Topical Steroids Induced Adrenal Insufficiency
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Topical steroids are considered to be a treatment option for many dermatological conditions. One of the major systemic side-effects of the topical steroids is the suppression of the hypothalamic-pituitary-adrenal axis resulting in adrenal insufficiency.

A fifty-year-old female with a known case of Xerosis was using diluted clobetasol propionate 0.05% cream and developed secondary adrenal insufficiency due to misuse of the topical steroid.

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Topical corticosteroids have played a major role in the treatment of most of the dermatological disorders since 1952. Systemic absorption of these agents may contribute to a variety of local and systemic side effects. Numerous studies have documented the potential for super-potent topical corticosteroids (such as clobetasol propionate) to suppress the hypothalamic-pituitary-adrenal axis (HPA). Factors that might increase the likelihood of suppressing the HPA include the amount applied, the percentage of body surface area, frequency of application, skin barrier quality, duration of the treatment, and the potency of the topical steroids.

The aim of this report is to present a patient with secondary adrenal insufficiency induced by prolonged use and misuse of a potent topical steroid that was used to treat Xerosis.

THE CASE

A fifty-year-old female with a known case of hypertension, dyslipidemia, gout, Xerosis, and diabetes mellitus was taking metformin and Lantus (insulin glargine). She presented with recurrent hypoglycemia for the last 2 months, for which her anti-diabetic medications (metformin and Lantus) had been stopped. However, she continued having hypoglycemia episodes once or twice per day. It was prescribed to use as necessary and on the affected area of the skin only. However, the patient was using it daily all over her body to relieve her itchiness.

C-peptide and insulin were normal. Random cortisol and adrenocorticotropic hormone (ACTH) levels were both low (cortisol 54, nmol/L, normal range, 83–833 nmol/L; ACTH, 3.27 pg/mL, normal range, 4.7–48.8 pg/mL). The synacthen test was performed (250 μg of synacthen was administered) to evaluate the hypophyseal–adrenal axis, and there was an insufficient response (cortisol at 0 minutes, 49 nmol/L; at 30 minutes, 351.9 nmol/L; and at 60 minutes, 430 nmol/L), which indicates adrenal insufficiency.

CT scan of the abdomen revealed no gross pathology. MRI of the pituitary was performed to rule out a pituitary adenoma.

The patient was diagnosed with secondary adrenal insufficiency resulting from the withdrawal of prolonged topical corticosteroid treatment. The patient was given intravenous hydrocortisone during her hospital stay. The patient’s condition and hypoglycemia episodes improved and the hydrocortisone was switched to oral administration. The patient was discharged on oral hydrocortisone 40–20–20 mg, the topical steroid was discontinued. She was advised to use Elica (mometasone furoate) instead. On follow-up, the patient’s condition had improved and hydrocortisone was tapered down.

DISCUSSION

Topical steroids have anti-inflammatory and anti-proliferative features; they have been the first-line treatment for chronic inflammatory skin disorders over the past decades. As with any medication, the use of potent topical steroids such as clobetasol propionate 0.05% (CP 0.05%), has the potential for a variety of side-effects including local reactions such as skin atrophy, telangiectasia, striae, steroid rosacea, acne, perioral dermatitis, hypertrichosis, hypopigmentation, and alteration in skin elasticity and mechanical properties.

Systemic side-effects include adrenocortical insufficiency resulting from topical steroids, which is caused by suppression of the HPA axis. However, this is highly debated, and it is usually associated with unregulated long-term use of potent topical steroids. Death from misuse of potent topical steroids related to an Addisonian crisis has been reported, although it is rare.

A study showed that four patients used clobetasol propionate 0.05% over a long period, and they developed secondary adrenal insufficiency 4 months after stopping the treatment. In our case, the patient had been using clobetasol propionate 0.05% since 2015 and had stopped 2 months before presenting with hypoglycemia.

Dhar et al showed that in some people, normal or clinically insignificant suppression of the HPA axis during treatment with topical steroids occurred. However, others reported a sustained suppression following discontinuation of treatment. In our case, the patient sustained suppression following discontinuation of treatment of topical steroids.

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Castela et al found that most of the reported cases of HPA axis suppression were usually due to misuse of the topical steroids through prolonged daily application and over a large surface area. Super-potent steroids increase the risk of suppression of the HPA axis. In our case, the patient used to excessively apply the topical steroid.

Steroid potency is linearly related to the cortisol level. A study revealed that if more than 50 g was applied per week, adrenal suppression is to be expected. However, as little as 2 g per day of clobetasol propionate 0.05% can cause a decrease in plasma cortisol within a few days. Our patient had applied clobetasol propionate 0.05% all over her body every day, although it had been prescribed only for use as needed.

If adrenal insufficiency is suspected, the morning cortisol level is the first test that might make a diagnosis, followed by a synacthen test. A blunted response to stimulation will confirm the diagnosis of adrenal insufficiency. In our case, the test revealed a level of cortisol below 420 nmol/L.

Another test is the insulin tolerance test to assess the integrity of the HPA axis. This test measures the ability of the adrenals to respond to insulin-induced hypoglycemia. If the axis is intact, there will be an increase in cortisol production by the adrenals, while no increase in production strongly supports the diagnosis of adrenal insufficiency. However, we could not perform the test because the patient’s main complaint was hypoglycemia, which was induced by the adrenal insufficiency. Another test is the metyrapone test, which is a provocation test. In this test, 30 mg/kg of metyrapone is given at midnight, and cortisol and 11-deoxycorticisol are checked at 8 am the following day. Levels of 11-deoxycorticisol >200 nmol/L regardless of the cortisol level indicate an intact HPA axis.

If the diagnosis of secondary adrenal insufficiency caused by topical steroids is confirmed, simultaneous replacement of oral steroids with a reduction in the potency and the amount of topical steroids is needed.

However, it has been reported that recovery from topical steroid-induced adrenal insufficiency is either time-dependent or spontaneous. One study showed that temporary reversible suppression was found in eight of 40 (20%) patients with psoriasis who were treated with potent topical steroids. It is recommended to test the HPA axis after stopping the steroid treatment. A study revealed that the patients’ serum cortisol and ACTH levels returned to the normal range after 1 to 4 months of follow-up. In our case, the recovery was not spontaneous.

CONCLUSION

Topical steroids can induce adrenal insufficiency, and although this is highly debated, the risk could not be ignored. Physicians should keep in mind the side-effects and avoid long-term use. It has been recommended not to exceed 4 weeks of topical steroid use, with doses of less than 50 g per week, and to use low-potency steroids to control the symptoms. However, the choice of the topical steroid should be determined by the area that is affected and the severity of the condition.

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