Following completion of cancer therapy, she was evaluated for parathyroidectomy. Preoperative assessment revealed NYHA class II heart failure, with reduced ejection fraction (36%) and severe tricuspid regurgitation attributed to trastuzumab-related cardiomyopathy. Despite optimal medical therapy, she was deemed high-risk for surgery. Cinacalcet failed to achieve sustained calcium control with levels exceeding 3 mmol/L. She was therefore referred for PEA.

Post-procedure, iPTH decreased 80% by Day 5 (54.9–10.6 pmol/L), with sustained normocalcemia (2.25 mmol/L) at 10 days without further need for cinacalcet.

CONCLUSION

This case illustrates that PEA can serve as definitive therapy for PHPT in patients unsuitable for surgery. It provides rapid and sustained biochemical control, while avoiding operative risk, supporting its role in individualized management.

EP_A092

EXPANDING THE SPECTRUM OF VITAMIN D-DEPENDENT RICKET TYPE 2: DOMINANT-NEGATIVE VDR MUTATION AND POSTPUBERTAL CALCIUM ADAPTATION

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INTRODUCTION

Vitamin D-dependent rickets type 2 (VDDR2) is traditionally defined by biallelic vitamin D receptor (VDR) mutations causing resistance to $1,25(OH)_2D$. We describe a case of the classical VDDR2 phenotype with a single VDR mutation and an interesting physiological adaptation.

CASE

A female diagnosed with rickets at age three presented with a femoral fracture, severe short stature, hypocalcemia (2.1 mmol/L; NR 2.35–2.70), hypophosphatemia (0.8 mmol/L; NR 1.5–2.10), and evidence of renal phosphate wasting (TMP/GFR 0.5 mmol/L; NR 1.5–2.4). Biochemistry showed markedly elevated alkaline phosphatase (1,227 IU/L; NR 50–136) and secondary hyperparathyroidism (20.7 pmol/L; NR 0.8–7.8). Despite hypocalcemia, $1,25(OH)_2D$ was significantly elevated (>450 pmol/L; NR 60–150), consistent with VDDR2. There was no initial family history; however, subsequent evaluation of her mother—prompted by the patient's diagnosis—revealed a similar biochemical profile, along with short stature (142 cm) and a history of multiple fractures. Genetic analysis in both individuals identified a heterozygous missense mutation in exon 10 of the VDR gene, affecting the ligand-binding domain, supporting a pattern of dominant inheritance. The patient was treated with cholecalciferol (1,200 IU daily), calcitriol (5–6 µg daily), and calcium carbonate (2,000 mg daily). Although biochemical responsiveness to therapy was evident, poor adherence resulted in suboptimal metabolic control throughout childhood and adolescence, including a second fracture at age 15 and a final adult height of 124 cm. Notably, calcium and phosphate levels progressively normalized after puberty, with sustained biochemical stability despite the patient omitting the treatment.

CONCLUSION

This case provides two important insights. First, it represents the fourth reported case worldwide demonstrating a dominant-negative effect of a VDR gene mutation, whereby a single mutant receptor interferes with wild-type VDR function. Second, it highlights postpubertal calcium adaptation, in which vitamin D–independent intestinal absorption may restore mineral homeostasis, and disease severity can attenuate over time through adaptive physiological mechanisms.

EP_A093

GIANT PARATHYROID ADENOMA WITH DELAYED HUNGRY BONE SYNDROME: A CASE REPORT

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INTRODUCTION

Giant parathyroid adenomas (GPAs), defined as lesions >3.5 g, are rare. Their size, biochemical severity, and compressive features often mimic carcinoma, creating diagnostic and surgical challenges.

CASE

A 33-year-old female was incidentally found to have hypercalcemia during evaluation after her newborn developed severe hypocalcemic seizures requiring NICU admission. Maternal calcium was 2.95 mmol/L with hypophosphatemia. Subsequent reviews showed persistent hypercalcemia (3.15–3.3 mmol/L), hypophosphatemia (0.32–0.51 mmol/L), and markedly elevated intact parathyroid hormone (85–96 pmol/L). She had vitamin D deficiency, very high alkaline phosphatase (1,329 U/L), and progressive

bone pain with reduced mobility. Bone mineral density revealed Z scores of −2.9 (hip) and −3.3 (lumbar spine).

