provided 25% total fat, 1.5 g/kg reference weight of protein, and 100g of carbohydrates. Serum aldosterone was drawn fasting in upright position at 0, 2, 4, and 6 weeks. Scatter plots were used to explore the residual and predicted associations between aldosterone with other measures after accounting for time and group effect.Results: Twenty-four participants in the ketogenic diet groups were matched for age and body mass index, then randomized to either the KD+PL or KD+KS group. A separate group of 12 matched participants were specifically recruited for the LFD group. The median age was 33 years. Weight decreased 6, 8, and 7 kg on average in the KD+KS, KD+PL, and LFD groups, respectively, over 6 weeks ($p<0.05$ for all). Systolic blood pressure (SBP) improved from 117 and 115 mmHg in the KD+KS and KD+PL groups to 110 mmHg over 6 weeks while the baseline mean SBP 118 in the LF group did not change. Baseline mean aldosterone of 13.6 and 13.6 ng/dL in the KD+KS and KD+PL groups increased to 33.3 and 27.3 ng/dL over 6 weeks ($p<0.001$). Baseline mean aldosterone of 8 ng/dL in the LF group non-significantly changed to 11.5 ng/dL over 6 weeks ($p>0.05$). Using predicted value associations, increases in ketones were positively associated with higher aldosterone ($R2=0.86$; $p<0.001$). Conclusion: Participants on a ketogenic diet had significantly elevated aldosterone levels throughout the study while participants on low fat diet had little change. Unexpectedly, aldosterone was significantly higher in the high sodium vs. low sodium ketogenic diet. There was a significant association between ketones and aldosterone suggesting that ketones may play a stimulatory role on aldosterone synthesis or secretion.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS II

The Association of Paget's Disease With Inclusion Body Myositis and Fronto Temporal Dementia (IBMFTD)

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MON-LB70

The association of Paget's Disease with Inclusion body myositis and Fronto Temporal Dementia (IBMFTD)

Background:Inclusion body myopathy associated with Paget disease of bone (PDB) and/or frontotemporal dementia (IBMPFD) is a rare, autosomal dominant condition, characterized by adult-onset muscle weakness, early-onset PDB, and premature frontotemporal dementia. Paget's disease is a chronic disorder of bone resulting in increased bone resorption, followed by a disorganized and excessive formation of bone.

Clinical Case:A 43 year old gentleman was referred to neurology services with foot drop, limb weakness and cognitive impairment. Following a prolonged period of diagnostic evaluation a mutation in valosin-containing protein (VCP) gene was uncovered

IBMPFD has a variable phenotype which may include PDB. This gentleman denied bony pain and had an alkaline phosphatase within reference range. Plain film radiographs at multiple sights demonstrated no signs of PDB. An MRI whole body was performed which reported coarse trabecular markings in L2 vertebral body and multilevel degenerative changes with bridging osteophytes in the lumbar spine consistent with PDB.

At initial review in endocrine clinic, he denied fractures or bone pain. He had no signs of increased cardiac output or cranial nerve deficits. A radionuclide bone scan identified intense radiopharmaceutical accumulation in L2 vertebral body consistent with MRI findings and also curvilinear increased activity in the left occipital bone and low-grade activity in the left hip, thus confirming polyostotic Paget's disease.

He received a 5mg IV infusion of zolendronate, side effects of which included myalgia, pyrexia and lethargy.

Six months following the zoledronate infusion a repeat bone scan demonstrated that the extent of uptake at affected sites had decreased significantly.

He subsequently fractured his left femur following a mechanical fall. PDB can affect up to 50% of patients with IBMFTD. PDB can lead to complications such as bone pain, localized pain and deformity of the long bones, pathologic fractures and deafness. This case highlights the association of Paget's disease with IBMFTD and as it can be asymptomatic, as in our case, radiological imaging is required for diagnosis. It also reminds us that Paget's disease can be due to genetic causes. Understanding the role of VCP in the cell cycle may help in further understanding bone physiology.

Neuroendocrinology and Pituitary

CASE REPORTS IN SECRETORY PITUITARY PATHOLOGIES, THEIR TREATMENTS AND OUTCOMES

Acute Sterile Meningitis as a Primary Manifestation of Pituitary Apoplexy

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SAT-LB54

Background: Pituitary apoplexy (PA) is a rare endocrinopathy that requires prompt diagnosis and treatment. Presentation with acute neutrophilic meningitis is uncommon.

Clinical Case: A 67-year-old man presented to our hospital with a 2-week history of worsening bilateral frontal headache, nausea, and dry heaving. On admission, the patient was somnolent with a score of 13 on the GCS assessment (E2, V5, M6). The neurological exam was overall normal with normal ocular motion and intact cranial nerves, except for a left eye peripheral vision defect. Plain head CT revealed a well-circumscribed ovoid pituitary mass with suprasellar enlargement, consistent with a pituitary macroadenoma. Sellar MRI showed a pituitary mass, roughly 20 x 19 x 24 mm, bulging into the suprasellar cistern with optic chiasm elevation. Analysis of pituitary function revealed low ACTH concentration of 2.8 pg/mL (n = 7.2 - 63.3 pg/mL), a low random cortisol level of 1.7 ug/dL (n = 2.9 - 19.4 ug/dL), a low TSH of < 0.1 uIU/mL (n = 0.35 - 4.9 uIU/mL), a low free T4 level of 0.72 ng/dL (n = 0.77 - 1.48 ng/dL), a low LH of 0.8 IU/L (n = 1.7 - 8.6 IU/L) with a very low total testosterone

