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Background:PRES is a rare but severe condition with highly variable neurologic manifestations ranging from headaches to seizures, coma and radiologic findings of focal vasogenic edema[1]. It is commonly caused by hypertension, chronic renal failure, preeclampsia / eclampsia and immunosuppressants. We are reporting a rare presentation of PRES caused by severe hypercalcemia.
Clinical Case: A 29- year old female presented with frontal headaches, visual disturbance, emesis and confusion. Her medical history was relevant for hyperthyroidism treated with partial thyroidectomy (on methimazole) and complicated by iatrogenic hypoparathyroidism. The resulting hypocalcemia was managed with calcitriol and calcium supplementation. On presentation, the patient was awake but disoriented. Physical examination was remarkable for right-sided hemianopsia. Admission blood pressure (BP) was 192/127 suggestive of hypertensive emergency. Initial laboratory tests revealed severe hypercalcemia (calcium: 18.7 mg/dL, ionized: 2.1 mmol/L), acute kidney injury (creatinine of 2.5 mg/dL, (baseline = <1), elevated 1, 25-dihydoxy vitamin D: 65.1 pg/mL, PTH <1 pg/mL, and negative urine toxicology. Head CT without contrast revealed symmetric bilateral parieto-occipital parenchymal hypoattenuation and MRI confirmed the aforementioned findings to be consistent with PRES. The patient was admitted to the ICU and started on Nicardipine intravenous (IV) infusion, IV fluids and calcitonin. Other causes of severe hypercalcemia such as multiple myeloma and hypercalcemia of malignancy were ruled out. Home calcium and calcitriol supplements were discontinued due to suspicion of intoxication. After correction of serum calcium levels her encephalopathy, hypertension and AKI resolved. She was subsequently transferred to the medical floor in stable condition. Calcium supplementation was resumed when serum calcium level normalized and calcitriol was held until further follow up of calcium levels as outpatient.
Conclusion: Severe hypercalcemia is a rare cause of PRES secondary its effect on vascular smooth muscle vasoconstriction and increased vascular resistance leading to severe hypertension. Thus, it is imperative to establish a prompt diagnosis and rule out hypercalcemia in all patients presenting with PRES to prevent its devastating neurologic complications. **Reference:** Fugate JE, Rabinstein AA. Posterior reversible encephalopathy syndrome: clinical and radiological manifestations, pathophysiology, and outstanding questions. Lancet Neurol. 2015 Sep;14(9):914–925. doi: 10.1016/S1474-4422(15)00111-8. Epub 2015 Jul 13. Erratum in: Lancet Neurol. 2015 Sep;14(9):874. PMID: 26184985.

Bone and Mineral Metabolism
BONE AND MINERAL CASE REPORT

A Curious Case of PTH Independent Hypercalcemia Secondary to Silicone Injections

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Background: Hypercalcemia is a commonly encountered clinical problem with numerous etiologies. Granulomas formed secondary to foreign bodies are a rare but increasingly recognized cause of hypercalcemia. **Clinical Case:** A 49-year old African American woman, who had received silicone injections for buttock augmentation 15 years ago, was found to have severe hypercalcemia after she presented with complaints of chronic constipation, muscle cramping, polyuria, and mental fog. Her labs on admission showed severe hypercalcemia Ca 17.9mg/dL (normal: 8.4–10.6 mg/dL), with a suppressed PTH 4 pg/mL (normal 14–54 pg/mL). Prior labs from 5 years earlier, had shown an elevated $1,25(OH)_2D$, therefore differentials including lymphoma and chronic granulomatous diseases, particularly sarcoidosis, were high on the list of possible diagnosis. Additional labs showed a normal PTH-RP 19 pg/mL (normal 14–27 pg/mL), normal ACE levels 64 U/L (normal 9–67 U/L), low $25(OH)D_2$ 1 ng/mL and normal 1,25(OH)2D 62 pg/mL. Her exam was notable for multiple indurated and firm masses palpable over the bilateral gluteal region and lateral thighs. CT abdomen/pelvis showed extensive and markedly confluent infiltration with intervening globules of macroscopic fat throughout the subcutaneous fat layers of the buttocks and lateral hips and speckled linear calcifications consistent with granulomatous reaction. With aggressive fluid hydration and calcitonin, her calcium levels decreased over the following 48 hours, but remained at 12–13 mg/dL. She was started on 30 mg of prednisone daily and her calcium levels dropped to 10.9 mg/dL the following day. She was discharged home on prednisone, her calcium levels remained suppressed, and her prednisone dose was slowly tapered during the following months. She was referred for plastic surgery evaluation and is being evaluated for possible surgical debridement. **Conclusion:** Hypercalcemia secondary to foreign body granulomas is a rare clinical entity. The diagnosis is usually established through a thorough history and examination. Lab findings may be variable. Treatment of these patients can be challenging, and corticosteroids are the mainstay of treatment in most cases[1]. Surgical debridement of granulomas has been reported with good results; however, further investigation and longer follow-up is needed[2]. **References:** 1.Tachamo, N., Donato, A., Timilsina, B., Nazir, S., Lohani, S., Dhital, R., & Basnet, S. Hypercalcemia associated with cosmetic injections: A systematic review. *European Journal of Endocrinology,* 2018; 178(4): 425–4302.Edwards, B.J., Saraykar, S., Suna, M., Murphy, W. A., Lin, P., Gagel, R. Resection of granulomatous tissue resolves silicone induced hypercalcemia, *Bone Reports*, 2016; 5:163–7

