

Introduction

Carboplatin is an alkylating agent often used in chemotherapy. This agent can cause hypomagnesemia which in turn causes often severe hypomagnesemia. This phenomenon has been described but is often under reported and under treated. We report a case involving life-threatening hypocalcemia after a course of carboplatin.

Case

A 60 years old African American female with Stage IV Adenocarcinoma of the lung presented with severe body ache and shortness of breath after a course of chemotherapy including carboplatin. Labs at admission revealed pancytopenia, BUN 45 mg/dL, creatinine 2.3 mg/dL, corrected calcium 4.9 mg/dL, phosphorus 3.4 mg/dL, magnesium 0.8 mg/dL, 25-hydroxy vitamin D 9.2 mg /dL and PTH intact 969.1 pg/ml. Corrected QT interval was 495 ms.

Over the course of first 4 days, she received 16 grams of IV calcium gluconate, 12 grams of magnesium sulfate, as well as oral calcitriol 0.5 mcg daily, oral calcium carbonate and magnesium oxide. Low potassium was also replaced. Calcium level normalized after the magnesium level was corrected. Even though calcium and magnesium were corrected, on day 6 repeated PTH was 986.4 pg/ml. QT interval was corrected.



Fig.1 EKG at presentation; note that the QT interval is prolonged (QTc 495 ms)

Carboplatin Chemotherapy and PTH Resistance: Perilous Duo

Pinsker, Richard W MD FACPM FACE ; Swe, Nyein Chan MD; Ahsan, Muhamad MD; Kukar, Narinder MD FACP FACE Jamaica Hospital Medical Center, Jamaica, NY, United States



Renal tubular damage caused by carboplatin can cause urinary magnesium Hypomagnesemia can cause hypocalcemia by inhibiting PTH release and inhibiting the action of PTH in peripheral tissues, bone and kidney. This PTH resistance leads to inappropriately high or normal PTH as was seen in this case. Reduced action of PTH in the kidney decreases hydroxylation of 25-hydroxy vitamin D further decreasing the calcium level.

Hence magnesium replacement is the key to correct hypocalcemia in this case. Plasma magnesium level is the primary regulator of magnesium absorption in renal tubules, so abrupt elevation of plasma magnesium can shut down this renal absorption of Correction of magnesium must therefore be magnesium. sustained. Hypomagnesemia from carboplatin may persists for months or even years.



Fig. 2 Magnesium reabsorption along the nephron. The glomerulus filters the blood and facilitates thereby the entrance of Mg2⁺ into the tubular system that subsequently mediates the reabsorption of 90–95% of Mg2⁺. Approximately 10– 25% of Mg2⁺ is reabsorbed in the proximal tubule (PT). 50–70% of Mg2⁺ is absorbed along the thick ascending limb (TAL) of the loop of Henle. The final Mg²⁺ concentration in urine is determined in the distal convoluted tubule (DCT) where only 10% of Mg2⁺ is reabsorbed. Renal toxicity caused by carboplatin loses Mg²⁺ from the renal tubules.

Carboplatin can cause renal toxicity with incidence as high as 20%. wasting and consequently hypomagnesemia.



Conclusion

Awareness of carboplatin induced hypomagnesemia and PTH resistance or PTH deficiency causing hypocalcemia is very important to clinicians. Magnesium replacement is the key to the treatment of hypocalcemia. Besides, magnesium is the major intracellular divalent cation and is involved in more than 300 enzymes mediated processes. Early detection of hypomagnesemia and hypocalcemia induced by carboplatin chemotherapy and early magnesium and calcium replacement can prevent morbidity and mortality.

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Fig. 3 Biosynthetic events in the production of PTH within the parathyroid cell. The CaSR, or CaR, senses changes in extracellular calcium that affect both the release of PTH and the transcription of the *preproPTH* gene.

PTH acts on bone, intestinal mucosa, and kidney. By its integrated effects on the kidney, gut, and bone, PTH acts to increase the inflow of calcium into the extracellular fluid and thus defend against hypocalcemia. Removal of parathyroid gland or absence of PTH action results in profound hypocalcemia and ultimately in tetany and even death.

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