CLINICAL CASE

Magnesium Deficiency in a Patient on Chemotherapy-Radiotherapy Treatment for Cervical Cancer: Case Report and Review

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Abstract

Introduction: Magnesium deficiency is a common entity in cancer patients owing to cisplatin-containing chemotherapeutic schemes. Combination with radiotherapy in certain tumors where the gastrointestinal tract is part of the treatment field can elicit this entity. Clinical case: The case is presented of a 35-year-old woman diagnosed with uterine cervix cancer on treatment with concomitant chemotherapy plus radiotherapy. Owing to the tumor extension and lymph node involvement, the radiation treatment field was broad, with important doses at the level of the small intestine. During treatment, the patient had important diarrhea due to magnesium deficit. Results: Testing for hypomagnesemia is not common in clinical practice, but it should be contemplated in patients on treatment with cisplatin-containing chemotherapeutic schemes and extended-field pelvic radiotherapy. Discussion: Knowing this entity and providing adequate treatment can prevent quality of life deterioration in affected subjects and possible early treatment discontinuation due to poor tolerance. (creativecommons.org/licenses/by-nc-nd/4.0/).
INTRODUCTION

Magnesium deficiency is a known side effect in patients on chemotherapeutic treatment with cisplatin. Hypomagnesemia is defined as serum level of the ion lower than 1.8 mg/dl (1.5 mEq/l), and its relationship with the use of cisplatin is dose-dependent, with its frequency increasing with each administered cycle\textsuperscript{1-3}. It is one of the more common hydro-electrolytic disorders, but its clinical manifestations are unspecific. Clinical signs and symptoms are basically asthenia, confusion, irritability, convulsions, and neuromuscular or cardiac alterations\textsuperscript{4}. Its diagnosis is difficult since determination of serum magnesium is not common practice. In addition, there is close relationship between magnesium levels and phosphorus and potassium levels, which makes it hard to distinguish whether clinical symptoms are due to one or another ion.

Uterine cervix cancer treatment is based, except for very early stages, on the combination of chemotheraphy and radiotherapy. The use of weekly cisplatin at a 40 mg/m\textsuperscript{2} dose, together with pelvic radiotherapy at doses up to 46-50 Gy, followed by brachytherapy, is the most widely used scheme. Surgery alone is reserved for stages IA and IIB. If tumor stage is advanced, the radiotherapeutic field can be broader, reaching in the upper limit the iliac bifurcation or the para-aortic lymph nodes, which significantly increases the possibility of radiation enteritis and, hence, malabsorption problems.

Treatement is based on correction of the underlying process whenever this is possible. If deficiency occurs in early stages of oncological treatment, magnesium salts can be administered by the oral route. If there is vital compromise, vials of magnesium sulfate 15\% diluted in dextrose 5\% solution are administered in 20 minutes, continuing on the ensuing days until the deficiency is corrected. Bolus administration should be avoided owing to possible cardiac complications that may derive from it\textsuperscript{5,6}.

CLINICAL CASE

The case is presented of a 35-year-old woman who had experienced menstrual cycle-unrelated bleeding and hypogastric pain for more than one year. In view of the described clinical symptoms, the patient attended the Gynecology Department. On physical examination she had normal external genitals and vagina, with cervix completely lateralized to the left. On bimanual examination, rigidity was found on the upper third of the left anterolateral vaginal wall, with supravaginal cervical tumor growth. On digital rectal examination, normal right parametrium was found, with the left one not being assessable due to the tumor lesion growth. The cervix touched the anterior side of the rectum. A gynecological ultrasonography showed a 5.2 x 3.4 cm cervical lesion with abundant vascularization and deep invasion without parametrical involvement.

