to Predict the Future Fracture Risk?

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Background: Cushing's disease may present with a variety of clinical features, including osteoporosis and fracture. Due to the inhibitory effects of cortisol on osteoblastic activity and enhancing effects on osteoclastic activity, these patients are more prone to have osteoporotic fractures. We report a case of ACTH dependent Cushing's disease presenting with recurrent atraumatic pelvic fractures in a woman despite normal bone mineral density for her age. **Clinical Case:** A 56 year-old-woman was referred to the endocrinology department for suspected Cushing's syndrome following a recent atraumatic fracture of right pubic ramus. She had a history of weight gain and easy fatigue. On examination, she had subtle changes suggestive of Cushing's syndrome, including mild truncal obesity, minimal bruising and moon face. She had been taking hormone replacement therapy for 3 years for the post-menopausal symptoms. Her bone mineral density was normal for her age on a recent DEXA scan [femoral neck T score: -0.9, Z score: 0.1, lumbar spine (L1-L4) T score: -1.2, Z score: -0.1]. Her vitamin D, serum calcium and parathyroid hormone levels were normal. Her 24-hour urinary cortisol was 688 nmol/day (reference range: <200 nmol/day), low dose dexamethasone suppression cortisol 525 nmol/L (reference range: <50 nmol/day), ACTH 96 ng/L (reference range: <50 ng/L), indicating ACTH dependent Cushing syndrome. MRI pituitary showed 7 mm right sided hypoenhancing area suggestive of a pituitary microadenoma. CT neck, thorax, abdomen and pelvis did not show any source of ectopic ACTH secretion but did show generalised osteopenia, with old fractures of the ribs and left ilium. She was referred for transsphenoidal resection of pituitary tumour. While awaiting pituitary surgery she was treated with metyrapone: at this time she suffered a further atraumatic fracture of the left pubic ramus. **Conclusion:** Glucocorticoid excess predominantly affects trabecular bones (pelvis, ribs, lumbar spine) as compared to cortical bones. Due to micro-architectural changes, reduction in bone strength is disproportionately greater than would be expected from BMD measured by DEXA. Clinicians should be aware that recurrent fracture of trabecular bones may indicate Cushing's disease even though other clinical features of cortisol excess are minimal or absent.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORT

Response of Severe Osteomalacia to High Dose Vitamin D3 Replacement in a Patient With Ulcerative Colitis and Liver Transplantation on Immunosuppressive Therapy

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Background: Bone disease is common in inflammatory bowel disease (IBD), more frequently in Crohn's disease than ulcerative colitis (UC). We present the case of a patient with prior history of ulcerative colitis with severe 25 OH vitamin D deficiency and metabolic bone disease. **Case:** 67 year old male with h/o ulcerative colitis, colon cancer s/p proctocolectomy and ileostomy, chemo-radiation, h/o primary sclerosing cholangitis (PSC) and orthotopic liver transplantation (OLT) 20 years prior presented with presented with severe muscle aches, severe limitation in mobility and severe vitamin D deficiency. He had been on chronic prednisone and tacrolimus, mycophenolate. Three years after OLT, he had fragility fractures at different times in both hips requiring hip arthroplasty. Labs were significant for persistently elevated alkaline phosphatase (ALP) up to 1569 U/L for last 10 years, bone specific ALP at 423.6 mcg/L, Calcium 9 mg/dl, phosphorus 2 mg/dl, 25 OH vitamin D was 4 ng/ml, 1, 25-hydroxy vitamin D (25-OHD) was 34 ng/ml, PTH was 189 pg/ml, urine calcium/creatinine ratio was 50 mg/g and urine NTX at 223 nM BCE/mM. Celiac screen was negative and tacrolimus levels were within normal range. Patient had extensive workup by gastroenterology for elevated ALP including three liver biopsies which were unrevealing. A bone scan showed increased uptake in thoracic region and metaphyses of large joints. A diagnosis of osteomalacia and secondary hyperparathyroidism was made and he was started on high dose vitamin D gradually increased to 8000 units thrice a day. Within few weeks, he noted marked improvement in mobility, bone pain and need for pain medications. In few months, BSAP decreased to 144.9 mcg/l, NTX and PTH also improved. 25 OH has also increased slightly to 13. He continues on high dose vitamin D and 1200mg of calcium daily. **Discussion:** Our patient likely had severe osteomalacia due to prolonged vitamin D deficiency, caused by multiple etiologies. Firstly, poor absorption in UC might lower 25-OHD levels. Secondly CYP3A enzymes are involved in the metabolism of calcineurin inhibitor tacrolimus as well as vitamin D, this could result in enhanced vitamin D metabolism, which would explain persistently low vitamin D level despite replacement with such high doses. The significant improvement in his symptoms with supplementation resulting in increased mobility despite not having a normal vitamin D level suggest other pleiotropic effects of vitamin D on muscle and bone as well. Additionally effects of liver transplantation on vitamin D metabolism need to be explored further.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORT

Severe Hypercalcemia as Rare Manifestation of Acute Lymphoblastic Leukemia in Adolescent

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Background: Hypercalcemia is a rare manifestation of acute lymphoblastic leukemia (ALL). Several studies reported that severe hypercalcemia is very uncommon in pediatric ALL, but there is no report regarding ALL in adolescence and young adult (AYA) which comprises distinct entity with diverse prognosis.

