functions should both be monitored during the clinic follow-up for children with short stature or obesity in order to early diagnosis of craniopharyngioma.

Neuroendocrinology and Pituitary

CASE REPORTS IN SECRETORY PITUITARY PATHOLOGIES, THEIR TREATMENTS AND OUTCOMES

Cushing's Disease with Two ACTH-Producing Pituitary Tumors

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SAT-248

Objective: The objective of this case report is to discuss a case of Cushing's disease with two ACTH-producing pituitary tumors and emphasize consideration of repeat surgery as a treatment modality for unsuccessful initial surgery.

Methods: We present a case of a patient with Cushing's disease with two ACTH-producing pituitary tumors and a literature review.

Results: A 36 year-old female found to have left supraclavicular fossa swelling was screened for Cushing's syndrome. Midnight salivary cortisol levels elevated at 0.636 ug/dL and 0.316 ug/dL (<0.010–0.090 ug/dL). 24-hour urine cortisol 162 ug/24 hr (0–50 ug/24 hr). 1-mg dexamethasone suppression test 14.0 ug/dL. Serum morning cortisol 26.4 ug/dL with corresponding ACTH 66.7 pg/mL (7.2–63.3 pg/mL). MRI brain with and without contrast showed a 7-mm relatively hypoenhancing lesion of the anterior pituitary gland. 8-mg dexamethasone suppression test 2.7 ug/dL. She underwent transsphenoidal surgery (TSS) and pathology was consistent with a pituitary adenoma staining positive for ACTH. No residual tumor was seen. Postoperative morning serum cortisol 17.0 ug/dL and ACTH 79 pg/mL (9–46 pg/mL). She had repeat TSS and the area of resection was clean with no residual tumor but a second adenoma was found that was not visualized on MRI and was distinct from the initial lesion. Postoperative morning cortisol 0.7 ug/dL and ACTH <9 pg/mL (9–46 pg/mL). Pathology was consistent with pituitary adenoma staining positive for ACTH. She is now on steroids for central adrenal insufficiency.

Discussion: First-line treatment for Cushing's disease is surgical resection of the primary lesion (Nieman LK, Biller BMK, et al. Treatment of Cushing's syndrome: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2015; 100(8):2807–2831). Remission rates are 73–76% for selectively resected microadenomas but 43% for macroadenomas (Nieman et al. 2015). For patients who undergo a noncurative surgery, second-line therapies include repeat TSS, radiotherapy, medical therapy, and bilateral adrenalectomy. Repeat TSS is recommended particularly in patients who had evidence of incomplete resection or a pituitary lesion on imaging although this was not the case with our patient. Repeat TSS is cited to be successful in about 50–60% of cases (Patil CG, Veeravagu A, et al. Outcomes after repeat transsphenoidal surgery for recurrent Cushing's disease. *Neurosurgery*. 2008;63(2):266–270) but carries an increased risk of hypopituitarism and lower likelihood of remission compared to initial surgery. Remission can be achieved more rapidly compared to other second-line treatments.

Conclusion: In Cushing's Disease with unsuccessful initial surgery, consideration for repeat TSS may be considered when there is access to an expert pituitary surgeon.

Adrenal

ADRENAL PHYSIOLOGY AND DISEASE

Skin Glucocorticoid Metabolism in Burn Injury: Towards Novel Treatments That Reduce Scarring

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SUN-217

The most common and severe complication of burn injury is the development of excessive scarring/tissue fibrosis. No current treatments reduce scarring after burns. Prolonged exposure to high levels of glucocorticoids (Cushing's syndrome) detrimentally impacts skin, leading to reduced collagen production and impaired wound healing. Skin can generate active glucocorticoids locally through expression and activity of the 11β-hydroxysteroid dehydrogenase type 1 enzyme (11β-HSD1). We hypothesised that local glucocorticoid activation by 11β-HSD1 is an important regulator of wound healing, fibrosis and scarring after burn injury. We additionally proposed that pharmacological manipulation of this system would improve outcomes of burn wound healing.

We examined glucocorticoid metabolism (by RT-PCR, immunohistochemistry and specific enzyme activity assays) in burn and non-burn skin from burn injury patients (n=14) and mouse models of burn injury (1cm^2 full thickness burn in C57Bl/6 mice). We utilised mice with genetic or pharmacological deletion of 11β-HSD1 in skin to evaluate the effects of 11β-HSD1 on burn injury healing, wound fibrosis and skin properties (by atomic force microscopy and tensile property testing) after wound healing. We also developed slow release scaffolds containing therapeutic agents including inactive glucocorticoids (prednisone) that are selectively reactivated in skin cells expressing 11β-HSD1.

