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CASE REPORT

Education

A case of iatrogenic Cushing syndrome and subsequent adrenal insufficiency from a hidden ingredient in the supplement Artri Ajo King

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Abstract

Dietary supplement use is common in the United States. Supplements are regulated by the US Food and Drug Administration (FDA) under a separate set of guidelines from typical food and drug products. This case report describes a patient who presented to the emergency department (ED) with abdominal pain, vomiting, and generalized weakness. On detailed history, we learned that he had been taking a supplement called Artri Ajo King for 18 months, followed by recent abrupt cessation before his ED presentation. He was subsequently found to have a low serum cortisol level and was diagnosed with secondary adrenal insufficiency by a cosyntropin stimulation test. Ultimately, he was started on hydrocortisone with resolution of his symptoms. This case illustrates the consequence of allowing dietary supplements to be sold before FDA evaluation as well as the importance of physicians eliciting history of supplement use and offering a culturally competent discussion with their patients regarding supplement use.

KEYWORDS
adrenal insufficiency, Artri Ajo King, Cushing syndrome, supplement

1 | INTRODUCTION

Major quality concerns exist surrounding the ingredients of dietary supplements.[1] The 1994 Dietary Supplement Health and Education Act allowed supplements to be available to consumers without premarket evaluation by the US Food and Drug Administration (FDA).[2] Supplements are only regulated by the FDA after reaching the market if found to have adulterated or misbranded ingredients. This resulted in unregulated ingredients reaching the market for widely available supplements.[2] Common quality issues range from microbial contamination to heavy metal contamination to prescription drug alteration.[1]

In April 2022, the FDA released a formal warning regarding the product Artri Ajo King (AK). "Artri" or "Ortiga," which is a supplement marketed for joint pain, muscle pain, osteoporosis, and cancer, is readily available online and in retail stores.[3,4] Laboratory analysis performed by the organization demonstrated ingredients not included on the product label, most notably diclofenac, methocarbamol, and dexamethasone. This may lead to the consumer experiencing undesired adverse effects or unanticipated medication interactions. Specifically, ingesting exogenous steroids such as dexamethasone can lead to iatrogenic "Cushing syndrome," which is hypercortisolism characterized by clinical features of obesity, hirsutism, round facies, striae, bruising, muscle weakness, depression, dyslipidemia, hypertension, and hyperglycemia.[5] In the setting of chronic corticosteroid use as may occur with supplementation, sudden withdrawal leads to physiologic consequences, most notably adrenal insufficiency (AI).[6]

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1.1 | Case

A 52-year-old Spanish-speaking man with a medical history significant for hypertension, hyperlipidemia, prediabetes, and arthritis presented to the emergency department (ED) with generalized abdominal pain, nausea, and vomiting during the past month. He reported 3 to 4 episodes of non-bloody emesis daily and was on a clear liquid diet as a result of an inability to tolerate solid foods. He endorsed 20 pounds of weight loss during the preceding month. He was having normal bowel movements without blood. His family reported significant weakness that now required a walker for assistance with ambulation. Multiple previous visits to the ED did not identify the etiology of his symptoms. After a review of his medications, it was noted that he had recently discontinued use of a supplement, AK, after a recent hospitalization, and this seemed to be when his symptoms began. He had previously been taking this supplement for 1.5 years for arthritis, during which time he reported symptoms of a 50-lb weight gain, fat over the posterior neck, abdominal striae, face rounding, and muscle weakness.

