for management of PHPT. However, in cases of VTE where PHPT is diagnosed, parathyroidectomy should be considered to potentially improve hypercoagulability and reduce the risk of subsequent VTE.

Tumor Biology

TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

Humoral Hypercalcemia of Malignancy Caused by Squamous Cell Carcinoma of the Penis

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SAT-120

Background. Humoral hypercalcemia of malignancy (HHM) accounts for approximately 80% of hypercalcemia associated with cancer. We present an unusual case of HHM caused by recurrent squamous cell carcinoma of the penis. **Case.** A 45 year old male was brought to the emergency department (ED) due to worsening confusion over 48 hours. History was notable for squamous cell carcinoma of the penis initially diagnosed 12 years ago and managed by partial penectomy and ilioinguinal lymphadenectomy. Recurrence had been diagnosed approximately 30 days before presentation to the ED. The patient was somnolent, disoriented, and unable to follow commands. Admission laboratories were remarkable for new occurrence of hypercalcemia (serum calcium corrected for low albumin 17.0 mg/dL, 8.6–10.3) and acute renal failure (Cr 1.7 mg/dL, 0.6–1.3; BUN 44 mg/dL, 7–25). No masses or hemorrhages were observed on head imaging, though computed tomography of the chest, abdomen, and pelvis revealed multiple lung and liver masses and lytic bone lesions. Biopsy of a rib mass confirmed metastatic squamous cell carcinoma. Intact PTH level was suppressed at 1 pg/mL (12–88), but parathyroid hormone related protein (PTHrP) was significantly elevated at 120 pM (0.0–2.3). HHM due to PTHrP was diagnosed. Corrected calcium level reached a nadir of 9.5 mg/dL on hospital day seven after saline hydration, calcitonin, and zoledronic acid, but high dose denosumab (120 mg weekly) was started hospital day 10 after corrected calcium level increased to 11.7 mg/dL. Despite corrected calcium levels consistently in the range of 10.5–11.5 mg/dL for the remainder of hospitalization, the patient's mental status failed to improve. He expired on hospital day 24. **Conclusions.** Squamous cell carcinoma of the penis is rare in the United States, with only about 2,000 cases diagnosed annually. Though squamous cell carcinomas are collectively the most common cause of PTHrP-related hypercalcemia, there are only a few cases of PTHrP-related hypercalcemia due to squamous cell carcinoma of the penis documented in the peer reviewed literature. As in our patient's case, other penile carcinoma patients with PTHrP-related hypercalcemia have had regionally advanced or metastatic disease and limited therapeutic response to bisphosphonates. Our patient's survival after occurrence of hypercalcemia was also similar to other published cases of penile carcinoma complicated by PTHrP-related hypercalcemia. This case confirms the potential for penile carcinoma to cause HHM through hypersecretion of PTHrP like squamous cell carcinomas of the lung, head, and neck. Denosumab may be a more effective treatment option than a bisphosphonate based on the therapeutic experience in this case and others. PTHrP-related hypercalcemia appears to be a strong indicator of limited life expectancy for penile carcinoma as for other malignancies.

Cardiovascular Endocrinology

PREVALENCE, DIAGNOSIS, AND MECHANISMS OF HYPERALDOSTERONISM

Prospective Multicentre Study Comparing ^{11}C-metomidate PET CT with Adrenal Vein Sampling (AVS) in the Detection of Unilateral Aldosterone-Producing Adenomas (APAs)

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OR34-07

Approximately 50% of Primary Aldosteronism (PA) cases are unilateral, potentially curable by adrenalectomy. However far fewer patients progress to surgery, partly due to difficulties in identifying unilateral disease. AVS is the current criterion standard method for lateralisation. However it is an invasive procedure, technically difficult to perform, and only available in few specialist centres. MATCH is a prospective, multicentre study comparing the diagnostic accuracy of AVS with ^{11}C-metomidate PET-CT, a non-invasive functional scan (ClinicalTrials.gov Identifier NCT02945904).

Patients fulfilling Endocrine Society criteria for PA undergo both investigations in random order. At a multidisciplinary meeting PET-CT results are scored first, followed by AVS. Patients are offered surgery if one or both investigations indicate unilateral disease. Each investigation will be re-scored by an independent, blinded endpoints committee, without knowledge of other investigations or outcomes in the same patient. Hierarchical primary outcomes are the change in aldosterone renin ratio (ARR) and average home SBP readings. If no superiority is observed for either investigation, non-inferiority of PET-CT will be tested. MATCH is

