

arcuate nucleus of the hypothalamus. This gene targeting strategy leaves pituitary *Pomc* expression unaffected. These mice are hyperphagic starting at weaning, and develop progressive obesity, infertility and insulin resistance over their lifetime. RM-493 (setmelanotide) is a melanocortin-4 receptor agonist that has shown promise in treating humans with *Pomc* null mutations. In this preclinical study, we investigated the effects of chronic RM-493 treatment using subcutaneously implanted osmotic minipumps in two groups of male mice: Arc-*Pomc* knockout mice, fed regular chow throughout the study period, and their wildtype counterparts, fed a 45% high-fat diet. Each of these groups of mice was randomized into three treatment cohorts at weaning: one that was given RM-493 throughout the entire study period (4–24 weeks of age, “RM-493” group), one that was given RM-493 only for the first 4 weeks of the study (4–8 weeks of age, “switch” group) and then switched to vehicle, and one cohort that received vehicle for the entire study (“vehicle” group). We serially measured body weight, food intake, body composition, glucose tolerance, insulin tolerance, and several measures of metabolism using the Comprehensive Lab Animal Monitoring System, including oxygen consumption, energy expenditure, ambulatory activity and lipid and glucose oxidation.

Among other results, at the end of the study (24 weeks of age), Arc-*Pomc* knockout mice in the RM-493 group weighed significantly less than either the switch or vehicle groups ($p < 0.05$). Arc-*Pomc* knockout mice on RM-493 also had higher energy expenditure when compared to the switch and vehicle groups ($p < 0.05$). In addition, RM-493 improved the glucose-insulin index for Arc-*Pomc* knockout mice ($p < 0.05$). According to our preliminary results, wildtype mice on high-fat diet, treated chronically with RM-493, did not differ in any of these measurements from their switch and vehicle groups.

We conclude that the obesity syndrome caused by a loss of hypothalamic *Pomc* expression was completely blocked by RM-493 treatment started before the onset of obesity, with no apparent desensitization to the drug's action over 20 weeks. However, the beneficial effects of a single month's treatment were steadily reversed within one month after switching to vehicle treatment. In contrast to the dramatic effects of RM-493 in the genetic obesity syndrome, at this time, there does not appear to be any phenotypic changes in wild-type mice with RM-493 administration on the development of obesity or secondary metabolic disruptions in response to high-fat diet consumption.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS II

Diabetic Amyotrophy; A Rare Cause of Muscle Weakness

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Background: Diabetic amyotrophy is a rare complication of type 2 diabetes mellitus. There is little existing evidence contributing to projected outcomes for patients recovering from diabetic amyotrophy. Clinical Case: A 42 year-old man

presented with lower extremity muscle pain and progressive proximal muscle weakness over 8 months. He developed asymmetrical muscle weakness in the lower extremities with diffuse pain and sensitivity to touch. He also had 80 pounds weight loss, diarrhea, and erectile dysfunction over the same time period. He had a past medical history of asthma, chronic migraines, and type II diabetes mellitus with A1c 7.1. His medications included high dose prednisone to treat his chronic migraines and asthma. Exam revealed generalized muscle atrophy, asymmetric proximal weakness, areflexia, with sensory loss in bilateral lower limbs. ESR, CRP, ANA, anti-HMG CoA reductase, CK, aldolase, SPEP, and myomarker panel were all within normal limits. Treponema pallidum and Bartonella serologies were negative. CSF evaluation was not suggestive of any demyelinating or neuromuscular disease. Full body STIR MRI demonstrated muscle edema in abductor, gluteus minimus, and paraspinal muscles bilaterally. EMG testing revealed acute to subacute active asymmetrical polyradiculoneuropathy and evidence of chronic proximal myopathy. Based on clinical presentation, EMG findings, and lack of evidence to support alternative diagnoses, he was diagnosed with diabetic amyotrophy and was started on IVIG and methylprednisolone with improvement in pain but very minimal improvement in weakness. Unfortunately, the expected clinical course following a diagnosis of diabetic amyotrophy is one of minimal improvement with treatment, as was the case in our patient. Conclusion: Diabetic amyotrophy is a rare complication of type 2 diabetes mellitus which typically presents with muscle weakness followed by severe pain in the thighs, hips, and buttocks. Compared with other neurologic complications of diabetes, amyotrophy is relatively uncommon, affecting approximately 1 percent of patients. This low prevalence and the broad differential for proximal muscle weakness makes it challenging to diagnose. It remains a diagnosis of exclusion, though EMG studies showing polyradiculoneuropathy in the proximal leg musculature is suggestive. Clinical improvement is slow and often incomplete. Physical and occupational therapy are a mainstay of treatment which may also include IVIG and steroids aimed at treating associated pain. Endocrinologists should have a high clinical suspicion for diabetic amyotrophy in the appropriate clinical context. When considering the diagnosis and discussing treatment options with patients, this case highlights the important role of endocrinologists discussing expectations associated with projected outcomes while attempting to manage diabetic amyotrophy.

Neuroendocrinology and Pituitary

CASE REPORTS IN UNUSUAL PATHOLOGIES IN THE PITUITARY

Lymphocytic Hypophysitis Mimicking Tolosa Hunt Syndrome

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SUN-286

Introduction:

Lymphocytic hypophysitis often presents with headache, hypopituitarism and visual disturbance, the latter from

optic nerve compression. Rarely, it can present with diplopia from cranial nerves III, IV and VI (3.7%) and cavernous sinus involvement (1).