On presentation to the ED, he appeared fatigued, but was non-toxic. His initial vital signs were temperature, 97.7°F; heart rate, 93 beats per minute; respiratory rate, 16 breaths per minute; blood pressure, 132/90 mmHg; and pulse oximetry, 99% on room air. His physical examination was notable for tenderness to palpation in the epigastric region of the abdomen without any rebound or guarding. He was noted to have abdominal striae (Figure 1). His neurological exam showed globally decreased 4 of 5 strength in all extremities. His initial laboratory studies showed multiple electrolyte abnormalities, including potassium of 2.9 (3.5–5.5 mmol/L), magnesium of 1.4 (1.6–2.6 mg/dL), and calcium of 12.3 (8.4–10.5 mg/dL). The remainder of his laboratory studies were normal. A computed tomography scan of the abdomen was also performed, which was only significant for a fat-containing umbilical hernia and hepatic steatosis. He was treated with fluid resuscitation and electrolyte replacement and was admitted to the hospital. History of supplementation use and cessation were communicated to the inpatient team for further AI workup.

The next morning, his serum cortisol was 1.2 (≥2.0 μg/dL) and his adrenocorticotropic hormone (ACTH) was 32.2 (7.2–63.3 pg/mL). Endocrinology was consulted because of the concern for AI. A cosyntropin stimulation test was performed, and his cortisol went from 1.4 to 8.6. These results were consistent with AI and thought to be secondary to hypothalamic-pituitary-adrenal (HPA) axis suppression from exposure to an exogenous glucocorticoid. He was started on a steroid regimen with significant improvement in his symptoms while inpatient. He was ultimately discharged on hydrocortisone 15 mg in the morning and 10 mg in the afternoon.

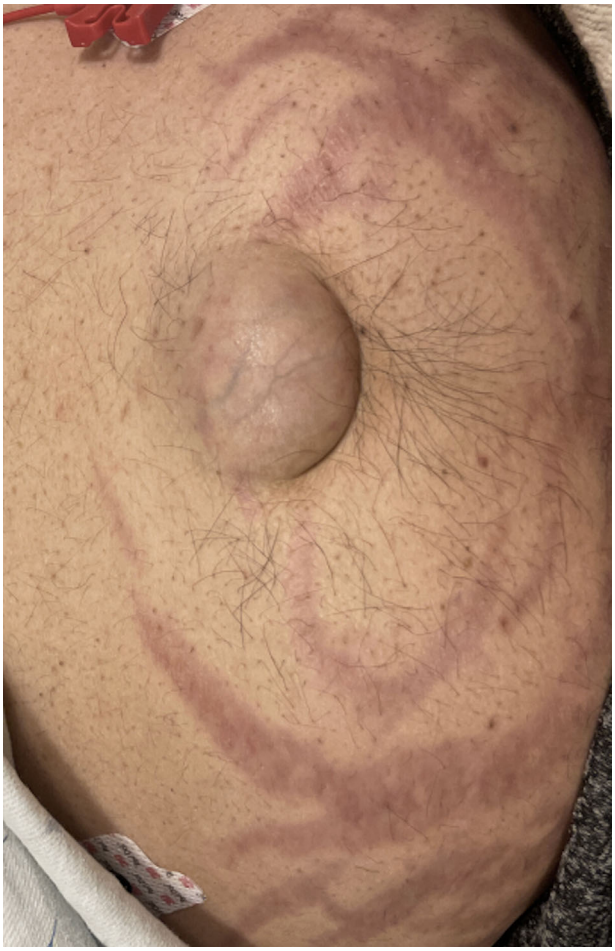

FIGURE 1 Abdominal striae in a patient with iatrogenic Cushing syndrome.

2 | DISCUSSION

This case highlights the importance of obtaining a complete history, including medications and over-the-counter supplements. This patient presented to the ED with symptoms concerning for AI, including a 20-lb weight loss within 1 month and generalized weakness that affected the patient's ability to ambulate. In addition, he was found to have minor electrolyte derangements on workup, including hypokalemia, hypomagnesemia, and hypercalcemia. This patient had been taking the supplement AK, which contained unlisted glucocorticoids that led to iatrogenic Cushing syndrome, followed by AI after an abrupt withdrawal.

