have been treated with fluconazole, which has a favourable side effect profile and yields good results. Adjusted calcium reduced to 2.62 nmol/L, 25 OH Vitamin D normalised to 111 nmol/L and 24:24,25 dihydroxyvitamin D ratio is now 17. Patient's liver functions and full blood count has been monitored regularly during the course of treatment and the drug was well tolerated. **Conclusion:** Genetic causes of hypercalcemia can be left undiagnosed for long periods and there is a lack of proven or definitive therapeutic agents for correction of elevated calcium. Here fluconazole has been shown to reduce the hypercalcaemic burden and effectively lowered the Vitamin D levels in this case of a *CYP24A1* mutation. This study augments fluconazole use in these cases but further studies are needed to elucidate the long term safe usage.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORT

Delayed Diagnosis of Congenital Hypoparathyroidism in a Kindred of Three Patients With Autosomal Dominant Deafness

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Background: Congenital hypoparathyroidism can be related to autosomal dominant mutations or deletions in GATA-binding protein 3 gene on chromosome 10[1,2]. Affected patients present with a triad of hypoparathyroidism, renal dysplasia and neurosensorial deafness. We hereby present the case of a patient with the rare Barakat syndrome, also known as HDR syndrome. **Clinical Case:** A 11-year-old girl, diagnosed with deafness at birth, was brought to medical attention because of menorrhagia requiring blood transfusions two months after menarche. A pelvic ultrasound demonstrated a septate uterus as well as right multicystic dysplastic kidney with solitary left kidney and ovary. As her maternal grandmother, mother and older sister suffered from congenital deafness and her mother also had a kidney cyst, the patient was referred to genetics to identify a unifying cause of the autosomal dominant pattern of deafness and urogenital anomalies. Chromosome microarray analysis revealed a copy number change on chromosome 10p14 of 1925 kb predicted to result in the deletion of a single protein coding gene, GATA3. Embryonically, GATA3 is involved in the development of the inner ear, kidneys and parathyroid glands. The patient was lost to follow up so that a serum calcium was drawn three years later, revealing low ionized calcium of 1.06 mmol/L (N 1.16–1.29), low corrected total calcium of 2.11 mmol/L (N 2.30–2.62) along with PTH of 1.1 pmol/L (N 2.0–9.4), PO4 of 1.73 mmol/L (N 1.03–1.78) and creatinine of 64 umol/L (N 50–71). She was started on calcium carbonate 1000 mg TID and calcitriol 0.5 mcg BID and genetic analysis of the mother and sister revealed the same mutation compatible with Barakat syndrome. Compliance has been difficult, and when the patient transitioned to adult endocrinology three years later, she was on alfacalcidiol 2 mcg daily along with calcium carbonate 1500 mg daily and her labs were still suboptimal with a total corrected calcium of 1.82 mmol/L (N 2.22–2.54) and ionized calcium 0.98 mmol/L (N 1.16–1.29). Renal function determines the prognosis, and reassuringly her creatinine remains normal. Upon further questioning of the mother, she recalls that the patient had to be intubated for respiratory failure as a newborn, she had delayed milestones and also had seizure like activity during her infancy and early childhood. She had brought these symptoms to her family physician's attention however no further investigations were completed and serum calcium was not checked.

Conclusion: Early recognition of hypocalcemia symptoms is critical in identifying patients with congenital hypoparathyroidism, even more so when associated with other features that are part of complex familial syndrome such as Barakat syndrome.