level of < 3 ng/dL (n = 300 - 720 ng/dL) and normal prolactin, IGF-1 and GH levels. On hospital day 2, the patient had worsening encephalopathy with left eye ptosis and decreased vision. Repeat CT and MRI showed no interval change in the pituitary adenoma or evidence of bleeding. An immediate lumbar puncture was performed and CSF analysis revealed an increased leukocyte count of (1106/mm3) with 89% neutrophilic granulocytes, and increased total protein level of 138 mg/dL (n = 15 - 40 mg/dL), red blood cell count of 2040 without xanthochromia and glucose of 130 mg/dL (n = 40 - 70 mg/dL). Based on the laboratory results and new symptoms, empirical antibiotic (vancomycin, ceftriaxone, and ampicillin) therapy was started for suspected bacterial meningitis before the confirmation of the CSF culture study. CSF culture did not grow any organisms. Given the sudden visual impairment and neurological deterioration, the patient underwent transsphenoidal resection of the tumor with free nasal mucosal graft reconstruction. Histological examination revealed a necrotic pituitary adenoma with apoplexy and no evidence of hemorrhage. Postoperatively, his neurological exam greatly improved. His left pupil was reactive to light and the third palsy was improving.
Conclusion: This case reinforces the importance of including PA in the differential diagnosis of acute headache, particularly in patients presenting with visual disturbances. Patients with PA often present with sterile meningitis due to increased debris and blood in the subarachnoid space which closely mimics acute bacterial meningitis. While MRI remains a sensitive imaging modality for the detection of PA, the latter remains a clinical diagnosis. Timely diagnosis with high clinical suspicion and treatment is essential.

Thyroid

THYROID CANCER CASE REPORTS I

The Anti-Tumor Activity of the Selective Ret Inhibitor Selpercatinib (LOXO-292) in Medullary Thyroid Cancer Is Independent of the Specific RET Mutation

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SUN-LB75

The RET receptor tyrosine kinase proto-oncogene is activated by somatic or germline mutations in a majority of medullary thyroid cancers (MTC). However, treatment of MTC has been challenging due to the lack of effective and tolerable RET-specific therapy, thus testing tumors for the presence of somatic *RET* mutation has not been warranted. In a first-in-human, phase 1/2 clinical trial (LIBRETTO-001, NCT03157128), selpercatinib (LOXO-292), an investigational, highly selective, potent small molecule RET kinase inhibitor, demonstrated significant and durable anti-tumor activity in patients with advanced *RET*-mutant MTC or with diverse *RET* fusion-positive cancers (1). Among the primary analysis set of patients with *RET*-mutant MTC previously treated with cabozantinib and/or vandetanib (N=55), the investigator-assessed objective response rate (ORR) per RECIST 1.1 was 56% (95% CI 42.3-69.7, n=31/55). Duration of response was not reached with a 10.6-months median follow-up (data cutoff date 17-Jun-2019). Here, we evaluated investigator-assessed ORR per RECIST 1.1 and clinical benefit rate (CBR) in this previously treated patient population by *RET* alteration and by germline or somatic testing used for enrollment. The ORR remained consistent across subgroups with *RET* M918T (49%, 95% CI 30.8-66.5, n=16/33), V804M/L gatekeeper mutations (60%, 95% CI 14.7-94.7, n=3/5), extracellular cysteine mutations (43%, 95% CI 9.9-81.6, n=3/7), other mutations (90%, 95% CI 55.5-99.7, n=9/10), and germline (50%, 95% CI 6.8-93.2, n=2/4) or somatic (57%, 95% CI 42.2-70.7, n=29/51) testing. The CBR, defined as the proportion of patients with best overall response of confirmed complete response, confirmed or unconfirmed partial response, or stable disease lasting 16 weeks or more, in this patient set was 87% (95% CI 75.5-94.7, n=48/55). The CBR remained consistent across subgroups with *RET* M918T (88%, 95% CI 71.8-96.6, n=29/33), V804M/L gatekeeper mutations (80%, 95% CI 28.4-99.5, n=4/5), extracellular cysteine mutations (71%, 95% CI 29.0-96.3, n=5/7), other mutations (100%, 95% CI 69.2-100.0, n=10/10), and germline (75%, 95% CI 19.4-99.4, n=3/4) or somatic (88%, 95% CI 76.1-95.6, n=45/51) testing. The primary technologies used to identify *RET* alterations were tumor next-generation sequencing (n=43) and polymerase chain reaction (n=9). As previously reported, selpercatinib was well tolerated with an acceptable safety profile (1). These results indicate broad anti-tumor activity for selpercatinib in patients with *RET*-mutant MTC irrespective of the specific *RET* mutation, and support implementation of *RET* mutation testing for patients with advanced MTC, including somatic testing, to identify patients who may benefit from selpercatinib. **Reference:** (1) Wirth et al., Ann Oncol. 2019 Oct; 30(supplement 5): v933.