The 2-part function of the HPA axis is to maintain a basal cortisol rate in addition to generating a cortisol response to stimuli.[5] This system entails a feedback system that includes a cortisol-releasing hormone (CRH), ACTH, and cortisol.[5] A cortisol peak is exhibited soon after waking in the morning, with trough levels around midnight.[5] With the prolonged use of exogenous glucocorticoids and an abrupt cessation of use, the HPA axis can be suppressed, leading to secondary AI.[7] This occurs when the stimulation provided by the exogenous glucocorticoids act to decrease the amount of CRH secreted by the pituitary gland. This decreases the production of ACTH and cortisol levels. The attenuation of the HPA axis is evident when the glucocorticoids are abruptly stopped, and the adrenal cortex is unable to compensate by producing cortisol on its own. This leads to insufficiency symptoms such as severe fatigue, abdominal pain, nausea, vomiting, diarrhea, and

weight loss. The suppression of the HPA axis can persist for up to 12 months after the cessation of exogenous glucocorticoid use.[8]

This HPA axis suppression is evidenced by our patient's basal cortisol level, resulting in lower-than-average levels at 1.2 μg/dL (reference range, ≥2.0 μg/dL). The cosyntropin stimulation test is used to differentiate between various forms of AI.[8] Cosyntropin is a derivative of ACTH used to differentiate between primary and secondary AI.[9] The patient's cortisol levels were responsive to a prolonged stimulation of ACTH by cosyntropin, which rules in secondary AI. This signifies that the pituitary gland and HPA axis are functioning and able to respond to stimulation appropriately, ruling out a primary AI.[9] Although primary AI often presents with hyponatremia and hyperkalemia because of the mineralocorticoid deficiency, these electrolyte changes may be less dramatic or not present in secondary AI.[6] This was exemplified by this case, in which the patient's serum sodium was normal at 137 mmol/L and serum potassium low at 2.9 mmol/L; the latter may have been attributed to the patient's persistent vomiting.

This case highlights the potentially life-threatening consequences of allowing supplements to go directly to consumers without evaluation.[1] Non-prescription access to AK products makes it important to report not only the increasing numbers of Cushing syndrome cases but also the long-term consequences of abruptly halting the use of the product without appropriate tapering by a licensed physician. There are 2 prior case reports in the endocrinology literature outlining Cushing syndrome secondary to AK use and 1 case report describing AI.[10,11] All 3 patients in these past reports were able to connect with a physician for tapering guidelines and were safely titrated back to baseline with the use of hydrocortisone. Our case report is unique because at ED presentation, our patient had AI as a result of prolonged supplementation and subsequent cessation of AK. This case highlights the importance of complementary and alternative medicines when obtaining a full history from patients.[12] The FDA is aware of the physiologic effects of AK and has appropriately issued warning to various distributors of these products, but as with our patient, the supplement may be still available from other sources or outside of the United States.[4]

The impact of physician language concordance and cultural norms with medical outcomes is also a paramount point of discussion in this case report. A prior study showed that up to 80% of Hispanic patients reportedly use herbal supplements; however, only 17.4% of physicians were reported to have asked about them.[13] This demonstrates the cultural discordance between patients and physicians when prioritizing the discussion about supplement use. This creates not only a barrier between patient–physician relationships but also it leads to incomplete differential diagnoses with missed opportunities for life-altering interventions.

3 | CONCLUSION

Patient presentations with vague complaints and non-specific laboratory abnormalities can be a challenge to assess in the ED. We describe a case of iatrogenic Cushing syndrome followed by AI as a result of a hidden glucocorticoid in the supplement AK. This case emphasizes the importance of asking patients about supplement use in a culturally concordant manner, assessing for the presence of unlisted ingredients in unregulated supplements, and recognizing exogenous Cushing syndrome or subsequent AI with medication cessation. Physicians are strongly encouraged to report cases such as this to the FDA MedWatch to ensure appropriate action is taken to regulate and prevent harm to patients.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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