Topical Corticosteroid-Induced Adrenal Insufficiency: A Case Report

Nada Ghazi AlQadri a    Nouf Aljomah b    Hend M. Alotaibi c

a College of Medicine, Alfaisal University, Riyadh, Saudi Arabia; b College of Medicine, King Saud University, Riyadh, Saudi Arabia; c Department of Dermatology, King Saud University Medical City, Riyadh, Saudi Arabia

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Abstract
Topical Corticosteroids (TCS) are the most commonly prescribed medications in Dermatology practice. They are considered safe and effective if used at the appropriate location and for the appropriate duration. Local side effects due to TCS are not uncommon. However, systemic side effects are rare. Herein, we present a patient who developed adrenal insufficiency secondary to the use of TCS.

Introduction
Topical corticosteroids (TCS) are the most commonly prescribed medications in dermatology practice. They are considered the mainstay treatment for numerous inflammatory skin diseases due to their anti-inflammatory and immunosuppressive properties. If used in the proper way, they are safe and effective, and their adverse effects are rare. However, TCS abuse is becoming increasingly common by both physicians and patients [1]. Their excessive use can result in both local and systemic side effects. Most common local side effects include atrophy, striae, rosacea, perioral dermatitis, acne, and purpura. However, systemic side effects are much less common and include glaucoma, hyperglycemia, diabetes mellitus, and Cushing syndrome [2, 3]. Herein, we present the case of an 82-year-old female who developed adrenal insufficiency secondary to the use of TCS.
Case Report

An 82-year-old female presented to the Dermatology Department at King Saud University Medical City. She is a known case of diabetes mellitus and hypertension, which are controlled on treatment. Her main complaint was generalized itchiness that started >5 years ago.

Cutaneous examination revealed multiple excoriations marks over the arms and legs with few brown macules and patches; however, there were no primary skin lesions or stria. Two skin punch biopsies were taken from the left arm which revealed pigment incontinence with rare eosinophils in the dermis and mild deposition of fibrinogen in the blood vessel walls. The direct immunofluorescence study showed no IgA, IgM, IgG, or C3. In order to control the pruritus, the patient reported that she had been using TCS for the past 3 years without any physician's supervision. During the first year, she was using hydrocortisone butyrate cream 0.1% (30 mg/week) when she noticed an improvement. In the 2 years following, she would apply hydrocortisone butyrate cream 0.1% (60 mg/day) all over her body for 1 month, and then she would use a combination of hydrocortisone butyrate cream 0.1% (60 mg/day) and mometasone Furoate 0.1% and miconazole Nitrate 2% (50 mg/day) for 1 week. And finally, she would switch to clobetasol propionate 0.05% (25 mg/day) for 2 weeks. And she would repeat the same cycle of medications over and over again. However, while she was still using the TCS, she started experiencing symptoms such as weight loss, fatigue, and dizziness sometimes even leading to a loss of consciousness, nausea, and vomiting for 1 month. Therefore, she was referred urgently to endocrine clinics, and she was admitted in the internal medicine ward for further evaluation. Laboratory investigations were done (Table 1). The short synacthen test revealed an adequate response. An MRI of the pituitary gland was done with no abnormalities noted, which confirmed the diagnosis of central adrenal insufficiency secondary to chronic TCS use. The patient was advised to stop TCS and was started on oral hydrocortisone (20 mg/day) which was later tapered down (15 mg/day). The patient reported a significant improvement in symptoms once substitution treatment with oral hydrocortisone was initiated and the serum electrolytes normalized.

Discussion

Ever since its introduction in 1952, TCS has become a cornerstone treatment for multiple inflammatory dermatoses [4]. They work on the nuclear level and produce anti-inflammatory, immunosuppressive, and anti-mitogenic effects [5]. TCS is classified into 7 classes according to their potency. Choosing the proper TCS depends on multiple factors which include the

| Laboratory Investigation          | Result            | Normal Ranges          |
|-----------------------------------|-------------------|------------------------|
| Serum sodium                      | 133 mEq/L (low)   | 135–145 mEq/L          |
| Serum potassium                   | 3.4 mEq/L (low)   | 3.5–5 mEq/L            |
| Random cortisol level             | 13.8 mcg/dL (low) | >15 mcg/dL             |
| ACTH level                        | 0.5 pg/mL (low)   | 6–76 pg/mL             |
| Random serum glucose              | 14.8 mmol/L (high)| 4.4–7.8 mmol/L         |
| Total serum protein               | 65 g/L (normal)   | 60–83 g/L              |
| Haemoglobin                       | 12.1 g/dL (normal)| 12–15.5 g/dL           |

ACTH, adrenocorticotropic hormone.
anatomical area being treated, the severity of the disease and the extent of the body surface area involved. Local side effects usually occur with prolonged use and are dependent on the TCS potency, vehicle, and the application site. Common local side effects include skin atrophy, striae, acne, rosacea, perioral dermatitis, and pigment alteration. Due to a low percutaneous absorption, systemic side effects are much less common and include glaucoma, HPA axis suppression, Cushing syndrome, hypertension, hyperglycemia, and diabetes mellitus. As a general rule, treatment with TCS should not exceed 2–4 weeks. And superpotent TCS such as clobetasol propionate should not be used for >2 weeks with a total dose not exceeding 60 g per week, after-which, tapering down the treatment should be done to avoid local and systemic adverse effects. When prescribing TCS, proper counseling about the frequency and duration of treatment should be performed and the potential adverse effects should be explained to the patient. Moreover, providing a follow-up appointment or monitoring to the patient is recommended [4, 6]. In this case, the patient used 3 low, medium, and superpotent TCS simultaneously for 3 consecutive years which lead to the development of secondary or central adrenal insufficiency. Secondary adrenal insufficiency is defined as adrenal suppression caused by a deficiency of adrenocorticotropic hormone (ACTH) which is suppressed by the excessive use of exogenous corticosteroids. Symptoms include fatigue, weakness, weight loss, nausea, vomiting, diarrhea, and increased skin pigmentation, which is similar to Addison disease. Adrenal suppression can be detected by 1 of 2 ways either by measuring basal cortisol level or by evaluating ACTH response to low glucose level or cortisol level. Synacthen test, or ACTH stimulation test, is a diagnostic tool, and it tests the adrenal gland response to ACTH [7].

**Conclusion**

TCS is frequently prescribed by dermatologists and primary care physicians. They are highly effective in treating inflammatory skin diseases. However, patients are often unaware of their serious and potentially fatal systemic side effects if used incorrectly. Therefore, we encourage primary care physicians and dermatologists to provide their patients with a proper counseling about the proper usage of TCS and their potential side effects if used excessively or incorrectly in order to avoid the occurrence of local and systemic side effects, which could be fatal.

**Statement of Ethics**

A signed consent was provided by the patient to publish this case. And the study protocol was approved by the institute’s committee.

**Conflict of Interest Statement**

The authors declare that there is no conflict of interest.

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Author Contributions

Nada Ghazi AlQadri: writing manuscript, Nouf AlJomah: writing manuscript, and Hend Alotaibi: writing and editing manuscript.

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