was delayed due to poor functional status and concurrent discovery of an EBV-positive nasopharyngeal carcinoma. Prior to surgery patient was treated with phosphorus and calcitriol supplements. Post-operatively serum phosphorus and FGF-23 levels were normalized. Patient also improved clinically. Patients treatment course was complicated by secondary hyperparathyroidism; however, this improved following surgery. **Conclusion:** Diagnosis of TIO can be delayed due to its nonspecific symptoms. Thus, in patients with chronic bone pain, muscle weakness, and atraumatic fractures, TIO should be kept on the differential and these patients should undergo thorough biochemical and imaging evaluation. Tumor localization could be challenging. Patients should be managed with supplements of active vitamin D and phosphorus with goal to normalize phosphorus level to prevent further bone demineralization prior to surgery. However, surgical intervention remains the mainstay of management as this is curative of TIO.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORT

Successful Early Treatment of Severe Neonatal Hyperparathyroidism With Cinacalcet

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Introduction: Neonatal severe hyperaparathyroidism (NSHPT) can cause significant bone disease early in life and prompt treatment is therefore necessary. Cinacalcet is a calcimimetic primarily used in adult patients with hypercalcemia to treat secondary hyperparathyroidism, but has only been trialed in neonates with NSHPT. Successful treatment appears to be dependent on the mutation leading to hypercalcemia. We describe a neonate born with severe hypercalcemia and a suspected mutation of the calcium sensing receptor (CaSR) who received successful early treatment with cinacalcet and decrease in calcium levels.

Case Report: A full-term baby girl was found to have rapid breathing at 2.5 hours of life requiring CPAP. A chest x-ray demonstrated bone demineralization with rib fractures. Lab evaluation demonstrated hypercalcemia (total calcium = 12 mg/dl) with an inappropriately elevated PTH level of 386 pg/mL, hypophosphatemia (3.3 mg/dL), normal magnesium (2.0 mg/dL), a normal urine calcium to creatinine ratio of 0.26 and calcium to creatinine clearance ratio of 0.05 and a slightly low vitamin D-25 of 28.8 ng/mL.

The father had a history of asymptomatic hypercalcemia without a diagnosis. Paternal genetic testing identified a heterozygous pathogenic CASR defect: c. 554G>A (p.Arg185Gln). This has been described in patients with NSHPT.

The patient was initially treated with IV fluids and Lasix, but calcium levels did not decrease. Cinacalcet therapy was given on day of life 10. Patient had a decreased PTH to 231 pg/ mL after one day. After 26 days of treatment, patient's PTH level decreased to 63 pg/mL. Patient was weaned off of CPAP and was discharged home.

Discussion: Cinacalcet, a calcimimetic that works at the level of the CASR, was able to successfully and significantly decrease PTH levels in a neonate patient with NSHPT. Treatment options are limited in patients with this condition and we believe prompt treatment with this therapy facilitated patient's discharge. The patient's osteopenia secondary to the NSHPT and subsequent rib fractures resulted in a prolonged requirement of CPAP. Early recognition and treatment, even prior to results of genetic testing, prevented further fractures. We demonstrate the potential benefit of calcimimetics in a case of NSHPT where conventional treatment was ineffective. More importantly, we anticipate improvement in osteopenia and any future comorbidities secondary to this condition. Continued success with this treatment is yet to be evaluated.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORT

Successful Medical Management of a Non-Localising Case of Tumour-Induced Osteomalacia

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Introduction: TIO is a rare paraneoplastic syndrome characterised by renal phosphate wasting due to fibroblast growth factor-23 (FGF23) over-secretion from a phosphaturic mesenchymal tumour (PMT). While surgery is potentially curative, localisation is often challenging.

Clinical Case: A 53 year old lady presented with recurrent fragility fractures in the spine (T10-L1, L4, S1-2), right femoral neck fracture and pelvic fractures at the bilateral superior and inferior pubic rami, associated with a 2 year onset of lower limb pain and proximal myopathy. Power was 2/5 proximally, rendering her progressively chairbound. She had no family history of fragility fractures. Biochemistry revealed hypophosphatemia of 0.48 mmol/l (NR 0.86–1.45 mmol/l), normal adjusted calcium of 2.32 mmol/l (NR 2.15–2.55 mmol/l), hyperphosphaturia (TmP/GFR 0.39 mmol/l, NR 0.88–1.42 mmol/l), mildly insufficient 25(OH)D level of 25 μg/l, inappropriately suppressed $1,25(OH)_2D$ at 13 pg/ml (NR 18–78 pg/ml) and raised FGF23 at 484 RU/ml (NR<180 RU/ml). Localisation of the PMT was unsuccessful, despite multiple investigations including 68-Gallium-DOTANOC PET-CT, bilateral lower limb MRI for non-specific inguinal lymph nodes and various ultrasonographic evaluation of soft tissue lesions including biopsy of a benign breast tumour. Surgical removal of the breast papilloma did not affect FGF23 levels. In the absence of any suspicious lesion, selective venous sampling was not performed due to uncertain utility. She was treated medically, requiring 16mmol oral phosphate, 1000 IU cholecalciferol and 0.5mcg calcitriol daily, with a view to perform interval DOTA-peptide scan. Despite an increase in FGF23 to 760 RU/ml over 29 months, phosphate level was maintained in the low-normal range and alkaline phosphatase, as a marker of disease activity, normalised from 370 U/l to 92 U/l (NR 40-130U/l). Development of secondary hyperparathyroidism improved with uptitration of calcitriol. There was no hypercalciuria on monitoring of

urinary calcium. Symptoms of generalised body pain resolved, and her bone mineral density (BMD) improved over 47 months of medical therapy. Power improved to 4/5, and she was able to ambulate with assistance. BMD at the femoral neck, total hip and lumbar spine increased by 68.2%, 44.6% and 65.2% respectively.

