Symptomatic hypocalcemia following intravenous administration of zoledronic acid in a breast cancer patient

Mishra A

Bisphosphonates are increasingly being incorporated in the management of patients with breast cancer.[1] With wider adoption of bisphosphonates, the incidence of some rare complications like hypocalcaemia might go up, particularly in vitamin D deficient populations. Here we would like to share our experience of managing a patient, who developed symptomatic hypocalcaemia after intravenous (IV) infusion of zoledronic acid, to highlight the need of anticipating this preventable, and potentially fatal complication.

A 70-year-old lady presented to us with right breast cancer with multiple skeletal metastases. She was put on chemotherapy along with three-weekly IV infusion of 4 mg zoledronic acid. Her serum calcium (10.5 mg%) and creatinine (0.9 mg/L) were within normal limits. After receiving the second dose of zoledronic acid she developed symptomatic hypocalcaemia. She initially complained of tingling and numbness and later became irritable. Serum calcium estimation was done and it was 6.2 mg% (range 8.4-10.4 mg%), serum albumin was 2.39%. Serum creatinine, sodium, potassium and electrocardiogram recordings were within normal limits. Hypocalcemia was managed with IV calcium gluconate followed later with oral calcium and Vitamin D supplementation. Simultaneously, serum 25 hydroxy vitamin D level was estimated and was found to be grossly low (<5 ng/mL, normal range: 9-47 ng/mL) indicating preexisting vitamin D deficiency. Patient was put on therapeutic doses of Vitamin D along with daily calcium supplementation. Naranjo adverse drug reaction probability score indicated a possible relationship (Score 3) between symptomatic hypocalcaemia and zoledronic acid therapy in this patient.[2] We now estimate serum Vitamin D levels in all patients likely to receive bisphosphonates and correct Vitamin D deficiency if found so.

Bisphosphonates, in general have a good safety profile. Though mild biochemical hypocalcaemia is common with administration of bisphosphonates, there are anecdotal reports of patient developing symptomatic hypocalcaemia following IV administration of pamidronate or zoledronic acid.[3-7] Overall, the rate of development is related with the potency of the bisphosphonate. In most of the published reports, apart from nutritional deficiency of Vitamin D, impaired renal function had been sighted as the main reason for development of symptomatic hypocalcaemia. Renal insufficiency leads to impaired conversion of Vitamin D to its active metabolite (1,25, hydroxy Vitamin D), and is a possible contributory cause of hypocalcaemia.[3-7]

Bisphosphonates are likely to be used more frequently in future. In Vitamin D deficient populations like ours, there is a huge number of potentially vulnerable patients for developing symptomatic hypocalcaemia. Therefore, there is a need for greater awareness and taking precautionary measures to prevent this potentially life-threatening complication.

References