

Cushing Syndrome Induced by Topical Corticosteroids for the Treatment of Lichen Sclerosus



Manisha Notay MBBS¹, Nasim Fazel MD, DDS¹, Smita Awasthi MD^{1,2,*}

¹ Department of Dermatology, University of California, Davis, Sacramento, California

² Department of Pediatrics, University of California, Davis, Sacramento, California

ABSTRACT

Background: Lichen sclerosus is a chronic inflammatory dermatological condition with a predilection for the anogenital area.

Case: We describe a case of iatrogenic Cushing syndrome from the administration of high-potency topical steroids for vulvar lichen sclerosus in a 6-year-old girl. Her symptoms resolved after the cessation of topical steroid treatment.

Summary and Conclusion: This case brings attention to iatrogenic Cushing syndrome as a potential complication when using high-potency topical corticosteroids in the anogenital region.

Key Words: Lichen sclerosus, Pediatric, Topical steroids, Cushing syndrome

Introduction

Lichen sclerosus (LS) is a chronic inflammatory dermatological condition, mainly affecting the anogenital region. Although it most commonly affects postmenopausal women, 7%-15% of patients are prepubertal girls. The prevalence is estimated to be 1 in 900-1100.¹ Pediatric LS most commonly presents with vulvar and anal pruritus, soreness, dysuria, bleeding, and constipation. On examination, the skin can appear atrophic (often described as cigarette-paper like atrophy), with erosions, erythema, and/or purpura. Alteration of the vaginal and vulvar architecture can also occur, including labial fusion and clitoral obliteration. Female patients can develop a figure of 8 pattern, which describes involvement encircling the vagina and anus.² High-potency topical steroids are commonly used in the treatment of pediatric LS.¹ Cushing syndrome is a rare complication from the administration of topical steroids in the pediatric population.³ Herein we describe a case of Cushing syndrome due to the administration of topical steroids for the treatment of pediatric vulvar LS, which, to our knowledge, has not been previously reported.

Case

A 6-year-old girl with a 1-year history of vulvar LS was referred to the dermatology outpatient clinic for treatment. She had previously been treated with triamcinolone 0.5% ointment; however, despite this she continued to experience symptoms of pruritus and burning. She subsequently started a regimen of topical clobetasol 0.05% ointment twice daily. Upon follow-up, 1 month later, she had symptomatic improvement, as well as a reduction in vulvar

atrophy and hypopigmentation. Because of her clinical improvement, the clobetasol 0.05% ointment was reduced to once-daily application. However, the option to switch to a lower potency topical steroid was deferred because of persistent symptoms as evidenced by continued pruritus, dysuria, petechiae, and cigarette paper-like atrophy. She was asked to follow-up within 4 weeks; however, her family cancelled her appointment and did not reschedule.

Eight weeks after initiating clobetasol 0.05% ointment (60-g tube), she presented to the pediatric outpatient clinic with facial swelling and was then referred to Endocrinology. On examination, she was noted to have moon facies (Fig. 1) and mild facial plethora, with no evidence of fat pad deposition on her upper back, striae, acne, hirsutism, proximal muscle weakness, or easy bruising. She had gained 1.6 kg over the course of 8 weeks, maintaining normal growth velocity. She was Tanner stage 1 for breast and pubic hair development. Her vital signs, including blood pressure, were within normal limits. Her blood glucose was also normal. Ophthalmologic examination revealed no evidence of increased intraocular pressure or cataract formation.

After urgent follow-up with dermatology, a slow taper off topical steroids was initiated. The patient was tapered first to triamcinolone 0.05% ointment daily for 2 weeks, then to desonide 0.05% ointment daily in the morning and pimecrolimus 1% cream in the evening for 2 weeks. She was then transitioned to pimecrolimus 1% cream twice daily. She was successfully weaned off steroids without any symptoms suggestive of adrenal insufficiency; thus, she did not have an adrenocorticotropic hormone or urinary cortisol level checked by Endocrinology. The patient's facial appearance returned to normal after the topical steroid taper (Fig. 2). Unfortunately, her LS flared and her symptoms of burning, pruritus, and dysuria returned, but were eventually controlled with 3 days of triamcinolone 0.1% ointment per week and 4 days of tacrolimus 0.1% ointment per week. Her weight, height, and blood pressure are

The authors indicate no conflicts of interest.

* Address correspondence to: Smita Awasthi, MD, UC Davis Department of Dermatology, 3301 C St, Suite 1400, Sacramento, CA 95816; Phone: (916) 734-4510

E-mail address: sawasthi@ucdavis.edu (S. Awasthi).



Fig. 1. Cushingoid appearance of the face.

monitored at every appointment and have been within normal limits and no further signs of Cushing syndrome have been noted on exam.

