12 h, with fewer treatment-specific ones, except for *rec*FSH, which exhibited stronger responses with more specifically associated processes. Similar results were found for down-regulated cell processes, with a greater number of processes at 6 h or 12 h, depending on the particular glycoform. In general, there were fewer down-regulated than up-regulated processes at both 6 h and 12 h, with FSH^{21} exhibiting the largest number of down-regulated associated processes at 6 h (10 *vs* 3 processes for *e*FSH, one process for FSH^{24}, and one for *rec*FSH), while *e*FSH exhibited the greatest number at 12 h (19 processes *vs* 4 for FSH^{21}, 13 for FSH^{24}, and 7 for *rec*FSH). Two signaling cascades, largely linked to Rap-1 and cAMP pathways, were differentially activated by the glycoforms, with each glycoform exhibiting its own molecular signature. These transcriptomic data support previous biochemical observations demonstrating glycosylation-dependent differential regulation of intracellular signaling pathways triggered by FSH in granulosa cells.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS I

Hypercalcemia Due to Castleman's Disease

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SAT-366

Castleman's disease is a group of poorly understood lymphoproliferative disorders in which pro-inflammatory cytokines are hyper-produced, causing a constellation of symptoms. This patient was diagnosed with a rare subtype of idiopathic multicentric Castleman's called TAFRO, which is a subclass characterized by thrombocytopenia (T), anasarca (A), fever (F), reticulin fibrosis (R), and organomegaly (O). This is a case of hypercalcemia likely secondary to Castleman's disease. To our knowledge, only two such cases have been reported, and none with this rare subtype of the disease. The mechanism of hypercalcemia in Castleman's disease is thought due to lymph node macrophages expressing vitamin D activating enzyme 25-hydroxyvitaminD 1-alpha-hydroxylase, and possibly due to increased bone-turnover from osteoclasts production by IL-6. The treatment is managing the primary cause of the disorder: high doses of systemic steroids, immunosuppressants and IL6-inhibitors. We present a case of a 53 year old Hispanic female with a PMH of type 2 diabetes mellitus. She had hypercalcemia with a corrected calcium 12 mg/dl and a normal PTH 16.2pg/ml, with low levels of 1,25-OH vitamin D 8.3pg/ml, and 25-OH vitamin D 16.6ng/ml. PTHrP was undetectable. Phosphorous was normal at 3.3 mg/dl. Given that the iPTH was low normal, and with low 25-OH and 1,25-OH vitamin D levels, primary hyperparathyroidism was thought unlikely. SPEP showed a chronic disease pattern. TSH was also noted to be normal. Quantiferon tuberculin test, HHV6, HHV8 and HIV were negative. IgG, IgA, IgM levels were normal. She also had elevated alkaline phosphatase at 108 U/L. No other bone markers were checked. After steroid therapy, her corrected calcium came down to 10.1. Her Castleman's disease was diagnosed via histopathology of lymph node biopsy showing follicular hyperplasia with atretic germinal centers, penetrating blood vessels, expanded mantle zones, hypervascular interfollicular regions and intense interfollicular plasmacytosis consistent with Castleman's disease. Initial CT Chest with contrast showed diffuse lymphadenopathy in the retropectoal, axillary, prevascular, pretracheal, paratracheal, and retroperitoneal regions. She had anasarca with ascites, requiring paracentesis with ascites fluid that was negative for malignancy. She was also diagnosed with acute thrombotic microangiopathy via kidney biopsy for workup of thrombocytopenia and acute renal injury. She was initially treated with PLEX and dexamethasone 40mg, then switched to methylprednisolone, was also tried on riuxamab and cylclosporine. She failed therapy with an IL-6 inhibitor, Siltuximab, due to pulmonary edema requiring hospitalization. Currently, she is on a drug holiday and will resume lower doses of cyclosporine. Clinicians should consider an underlying lymphoproliferative disorder in the differential for a patient with hypercalcemia.

Bone and Mineral Metabolism

BONE DISEASE FROM BENCH TO BEDSIDE

Burosumab Resulted in Greater Clinical Improvements Compared with Higher-dose Conventional Therapy in Children with X-linked Hypophosphatemia (XLH)

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SUN-356

In XLH, excess circulating FGF23 causes hypophosphatemia, rickets, lower limb deformity, and impaired growth and mobility. An active-controlled, phase 3 trial (CL301; NCT02915705) showed treatment with burosumab, a fully human monoclonal antibody against FGF23, resulted in significantly greater improvements in all of these outcomes in children with XLH, compared with continuing oral phosphate and active vitamin D as conventional therapy (Pi/D) per established guidelines. In a post-hoc analysis, we compared children who received burosumab vs those who received an average 64-week oral phosphate daily dose >40 mg/kg (higher-dose Pi) vs ≤40 mg/kg (lower-dose Pi). Sixty-one children with XLH (1–12 years-old) were randomized 1:1 after a 7-day Pi/D washout to receive burosumab (n=29) starting at 0.8 mg/kg subcutaneously Q2W or to resume Pi/D (n=32) titrated by their investigator, for 64 weeks. Eligibility criteria included Rickets Severity Score (RSS) ≥2.0 despite prior Pi/D treatment. Of the 32 subjects randomized to Pi/D, 12 received average higher-dose Pi and 20 received average lower-dose Pi (as specified above). The primary endpoint was rickets healing, using the Radiographic Global Impression of Change (RGI-C) Scale. At week 64, the improvement in the least square (LS) mean (LS mean [±SE; 95%CI]) RGI-C Global Score for rickets was greater on burosumab (+2.06 [0.072; 1.92, 2.20]) compared with either higher-dose (+1.02 [0.241; 0.55, 1.50]) or lower-dose (+1.04 [0.162; 0.73, 1.36]) Pi. The mean decrease in the total RSS from baseline was also

