Refractory Hypercalcemia of Malignancy: Responsiveness to Denosumab and Zoledronate

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Background

Hypercalcaemia secondary to malignancy is rare in children and adolescents. PTH-rP (Parathyroid hormone related peptide) secreted by malignant cells is an important humoral factor that increases bone resorption and renal calcium retention causing hypercalcaemia. We report 2 cases of hypercalcaemia of malignancy refractory to treatment with pamidronate and corticosteroids but responsive to treatment with Denosumab and Zoledronic acid.

Case 1

A 17-year-old boy with epidermolysis bullosa presented with advanced squamous cell carcinoma of the left leg and symptomatic hypercalcaemia (serum adjusted calcium, 4.2mmol/l). PTH was suppressed at 0.7pmol/l. Serum 25 hydroxy vitamin D level was 31nmol/l (normal range > 50nmol/l). PTH-rP and 1, 25 dihydroxy vitamin D levels were elevated at 2.1pmol/l (0.0-1.8) and 173pmol/l (43 – 143) respectively. The management is shown below(Figures 1,2,3).

Figure 1: Initial management of Hypercalcaemia (Week 1) HH denotes hyper hydration

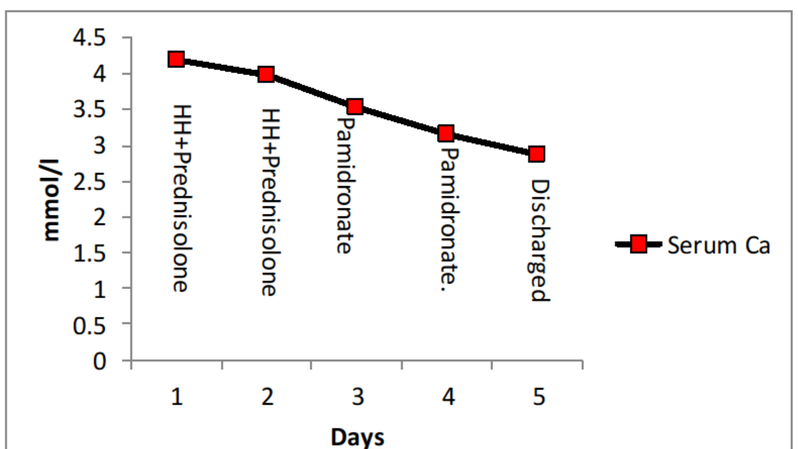


Figure 2: Management of Hypercalcaemia (week 2)

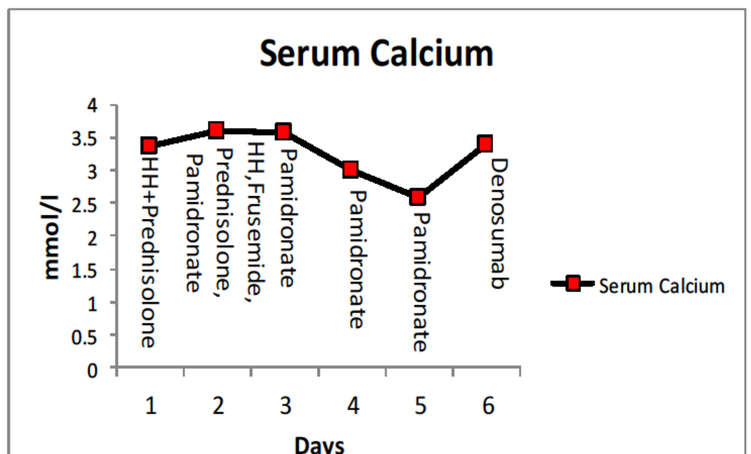
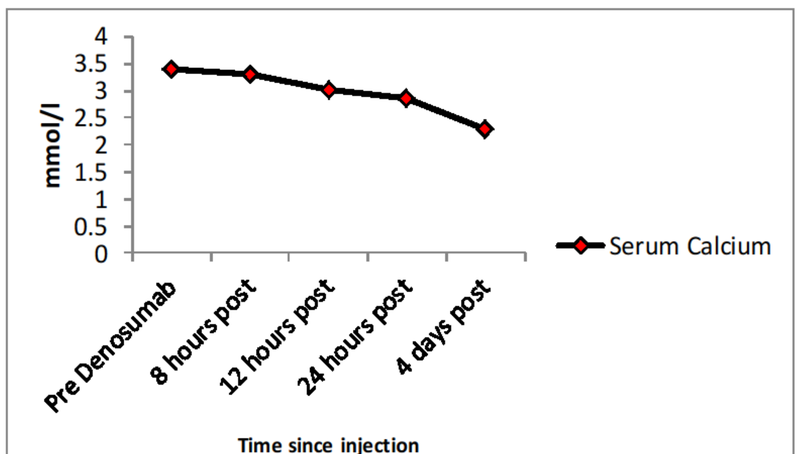


