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CASE REPORT ON AN EFFECTIVE AGENT IN MANAGING HYPERCALCEMIA WITH SEVERE RENAL IMPAIRMENT

Mahesh D. M.*, Vinay Patil, Praveen Kumar and Anand Srivastava

India.

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***Corresponding Author**
Mahesh D. M.
India.

ABSTRACT

Bisphosphonates are first line drugs in the acute management of hypercalcemia in those with normal kidney function, but are contraindicated in those with patients with low GFR. In those with renal dysfunction, both over hydration and bisphosphonates cannot be used, thus making it difficult to reduce calcium levels and hence patients are subjected to haemodialysis and its risks. We report a case of bilateral renal calculi and acute kidney injury secondary to primary hyperparathyroidism (PHPT) with severe hypercalcemia (12.3 mg/dL), in whom denosumab (RANKL inhibitor) was used to effectively lower the calcium levels.

KEYWORDS: Hypercalcemia, Renal dysfunction, Hyperparathyroidism, Denosumab.

INTRODUCTION

Acute management of hypercalcemia includes hydration and Bisphosphonates as are first line drugs. However bisphosphonates are contraindicated in those with renal dysfunction, thus making it difficult to reduce calcium levels and hence patients are subjected to haemodialysis and its risks. We report a case of acute kidney injury secondary to severe hypercalcemia in whom we used denosumab (RANKL inhibitor) to effectively reduce the calcium levels.

CASE REPORT

We present a 65-year-old gentleman who was admitted with vomiting, abdominal pain, bone pain, muscle pain and weakness for 2-3 weeks. He also had reduced urine output for 2 days prior to admission. On evaluation he had raised urea and creatinine levels [Table-1] with estimated Glomerular filtration rate (GFR) of 28.65 mL/min/1.73 m^2. On abdominal ultrasonography he had bilateral renal calculi (Left >Right) with right mid ureteric calculus (6.5 x 4.0 mm) just below the level of iliac vessels crossing at S2 sacral level with proximal

hydroureteronephrosis. He underwent URS DJ STENTING 04/11/19]. His albumin corrected serum calcium at presentation was 12.23 mg/dL and intact PTH was 1,897pg/mL (*N* = 8–50). USG neck revealed Large well defined hypo echoic focal lesion measuring 3.7 x 2.0 x 2.4 cm posterior to the right lobe of thyroid- likely representing parathyroid adenoma. Hence he was diagnosed to have primary hyperparathyroidism (PHPT) with severe hypercalcemia. He was treated with saline with which calcium declined to 11.2 mg/dL. However, after 72 h, his serum calcium levels remained >11 mg/dL. In view of persistent vomiting and refractory hypercalcemia in the background of renal dysfunction disease, we used denosumab, a Rankl inhibitor, as bisphosphonates were contraindicated due to low GFR.[1] Following administration of denosumab 60mg subcutaneously, his calcium level reduced to 9.7 mg/dL in 48 hours. His symptoms got better and serum creatinine reduced to 2.52mg/dl.

Table 1: Serial serum lab parameters before and after giving injection denosumab.

Serum levels [normal]	At admission	Day 1 Post Denosumab	Day 3 Post Denosumab
CALCIUM [8.6-10.4mg/dl]	12.23	11.2	9.7
ALBUMIN [3.5-4.5g/dl]	3.8	4.0	3.8
CREATININE [0.8-1.1]	4.20	3.44	2.52
UREA [< 20 mg/dl]	103.7	95	56.4
Sodium [136-145 mEq/L]	139	141	141
Potassium [3.6-5.0mEq/L]	5.92	5.26	4.2
Bicarbonate (22-24mmol/L]	12	15	19.8

DISCUSSION

Acute hypercalcemia is a rare but potential life-threatening condition. Management for hypercalcemia should be aimed both at lowering the serum calcium concentration and, if possible, correcting the underlying cause. Treatments that effectively reduce serum calcium include those inhibiting bone resorption, increase urinary calcium excretion, or decrease intestinal calcium absorption. The appropriate choice varies with severity of hypercalcemia and renal function. Bisphosphonates are one of first line drugs approved for the treatment of acute hypercalcemia in patients with normal renal function. Denosumab, a fully human IgG2 monoclonal antibody against RANKL, is an alternate option in hypercalcemia that is refractory to bisphosphonates or contraindicated with its use. Denosumab interferes with RANKL signalling inhibits the maturation, function and survival of osteoclasts and thereby inhibits bone resorption.[2] Bisphosphonates like zoledronic acid are contraindicated in those with low GFR. Unlike bisphosphonates, denosumab is not cleared by the kidney, and hence, it can be safely used in patients with chronic kidney disease.[3] Though denosumab has been

approved and used for hypercalcemia of malignancy, literature is limited on its use in patients with refractory hypercalcemia secondary to primary hyperparathyroidism with acute kidney injury prior to surgery excision of parathyroid.[4] Although calcimimetic like cinacalcet has been utilized in PHPT, its impact on reducing calcium is not usually immediate and may lead to worsening of nephrocalcinosis.[5] The median time to response (time taken to lower calcium to <11.5 mg/dL) for denosumab has been described as 9 days (7–10 days).[6] in our patient, the serum calcium decreased by day 3. In view of its renal safety and quick action, our case demonstrates that denosumab is a potential drug for lowering calcium levels and safe especially in those with renal impairment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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