Exogenous Cushing Syndrome Caused by a “Herbal” Supplement

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ABSTRACT

Background/Objective: Exogenous Cushing syndrome is usually diagnosed in the setting of known glucocorticoid exposure; however, occult glucocorticoid use is possible. We present 2 cases of patients who developed Cushing syndrome while taking Artri King (AK), an over-the-counter “herbal” supplement for joint pains reported to contain glucocorticoids.

Case Report: Patient 1, a 49-year-old woman, reported rapid weight gain, large stretch marks, poor wound healing, and recent diagnoses of type 2 diabetes mellitus and hypertension over a course of 1 year. Her serum AM cortisol level was <0.5 µg/dL (reference range, 4.0-22.0 µg/dL) and adrenocorticotropic hormone (ACTH) level was <5 pg/mL (reference range, 5-60 pg/mL). Synthetic glucocorticoid screening revealed a dexamethasone level of 210 ng/dL (reference value < 100 ng/dL) while she was taking AK; 5 days after stopping the supplement, the level was 24 ng/dL (reference value < 20 ng/dL). Patient 2, a 61-year-old woman, presented with weight gain, fatigue, swelling, and recent diagnoses of prediabetes and hypertension over a span of 6 months. Her serum AM cortisol level was <1.0 µg/dL (reference range, 8.0-25.0 µg/dL) and ACTH level was <5 pg/mL (reference value < 46 pg/mL). She stopped AK, and 1 month later, her AM cortisol level rose to 9.1 µg/dL (reference range, 8.0-25.0 µg/dL) and ACTH level rose to 68 pg/mL (reference value < 46 pg/mL).

Discussion: Supplements containing hidden glucocorticoids and causing Cushing syndrome have been reported in rare cases and can pose a diagnostic challenge for providers.

Conclusion: Exogenous glucocorticoid use because of unregulated herbal supplements should be considered when Cushing syndrome is suspected. © 2022 AACE. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Introduction

Cushing syndrome can present as weight gain, particularly around the abdomen; round facies; large striae; proximal muscle weakness; easy bruising; hypertension; and hyperglycemia. It can be caused by adrenocorticotrophic hormone (ACTH)-secreting pituitary tumors, ectopic ACTH-secreting tumors, and adrenal tumors or hyperplasia; however, the most common cause of Cushing syndrome is exogenous glucocorticoid use.1 In most patients, the diagnosis of exogenous Cushing syndrome is straightforward because they are treated with known systemic glucocorticoids for inflammatory conditions. However, cases of Cushing syndrome with unknown glucocorticoid use because of supplements have been reported. Artri King (AK) (Natural de Mexico LLC), is an over-the-counter supplement marketed as a natural remedy for joint pains. Although AK does not list any glucocorticoids as an ingredient on its label, laboratory analyses by regulatory agencies have reported that their products contain glucocorticoids and advise against their use.2,3 Here, we present 2 cases of patients who we suspect developed exogenous Cushing syndrome because of unknowingly taking glucocorticoids present in this “herbal” supplement.

Case Report

Patient 1 was a 49-year-old woman who was admitted to the hospital for a left lower extremity wound and cellulitis. She reported gaining 150 pounds of weight, developing fluid retention, new large stretch marks, proximal muscle weakness, poor wound healing, easy bruising, facial puffiness, some minor acne on her
no clear offending agents were noted to be taken by our patients at the time of presentation; however, both were taking AK. The product label lists glucosamine, condroitin, colageno, vitamina C, curcuma, ortiga, omega 3, and MSM (which we believe translates to glucosamine, condroitin, collagen, vitamin C, curcumin, nettle, omega-3 fatty acids, and methylsulfonylmethane in English) as its ingredients. Still, we suspected it to be the source of glucocorticoids based on a process of elimination. In addition, an online search of AK revealed news articles stating that testing of this company's products have led to the conclusion of potential dangers of using unregulated over-the-counter supplements.