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Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORT

Denosumab Induced Severe Hypocalcemia in a Patient With Metastatic Prostate Cancer

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Background: Denosumab can lead to severe hypocalcemia in patients with underlying risk factors such as vitamin D deficiency, low PTH, hypomagnesemia, and CKD. Denosumab is a monoclonal antibody against RANKL, reducing the activity of osteoclasts and thus reducing the release of calcium in the bloodstream causing hypocalcemia. Hypocalcemia can range from mild to severe symptoms requiring prolonged hospitalization. Medications such as zoledronic acid and Denosumab are known to reduce the occurrence of Skeletal related events (pathological fracture, spinal cord compression, and radiation to bone). For metastatic prostate cancer, about 90% can develop bone metastasis with significant morbidity and mortality [1]. Our patient presented with severe hypocalcemia after denosumab use without any above risk factors. **Clinical Case:** A 66-year-old male with a medical history of Prostate cancer with Metastasis to chest and bone presented to ER with syncope. Patient-reported poor oral intake, nausea, and vomiting for the last few days. In the ER, the patient was found afebrile, bp 116/76, HR 92, saturating 100% on room air. On examination, the patient was found lethargic, malnourished, foley in place due to chronic urinary retention. The abdomen was soft and non-tender. Laboratory findings were significant for Hb 9.1, Na 133, K3.6, bicarb 21, total calcium (Ca) 4.2, ionized Ca 0.63 and corrected Ca 5.4, magnesium 1.6, phosphorus 2.1, albumin 3.3, ALT 218, AST 229, ALP 1607. Lipase 82, Total bilirubin 1.5, direct bilirubin 0.8. Spot Urinary Ca 0.7, Vitamin D 25 OH 36.9, serum PTH 225 pg/mL. Serum cortisol AM 20.9, BUN 16, and serum Creatinine 1.0. The patient was started on 11g calcium gluconate in 1L dextrose @ 50c/hr and calcitriol 0.25mcg twice daily. Serum Ca level was monitored every 6 hours and reached 6.7. Later was started on Ca carbonate

1250 TID with meals. Finally, after electrolyte correction, the patient clinically improved and was discharged with the plan to follow Calcium at the outpatient clinic. On review of previous labs at the oncology clinic, the patient received Denosumab at his oncologist's clinic 10 days before this hospital admission, last Ca level from 6 months ago 8.6, the patient was not any vitamin D or Ca supplement. **Conclusion:** Many case reports have been published on severe hypocalcemia after denosumab usage. Several patients had underlying risk factors such as vitamin D deficiency, osteoblastic lesion, and AKI leading to an additional cause of hypocalcemia. We emphasize careful monitoring of serum Ca levels particularly in the first few weeks of treatment even without significant risk factors for hypocalcemia. **References:** [1] Metastatic patterns of prostate cancer: an autopsy study of 1,589 patients. Bubendorf L, Schöpfer A, Wagner U, Sauter G, Moch H, Willi N, Gasser TC, Mihatsch MJ. . Hum Pathol. 2000 May; 31(5):578–83