Conclusion: This is a challenging case of TIO which has failed to localise despite best efforts. One must consider FGF23-independent and dependent causes of osteomalacia when patients present with severe frailty and hypophosphatemia as substantial morbidity results from delayed diagnosis and treatment. TIO-related PMTs can be difficult to localise, even with a combination of functional and anatomical imaging. With medical therapy, bone mineralisation and symptoms can improve significantly. Patients need to be monitored for complications of long-term phosphate and calcitriol replacement.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORT

Successful Parathyroidectomy May Not Resolve Hypercalciuria in Patients With Primary Hyperparathyroidism

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Background: Hypercalciuria, with twenty-four-hour urinary calcium of >400 mg/day, is one of the indications for parathyroidectomy in patients with primary hyperparathyroidism. We report five cases where hypercalciuria is not resolved following a successful parathyroidectomy (normalization of serum calcium) in such patients. Here resolution of hypercalciuria is defined as twenty-four-hour urinary calcium of less than 200 mg/day. **Clinical Case:** This is a case series of five patients who remained hypercalciuric at 6 to 19 months after successful parathyroidectomy. Pre-parathyroidectomy, average PTH was 95 pg/dL (Min 69 pg/dL, Max 120 pg/dL), average serum calcium was 11.0 mg/dL (min 10.3 mg/dL, max 12.0 mg/dL), and average twenty-four-hour urinary calcium was 455 mg/day (min 386 mg/day, max 551 mg/day). Calcium levels were corrected to normal range post-parathyroidectomy and remained in normal range. However, hypercalciuria did not resolve. Post-parathyroidectomy, average PTH was 44 pg/dL (min 25 pg/dL, max 69 pg/dL), average serum calcium was 9.6 mg/dL (min 9.3 mg/dL, max 9.8 mg/dL), and average twenty-four-hour urinary calcium was 284 mg/day (min 201 mg/day, max 376 mg/day). Two patients who had history of nephrolithiasis prior to parathyroidectomy continued to develop nephrolithiasis at six and sixteen months after successful parathyroidectomy. **Conclusions:** This case series showed that hypercalciuria may not resolve following a successful parathyroidectomy in patients with primary hyperparathyroidism and elevated twenty-four-hour urinary calcium at 6 to 19 months after surgery. Further observations to evaluate long term effects of parathyroidectomy on hypercalciuria is needed.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORT

The Importance of Interpreting Urine Calcium:Creatinine Ratio in PHPT Within Ethnic Context

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A 56-year-old Afro-Caribbean lady was found to have incidental hypercalcaemia on routine GP investigations. Tiredness was the only elicitable hypercalcaemic symptom and aside from early menopause at age 40, she had no significant past medical or family history. Examination was unremarkable. Blood results showed a raised adjusted calcium 2.68mmol/L (2.2–2.6), normal phosphate 1.06mmol/L (0.80–1.50), raised parathyroid hormone (PTH) 14.1pmol/L (1.6–7.2) and low 25-hydroxyvitamin D 28.1nmol/L (70–150).

She had osteopaenia of the femora and left radius on DEXA scan but no nephrocalcinosis on renal ultrasound. On initial investigation, her urinary calcium output was low at 1.55mmol/day resulting in a 24h calcium:creatinine ratio (UCCR) of 0.0065. Although suggestive of Familial Hypocalciuric Hypercalcaemia (FHH), her notable Vitamin D deficiency was considered to contribute to the observed hypocalciuria. After Vitamin D repletion, a repeat UCCR improved to 0.012, however, remained in the indeterminate range. No known pathogenic variant was identified on genetic analysis for FHH.

Her PTH and Calcium levels remained persistently high within 9.7–17.1pmol/L and 2.65-2.82mmol/L respectively, suggestive of Primary Hyperparathyroidism (PHPT) given the end organ damage and negative genetic studies. Based on her symptom of fatigue, osteopaenia at a young age and hypercalcaemia, localisation studies were arranged which showed no definitive evidence of a parathyroid adenoma and explorative surgery was planned.

The negative genetic testing, PTH level 17.1pmol/L, osteopaenia, low-normal magnesium and phosphate level collectively support a diagnosis of PHPT in this case, despite a low UCCR which however is observed in some PHPT patients. Indeed, a lower UCCR ratio has been reported in the healthy Afro-Carribean population across all age groups, as well as in Afro-Carribean patients with PHPT [1]. The underlying mechanism for this is yet to be determined but may be due to increased renal sensitivity to PTH or altered activity of the tubular calcium reabsorptive pathways. One can further speculate regarding an evolutionary reason behind a protective homeostatic system favouring renal calcium reabsorption over excretion in this frequently vitamin D deficient population.