ORIGINAL RESEARCH PAPER
Volume - 15 | Issue - 08 | August - 2026 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

MULTIFACTORIAL HYPOCALCEMIA: AN INTERESTING CASE REPORT

Internal Medicine

Dr Sanjay P Khare Head-Academics and Clinical Training: Apollo Hospital Navi Mumbai
Dr Minal Chaudhary DNB Student Apollo Hospital Navi Mumbai

ABSTRACT

It is always a challenge to diagnose a patient accurately, ESPECIALLY from the wrong side of presentation. For example, It is easy to wax eloquent theoretically on any given topic, but to correctly diagnose the exact aetiopathology from an incoherent patient and that too in an emergency situation is indeed good applied medicine. Here we describe a complicated case with multifactorial aetiology.

KEYWORDS

Denosumab, Severe Hypocalcaemia, Secondary Hyperparathyroidism, Vitamin D Deficiency, Renal Insufficiency, Calcium Supplementation, Pleural Mesothelioma.

CASE PRESENTATION

A 56-year-old male presented with vague nonspecific complaints of muscle cramps in back and calves, tingling, Numbness (especially periorally and in extremities), irritability, Reduced intellectual/social capacity and was reported by his relatives as "having withdrawn with reduced alertness". He was visibly uncomfortable and grossly symptomatic and hence had been brought to ER by his relatives.

The patient was a known case of hypertension, hypocortisolism, and dilated cardiomyopathy (DCMP). He had been diagnosed a few months earlier with left-sided pleural mesothelioma with bony metastasis and was undergoing immunomodulatory therapy. On further enquiry, it was noted that he had received denosumab therapy approximately two weeks prior to current Presentation. Although calcium and vitamin D supplementation had been prescribed, he had omitted taking it.

On admission, the patient was hemodynamically stable. Clinical examination revealed signs suggestive of neuromuscular irritability without focal neurological deficit. Chvostek sign and Trosseau sign were positive. Clinically itself hypocalcemia was thought of and proven over next few minutes.

LABORATORY INVESTIGATIONS:

Test	Day 1	Day 3	Ref Value
Total Ca.	<5.0	5.0	8.6–10.2 mg/dL
Ionic Calcium	0.5	—	1.05–1.30 mmol/L
P.	2.0	—	2.5–4.5 mg/dL
Mg.	1.3	1.8	1.6–2.6 mg/dL
Creatinine	1.59	1.42	0.9–1.3 mg/dL
Vit. D	17.6	—	30–100 ng/mL
PTH	598.7	—	10.0–65 pg/mL
Albumin	2.8	—	3.5–5.2 g/dL

Corrected Calcium: 5.96 mg/dL

The patient also had microalbuminuria. Ultrasonography of the neck was performed to evaluate for alternative causes of hyperparathyroidism; however, no significant abnormality was detected.

The markedly elevated PTH in the setting of profound hypocalcemia was suggestive of Secondary hyperparathyroidism following CKD, precipitated by denosumab therapy, compounded by underlying vitamin D deficiency and worsened by noncompliance with recommended supplementation.

MANAGEMENT

Once diagnosis was secured, total deficit was calculated by the formula (Corrected Calcium=Measured Calcium+ 0.8 * (4.0- Pt's serum Albumin).

The patient was initiated on multiple doses of intravenous calcium gluconate administered at Fixed intervals, followed by oral calcium supplementation. Hypomagnesemia causes resistance to effects of administered Ca and Vit d, blocks PTH action in bone and kidneys and also causes reduced PTH secretion. Vit D is an important cofactor for normal PTH action and needs to be corrected urgently. Concurrent correction of Hypomagnesemia was achieved using intravenous magnesium sulphate ($MgSO_4$). Vitamin D replacement therapy was also initiated with oral vitamin D capsules.

Supportive management included adequate hydration and optimization of antihypertensive therapy. The dose of fludrocortisone was reduced considering the underlying clinical status and finally omitted altogether.

Renal function was closely monitored, and serum creatinine demonstrated gradual Improvement during hospitalization.
High Calcium and low Phosphate diet was recommended and implemented.

OUTCOME AND FOLLOW-UP

The patient remained hemodynamically stable throughout the hospital stay and demonstrated significant clinical improvement with resolution of neuromuscular symptoms and improved responsiveness. Although biochemical hypocalcemia persisted at the time of discharge, the patient was asymptomatic. He was discharged on oral calcium and vitamin D supplementation with advice for strict compliance and scheduled follow-up for serial calcium monitoring.

