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 trans-sphenoidal 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 predominately 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 atraumatic fractures 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, 25-hydroxy vitamin D (25-OH) was 34 ng/ml, PTH was 189 pg/ml, urinary 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.