greater on burosumab (-2.23 [0.117; -2.46, -2.00]) compared with higher-dose (-0.87 [0.264; -1.39, -0.35] or lower-dose (-1.09 [0.180; -1.45, -0.74]) Pi. Similarly, the mean RGI-C Lower Limb Deformity Score was greater on burosumab (+1.25 [0.170; 0.92, 1.59]) compared with either higher-dose (+0.32 [0.188; -0.05, 0.69]) or lower-dose (+0.26 [0.146; -0.02, 0.55]) Pi. Adverse events including hypersensitivity and injection site reactions, were more frequent with burosumab, and were mild to moderate in severity overall. No discontinuations occurred. In conclusion, children with XLH treated with burosumab had greater improvements in rickets and lower limb deformity compared with subjects receiving higher or lower doses of Pi.

Bone and Mineral Metabolism

PARATHYROID HORMONE TRANSLATIONAL AND CLINICAL ASPECTS

The Use of Imaging in Primary Hyperparathyroidism

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SAT-398

Primary hyperparathyroidism is characterized by excessive dysregulated production of parathyroid hormone (PTH) by 1 or more abnormal parathyroid glands. Preoperative localization is important for surgical planning in primary hyperparathyroidism. Previously, it had been published that ultrasound (sensitivity of 76.1%, positive predictive value of 93.2%) and nuclear scintigraphy (Sestamibi-SPECT) (sensitivity of 78.9%, and a positive predictive value of 90.7%) are first line imaging modalities[1]. Currently, the imaging modality of choice varies according to region and institutional protocol. The aim of this study was to evaluate the imaging modality that is associated with an improved remission rate based on concordance with operative findings. A secondary aim was to determine the effect of additive imaging on remission rates. This was an IRB-approved retrospective review of 2657 patients with primary hyperparathyroidism undergoing surgery at a tertiary referral center from 2004–2017. Analyses were performed with SAS software using a 95% confidence interval ($p<0.05$) for statistical significance. After excluding re-operative and familial cases, 2079 patients met study criteria. There were 422 (20.3%) male and 1657 (79.7%) female patients with a mean age of 66 (+12.2) years, of which 1723 (82.9%) of patients were white and 294 (14.1%) patients were black. Ultrasound (US) was performed in 1891 (91.9%), sestamibi with SPECT (sestamibi/SPECT) in 1945 (93.6%), and CT in 98 (4.7%) patients. Of these, 1721 (82.8%) had combined US and sestamibi/SPECT. US was surgeon-performed in 94.2% of cases and 89.9% of the patients underwent a four gland exploration. Overall, US concordance was 52.4%, sestamibi/SPECT was 45.5%, and CT was 45.9%.US and sestamibi/SPECT both had an improved remission rate if concordant with operative findings, while CT had no effect (US p=0.04; sestamibi/SPECT p=0.01; CT p=0.50). The overall remission rate was 94% (CI=0.93–0.95), however, increasing the number of imaging modalities performed did not increase the remission rate (p=0.76) or concordance with operative findings (p=0.05). Despite having low concordance rates, US and sestamibi/SPECT that agreed with operative findings were associated with higher remission rates. Therefore, when imaging is to be used for localization, our data support the use of US and sestamibi/SPECT as the initial imaging modalities of choice for preoperative localization.

[1]Kuzminski SJ, Sosa JA, Hoang JK. Update in Parathyroid Imaging. *Magn Reson Imaging Clin N Am*. 2018;26(1): 151–166.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS II

The Case of Dueling Femurs

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MON-371

Introduction: Paget's disease of the bone is characterized by excessive osteoclastic bone resorption followed by formation of disorganized bone; which is often focal. Bone pain and deformities are common features and it often leads to complications such as pathological fractures, deafness or neurologic deficits. Elevated bone turnover markers and alkaline phosphatase reflect ongoing exaggerated bone resorption and osteoblastic activity. We present an unusual scenario of post-menopausal osteoporosis and Paget's disease occurring in the same patient.

Clinical Case: 86-year-old female with history of Type 2 Diabetes Mellitus, Hypertension,

Hypothyroidism, degenerative joint disease of lumbar spine with prior interbody fusion and laminectomy was referred to our clinic by Orthopedics for evaluation of newly diagnosed Paget's disease. 2 months ago, she noticed severe right hip pain limiting daily activities. She denied any

history of falls, fractures or family history of Paget's. Physical exam was notable for tenderness to right sacroiliac joint and right femoral trochanteric region. Work up included MRI of Lumbar spine and Pelvis, Pelvis X-ray, DEXA scan and routine blood work.

Interestingly, her DEXA scan showed T score of +2.9 in Right hip and -3.1 in Left hip. On Pelvis X-ray cortical thickening, coarse trabecula and osteoarthritic changes were noted in right femur and hip, consistent with Paget's disease. Left femur showed strikingly thinner cortices compared

to the right, due to underlying osteoporosis. MRI of lumbar spine and pelvis was consistent with polyostotic Paget's involving L3-L5, Sacrum and Right femur. Nuclear bone scan showed areas of uptake including anterior calvarium, lumbar spine, right hip, right femur, 8th rib, left mid tibia and 1st metatarsal of left foot. Since the distribution of uptake seemed atypical for Paget's, a skeletal survey was obtained which was negative for bone lesions suggestive of malignancy.