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Transient Pseudohypoparathyroidism Due To Amphotericin B–Induced Hypomagnesemia in Term Neonates With High Anorectal Malformation

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Abstract

Hypomagnesemia is a rare cause of transient pseudohypoparathyroidism.

This case report describes a neonate with anorectal malformation, who was started on amphotericin B on day 9 of life to manage fungal sepsis. The neonate developed hypocalcemia and hypomagnesemia, and serum level of parathyroid hormone was high, along with tetany, stridor, and respiratory distress.

Hypomagnesemia induced by amphotericin B results in transient pseudohypoparathyroidism.

Key Words: Transient pseudohypoparathyroidism, hypomagnesemia, amphotericin B, hypocalcemia, fungal sepsis, anorectal malformation

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Introduction

Magnesium (Mg) is the second most abundant intracellular cation.[1] It acts as a cofactor in various biological reactions. Although the primary site of absorption of Mg is the small bowel, Mg is absorbed in the large bowel also in small quantities.[2] The serum Mg concentration is primarily regulated in the kidney, and only 3% to 5% of total filtered amount is excreted into the urine.[3] Of the total filtered amount, 20% to 25% is reabsorbed in the proximal tubule, approximately 50% to 60% is reabsorbed in the thick ascending limb of the loop of Henle, and the remaining 5% to 10% is reabsorbed in the distal convoluted tubule (DCT).[3] Being

the last site of Mg reabsorption, DCT finely regulates Mg excretion.[2]

Amphotericin B (AMB), a polyene macrolide antibiotic, is one of the most effective drugs for the treatment of systemic fungal infections in neonates. Its antifungal action is mediated through ion-permeable pores formed by the association of AMB with ergosterol in the fungal cell membranes, which results in nephrotoxicity.[4,5] AMB induces specific tubular damage in the DCT and the thick ascending limb of the loop of Henle, which is the primary site of Mg reabsorption.[6]

This is a case report of a term neonate who underwent sigmoid colostomy for high anorectal malformation (H-ARM), receiving AMB for fungal infection and presenting with stridor, tetany, and transient pseudohypoparathyroidism. Our observation illustrates that Mg deficiency can induce peripheral resistance to parathyroid hormone (PTH) and therefore subsequently lead to hypocalcemia, stridor, and tetany.

Case Description

An early-term (38 wk), male, small-for-gestational age (SGA) neonate weighing 1.85 kg was born by lower segment cesarean section. The neonate was noticed to have imperforate anus at birth. Sigmoid colostomy was performed on day 1 of life in view of H-ARM. The neonate required noninvasive respiratory support till day 11. On day 3, meropenem antibiotic was started as the neonate tested positive on sepsis screening. However, on day 9, AMB was also added on further clinical deterioration and suspicion of fungal sepsis. On day 19, the neonate developed inspiratory stridor because of respiratory distress, following which oxygen supplementation was started. Results of blood gas showed all parameters to be normal, except low ionic calcium (Ca) level (0.782 mmol/L; normal range 1.12–1.32 mmol/L). Ionic Ca level did not improve despite supplementation with IV calcium gluconate. On day 21, the neonate had tetany along with stridor and respiratory distress. Hence, detailed laboratory investigations were performed, which revealed low serum Ca (6 mg/dL; normal range 8.5–10.5 mg/dL); low serum Mg (1.33 mg/dL; normal range 1.5–2.2 mg/dL); high serum phosphorus (13.7 mg/dL; normal range 3.9–6.9 mg/dL); decreased serum 25-hydroxyvitamin D level (18.6 ng/mL; normal range 30–100 ng/mL), and high serum PTH level (97.28 pg/mL; normal range 15–68 pg/mL). This variation in PTH and other electrolyte levels was thought to be because of AMB-induced hypomagnesemia. Hence, AMB was stopped on day 22. Supplementation of IV calcium gluconate and IV magnesium sulfate was continued for 72 hours, after which tetany, stridor, and respiratory distress subsided. IV supplementation of Ca and Mg was discontinued once these symptoms subsided. The neonate was continued on oral calcium supplements subsequently. Laboratory investigations were repeated after 48 hours of stopping AMB, the results of which revealed normalization of ionic Ca (1.31 mmol/L), serum Ca (10.99 mg/dL), and serum Mg (2.51 mg/dL), and serum phosphorus (8 mg/dL) levels. Serum levels of all electrolytes were within normal range after 1 week. The neonate was discharged in a hemodynamically stable condition.

Discussion

Mg deficiency is caused by either gastrointestinal loss or renal loss. As majority of Mg absorption occurs in the small bowel,[2] this cause is unlikely in this case. AMB can induce azotemia, impair renal concentration, and cause renal tubular acidosis and electrolyte imbalance such as hypokalemia or hypomagnesemia.[7] Hence, the most probable cause of hypomagnesemia in this case was AMB. Hypocalcemia is a typical presentation in hypomagnesemia[8] and can manifest with tetany, stridor, and respiratory distress, as seen in this neonate. Impairment of PTH secretion is the most important factor in the pathogenesis of hypocalcemia in Mg deficiency.[8] Also, impairment of PTH secretion results in low to inappropriate PTH levels in contrast to high PTH level in this case. Very few cases of hypomagnesemia induced either by AMB or any other etiology, presenting with hypocalcemia, tetany, and stridor-like symptoms, are reported in adults.[9-12] In all these reported cases, hypocalcemia and associated symptoms were due to hypoparathyroidism.

Rude et al[13] reported increased serum PTH level in some adult patients with Mg deficiency, which indicates

the state of peripheral resistance to PTH or functional hypoparathyroidism or pseudohypoparathyroidism similar to this case. This rare phenomenon most probably impairs adenylate cyclase activation by PTH in target organs.[14] Thus, either impairment of PTH secretion (hypoparathyroidism) or peripheral resistance to PTH in target organs (pseudohypoparathyroidism) are the main causes of hypocalcemia in Mg deficiency.

Nevertheless, reports on transient pseudohypoparathyroidism due to AMB-induced hypomagnesemia in the neonatal age group are scarce. To the best of our knowledge, this is the first case of AMB-induced hypomagnesemia, presenting with transient pseudohypoparathyroidism, hypocalcemia, tetany, stridor, and respiratory distress, reported in the neonatal age group.

Conclusion

In this case, the most likely diagnosis was transient pseudohypoparathyroidism caused by AMB-induced hypomagnesemia, which leads to hypocalcemia and associated symptoms such as tetany and stridor. Initially, hypocalcemia was unresponsive to IV Ca supplementation, but was normalized after supplementation of both Mg and Ca. Withdrawal of AMB resulted in normalization of all laboratory parameters. This case study highlights pseudohypoparathyroidism as a rare consequence of hypomagnesemia.

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