Studies to find the extension of disease were carried out, with pelvic magnetic resonance imaging reporting a 5.5 x 4.5 x 4.0 cm cervical mass, with presence of a 1.2 cm right iliac chain adenopathy without parametrical, vaginal, ureteral, bladder, or rectal invasion. A positron emission tomography-computed tomography scan revealed hyper-uptake (SUVmax 16.55) on cervical region with 5.5 cm diameter and at the right iliac chain (SUVmax 12.30). Biopsy of the lesion was taken, which yielded the result of adenosquamous carcinoma of the cervix.

The case of this patient was presented to the multidisciplinary committee for gynecological tumors of our hospital and, in view of the anatomopathological and radiological result, FIGO IIIB, treatment with chemotherapy and radiotherapy was decided on. The patient was started on chemotherapeutic treatment with weekly cisplatin at 40 mg/m\textsuperscript{2} in combination with radiotherapy. The radiotherapeutic planning target volume reached up to the L4-L5 vertebrae at its upper limit. During the third chemotherapy cycle, and with a radiotherapy dose of 22 Gy of 50 planned, the patient experienced nausea, vomiting, and intense diarrhea that did not improve in spite of loperamide administration and dietary changes. Together with this there was a 7 kg weight loss in 20 days and significant asthenia. In addition, her relatives reported she was more irascible and had memory losses.

Blood count and chemistry was obtained, with K+ values of 3.4 mEq/l and Mg\textsuperscript{++} 1.3 mg/dl standing out. Tablets with 404.85 mg of magnesium lactate every eight hours for five days were prescribed. The patient started noticing improvement of her gastrointestinal and memory symptoms. New blood tests after treatment completion showed magnesium levels of 2.2 mg/dl.

DISCUSSION

The use of pelvic radiotherapy is one of the least known causes of magnesium deficiency, which is increased if the patient requires chemotherapy with cisplatin. There are several tumors with large pelvic fields of radiation therapy that can elicit radiation enteritis (uterine cervix, endometrium, prostate, rectum, or anal canal) and, therefore, nutrient malabsorption. Although at-risk organ-limiting doses are known, many times these cannot be complied with due to tumor extension or lymph node involvement.

In spite of being a known side effect in the literature (Table 1), there are few studies assessing the prophylactic use of magnesium with the use of cisplatin. Hunter, et al.\textsuperscript{7} studied the beneficial effect of magnesium sulfate supplementation in more than 200 patients on cisplatin and radiotherapy combined treatment. In addition, they reported that patients with diabetes mellitus and/or hypertension were at higher risk of developing magnesium deficiency, owing to renal problems. The analysis by Evans, et al.\textsuperscript{8} evaluated a sample of 28 patients with gastrointestinal cancer treated with chemotherapy with cisplatin, 5-fluorouracil and epirubicin, demonstrating statistically significant improvement with magnesium supplementation after the third cycle of cisplatin. There are more recent studies by Yamamoto, et al.\textsuperscript{9} and the Iranian group clinical trial\textsuperscript{10}, which also report improvement with the prophylactic use of magnesium supplements in cancer patients who are to receive chemotherapy with cisplatin. The retrospective study by Kidera, et al.\textsuperscript{11} analyzed the beneficial effect of magnesium supplements in different solid tumors, including lung cancer.

In everyday clinical practice, knowing magnesium serum values prior to initiating oncological treatment with cisplatin and pelvic radiotherapy may prevent situations...
of deficiency that elicit clinical manifestations in patients on treatment. In our case, the patient’s quality of life had significantly deteriorated since the beginning of oncological treatment and there was doubt whether she would be able to complete it. Magnesium supplement administration produced an improvement of her clinical conditions, especially at the gastrointestinal level.

CONCLUSIONS
Magnesium deficit on treatment with cisplatin and radiotherapy with extended pelvic fields is a common entity in clinical practice that sometimes is not diagnosed, which results in important gastrointestinal clinical symptoms in affected patients. Routinely performing magnesium level controls and supplementing in case these are low is a beneficial solution for these subjects.

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DECLARATION OF INTEREST
The author declares not having any conflicts of interests.

REFERENCES