MANAGEMENT OF 1,25-DIHYDROXYVITAMIN D (1,25-OHD) MEDIATED HYPERCALCEMIA OF UNKNOWN ETIOLOGY

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Background: We describe the diagnostic dilemma and treatment challenges faced in a rare case of 1,25-OHD mediated hypercalcemia.

Materials/Methods: Case report

Results: A 13 year old boy presented with hypercalcemia (calcium 15.5 mg/dl), a non-specific rash, malaise, pancytopenia and acute kidney injury. He was incidentally also noted to have hypogammaglobulinemia a few months prior to presentation. Labwork was suggestive of hypercalcemia mediated by 1,25-OHD (level >200 pg/ml). 25-hydroxy vitamin D was normal (29 ng/ml) and PTH was appropriately suppressed (<4 pg/ml). Workup for various etiologies associated with ectopic production of 1,25-OHD was initiated. Hypercalcemia was initially managed with intravenous hydration, furosemide and calcitonin. However after a brief period of improvement, calcium levels started to rise again despite increasing calcitonin dose and frequency. Kidney function also started to worsen. Extrarenal 1-alpha hydroxylase activity can be suppressed using steroid therapy, however it was contraindicated at the time given that malignancy and other infectious etiologies had not been excluded. At that point, a trial of zoledronic acid was done with subsequent resolution of hypercalcemia. However, this was only temporary given that the underlying disease process driving the production of 1,25-OHD had not been addressed. Various other treatment options were considered including a repeat dose of bisphosphonate, denosumab, ketoconazole and hydroxychloroquine, but since hypercalcemia was only mild, supportive measures were continued. An extensive workup revealed splenomegaly, lymphadenopathy, bilateral renomegaly and bilateral pulmonary ground glass opacities and nodules. Infectious workup and bone marrow biopsy were negative. An elevated angiotensin converting enzyme (ACE) level (359 units/L) suggested an underlying granulomatous process and renal biopsy showed non-caseating granulomas. The most likely diagnosis was thought to be sarcoidosis, however presence of hypogammaglobinemia also raised suspicion for a granulomatous form of Common Variable Immunodeficiency (CVID) which, albeit rare, has been reported to be associated with hypercalcemia. Empiric treatment with steroids and IVIG was initiated, following which calcium and 1,25-OHD normalized.

Conclusions: Granulomatous form of CVID is rare, but should be considered in a patient presenting with 1,25-OHD mediated hypercalcemia and hypogammaglobulinemia. Treatment can be challenging, particularly if steroids are initially contraindicated.