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BCG-Osis, a Rare Cause of 1,25 Hydroxy Vitamin D Mediated Hypercalcemia

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Background: Non-parathyroid hormone (PTH) mediated hypercalcemia is mostly related to malignancy and less commonly caused by granulomatous diseases. We report a rare case of severe hypercalcemia caused by systemic granulomatous disease after intravesical Bacillus Calmette-Guerin (BCG) treatment for bladder cancer (BCGosis). **Clinical Case:** 74-year-old male with history of bladder cancer treated with intravesical BCG a year ago, was hospitalized with confusion, weakness, recurrent falls and polyuria for a few days. He had night sweats and 50 lb weight loss over 6 months. Lab evaluation showed hypercalcemia with calcium 10.9 mg/dL, albumin 3.6 g/dL, corrected calcium 11.2 mg/dL, PTH 12 pg/ml, and 25 OH vitamin D 44ng/ml. He had normal thyroid hormone levels, serum electrophoresis and PTHrP <2 pmol/L. CT chest/abdomen/pelvis without contrast revealed sub-cm pulmonary nodules and non-obstructive renal calculi and bone scan showed no evidence of osseous metastases. He was treated with intravenous (IV) hydration and pamidronate 60 mg infusion, and his corrected calcium improved to 9.7 mg/dL. He was admitted again 3 weeks later with hypercalcemia, calcium 11.9 mg/DL, albumin 3.2 g/dL, corrected calcium 12.5 mg/dL, 25 OH vitamin D 24 ng/ml, PTH 14.6 pg/ml, and PTHrP <2 pmol/L. He received IV hydration and zoledronic acid 4 mg infusion. 3 weeks later he was hospitalized for the third time for recurrent hypercalcemia and worsening renal failure, calcium 13.2, albumin 2.6 g/dL, corrected calcium 14.2 mg/dL, PTH 19.2 pg/ml. 1,25 OH vitamin D checked this time was elevated at 113 pg/mL. He received another infusion of zoledronic acid 4 mg infusion and 10 days later required denosumab 120 mg for resistant hypercalcemia. PET CT scan showed multiple hypermetabolic foci in right neck, right anterior 4th rib, scrotum, and around left kidney and aorta. He underwent biopsy of the right rib lesion which demonstrated + AFB on smear and histiocytic inflammation, which led to diagnosis of BCGosis, with subsequent cultures positive for Mycobacterium bovis. He was started on multi drug regimen with rifampin, isoniazid and ethambutol. Follow up labs at 4 weeks showed normalization of calcium 8.9 mg/dL, albumin 3.2 g/dL, corrected calcium 9.78 mg/dL, PTH 54 pg/ml and low 1,25 OH vitamin D 17 pg/mL. Calcium and 1,25 OH vitamin D levels were stable at 4 months follow up. **Conclusion:** Intravesical BCG treatment can be associated with systemic reactions in 1- 5% of patients. Granulomas associated with disseminated BCG infection can lead to hypercalcemia due to increased 1-alpha-hydroxylase activity in macrophages, causing elevated 1,25 OH vitamin D levels. Therefore, evaluation of 1,25 OH vitamin D levels is critical to determine the etiology of hypercalcemia. Treatment of underlying BCGosis with anti-tuberculosis treatment is key in management of hypercalcemia along with supportive treatments that may include IV hydration, bisphosphonates and/or glucocorticoids.

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