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Case Report

Unmasking Iatrogenic Cushing's Syndrome

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Abstract

Cushing's Syndrome is a well-characterized clinical manifestation of hypercortisolism and results from a variety of etiologies, most commonly from exogenous glucocorticoids. Iatrogenic Cushing's Syndrome related to dietary supplements remain underreported; the quality, safety, labeling, and marketing of dietary supplements differs from that of drugs, and ineffective regulation poses potential risks to consumers. We describe one case of Iatrogenic Cushing's Syndrome and secondary adrenal insufficiency due to use of the dietary supplement "Artri King" for joint pain.

Keywords: *Iatrogenic Cushing Syndrome; Secondary Adrenal Insufficiency; Dietary Supplement Regulation*

Abbreviations

HPA: Hypothalamic-Pituitary-Adrenal; ACTH: Adrenocorticotropic Hormone; SIAI: Steroid-Induced Adrenal Insufficiency; FDA: Food and Drug Administration; USP: US Pharmacopoeia

Introduction and Case Presentation

We describe the case of a 59-year-old male with a history of hypertension, diabetes, osteopenia complicated by thoracic compression fractures, and central hypogonadism diagnosed 3 months prior; the patient presented to the emergency department at the Olive View - UCLA Health Medical Center with three weeks of severe fatigue, shortness of breath, malaise, lightheadedness, and nausea. Medication history on admission was notable for the absence of prescription glucocorticoids; on initial inquiry about the current use of dietary supplements or other over-the-counter medications, the patient reported none.

Vital signs remained stable throughout admission. Physical exam was remarkable for proximal myopathy, rounded facies, facial plethora, wide purple abdominal striae, central obesity with extremity wasting, dorsocervical fat pad, and lower extremity fungal skin infection (Figure 1). Laboratory values on admission were significant for hypokalemia to 2.6 mEq/L, requiring significant repletion (daily doses of 80 to 100 mEq intravenous potassium chloride to a goal of 4.0 mEq/L). MRI brain revealed no hypothalamic or pituitary abnormalities and CT of the adrenal glands were unremarkable.

Figure 1a

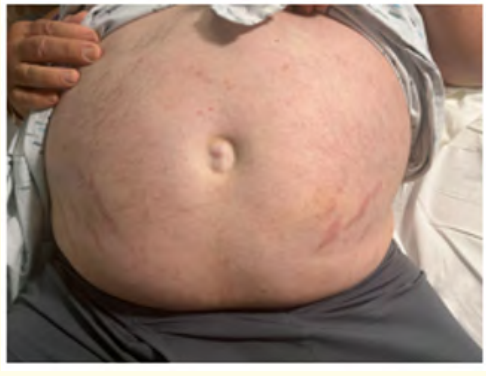

Figure 1b

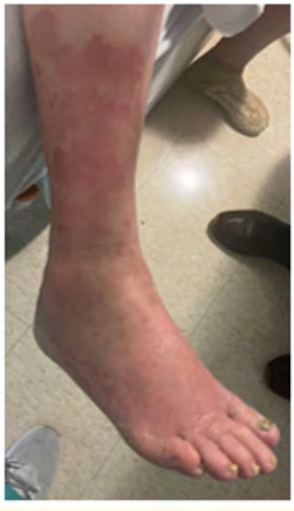

Figure 1c

Figure 1: *Physical exam findings consistent with Cushing's Syndrome. a) Rounded facies and facial plethora. b) Central obesity and purple striae. c) Lower extremity fungal skin infection and onychomycosis.*

Given a clinical presentation highly suggestive of Cushing's Syndrome, we revisited the medication history and revealed significant use of the dietary supplement "Artri King" (AK) for joint pain, a poorly regulated dietary supplement containing dexamethasone and diclofenac, unlisted on the product label [1]. The patient had regularly purchased the product at a local Mexican flea market and used up to one bottle per week for two to three years, then abruptly discontinued the drug 3 weeks prior to presentation when informed by a friend about the potential risks. When asked specifically, the patient reported that his clinical symptoms - including round facies, central obesity, and striae - progressed during his usage of the medication. His presenting constitutional symptoms in the setting of abrupt discontinuation of exogenous glucocorticoids are consistent with steroid-induced adrenal insufficiency (SIAI), one etiology of secondary adrenal insufficiency. Our patient demonstrated adrenal insufficiency, consistent with SIAI, on a 250 mcg ACTH stimulation test: baseline, 30 minutes and 60 minutes serum cortisol values were 2.5, 9.2, and 13.1 mcg/dL, respectively, and the peak serum cortisol value at 60 minutes is below the accepted threshold of 14 mcg/dL [2]. Our patient was subsequently provided a three-week glucocorticoid taper with outpatient follow up with endocrinology.

