Hypocalcaemia in Cetuximab Use from Hypomagnesaemia induced Hypoparathyroidism

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Introduction

Cetuximab is an epidermal growth factor receptor (EGFR) monoclonal antibody utilized in combination with chemotherapy for the management of RAS wild type metastatic colorectal cancer. Hypomagnesaemia is a common side effect of Cetuximab treatment.[1] We present the case of a patient who developed symptomatic hypocalcaemia with hypomagnesaemia related to Cetuximab treatment for metastatic colorectal cancer.

Case History

A 58 year old male presented to emergency with acute vomiting, paraesthaesia in fingers and toes. He had been undergoing Cetuximab and FOLFOX chemotherapy for metastatic colorectal cancer for the past 8 months with intermittent isolated hypomagnesaemia when ranges 0.35 – 0.69mmol/L, and concomitant hypocalcaemia when magnesium ranged 0.15 – 0.34mmol/L. On this presentation, he developed severe hypomagnesaemia of 0.10mmol/L, hypocalcaemia 1.55mmol/L, suppressed PTH 1.6pmol/L, 25OH Vitamin-D 68nmol/L, and both elevated 24 hour Mg urinary excretion 37.7mmol/day and calcium urinary excretion 16.7mmol/day. The patient was managed in ICU with intravenous magnesium, calcium replacement, and calcitriol. Calcitriol was continued on discharge, and despite ongoing intermittent hypomagnesaemia (0.34 – 0.68mmol/L) until 2 months post cessation of cetuximab, no further hypocalcaemia occurred.

Discussion

Cetuximab induced hypomagnesaemia may be related to its inhibition on the EGFR receptors highly expressed in the ascending limb of the Loop of Henle, leading to impaired renal resorption of magnesium via the transient receptor potential melastatin subtype6 (TRPM6) ion channel.[2] PTH suppression in severe hypomagnesaemia may be mediated by an increase in G-alpha subunit activation of the calcium-sensing receptor, leading to severe hypocalcaemia.[3] Administration of calcitriol in this context ameliorates of the effect of hypoparathyroidism until the suppressive effect of hypomagnesaemia resolves.

Conclusion

Severe hypomagnesaemia from Cetuximab use can induce hypocalcaemia via PTH suppression. Acute management include intravenous electrolyte and oral calcitriol replacement. Ongoing calcitriol replacement may need to be continued up to 2 months post cessation of Cetuximab to avoid recurrence of hypocalcaemia.

References

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