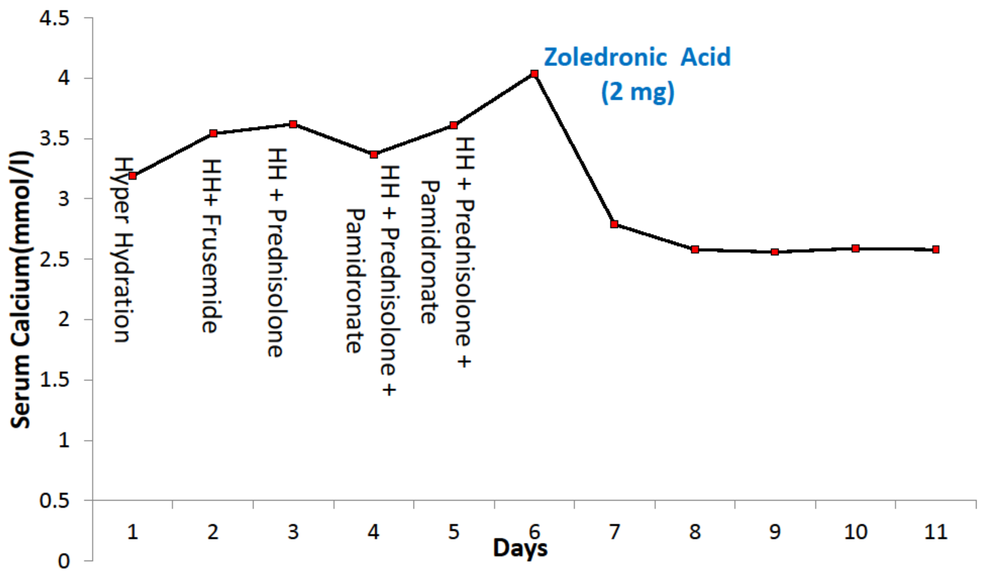
Figure 3: Response to Denosumab (60mg subcutaneous injection)No significant side effects to treatment noted



Case 2

A 17-year-old girl with pelvic rhabdomyosarcoma was hypercalcemic (serum adjusted calcium, 3.19mmol/l) with supressed PTH of 0.3pmol/l and serum phosphate of 2.2 mmol/l. Serum 25 hydroxy Vitamin D was 28nmol/l and renal profile was normal. The management is as shown in the graph below(Figure 4).

Figure 4: Management of Hypercalcemia. HH denotes Hyper Hydration



Discussion

Denosumab is a monoclonal antibody which neutralises RANKL (receptor activator of nuclear factor kappa-B ligand), inhibiting the function of osteoclasts thereby preventing generalized bone resorption. Zoledronic acid blocks osteoclast resorption and has a more potent calcium-lowering effect than pamidronate. These two drugs widen the treatment options for patients with refractory hypercalcaemia of malignancy.

Reference

Denosumab for Treatment of Hypercalcemia of Malignancy. J Clin Endocrinol Metab. 2014 Jun 10:jc20141001. Hu MI1, Glezerman IG, Leboulleux S, Insogna K, Gucalp R, Misiorowski W, Yu B, Zorsky P, Tosi D, Bessudo A, Jaccard A, Tonini G, Ying W, Braun A, Jain RK.

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