DISCUSSION

A standard adult has around 1.2 Kg of Calcium in body. More than 99% is lodged inside the bones. 50% of total calcium is ionized, 40% is protein bound and 10% circulates bound to ions like Phosphate, Carbonate etc. Ionized Calcium is credited with diverse physiological functions like neuromuscular transmission, Membrane stability, Bone structure, Blood coagulation, intracellular signalling, muscle contraction/relaxation etc. Needless to say, deficits in this important ion will auger poorly for sustenance of life itself.

Hypocalcemia is defined as total serum Calcium below 8.8 mg/dl or ionised calcium below 4.7 mg/dl. It may be acquired (more common) and hereditary/genetic (relatively few incidences).Common causes are hypoparathyroidism, Liver and Kidney disorders, poor diet, medications and surgery. Medications (Denosumab) too play an important contributory part. CKD causes decreased conversion of 25-Hydroxy vitamin D to its active form-1, 25-dihydroxyvitamin D which causes PTH secretion to flare up. Denosumab, a monoclonal antibody against receptor activator of nuclear factor kappa-B Ligand (RANKL), is commonly employed in the treatment of osteoporosis and Malignancy-related skeletal metastasis. Although generally well tolerated, it can precipitate significant hypocalcaemia, especially in individuals with renal impairment[2], vitamin D deficiency, or inadequate calcium supplementation. Severe hypocalcemia may manifest withneuromuscular symptoms, altered sensorium, and potentially fatal complications and may result in significant mortality and morbidity. Denosumab inhibits osteoclast formation, decreases bone resorption, increases bone mineral density and reduced fracture

risk. However, this comes at a risk of potential hypocalcemia and patients MUST be supplemented with calcium.

This case highlights the serious metabolic consequences associated with denosumab therapy, particularly on background of renal insufficiency, vitamin D deficiency, and inadequate adherence to calcium supplementation.

The resultant hypocalcemia triggered marked secondary hyperparathyroidism, evidenced by significantly elevated PTH levels. Timely diagnosis and aggressive correction of calcium, magnesium, and vitamin D deficits were crucial in preventing further neurological and cardiovascular complications. This case underscores the need for baseline assessment of calcium, vitamin D, and renal function before initiating denosumab therapy, along with continuous patient education regarding adherence to supplementation.

CONCLUSION

Hypocalcemia can be severe and potentially life-threatening, especially in patients with underlying renal dysfunction, vitamin D deficiency, Hypomagnesemia and poor compliance with calcium supplementation[3] especially on background of treatment with Denosumab.. Careful patient selection, regular biochemical monitoring, and strict adherence to calciumand vitamin D supplementation are essential to prevent adverse outcomes. Early recognition and prompt management can significantly reduce morbidity and prevent further clinical deterioration.

LEARNING POINTS

- Hypocalcemia should always be thought of especially in quaternary care hospitals.
- Calcium and vitamin D supplementation must be ensured in all patients receiving Denosumab therapy.
- Patients with renal insufficiency and vitamin D deficiency are particularly vulnerable to severe denosumab-induced hypocalcemia.
- Baseline and periodic monitoring of calcium, vitamin D, and renal function are essential during therapy[4].
- Proper counselling regarding compliance with supplementation can prevent potentially fatal complications.

It is a good idea to NOT to be happy with a single aetiology especially at level of a Quaternary hospital. Multiple aetiogies are often found.

REFERENCES:

1. Dadana S, Gundepalli S, Kondapalli A. Severe Refractory Hypocalcemia Caused by Denosumab. Cureus. 2023 Jun 2; 15(6):e39866. doi: 10.7759/cureus.39866. PMID: 37404446; PMCID: PMC10315058.
2. Jalleh R, Basu G, Le Leu R, Jesudason S. Denosumab-Induced Severe Hypocalcaemia in Chronic Kidney Disease. Case Rep Nephrol. 2018 Nov 4; 2018:7384763. doi: 10.1155/2018/7384763. PMID: 30519493; PMCID: PMC6241374.
3. Kalayanamitra R, Yaghnam I, Patel R, Groff A, Jain R. The Calcium Culprit: A Case Of Denosumab-induced Hypocalcemia. Cureus. 2019 May 28; 11(5):e4768. doi: 10.7759/cureus.4768. PMID: 31363449; PMCID: PMC6663059.
4. McCaleb RV, Johnson JT. SEVERE, PROLONGED, DENOSUMAB-INDUCED HYPOCALCEMIA WITH RECOVERY AFTER 111 DAYS OF HIGH-DOSE CALCIUM SUPPLEMENTATION. AACE Clin Case Rep. 2019 Jan 30; 5(1):e82-e85. doi: 10.4158/ACCR-2018-0295. PMID: 31967007; PMCID: PMC6876976.