LETTER TO THE EDITOR

SYMPTOMATIC HYPOCALCEMIA OWING TO ORAL RISEDRONATE THERAPY

Sir,

A 21-year-old man was admitted to our hospital because of intermittent diarrhea from his childhood and weight loss. Physical examination was normal (1.55 m height and 43 kg weight). Laboratory studies were as follows; serum total calcium (Ca\(^{2+}\)): 8.8 mg/dl, phosphorus: 5 mg/dl, magnesium: 1.6 mg/dl, albumin: 3.7 mg/dl, total protein: 5.7 mg/dl. Serum sodium, potassium, alkaline phosphatase levels, and renal, hepatic, and thyroid function tests were normal. Serum parathyroid hormone (PTH) level was 139 pg/ml. Antigliadin immunoglobulin A (IgA) antibody was positive. Severe villous atrophy in the proximal intestine was found in histopathologic examination. Bone mineral densitometry (DEXA) revealed significant osteoporosis (\(L_{-}\) \(- L_{+}\) \(- Z; \) and \(T\) scores were -3.24 and -3.23, respectively). According to these data, he was diagnosed with celiac disease and implemented on a gluten free diet, oral risedronate (35 mg/once a week), oral calcium (elemental calcium 1800 mg/day) and oral magnesium (1830 mg/day). Three days after the starting dose of risedronate, he experienced a full picture of hypocalcemia with physical and laboratory findings (albumin-corrected serum Ca\(^{2+}\) of 5.9 mg/dl) including long QT interval in the ECG. Other results were; phosphorus 3.1 mg/dl, magnesium 1.7 mg/dl, and albumin 3.4 mg/dl. Then, he was treated with intravenous calcium gluconate. He recovered well with this therapy, and discontinued risedronate and continued with oral calcium, magnesium and vitamin-D\(_2\) besides gluten free diet.

Use of the Naranjo adverse drug reaction probability scale indicated a possible (score: 4) relationship between symptomatic hypocalcemia and risedronate therapy in this patient.[1]

Bisphosphonates are recommended especially in old patients with celiac disease, and, given the serious consequences of spontaneous fractures can also be considered at younger ages.[2] These drugs, when given intravenous, have occasionally been reported to cause symptomatic hypocalcemia.[3] However, as in the present case, it is quite uncommon with oral administration[4] because of compensatory mechanisms such as increase in PTH secretion, which prevents hypocalcemia by enhancing renal absorption of calcium, vitamin-D production, and stimulating osteoclastic bone resorption. Depending on the potency of the bisphosphonate, the effect of PTH on bone resorption by osteoclasts is blocked to some extent during bisphosphonate treatment.

Gastrointestinal calcium absorption occurs mainly in the proximal ileum and decreases towards the distal parts. In our case, the diarrhea might have impaired calcium absorption in response to hypocalcemia. Presumably, gastrointestinal calcium loss caused hypomagnesemia as well. Since PTH secretion is stimulated by magnesium dependent adenyl cyclase, it is possible that hypomagnesemia exacerbated hypocalcemia by interrupting the normal feedback loop. Therefore, correction of the hypomagnesemia seems essential in such patients.

In conclusion, symptomatic hypocalcemia is a rare but possible complication of oral risedronate therapy. Patients with celiac disease should be checked for their calcium and vitamin-D status, and carefully followed-up during risedronate treatment.

REFERENCES


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