Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS I

Calcium Level in a Patient with Rhabdomyolysis. A Tale of Two Phases.

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SAT-339

Background: Calcium kinetics can be challenging during the different phases of rhabdomyolysis[1]. We herein report a case of sever hypercalcemia refractory to hemodialysis following a period of hypocalcaemia that developed in a patient with rhabdomyolysis.

Case: A 27-year-old male patient was diagnosed with meningoencephalitis complicated with septic shock, continuous seizures, rhabdomyolysis, acute kidney injury and oliguria. His creatinine was 219 μmol/L (53–115), urea was 8 mmol/L (2.5–6.4). Creatine kinase (CK) was significantly high above assay range. Corrected serum calcium was 1.82 mmol/L (2.12- 2.52), phosphate was 0.48 mmol/L (0.81–1.58). He required intermittent sessions of hemodialysis and antibiotics therapy which both have been initiated since the first day of admission. Initially he had hypocalcaemia but as rhabdomyolysis improved, his calcium levels started to rise to reach normal levels by day 13 post admission. By day 16, he started to gradually develop hypercalcemia. Initially, it was 2.73 mmol/L and in another 10 days it was 3.39 mmol/L and reached maximum of 3.90 mmo/L despite the intermittent dialysis sessions. PTH was supressed at 0.62 Pmol/L. Over that time, his renal functions and urine output were gradually improving.

The clinical impression was PTH independent hypercalcemia and the work up for that was initiated. CT chest, abdomen and pelvis did not reveal any suspicious masses, lytic bone lesions, or lymphadenopathies. His acid fast bacilli stain and culture were both negative. His chest imaging did not show any findings to suggest sarcoidosis. TSH was normal and random cortisol was 339.2 nmol/l with albumin 20g/L. HIV serology came back negative.

He received Calcitonin 500 IU BID for three days and Denosumab 120 mg SC in order to control the hypercalcemia along with, cautious intravenous hydration. Within one week after Denosumab therapy, serum corrected calcium decreased to 3.07 mmol/L. After another week, corrected calcium reached 2.53 mmol/L. When his urine output improved further and his calcium levels dropped, hemodialysis was discontinued. His calcium level later normalised to 2.49 mmol/L.

After ruling out the common differential of PTH independent hypercalcemia, and from the diuretic phase the patient went through with concomitant hypercalcemia following hypocalcaemia, it was concluded that the cause of hypercalcemia was rebound hypercalcemia following rhabdomyolysis recovery.

Conclusion: hypercalcemia can complicate the recovery phase of rhabdomyolysis. Careful monitoring of calcium levels and management are warranted.

References:

[1] Mohsin N, Budruddin M, Pakkyara A. Calcium Kinetic in a Patient with Acute Renal Failure due to Rhabdomyolysis: A Case Report and Review of Literature. Oman Medical Journal. 2010;25:324–326.

Bone and Mineral Metabolism

NEW FRONTIERS IN BONE AND MINERAL METABOLISM

A Natural History Study of Fibrodysplasia Ossificans Progressiva (FOP): 12-Month Outcomes

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OR29-05

Background: FOP is an ultra-rare, severely disabling genetic disorder characterized by episodic flare-ups and heterotopic ossification (HO) leading to restricted movement, physical disability, and early death. FOP may initially be misdiagnosed in ~90% of individuals leading to unnecessary and often harmful interventions. Patients with FOP are diagnosed and managed by multiple specialties, including endocrinologists.

Data from an ongoing, prospective, longitudinal, global, natural history study (NCT02322255) were used to investigate the progression of FOP, HO formation, and impact on physical functioning over time. We present results from the first 12 months of the 3-year study.

Methods: Males and females with FOP and a documented *ACVR1* R206H mutation participated. HO volume was assessed by low-dose whole body computed tomography (WBCT) scan, excluding the head. All imaging was interpreted at a blinded, central laboratory using prespecified procedures. Functional outcomes were evaluated using the Cumulative Analogue Joint Involvement Scale (CAJIS; for each joint: score=0 represents <10% involvement, score=1 represents 10–90% involvement, and score=2 represents >90% ankylosed across 15 major joints; total score range 0 to 30 [higher scores indicate more severe mobility limitations]) and the FOP Physical Function Questionnaire (FOP-PFQ; percent total score). Changes from Baseline at Month 12 were evaluated for new HO volume, CAJIS, and FOP-PFQ.

Results: Of 114 participants (pts) with Baseline data, 99 (4 to 56 years at enrollment; mean 17 years of age; 56% male) also had a Month 12 assessment. A total of 93 pts had evaluable WBCT scans at Baseline and Month 12 and were included in the HO analysis.

In total, 40% (37/93) of pts had new HO over 12 months; the mean volume of new HO in these pts was 57,706 mm^3

(SD=100,079 mm^3; median=20,753 mm^3; range: 522 to 438,826 mm^3). Of the pts with new HO, 65% (24/37) reported at least one flare-up (mean rate of 2.3 flare-ups/year).
Over 12 months, 60% (56/93) of pts did not have new HO; 43% (24/56) of them reported at least one flare-up (mean rate of 1.8 flare-ups/year).
Mean changes from Baseline in CAJIS and FOP-PFQ were minimal: CAJIS: 0.6 (SD=2.4; median=1.0; n=99) and FOP-PFQ: 4.4% (SD=11.2; median=3.7%; n=90); and were similar across pts with or without new HO.
Conclusions: In participants with FOP, although deterioration of physical function is expected over a patient's lifetime, CAJIS and FOP-PFQ scores did not worsen significantly in the relative short-term of this study. However, HO volume, quantified by WBCT, increased over the course of 12 months. These results show that measuring HO may be a viable way to monitor changes in FOP over short periods of time.

