosis panel: ATP6V0A4, ATP6V1B1, CA2, EHHADH, HNF4A, SLC34A1, SLC4A1, SLC4A4. Bartter Syndrome panel: ATP6V1B1, BSND, CA2, CASR, CLCNKA, CLCNKB, CLDN16, CLDN19, FXYD2, HSD11B2,KCNJ1, KCNJ10, KLHL3, NR3C2, SCNN1A, SCNN1B, SCNN1G, SLC12A1, SLC12A2, SLC12A3, SLC4A1, SLC4A4, WNK1. Gene related to Gitelman syndrome: SLC12A3

Renal tubular acidosis was treated with KCL 600mg PO TID, Na bicarb 1200mg PO BID and spironolactone 25 mg PO OD. The patient received radioactive iodine (RAI) as