Adrenal Insufficiency in a Peritoneal Dialysis Patient Taking Megestrol Acetate

KEY WORDS: Megestrol acetate; end-stage renal failure; adrenal insufficiency; hypoadrenalism.

Editor:

Megestrol acetate (MA) is a synthetic hormone that is currently approved for use as an appetite stimulant in

patients with cancer or AIDS. Clinical trials have demonstrated that MA is effective and safe in stimulating appetite in dialysis patients as well (1–3). Reported side effects include gastrointestinal upset, hyperglycemia, and fluid overload. These side effects have been mild and uncommon. However, a serious but often overlooked side effect of MA is suppression of the hypothalamic–pituitary–adrenal axis. Here, we report a peritoneal dialysis (PD) patient who experienced this life-threatening side effect of MA.

An 80-year-old Chinese woman was started on continuous ambulatory PD (CAPD) because of diabetic nephropathy. Despite all efforts to optimize her dialysis and extensive investigations to look for a treatable cause, her appetite remained poor. Megestrol acetate 80 mg twice daily was started as an appetite stimulant. Initial response was good, with improvement in serum albumin, dry weight, and subjective global assessment score.

Five months after treatment with MA, the patient was admitted for malaise, anorexia, hypotension, and hypoglycemia. On admission, her blood pressure was 90/60 mmHg, and she was clinically euvolemic. Physical examination was unrevealing. Hemoglobin was 10 g/dL (100 g/L). White blood cell count and serum C-reactive protein were normal. Serum sodium was 135 mEq/L; potassium, 3.8 mEq/L. Serum urea nitrogen, creatinine, calcium, and phosphate were unremarkable. Liver function was normal, and serum albumin was 3.3 g/dL (33 g/L). Chest radiography and urine culture were normal. Her insulin requirement (Mixtard 30 HM: Novo Nordisk, Bagsvaerd, Denmark) greatly declined from a usual dose of 60 U daily to 10 U daily after admission. A short synacthen test (1 µg) showed a low baseline cortisol level and blunted response, with cortisol levels of 2.6 µg/dL (72 nmol/L), 10.1 µg/dL (278 nmol/L), and 13.2 µg/dL (364 nmol/L) at 0, 30, and 60 minutes respectively. Adrenocorticotropin was 17 pg/mL (3.7 pmol/L) which was inappropriately low, suggestive of secondary adrenal insufficiency.

Megestrol acetate was stopped, and a hydrocortisone supplement was initiated. The patient's blood sugar and pressure normalized, and she resumed her usual dose of insulin. Applying the Naranjo algorithm (4), the patient had a score of 7, indicating a probable association between MA and adrenal insufficiency in this case.

Most reports on MA-induced adrenal insufficiency have involved patients with an underlying malignancy. It is believed that MA suppresses the endogenous hypothalamic–pituitary–adrenal axis through its glucocorticoid-like action. Naing *et al.* performed corticotropin-releasing hormone tests in 9 patients with MA-induced adrenal suppression. Of those patients, 6 showed an increase

in adrenocorticotropin, indicating that suppression was occurring at the hypothalamus in some MA-treated patients (5).

To our knowledge, there have been no reports of MA causing hypoadrenalism in patients with end-stage renal failure on dialysis. The symptoms of hypoadrenalism, anorexia, fatigue, nausea, and vomiting are common in dialysis patients. Hyponatremia, which is a common finding in adrenal-suppressed patients with normal renal function, is not a feature of hypoadrenalism in dialysis patients with no significant residual renal function. The diagnosis of hypoadrenalism may therefore be overlooked. The present report underlines the need to exercise extreme caution and a high index of suspicion when prescribing MA to dialysis patients. In view of this potential adrenal suppression, routine screening of morning cortisol and the empiric use of steroids in cases of serious illness or surgery are recommended for patients on MA.

DISCLOSURES

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REFERENCES

1. Lien YH, Ruffenach SJ. Low dose megestrol increases serum albumin in malnourished dialysis patients. *Int J Artif Organs* 1996; 19:147–50.
2. Costero O, Bajo MA, del Peso G, Gil F, Aguilera A, Ros S, *et al.* Treatment of anorexia and malnutrition in peritoneal dialysis patients with megestrol acetate. *Adv Perit Dial* 2004; 20:209–12.
3. Yeh SS, Marandi M, Thode HC Jr, Levine DM, Parker T, Dixon T, *et al.* Report of a pilot, double-blind, placebo-controlled study of megestrol acetate in elderly dialysis patients with cachexia. *J Ren Nutr* 2010; 20:52–62.
4. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, *et al.* A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981; 30:239–45.

5. Naing KK, Dewar JA, Leese GP. Megestrol acetate therapy and secondary adrenal suppression. *Cancer* 1999; 86:1044-9.

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