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OSTEOPOROSIS: DIAGNOSIS AND CLINICAL ASPECTS

Differential Effects of Abaloparatide and Teriparatide on Hip Cortical Volumetric BMD by DXA-Based 3d Modeling

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SUN-385
The osteoanabolic agent abaloparatide (ABL) has been shown to significantly increase total hip BMD over an 18-month period in postmenopausal women with osteoporosis. However, it remains unknown if these gains predominantly occur in the cortical or trabecular compartments of the proximal femur, and how they may differ from the effects of teriparatide (TPTD). Therefore, a 3D modeling approach was applied to DXA images from patients in the ACTIVE trial to estimate cortical and trabecular changes in the proximal femur over 18 months of treatment with placebo (PBO), ABL, or TPTD. A subset of 750 patients, 250 from each of the treatment groups in ACTIVE (PBO, ABL, TPTD) with non-missing BMD data were randomly selected with data stratified by study site and patient race/ethnicity. Hip DXA scans at baseline and months 6 and 18 were subjected to DXA-based 3D modeling to evaluate volumetric BMD (vBMD) in the cortical and trabecular compartments, as well as cortical thickness and cortical surface BMD (sBMD) (3D-SHAPER v2.10.1, Galgo Medical, Spain). Pairwise group comparisons were made for percentage change from baseline data using P-values derived from contrast tests based on an MMRM model adjusting for BMI, age, value at baseline, and DXA scanner. At 18 months, total hip areal BMD was significantly increased in both the ABL and TPTD groups (P<0.001 vs PBO), with gains from baseline significantly greater with ABL versus TPTD (4.2% vs 3.3%; P<0.05). Similar increases from baseline were observed with ABL and TPTD for both trabecular vBMD (9%) and cortical thickness (1.5%) at month 18 (both P<0.001 vs PBO). In contrast, cortical vBMD was significantly increased from baseline with ABL (1.3%) compared with PBO (-0.2%) and TPTD (0.4%) at month 18 (both P<0.05 vs ABL). Cortical sBMD, the product of cortical thickness and vBMD, was also increased with ABL (+2.8%) versus both PBO (-0.2%) and TPTD (+1.8%) at month 18 (both P<0.05). Although ABL and TPTD increased trabecular vBMD and cortical thickness similarly at the hip by DXA-based 3D modeling after 18 months, ABL significantly increased cortical vBMD and sBMD to a greater extent than TPTD. Additionally, ABL appears to increase cortical density relative to TPTD in clinically important regions of the proximal femur. Further studies may be warranted to investigate these differences and how they may impact hip strength.

Tumor Biology

TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

Missed Pituitary Apoplexy in a HIV Patient

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SAT-143
Background: Pituitary hemorrhage has a prevalence of up to 25% in macroadenomas. In apoplectic hemorrhage, loss of pituitary function is associated with significant mortality. Sudden hemorrhagic enlargement of a preexisting adenoma compresses surrounding structures; ophthalmoplegia, mydriasis and ptosis occur when cranial nerves in the cavernous sinus are affected. The classic clinical syndrome of headache, visual deficits, altered mental status and hypopituitarism, combined with imaging, confirms the diagnosis of pituitary apoplexy.
Clinical Case: A 73 year-old smoker with a history of transsphenoidal surgery 20 years ago for a pituitary adenoma, HIV (CD4 928), hypertension, diabetes, coronary artery disease presented with two days of altered mental status, lethargy and headaches. Patient was febrile to 104.1°F on arrival. Head CT was done prior to a lumbar puncture, which showed a 1.7 x 2.1 x 2.2 cm pituitary mass. CSF analysis was positive for xanthochromia, and revealed 220 RBCs, 275 WBCs, glucose 143 mg/dL, protein 154 mg/dL and an opening pressure of 9 mm H20. Meropenem and vancomycin were started for presumed meningitis. A hypopituitary state was found on labs: prolactin 1.9 ng/mL (4.6–21.4 ng/mL), ACTH 3.2 pg/mL (7.2–63.3 pg/mL), cortisol 3.6 ug/dL, TSH 0.164 uIU/mL (0.27–4.0 uIU/mL), free T4 0.6 ng/dL (0.7–1.5 ng/dL), T3 0.3 ng/mL (0.6–1.6 ng/mL), IGF-1 33 ng/mL (41–179 ng/mL), total testosterone 4 ng/dL (193–740 ng/dL), LH 0.3 mIU/mL and FSH 1.2 mIU/mL. Subsequent MRI showed a 2.2 x 2.4 x 2.9 cm pituitary macroadenoma extending into the suprasellar region with mass effect on the optic chiasm and lateral displacement of the cavernous sinus segment of internal carotid arteries bilaterally. An ophthalmologic exam could not be performed due to altered mentation. Endocrinology recommended cosyntropin testing to assess for adrenal insufficiency. The