### Clinical Relevance

We report 2 cases of patients who developed Cushing syndrome while on Artri King (AK), an over-the-counter “herbal” supplement that likely contains glucocorticoids as a hidden ingredient. Given the wide availability of this product, we believe that it is important to share the potentially devastating health effects of using AK.

### Discussion

Both our patients presented with weight gain and recently diagnosed hyperglycemia and hypertension, raising concern for hypocortisolism. Laboratory testing revealed suppression of their HPA axes; therefore, we suspected possible exogenous glucocorticoid use.

Oral, injected, topical, and inhaled glucocorticoids have all been implicated in cases of exogenous Cushing syndrome.

Because of its intrinsic glucocorticoid activity, megesterol acetate has also been shown to cause Cushing syndrome at high doses. 

Itraconazole and ritonavir, which inhibit the cytochrome P450 3A4 metabolism of glucocorticoids, can delay the clearance of some glucocorticoids and cause Cushing syndrome even with exposure to lower doses of glucocorticoids. Suppotitious and occult glucocorticoid use has also been reported.

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products found hidden ingredients, including dexamethasone, methylprednisolone, and diclofenac. We believe that patient 1 developed Cushing syndrome after her initial course of deflazacort and continued to have signs and symptoms of hypercortisolism later, with a suppressed HPA axis, because of taking AK. Patient 2 had recently used an ophthalmic steroid ointment; however, given the lack of improvement after discontinuing it, we thought that the ointment was unlikely to have contributed. Notably, she appeared to have a less striking presentation than patient 1, likely because of lower overall glucocorticoid exposure while on AK alone. Discontinuing AK led to weight loss in both the patients; however, because of prolonged suppression of their HPA axes, they currently require replacement glucocorticoid doses. Although we were not able to test the actual supplements used by our patients to confirm their contents, the decrease in dexamethasone level in patient 1 after discontinuing AK suggests that the likely source of dexamethasone was AK.

The U.S. Food and Drug Administration (FDA) has noted a growing trend of dietary supplements with hidden drugs or ingredients. Supplements are classified as food products, not medicines; therefore, they are not subject to the strict regulatory standards of the FDA. Many over-the-counter “adrenal support” supplements have been found to contain steroids, and even supplements containing adrenal extracts from animals are sold to the general public with claims of aiding adrenal function. AK is part of a line of multiple products for joint pains and arthritis. These supplements are promoted as being “all natural” and are available for sale through various retailers. Since the management of the cases of the patients presented here, the FDA has issued a public notification advising consumers not to purchase AK because their laboratory analysis revealed dexamethasone and diclofenac as unlisted ingredients. No further details were given about the specifics of how the FDA conducted the testing of the AK products. To our knowledge, there are no prior reported cases of an AK supplement causing Cushing syndrome published in the English medical literature. We found 1 medical publication written in Spanish that details a case of Cushing syndrome in a patient taking an AK supplement. Given the availability of AK to patients in the United States, we believe that it is important to describe the potentially devastating health effects of using this product in the English literature as well.

**Conclusion**

For cases of suspected Cushing syndrome in which glucocorticoid use is not revealed based on the patient’s history, laboratory evaluation can offer some clues. Markedly low levels of serum cortisol, ACTH, and 24-hour urine cortisol in a patient who does not appear to have adrenal insufficiency should lead to suspicion of exogenous glucocorticoid exposure. Furthermore, synthetic glucocorticoid screening can help confirm exogenous glucocorticoid use. Our 2 cases emphasize the possibility of developing Cushing syndrome by unknowingly ingesting glucocorticoids from a misleadingly labeled over-the-counter “herbal” supplement. Patients should be warned about the use of AK products, and medical providers should counsel their patients on the potential dangers of using unregulated over-the-counter supplements.

**Disclosure**

The authors have no multiplicity of interest to disclose.
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