Bone and Mineral Metabolism
BONE AND MINERAL CASE REPORT

A Novel GATA3 Variant Causing Familial Hypoparathyroidism, Renal Agenesis and Sensorineural Deafness Presenting With Atypical Symptoms of Chronic Hypocalcaemia

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Introduction: Familial hypoparathyroidism is a rare cause of hypocalcaemia. We report a case of long-standing hypocalcaemia secondary to hypoparathyroidism caused by a novel *GATA3* variant resulting in multiple organ involvement. **Case**: A 20 year old girl was referred to our bone metabolic clinic for hypocalcaemia. Her past medical history included Bechet's disease, epilepsy and depression. She had bilateral sensorineural hearing loss and encephalitis as a child. She underwent right nephrectomy for an atrophic non-functioning kidney at the age of 16. Current medication included hydroxychloroquine, diazepam, oral calcium and cholecalciferol. It was noted that the hypocalcaemia dated back to 8 years, she denied any typical symptoms of hypocalcaemia but she did report visual and auditory hallucinations, fatigue and had low seizure threshold. She sustained recurrent fractures of her arm, elbow and wrist. **Initial investigations**: Corrected calcium 1.88 (2.20-2.60mmol/L), Phosphate 1.54 (0.80–1.50mmol/L), PTH 1.2 (1.6–6.9pmol/), 25-OH vitamin D 37 (50-120nmol/L). Myeloma screen, thyroid, renal and liver functions were all within the normal reference range. **Other bone markers**: Serum Procollagen Type 1 Amino Terminal Peptide was mildly raised at 82 (19-69ug/L), CTX 0.42 (0.1-0.5ug/L), 1,25 OH Vitamin D 29 (55-139pmol/L), 24,25-dihydroxyvitamin D was normal with normal 25:24,25 Dihyroxyvitamin D ratio at 18 normal. Bone density was in the normal range for her age. MRI of the brain was normal with no evidence of calcification. There was a family history of hypocalcemia in her estranged father. Subsequent genetic analysis showed a novel likely pathogenic *GATA3* missense variant (c.961T>C p.(Cys321Arg). She was started on alfacalcidol and achieved near normocalcemia with adjusted calcium levels of 2.18nmol/L. **Conclusion:** Pathogenic variants in the *GATA3* gene are responsible for *Hypoparathyroidism*-deafness-renal dysplasia (HDR) syndrome. In our patient, a novel missense variant in *GATA3*, p.(Cys321Arg), has been detected. This variant disrupts one of four conserved cysteine residues within a zinc-finger domain, which is involved in DNA binding and is presumed to have a deleterious effect on protein function. Patients may have longstanding asymptomatic hypocalcaemia with atypical features hence genetic testing is recommended in patient with multi-organ involvement. Alfacalcidol successfully restored calcium homeostasis in this case.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORT

A Novel Mutation in SOST Gene Causes Sclerosteosis

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Background: Sclerostin is a *SOST* gene product that inhibits osteoblasts activity and prevents excessive bone formation by antagonizing Wnt signaling pathway. Sclerosteosis has been linked to the loss of function mutation in *SOST* gene. It is a rare autosomal recessive disorder characterized by craniotubular hyperostosis leading to gigantism, cranial nerves entrapment, and fatal cerebellar herniation.
Objectives To report a novel mutation of *SOST* gene in a patient with sclerosteosis.
Clinical Case: A 25-year-old female was referred to the endocrine clinic for suspected GH excess. The patient noted the onset of headache, progressive bilateral blurred vision and hearing disturbance, irregular menses, and generalized arthralgia; at the age of 23 years. Subsequently, she observed a progressive increase in the size of shoes and hands, proptosis, and protrusion of the chin. She was the second of seven siblings from non-consanguineous parents with normal antenatal and neonatal history except for syndactyly. All family members were phenotypically normal except for a sister with similar physical appearance who had cranial decompression 20 years back. MRI pituitary was done initially due the suspicion of pituitary adenoma and it revealed an enlarged sella turcica with normal pituitary gland. Surprisingly, the MRI showed diffuse osseous thickening with narrowing of skull base foramina, narrowing of optic and internal auditory canals, secondary compression of cerebral parenchyma and bilateral cerebellar tonsillar herniation. Further image revealed extremely increased bone mass density with Z-score values of +12, generalized increase cortical thickness, vertebral end plates sclerosis, and deformed left index finger. Biochemical and endocrine tests revealed normal GH, IGF -1, TSH, prolactin, short Synacthen test, FSH, LH, estradiol, calcium, phosphorus, PTH and alkaline phosphatase. Due to progressive worsening of vision with compressive optic neuropathy, optic nerve fenestration with decompression hemicraniotomy was performed. Sclerosteosis was suspected due to the predominant craniotubular hyperostosis with syndactyly. There was no definite therapy. Management aimed at relieving symptoms and preventing complications, so she was commenced on calcitriol and prednisolone to suppress the osteoclasts. Genomic sequencing of the *SOST* was performed. We identified a novel deletion mutation in *SOST* gene (c.387delG, p.D131fs*) which disrupts the sclerostin function causing sclerosteosis in this patient.
Conclusion: We describe a novel mutation in the *SOST* gene in a patient with sclerosteosis in Saudi Arabia, that has not been previously described. Closing the gap between the genomic knowledge and clinical applications will add the benefit of success in development of targeted therapies in such a fatal disease.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORT

A Rare Case of Perinatal Hypophosphatasia Treated With Asfotase Alfa

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