powered to detect 25% superiority, or non-inferiority within a margin of 18%. Factors predicting cure will be assessed as secondary outcomes. These include BP response to aldosterone antagonists, correlation of standardised uptake value (SUV) max ratio of adenoma to adjacent normal adrenal, and phenotyping / genotyping of tumours.
Target recruitment of 140 patients has been achieved. Interesting observations to date include a high prevalence of hypokalaemia (73%), reflective of our referral base and inclusion criteria. The surgery rate is also high at 66%, consistent with finding frequent patients in whom only one investigation yields a positive result. The following case illustrates such a patient. A slim 45-year-old lady with PA and failed ONDST had inconclusive AVS (selectivity index in right adrenal vein 2.6). PET-CT revealed a 29mm metomidate-avid left adrenal nodule (SUVmax ratio 1.52, >1.25 suggestive of unilateral disease). Left adrenalectomy was recommended based on PET-CT, and achieved biochemical and clinical cure. However she required hydrocortisone replacement for 14 months. Her relatively low right adrenal vein cortisol, despite successful cannulation, was attributed to contralateral suppression by co-secretion of cortisol from her adenoma. This was confirmed by finding high *CYP11B1* and *CYP11B2* mRNA expression in her tumour, typical of a *KCNJ5* mutation, confirmed as L168R on Sanger sequencing.
PA is a high risk subset of hypertension. Under-treatment has serious public health consequences. ^{11}C-Metomidate PET CT has the potential to simplify the investigation pathway and allow more patients to receive potentially curable treatment.

Adipose Tissue, Appetite, and Obesity

NEURAL MECHANISMS OF OBESITY

Hypothalamic P75 Neurotrophin Receptor Regulates Homeostatic Feeding and Food Anticipation

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SAT-602

Proper circadian alignment of feeding behavior is necessary to prevent metabolic disease, and thus it is imperative to identify the neural circuits and molecular players that coordinate energy homeostasis. Neurotrophin signaling has been implicated in both metabolic and circadian processes, thereby representing a good candidate for regulating neural circuits driving time-of-day dependent feeding and foraging behavior. Here, we demonstrate that mice lacking the p75 neurotrophin receptor, p75NTR, have a behavioral defect in their ability to adequately respond to energy deficit. In response to fasting, p75KO mice (1) decrease their refeeding food intake compared to controls. Furthermore, following several days of restricted feeding, they (2) are unable to develop food anticipatory behavior (FAA), a phenomenon believed to be the output of a food-entrained circadian oscillator that has yet to be anatomically defined. Strikingly, these two phenotypes are observed only during the daytime, and not at night. These defects lead to increased weight loss, but do not appear to be mediated by changes in peripheral hormones. Notably, these effects are also independent of a role of p75NTR in development, as a global, adult-inducible p75NTR knockout recapitulates the feeding behavior of germline knockout mice. Rather, we demonstrate that p75NTR is discretely expressed in two hypothalamic regions known to be important for feeding behavior, the arcuate (ARC) and dorsomedial (DMH) hypothalamus. We find that p75KO mice have reduced fasting-induced activation of ARC, but not DMH, neurons. In addition, we show that ARC AgRP neuron p75NTR is necessary for fasting-induced refeeding and daytime FAA. We further suggest that AgRP-p75NTR is necessary to mediate AgRP neuron phospho-CREB signaling in response to energy deficit. Finally, given previous reports of involvement of the DMH in food anticipation, we asked whether DMH-p75NTR is necessary for feeding behavior and food anticipation. Strikingly, we find that p75NTR in the DMH is also necessary for FAA, but not for the control of homeostatic feeding. These data establish p75NTR as a novel regulator of energy homeostasis that acts to gate behavioral responses to food scarcity. It further posits that p75NTR may functionally link two independent hypothalamic regions to a time-of-day dependence of circadian food anticipation.

Adrenal

ADRENAL - CORTISOL EXCESS AND DEFICIENCIES

Utility of Salivary Cortisol After 1 Mg Oral Dexamethasone in the Evaluation of Incidental Adrenal Tumors

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MON-165

The subclinical Cushing´s syndrome (SCS) is found in 20% of incidental adrenal tumors (AI). The overnight 1 mg oral dexamethasone suppression test (DST) with the measurement of circulating cortisol (F) is a sensitive method to rule out SCS. The assessment of salivary cortisol (SAF) as a surrogate of F became a non-invasive methodological advance. There are few data on the functional evaluation of AI through SAF in DST (SAF_{dex}). The aim of this retrospective study was to investigate the utility of SAF_{dex} for the detection of SCS in patients with AI. Subjects and Methods: 20 subjects with AI (7 male and 13 women; 65.0 ± 11.0 y/o; BMI: 26.5 ± 1.4) were studied. Sixteen had unilateral and 4 bilateral tumors (size: 10.0 - 90.0 mm; density (UH) was <10.0 in 17 cases and ≥ 10.0 in 3). They were not on drugs that may affect the HPA axis. Eight patients (1 male and 7 women; 20.0–60.0 y/o; BMI: 27.0 ± 3.0) with overt non ACTH dependent Cushing Syndrome (CS) were included as the reference group of active hypercortisolism. CS had unilateral adrenal tumors in 6 cases and bilateral in 2 (size: 11.0 -200.0 mm; density (UH) <10.0: n= 7 and >10.0: n=1). All subjects collected 24-hour urine for urinary free cortisol (UFC). After the urine collection, they obtained whole saliva samples at 23 h for cortisol (SAF_{23}). Subsequently, they received 1 mg oral dexamethasone. The following day at 8 h, simultaneous blood (F_{dex}) and saliva (SAF_{dex}) samples