Discussion

Cushing's Syndrome is a well-characterized clinical manifestation of hypercortisolism and results from a variety of etiologies, most commonly from exogenous glucocorticoids. One meta-analysis describes the incidence of secondary adrenal insufficiency in prescription glucocorticoids, ranging from 4.2% for nasal corticosteroids to 52.2% for intra-articular corticosteroids, with increased risk with increased dose and duration of treatment [3]. In SIAI, chronic high-dose glucocorticoid use suppresses the hypothalamic-pituitary-adrenal (HPA) axis via negative feedback at the hypothalamus and the anterior pituitary gland, decreases the secretion of adrenocorticotropic hormone (ACTH), and ultimately results in adrenal atrophy in the zona fasciculata and zona reticularis. Recovery of HPA axis function after prolonged suppression is variable and may take 6 - 12 months [4].

Cases of secondary adrenal insufficiency due to non-prescription drugs are documented but underreported, several - including our patient - due to the use of AK, a product marketed for joint pain, muscle pain, osteoporosis, and cancer [5-8]. In April 2022, the FDA released a public notification describing the risks of AK, previously sold online and in retail stores in the United States, including Amazon, Latin Foods Market and Walmart [1].

This case highlights the gaps in dietary supplement regulation in the United States, which differs from more stringent regulatory oversight of drugs. The Food and Drug Administration (FDA) regulates dietary supplement quality, safety, and labeling, and the Federal Trade Commission monitors advertisements and marketing; however significant challenges in enforcement remain. Drugs that do not achieve compliance with national standards set by the US Pharmacopoeia (USP) and National Formulary are considered adulterated or misbranded. By contrast, compliance is optional for dietary supplements, with limited participation from manufacturers - in 2015, only 6 brands of dietary supplements marketed in the United States were USP verified [9].

Conclusion

We share the experience of our patient, who presented with striking physical exam findings of Cushing's Syndrome and constitutional symptoms of adrenal insufficiency, in the setting of prolonged exogenous use and subsequent abrupt discontinuation of a dietary supplement containing unlisted glucocorticoids. Our patient's unique presentation highlights the importance of a thorough physical exam and comprehensive medical history, including over-the-counter and non-prescribed medication use. This case underscores the need to maintain a high index of suspicion for iatrogenic causes in patients with complex presentations and apparent endocrinopathies. His experience serves as a potent reminder of the significant quality and safety concerns that result from limitations in dietary supplement regulation in the United States, emphasizing the need for ongoing public awareness and education efforts.

Disclosure

Written informed consent was provided by the patient for the publication of an anonymized summary of his clinical history and photographs of his physical exam findings.

Bibliography

1. Research, Center for Drug Evaluation and. "Public Notification: Artri King Contains Hidden Drug Ingredients". FDA (2022).
2. Javorsky Bradley R., *et al*. "New Cutoffs for the Biochemical Diagnosis of Adrenal Insufficiency after ACTH Stimulation Using Specific Cortisol Assays". *Journal of the Endocrine Society* 5.4 (2021): bvab022.
3. Broersen Leonie H A., *et al*. "Adrenal Insufficiency in Corticosteroids Use: Systematic Review and Meta-Analysis". *The Journal of Clinical Endocrinology and Metabolism* 100.6 (2015): 2171-2180.
4. Younes Areej K and Noor K Younes. "Recovery of Steroid Induced Adrenal Insufficiency". *Translational Pediatrics* 6.4 (2017): 269-273.
5. Mikhail Nasser., *et al*. "Iatrogenic Cushing's Syndrome Caused by Adulteration of a Health Product with Dexamethasone". *International Journal of Endovascular Treatment and Innovative Techniques* 3.1 (2022): 6-9.
6. Patel Reema., *et al*. "Exogenous Cushing Syndrome Caused by a 'Herbal' Supplement". *AACE Clinical Case Reports* 8.6 (2022): 239-242.
7. Dunn Colin., *et al*. "A Case of Iatrogenic Cushing's Syndrome Following Use of an Over-the-Counter Arthritis Supplement". *Case Reports in Endocrinology* 2023 (2023): e4769258.
8. Saad-Omer Suhail M., *et al*. "Exogenous Cushing Syndrome and Hip Fracture Due to Over-the-Counter Supplement (Artri King)". *Cureus* 15.7 (2023): e41278.
9. Starr Ranjani R. "Too Little, Too Late: Ineffective Regulation of Dietary Supplements in the United States". *American Journal of Public Health* 105.3 (2015): 478-485.

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