The expression of 11β-HSD1 in human and mouse skin increased substantially after burn injury (7.1+/-1.8 fold increase on day 4–9 post burn compared to non-burn skin, $p<0.05$). Early after injury, expression was primarily in immune cells but at later stages in fibroblasts. Mice with 11β-HSD1 deletion experienced faster wound healing post burn (17% reduced wound area at day 7 compared to wildtype, $p<0.0001$) but when healed these wounds had excessive collagen density and skin thickening, and abnormal collagen fibre organisation (assessed by Masson's

Trichrome staining). The post burn scars formed in 11β-HSD1 knockout mice demonstrated different skin elastic properties compared to those formed in wildtype mice. In wildtype mice application of scaffolds loaded with inactive glucocorticoid (prednisone) significantly impacted wound healing demonstrating the feasibility of using enzyme substrates to improve wound outcomes.
The findings demonstrate the importance of skin 11β-HSD1 in wound healing and scarring after burn injury and indicate ways in which excessive scarring might be prevented.

Neuroendocrinology and Pituitary

PITUITARY AND NEUROENDOCRINE CLINICAL TRIALS AND STUDIES

Lower Oxytocin Levels Are Associated with Lower Bone Mineral Density and Less Favorable Hip Geometry in Hypopituitary Men

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OR32-05

Introduction: Hypopituitary patients are at risk for bone loss. Oxytocin (OT) and vasopressin (VP) are hypothalamic-posterior pituitary hormones with opposing actions on bone (anabolic and catabolic, respectively). Whether OT and/or VP contribute to impaired bone homeostasis in hypopituitarism is unknown.
Hypothesis: We hypothesized that lower plasma OT and higher VP levels would be associated with lower bone mineral density (BMD) and less favorable hip geometry and estimated strength in men with hypopituitarism.
Design: We performed a cross-sectional study of 37 men with hypopituitarism ages 20–60 (mean±SEM 45.8±1.9) years: 20 with anterior pituitary deficiencies only (APD) and 17 with central diabetes insipidus (CDI; marker of posterior pituitary dysfunction), of similar age, body mass index and number of adenohypophyseal deficiencies, on stable hormone replacement. Main outcome measures were fasting plasma OT and VP levels, and dual X-ray absorptiometry-derived BMD (lumbar spine, total hip, femoral neck, distal radius and subtotal body) and hip structural analysis (HSA; cortical thickness, section modulus, and buckling ratio at narrow neck, intertrochanteric region and femoral shaft). All analyses were adjusted for multiple comparisons using Holm-Bonferroni correction.
Results: Mean BMD Z-scores were lower at all sites and all HSA parameters at the intertrochanteric region as well as cortical thickness at the femoral shaft were less favorable in those participants who had fasting OT levels below the median than in those with higher levels ($P \leq 0.022$). There were no differences in any bone variables at any skeletal site in those with fasting VP levels below vs. above the median ($P \geq 0.232$). Lower fasting OT levels were positively associated with (1) lower BMD Z-scores at the lumbar spine, femoral neck, total hip and subtotal body ($P \leq 0.02$) and (2) less favorable hip geometry and strength variables (lower cortical thickness, lower section modulus and higher buckling ratio) at the intertrochanteric region in CDI ($P \leq 0.018$), but not APD participants ($P \geq 0.458$ and $P \geq 0.429$, respectively). The associations between OT and bone variables remained significant after adjusting for key determinants of BMD including lean body mass and IGF-1 levels. There were no relationships between plasma VP levels and bone variables in CDI or ADP groups ($P \geq 0.173$).
Conclusions: OT, but not VP levels, are positively associated with BMD at multiple sites as well as favorable hip geometry and estimated strength in men with hypopituitarism and CDI. Future studies will be important to determine whether OT could be used therapeutically to optimize bone health in patients with hypopituitarism.

Adrenal

ADRENAL - HYPERTENSION

Pheochromocytoma and Paraganglioma: An Emerging Cause of Secondary Osteoporosis

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MON-204

Context: Many endocrine diseases are known to cause secondary osteoporosis, which is potentially reversible by treatment of the underlying disease itself. Pheochromocytoma (PHEO) and paraganglioma (PGL) (PHEO and PGL: PPGLs) are the rare catecholamine-producing neuroendocrine tumors, which are associated with low bone mineral density (BMD). However, PPGLs have not been recognized as a cause of secondary osteoporosis. Indeed, even the prevalence of osteoporotic fracture in patients with PPGLs is currently unknown. Furthermore, whether surgical resection contributes to the improvement of BMD has never been addressed. **Objective:** This study was designed to evaluate 1) whether PPGLs increase the risk of vertebral fracture (VF), which is the most common type of osteoporotic fracture and 2) whether surgical resection of PPGLs contributes to the improvement of BMD. **Design and Settings:** A retrospective cross-sectional study in a single referral center. **Participants:** Among 443 patients with adrenal tumor (AT), we included 62 patients with histologically confirmed PPGLs and 61 patients with non-functional AT. **Intervention:** The prevalence of VF was examined in 49 out of 62 patients with PPGLs and 61 patients with non-functional AT. In 23 out of 62 patients with PPGLs, BMD was evaluated at baseline and after