Summary and Conclusion

LS typically exhibits a female predominance. The incidence of LS shows a bimodal distribution, mainly affecting prepubertal girls and postmenopausal women. This pattern is thought to be due to the low levels of estrogen in both of these populations. The pathogenesis of LS is thought to be autoimmune in origin.¹

LS is typically managed using ultrapotent topical steroids. A 6- to 8-week course of ultrapotent topical corticosteroids applied twice daily is considered to be a safe and effective treatment for LS.⁴ Studies in postmenopausal women have shown improvement in symptoms and histological findings after a 12-week course of clobetasol 0.05% cream.⁵ However, no randomized control trials exist regarding treatment in the pediatric population.¹ Small studies have shown topical steroids to be safe in this age group. Untreated LS is known to cause complications such



Fig. 2. Facial appearance after successful tapering of topical steroid treatment.

as obliteration of the labia minora and narrowing of the vaginal introitus due to the architectural changes.⁶ Labial fusion in female infants with untreated LS can occur. Prepubertal LS can be recurrent with some patients experiencing relapses after treatment.¹

Risk factors for the development of Cushing syndrome from the use of topical steroids include age, quality of skin, potency of topical steroid used, area treated, duration of treatment, and the use of occlusive dressings.⁷ Although our patient was treated within current treatment guidelines, the use of high-potency steroids on a mucosal surface for several weeks does confer an increased risk of Cushing syndrome. However, despite many female children and adults being treated in a similar fashion, to our knowledge, there are no case reports of Cushing syndrome. Our patient was treated for 8 weeks in total and finished one 60-g tube during this time.

Weight gain without a corresponding gain in height is one of the first features of Cushing syndrome in the pediatric age group. Children can also present with hypertension, facial plethora, headache, bruising, striae, and a delay in sexual development. When signs and symptoms suggest Cushing syndrome in a child, laboratory diagnostic evaluation to determine if hypercortisolism is present is usually only undertaken if exogenous glucocorticoid use has been excluded. Iatrogenic Cushing syndrome is most commonly caused by exogenous steroid use, typically oral or parenteral. Cushing syndrome due to topical application of steroids is considered to be a rare clinical complication. However, there are multiple case reports of iatrogenic Cushing syndrome in the pediatric population. Most cases occurred after the administration of topical steroids for the treatment of diaper dermatitis, a common dermatologic concern in the pediatric population. A review of the cases of Cushing syndrome that developed in children after topical steroid treatment showed that the median duration of steroid use was 2.75 months.⁷

As expected, the most commonly implicated topical corticosteroids are the class I ultrapotent steroids. Cushing syndrome due to topical corticosteroid use in children usually occurs after a shorter duration of treatment compared with in adults.⁸ The percutaneous absorption of topical steroids is greater in younger children compared with older children, which is thought to be due to the increased ratio of body surface area to body weight. After conducting a thorough literature search in PubMed, Ovid-Medline, and EMBASE we were unable to identify other reports of Cushing syndrome from LS or from the administration of topical steroids to the vulva or vagina in the pediatric population. Systemic absorption from vaginal application of estrogens is well documented. This might be in part due to the vascularity of the vulvar and vaginal mucosal surface, and the avoidance of first pass metabolism. Similarly, this likely contributes to the systemic absorption of steroids leading to iatrogenic Cushing syndrome in this case. Chronic steroid use, especially in the setting of iatrogenic Cushing syndrome, can cause suppression of the hypothalamic-pituitary-adrenal axis, thus gradual withdrawal is necessary with monitoring for adrenal insufficiency on tapering.

In conclusion, we present this case to increase awareness of the potential complication of iatrogenic Cushing syndrome when using ultrapotent topical corticosteroids in the

setting of vulvar LS in the pediatric population, which are the treatment of choice for this condition. When discussing treatment with care-givers it is vital to stress that they adhere to the treatment amount and duration. It is also important to emphasize the importance of timely follow-up so that treatment can be monitored for efficacy and complications.

References

1. Bercaw-Pratt JL, Boardman LA, Simms-Cendan JS, et al: Clinical recommendation: pediatric lichen sclerosis. *J Pediatr Adolesc Gynecol* 2014; 27:111
2. Dendrinis ML, Quint EH: Lichen sclerosis in children and adolescents. *Curr Opin Obstet Gynecol* 2013; 25:370
3. Ho CW, Loke KY, Lim YY, et al: Exogenous Cushing syndrome: a lesson of diaper rash cream. *Horm Res Paediatr* 2014; 82:415
4. Garzon MC, Paller AS: Ultrapotent topical corticosteroid treatment of childhood genital lichen sclerosis. *Arch Dermatol* 1999; 135:525
5. Dalziel KL, Millard PR, Wojnarowska F: The treatment of vulvar lichen sclerosis with a very potent topical steroid (clobetasol propionate 0.05%) cream. *Br J Dermatol* 1991; 124:461
6. Smith SD, Fischer G: Childhood onset vulvar lichen sclerosis does not resolve at puberty: a prospective case series. *Pediatr Dermatol* 2009; 26:725
7. Tempark T, Phatarakijirund V, Chatproedprai S, et al: Exogenous Cushing's syndrome due to topical corticosteroid application: case report and review literature. *Endocrine* 2010; 38:328
8. Demirsoy EO, Bilen N, Akturk AS, et al: Cushing's syndrome induced by high-potency topical corticosteroids. *Int J Dermatol* 2014; 53:e20