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORT

Denosumab Induced Severe Prolonged Hypocalcemia in Metastatic Prostate Cancer

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Background: Denosumab is a RANK-l inhibitor that, in addition to the treatment of osteoporosis, is used in patients with advanced cancer and metastatic bone disease to prevent skeletal-related events. Although denosumab is generally safe and effective, it can cause hypocalcemia which in some patients can be severe and life threatening. We present a case of severe prolonged hypocalcemia after a single dose of denosumab in a patient with metastatic prostate cancer. **Case:** A 78-year-old male with a past medical history of stage 4 prostate cancer on antiandrogen treatment with GnRH antagonist presented with severe hypocalcemia. Physical exam revealed a blood pressure 125/80 mm Hg, pulse 115 per min and weight 135 lb with negative Chvostek's and Trousseau's signs. The electrocardiogram showed supraventricular tachycardia with prolonged QT_c interval of 503 ms (<430 ms). Labs showed serum calcium 4.9 mg/dL (8.5–10.5), albumin 2.5 g/dL (3.6–5.1), corrected calcium 5.7 mg/dL, ionized serum calcium 0.64 mmol/L (1.05–1.3), creatinine 1.10 mg/dL (0.7–1.2), eGFR >60, phosphorus 2.0 mg/dL (2.5–4.5), magnesium 1.9 mg/dL (1.6–2.6), 25-OH vitamin D 29.7 ng/mL (30–100), 1,25 dihydroxy vitamin D 174 pg/mL (18–64), iPTH 244.0 pg/mL (11–68) and PSA 1860 ng/mL. Three weeks prior to presentation, the patient received 120 mg of subcutaneous denosumab. Pre-treatment serum calcium was 9.2 mg/dL (8.5–10.5), and Tc-99m bone scan showed multiple osteoblastic osseous metastatic lesions involving both axial and appendicular skeleton. The patient was diagnosed with denosumab-induced severe hypocalcemia and started on intravenous (IV) calcium gluconate infusion, oral phosphate 250 mg twice daily, and ergocalciferol 50,000 IU twice weekly. He required IV calcium gluconate up to 10 g per day in addition to oral calcium carbonate 2 g t.i.d. for 2 weeks to resolve hypocalcemia and normalize QT_c interval. Patient was discharged to nursing home on calcium carbonate 2 g q.i.d. with IV calcium gluconate as needed to keep corrected calcium >8.0 mg/dL. After discharge he required up to 4 g of IV calcium and 8 g of oral calcium per day. Unfortunately, he presented again with severe hypocalcemia 5 weeks after discharge. In addition to current regimen of oral and IV calcium boluses, low dose calcitriol was started. We were only able to maintain his serum calcium>8.0 mg/dL by administering high daily dose of oral calcium carbonate 8 g /day and calcitriol 2 mcg daily. Due to poor prognosis, he was transitioned to hospice care and died 2 weeks later. **Discussion:** There are not many case reports on severe prolonged hypocalcemia secondary to denosumab in cancer patients but normal kidney function. Our patient remained on high dose of calcium even 101 days after denosumab administration. **Reference:** 1. Milat F et al. Prolonged hypocalcemia following denosumab therapy in metastatic hormone refractory prostate cancer. Bone. 2013 Aug 1;55(2):305–8.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORT

Diagnostic Dilemma of Elevated FGF23 in a Patient With Osteomalacia: A Case Report

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Introduction: Tumor-induced osteomalacia (TIO) is a rare paraneoplastic syndrome due to FGF23 hypersecretion. It is mostly seen with benign mesenchymal tumors. Establishing the diagnosis could be challenging due to occult nature of the disease.
Case: A 54-year-old female presented with right thigh and upper back pain. On presentation, she had hypophosphatemia (1.8 mq/dl), low 25-hydroxyvitamin D (23 ng/ml), normal ionized calcium and normal iPTH (53 pg/mL). CT scan showed healing right 10^{th} rib fracture and right proximal femoral fracture. DEXA scan was remarkable for osteoporosis. 99m-Technetium nuclear bone scan displayed hyperactivity on bilateral femurs and multiple ribs concerning for stress fractures. Patient was thought to have osteomalacia from vitamin D insufficiency and started on ergocalciferol. Two months later, patient was diagnosed with invasive ductal carcinoma. She had unilateral mastectomy and adjuvant chemotherapy. Surveillance studies were negative for recurrence. Patient lost to follow up for 2 years until she returned with right hip and upper back pain. Her labs showed hypophosphatemia (1.2 mg/dL), normocalcemia, elevated iPTH (131 pg/mL), low 25-hydroxyvitamin D (26 ng/ml), low normal 1,25-dihydroxyvitamin D (25 pg/ml, normal: 18 -72) and elevated FGF23 (285 RU/ml, normal level <180). 24-hour urine studies showed phosphate of 330 mg and fractional phosphate excretion (FEPO4) of 12%. Nuclear bone scan reported subacute fractures in left 11^{th} and right 6^{th} ribs and right proximal femur. TIO was entertained as the unifying diagnosis. She was started on calcium, phosphate, ergocalciferol and calcitriol. Localizing studies with a PET scan showed FDG hyperactivity in the right vocal cord. Subsequent MRI showed asymmetric fat tissue between esophagus and left common carotid artery concerning for lipoma. She lost to follow up again during COVID-19 pandemic.