Clinical Case:

A 40 year old woman presented with left eye pain, blurry vision, ptosis and diplopia for 2 days, preceded by headache for 2 weeks. Exam was remarkable for left eye ptosis, mild proptosis, downward and outward gaze and inability to adduct her left eye. Endocrinological exam revealed free T4 0.67 ng/dL (NI 0.70 - 1.48), TSH 0.67 ng/dL (NI 0.70–1.48), estradiol <10 pg/mL, LH 1.0 mIU/mL, FSH 6.9 mIU/mL, prolactin 23.3 ng/ml (NI 5.2–26.5) and IGF-1 95 ng/mL (NI 52–328). Cortisol was not assessed as patient was already on steroids. Work-up revealed atypical ANCA (1:320) but normal C-ANA (<1:20), P-ANCA (<1:20), and the rest of immune work-up was negative including ACE, ESR, CRP, ANA, serine protease and myeloperoxidase. No systemic manifestations were present concerning for systemic autoimmune disease. CSF exam was unrevealing including a normal ACE level. MRI revealed an enlarged pituitary gland with suprasellar extension containing a focal area of T2 hyperintensity and slight T2 hypointensity at the posterior aspect of the gland. There was a midline, thickened infundibulum, enhancement of both cavernous sinuses and narrowing of right internal carotid artery without occlusion. Endoscopic endonasal transsphenoidal biopsy of pituitary lesion confirmed diagnosis of lymphocytic hypophysitis and did not meet criteria for IgG4 hypophysitis. After 4 weeks of prednisone, she had significant symptomatic improvement and repeat MRI showed decreased pituitary size but persistent abnormal enhancement of the pituitary gland and cavernous sinuses.

Conclusion:

The atypical and variable clinical and radiological findings of lymphocytic hypophysitis can mimic other inflammatory, infiltrative lesions, pituitary tumor with apoplexy and Tolosa Hunt Syndrome. Tolosa Hunt syndrome is an idiopathic granulomatous inflammation of the cavernous sinus involving cranial nerves II to VI and often presenting with painful ophthalmoplegia. Pituitary involvement and carotid artery narrowing have been observed (2). Our case highlights a patient with cranial nerve III palsy and significant cavernous sinus involvement, clinically concerning for Tolosa Hunt syndrome, but confirmed by biopsy to be lymphocytic hypophysitis. There are no specific serum markers to distinguish lymphocytic hypophysitis from other entities and when uncertain, diagnosis is best established by biopsy.

References:

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Bone and Mineral Metabolism

OSTEOPOROSIS: DIAGNOSIS AND CLINICAL ASPECTS

Validation of a Deep Learning Based Algorithm to Diagnose Vertebral Compression Fractures

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Vertebral Compression Fractures are common in patients above age 50, but are often undiagnosed. Patients with one VCF are at higher risk of other osteoporotic fractures. Zebra Medical Imaging developed a VCF detection algorithm, utilizing a combination of traditional machine vision segmentation and convolutional neural network (CNN) technology, to detect VCFs from evaluating CT images of the chest, and/or abdomen/pelvis.

We conducted an independent and blinded validation study to estimate the operating characteristics of the Zebra VCF detection algorithm in identifying VCFs on de-identified data from previously completed CT scans of chest and/or abdomen/pelvis from 1200 women and men aged 50 or older who had those scans (for multiple reasons) at the clinics and hospitals affiliated with the Cedars Sinai Medical Center. Each set of scans were independently read by two of three board certified, practicing neuroradiologists to identify and grade VCF at each evaluable vertebra (using the semiquantitative scale of Genant and colleagues). When there was disagreement between radiologists, the respective scans were reviewed by a senior neuroradiologist who provided a final evaluation. The final determination of presence and severity of VCF by the neuroradiologists was used as the reference standard. The Zebra VCF detection algorithm evaluated the CT scans in a separate workflow from that used by the neuroradiologists (The algorithm and neuroradiologists were blind to each other's evaluations).

The Zebra VCF algorithm was not able to evaluate CT scans for 113 patients. Of the remaining 1087 CT patients, 588 (54%) were women. Median age was 73 (range 51, 102; interquartile range 66, 81). The four neuroradiologists who evaluated the CT scans each had over 10 years of experience in neuroradiology. For the 1087 Zebra evaluated patients, 227 had at least one VCF (90 with mild VCF, 81 with moderate VCF, and 56 with severe VCF; 115 of the 1087 Zebra evaluated patients (10.6%) presented with two or more VCFs). The sensitivity and specificity of the Zebra VCF algorithm in diagnosing any VCF were 0.66 (95% confidence interval 0.59, 0.72) and 0.90 (95% confidence interval 0.88, 0.92) respectively; and for diagnosing moderate/severe VCF were 0.78 (95% confidence interval 0.70, 0.85) and 0.87 (95% confidence interval 0.85, 0.89) respectively.

The Zebra VCF algorithm works to identify approximately three-quarters of moderate to severe VCF in patients, aged 50 and above, who receive CT scans for other reasons. Implementing the Zebra VCF algorithm within radiology systems may help to identify patients at increased fracture risk and could support the diagnosis of osteoporosis, and thus be a valuable adjunct for population health.

Cardiovascular Endocrinology

HYPERTRIGLYCERIDEMIA; INFLAMMATION AND MUSCLE METABOLISM IN OBESITY AND WEIGHT LOSS I

Hypertriglyceridemia-Induced Pancreatitis in a Pregnant Female Treated with Plasmapheresis

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