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Case Report: Denosumab Induced Hypocalcemia Refractory to Calcium Supplementation

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Abstract

A 70 years old female with PMH of CAD, Hyperlipidemia and recently diagnosed poorly differentiated carcinoma of unknown primary with diffuse bone metastases presented to the ED with hypotension, diaphoresis and tachycardia. Nine days before presenting to the ED she was started on Nivolumab and Denosumab. She was initially admitted with sepsis but later no source of infection was found, and antibiotics were stopped on day three. On the day of admission her calcium was 7.3mg/dl, whereas one month back it was in the normal range, which further decreased to 5.8mg/dl on 3rd day of admission. Because of her worsening hypocalcemia her Vitamin D, phosphorus and PTH level was also checked. It was noted that Vit D and phosphorus were decreased and PTH was increased. Despite the calcium gluconate her calcium level were not increasing. Nephrology was consulted and was started on calcitriol and ergocalciferol. Subsequently her calcium level started to rise and went up to 7.3, four days after initiation of therapy.

Keywords: Nephrology; Hypotension; Diaphoresis; Tachycardia; Symptomatic hypocalcemia; Sarcomatoid

Introduction

Denosumab is human monoclonal antibody, RANKL inhibitor which works by preventing the development of osteoclasts. It is used for the treatment of osteoporosis, treatment-induced bone pain, bone metastasis, and giant cell tumor of the bone. One of the side effects of this medication is hypocalcemia and sometimes can cause severe symptomatic hypocalcemia. Levels of calcium should be measured before starting therapy and levels should be checked frequently after the start of therapy. Other calcium lowering drugs also should be taken into consideration before starting the medication. Our patient did not have calcium level taken at the time of medication nor had prior vitamin D and PTH level.

Case Presentation

A 70 years old female with PMH of COPD, CAD, Hyperlipidemia, depression and recently diagnosed with poorly differentiated carcinoma of unknown primary with diffuse bone metastases with sarcomatoid features presented to the ED with hypotension, diaphoresis and tachycardia with heart rate of around 120s. For her metastatic cancer she was started on Nivolumab 240mg every 2 weeks and Denosumab 120mg/month. 9 days after the first dose of Denosumab she presented to the ED. She was initially admitted with sepsis but later no source of infection was found, and antibiotics were stopped on day 3. On the day of admission her calcium was 7.3mg/dl, whereas 1 month back it was in the normal range ranging from 8.6-9.4mg/dl, which further decreased to 5.8mg/dl on 3rd day of admission. Patient also started to develop back spasm so was given calcium gluconate. Because her calcium was decreasing, her Vitamin D, phosphorus and PTH levels were also checked. Vitamin D was <12.8ng/ml, phosphorus was 1.4mg/dl and intact PTH was 564.1pg/ml. Despite the calcium gluconate her Calcium level were not increasing. Nephrology was consulted and was started on calcitriol 0.2mg daily and ergocalciferol 50,000U weekly for vitamin D deficiency. Subsequently her calcium level started to rise and went up to 7.3 at the time of discharge 4 days after initiation of therapy.

Discussion

Denosumab is a human monoclonal antibody given subcutaneously. It inhibits osteoclast mediated bone resorption in bone metastases from solid tumors and multiple myeloma. It blocks the RANK ligand from activating the osteoclasts. Tumor cell stimulates osteoblast to release RANK ligand, which in turn binds to RANK receptor in osteoclast and stimulates them to increase bone resorption. It is used for the prevention of skeletal-related events in patients with bone metastases from solid tumors. The recommended dose is 120mg subcutaneously every four weeks [1].

The side effects of Denosumab include increased serious infection risk, nonspecific dermatologic reactions and hypocalcemia [2]. Various case reports have been reported for denosumab induced hypocalcemia. The use of denosumab is associated with a significantly increased risk of developing hypocalcemia [3]. There have also been case reports on denosumab causing hypocalcemia in a patient with kidney disease [4].

A patient with low levels of vitamin D has a higher chance of getting hypocalcemia after denosumab. Level of calcium, phosphorus and vitamin D level should be checked and replaced before starting the therapy [1]. In the case of our patient, calcium level was one month old and vitamin levels were never checked before initiation of therapy, which might be the cause of her severely decreased calcium level. Mostly the hypocalcemia can be reversed by supplementation of oral or IV calcium. But in our case the patient was resistant to calcium supplementation.

There are some case reports in the literature for resistant hypocalcemia after denosumab therapy [5]. The preexisting vitamin D deficiency predisposes the patient to go into severe hypocalcemia and is refractory to calcium supplementation unless vitamin D is given.

Conclusion

Hypocalcemia is a known consequence of denosumab infusion and preexisting vitamin D deficiency predisposes the patient to go into severe hypocalcemia, which is resistant to calcium supplementation and may require vitamin D therapy.

References

1. Muqeet Adnan M, Bhutta U, Iqbal T, Abdul Mujeeb S, Haragsim L, et al. (2014) Severe Hypocalcemia due to Denosumab in Metastatic Prostate Cancer. Case Reports Nephrol 2014(565393): 1-3.
2. Anastasilakis AD, Toulis KA, Polyzos SA, Anastasilakis CD, Makras P (2012) Long-term treatment of osteoporosis: Safety and efficacy appraisal of denosumab. Ther Clin Risk Manag 8: 295-306.
3. Qi WX, Lin F, He AN, Tang LN, Shen Z, et al. (2013) Incidence and risk of denosumab-related hypocalcemia in cancer patients: a systematic review and pooled analysis of randomized controlled studies. Curr Med Res Opin 29(9): 1067-1073.
4. McCormick BB, Davis J, Burns KD (2012) Severe Hypocalcemia Following Denosumab Injection in a Hemodialysis Patient. Am J Kidney Dis 60(4): 626-628
5. Ali N, Farhat S, Imran S, Jafri M, Ahmed A, et al. (2016) Severe Refractory Hypocalcemia in a Patient with Metastatic Prostate Carcinoma Following Denosumab Injection. Journal of Clinical Case Reports 6(7): 7-9.

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