Multiphase computed tomography demonstrated a multilobulated 6.9 cm mass extending from C5 to T2, compressing the esophagus and raising suspicion for carcinoma. Endoscopic evaluation excluded mucosal invasion. She underwent en bloc left inferior parathyroidectomy with hemithyroidectomy. Intraoperative parathyroid hormone fell from 41.7 to 13.4 pmol/L, confirming complete excision. The gland measured 65 × 20 × 15 mm and weighed 18.4 g. Histopathology revealed a hypercellular parathyroid tumor with endocrine atypia but no invasion, consistent with a giant adenoma.

Postoperatively, calcium was initially stable (1.99 mmol/L at discharge) but fell to 1.68–1.82 mmol/L at 2 weeks despite high-dose supplementation. Hypocalcemia persisted for 6 weeks, consistent with delayed hungry bone syndrome, likely precipitated by preoperative vitamin D deficiency, markedly elevated alkaline phosphatase, and low bone mineral density. With intensive supplementation, calcium gradually stabilized, and symptoms improved.

CONCLUSION

GPAs can closely mimic carcinoma, with endocrine atypia complicating histopathological interpretation. This case illustrates both diagnostic overlap and the unusual, delayed onset of hungry bone syndrome, emphasizing the need for preoperative risk assessment, correction of metabolic deficiencies, and extended postoperative monitoring. Rare presentations such as delayed hungry bone syndrome refine management strategies and improve outcomes in primary hyperparathyroidism.

EP_A094

CLINICAL USE OF DENOSUMAB FOR REFRACTORY HYPERCALCEMIA: A RETROSPECTIVE CASE SERIES

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INTRODUCTION

Severe hypercalcemia is most commonly caused by primary hyperparathyroidism (PHPT) and malignancy. While standard therapies are effective in most cases, a subset of patients have persistent or refractory hypercalcemia. We present a retrospective case series detailing the clinical characteristics, biochemistry, and outcomes of patients treated with denosumab for hypercalcemia.

CASES

Seven patients with severe hypercalcemia were identified, comprising five with PHPT and two with malignancy-associated hypercalcemia. The mean age was 70.4 years (range 55–86), with 71% female (n = 5) and 29% male (n = 2). Baseline corrected calcium ranged from 2.92 to 4.59 mmol/L, with a mean of 3.26 mmol/L. In the PHPT cohort, parathyroid hormone (PTH) levels were significantly elevated (16.7–168 pmol/L), while malignancy patients had suppressed PTH (0.6 and 0.9 pmol/L).

Prior to denosumab, 4/7 patients (57%) received bisphosphonates, 3/7 (43%) received calcitonin, and 1/7 (14%) was treated with cinacalcet. Denosumab resulted in a mean reduction in corrected calcium of 0.22 mmol/L from 3.26 to 3.03 mmol/L.

Biochemical response was observed in 5/7 patients (71%). Of these, 3 patients (43%) achieved normocalcemia, while 2 patients (29%) demonstrated a partial response. The remaining 2/7 patients (29%) showed no significant improvement in calcium levels. Among responders, the mean time to calcium reduction to <3.0 mmol/L was 27 days (range 7–47). Repeat dosing was required in the majority of patients, with a mean of 1.7 doses per patient (range 1–4), indicating variability in both onset and durability of response. Among patients with PHPT, four underwent parathyroidectomy, and one declined surgery. Both patients with malignancy were managed nonsurgically.

CONCLUSION

Denosumab achieved normocalcemia in 43% of patients, with additional partial responses. Its effects were variable, with delayed response and frequent need for repeat dosing, supporting its role as an adjunctive or bridging therapy rather than as a definitive treatment.

EP_A095

THE HIGH BONE DENSITY PARADOX: PRIMARY HYPERPARATHYROIDISM IN THE SETTING OF OSTEOPETROSIS

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INTRODUCTION

Primary hyperparathyroidism (PHPT) is a common disorder that typically leads to increased bone turnover and reduced bone mineral density (BMD). Osteopetrosis, in contrast, is a rare, inherited disorder of defective osteoclast function, resulting in diffusely sclerotic but structurally fragile bones. The coexistence of both conditions is rare and can significantly alter the expected skeletal phenotype of PHPT.