Clinical Case: A 18-year-old male presented with prolonged fever, general weakness, fatigue, pale and decrease of body weight for 3 months. He also complained visual disturbances which progressively worsened for 1 month. On admission, systemic examination showed that he was alert, had tachycardia, proptosis of both eyes and splenomegaly. There was neither lymphadenopathy nor thyroid/parathyroid abnormality. Initial laboratory investigation revealed pancytopenia (hemoglobin of 6.8 g/dl, hematocrit of 19.1%, white blood cell count of 3.8 x 10^9/L with platelets of 58 x 10^9/L and no blast). There was severe hypercalcemia of 18 mg/dL, hypomagnesemia 1.14 mg/dL, with normal phosphorus level. His serum creatinine level slightly increased to 1.3 mg/dL with filtration rate of 79 ml/min/1.73 m^2. Bone marrow evaluation showed blast cells infiltration, consistent with ALL type L3. Leukemia phenotyping revealed B cell-lineage with aberrant exp CD5. CT scan orbita and brain showed bilateral retrobulbar mass and diffuse lytic lesion in skeletal bones due to leukemic cells infiltration. Patient was treated with supplemental oxygen, hydration targeting natriuresis, loop diuretic and steroid. The serum calcium level remained high, thus bisphosphonate was given. There was progressive decline of serum calcium level after therapy. The patient is then prepared to start chemotherapy.

Discussion: Hypercalcemia is associated with both PTH or PTH-independent mechanism, including malignancy. It complicates 5–20% of malignancy, but only 0.6–4.8% reported in leukemia. Hypercalcemia in malignancy may present due to: (1) direct invasion of cancer cells to bone and (2) secretion of humoral PTH-related peptide (PTHrP) which mimics PTH. Severe hypercalcemia without inadequate treatment is fatal. Initial treatment of hypercalcemia includes hydration, loop diuretic, calcitonin and bisphosphonate targeting decline of serum calcium level of 3–9 mg/dL in 24–48 hours. The main treatment of leukemia-related hypercalcemia is chemotherapy. Several cases of pediatric ALL reported normocalcemia after starting induction phase of chemotherapy and exerted good prognosis.

Conclusion: Hypercalcemia should be investigated in leukemia patients and vice versa. The main aim of therapy is to normalize the serum calcium level and treat underlying causes. In adolescent ALL, adequate treatment of hypercalcemia helps achieving better outcome.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORT

Severe Hypocalcemia and Vitamin D Deficiency in Adolescence - A Case Series

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Background: Hypocalcemia due to vitamin D (vit D) deficiency is uncommon among adolescents in the US. Only 3% to 6% of those ages 12- to 19-years-old have a vit D level <12 ng/ml.[1] We present three cases of severe hypocalcemia secondary to vit D deficiency in non-obese adolescents with restricted diets and limited sun exposure.

Clinical Cases: A 14-year-old Ethiopian male with history of absence seizures presented with bloody stool. Incidentally, labs revealed: Ca 5.6 (8.4–10.2) mg/dL, iCal 0.71 (1.2–1.38) mmol/L, PTH 295.1 (10.0–65.0) pg/mL, 25(OH)D <4 (20–100) ng/mL, Mg 1.9 (1.7–2.2) mg/dL, PO_4 3.8 (2.5–4.5) mg/dL. He endorsed weight loss and knee pain, but denied paresthesias, tetany and seizures. He was a vegetarian and had minimal sun exposure. EKG and femur X-ray were unremarkable. He was started on IV calcium gluconate initially. Oral calcium carbonate and cholecalciferol were started on days three and four. He was discharged on day ten with iCal 0.84 on oral calcium carbonate and calcitriol.

A 16-year-old male with history of autism, ADHD and bipolar disorder presented with a seizure. Labs revealed: Ca 5.7, iCal 0.62, PTH 372, 25(OH)D <4, Mg 1.9, PO_4 3.5. Exam showed tetany, carpopedal spasms and positive Trousseau and Chvostek signs. EKG revealed prolonged QTc of 480 (<450) ms. He had a restricted diet and minimal sun exposure. His mother described his gait as "waddling" for the past two years. X-ray revealed bilateral femoral head fractures and evidence of rickets. He underwent bilateral surgical repair. He was started on IV calcium gluconate initially. Oral calcium carbonate and cholecalciferol were started on days two and four. He was discharged on day 14 with iCal 1.01 on oral calcium carbonate and cholecalciferol.

A 16-year-old male with history of severe food allergies and restricted diet presented with a seizure. He visited urgent care three months prior for perioral tingling, muscle cramps and chest pain. He started a multivitamin for "low Ca" and "prolonged QTc." The ED labs revealed: Ca 4.8, PTH 414.8, 25(OH)D 11, Mg 1.9, PO_4 5.0, Alk Phos 539 (44–147) IU/L. Exam showed upper extremity twitching and QTc was 543 ms. He received 2 g calcium gluconate IV, then began oral calcium carbonate and cholecalciferol and continued supplementation following discharge on day six.

Conclusions: Vit D deficiency among adolescents is re-emerging, likely due to decreasing sun exposure, unbalanced diets and increasing obesity.[2] Adolescents with restricted diets due to allergy or behavioral disorders may be at higher risk of vit D deficiency. Increased screening of high-risk adolescents may lead to early identification of cases.

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Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORT

Severe Hypophosphatemia and Elevated FGF23 Level Following Zoledronic Acid Infusion

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Background: Severe hypophosphatemia may be seen following zoledronic acid infusion, however FGF23 elevation has not been previously reported.

Clinical Case: A 67-year-old man with Crohn's disease status post remote ileocolonic resection, malnutrition (BMI