Cuties, Creams and Cushing

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Keywords

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Abstract

Prolonged use of corticosteroids can lead to serious side effects, including Cushing's Syndrome (CS), a disorder caused by abnormally high levels of free plasma glucocorticoids, and hypothalamo-pituitary axis suppression. The cause of CS may be either natural production or external administration of steroids. Iatrogenic CS is most commonly caused by oral or injectable medications and rarely by topical application. The absorption rate is higher with transcutaneous than with topical application. Only few cases of CS after topical application have been reported. We present the case of a 2-month-old girl who developed CS due to prolonged use of topical steroids.

Introduction

Cushing's Syndrome (CS) is a condition associated with excessive cortisol secretion that may result from an ACTH-dependent cause such as ACTH production by a pituitary adenoma or an ACTH-independent cause such as an adrenal adenoma. It can be caused by to the external administration of steroids. The most common cause of CS is the administration of exogenous glucocorticoids, whereas endogenous glucocorticoid excess due to pituitary or adrenal tumors is comparatively infrequent. Patients with CS typically present with a variety of physical symptoms including facial redness and swelling, which can result in a rounded "moon face" appearance, a fatty deposit at the back of the neck called a "buffalo hump," truncal obesity, hirsutism, skin bruises, proximal muscle wasting, hypertension, hypertension, and growth abnormalities (1,2). The diagnosis of exogenous CS is made based on the clinical presentation of specific symptoms and confirmed by measuring basal cortisol levels at 8 AM. There has been a significant increase in incidence of adverse effects associated with the use of topical or systemic steroids. These individuals are often from lower socioeconomic backgrounds, have lower levels of education and awareness, and may have received inadequate or inappropriate information from healthcare providers (2).

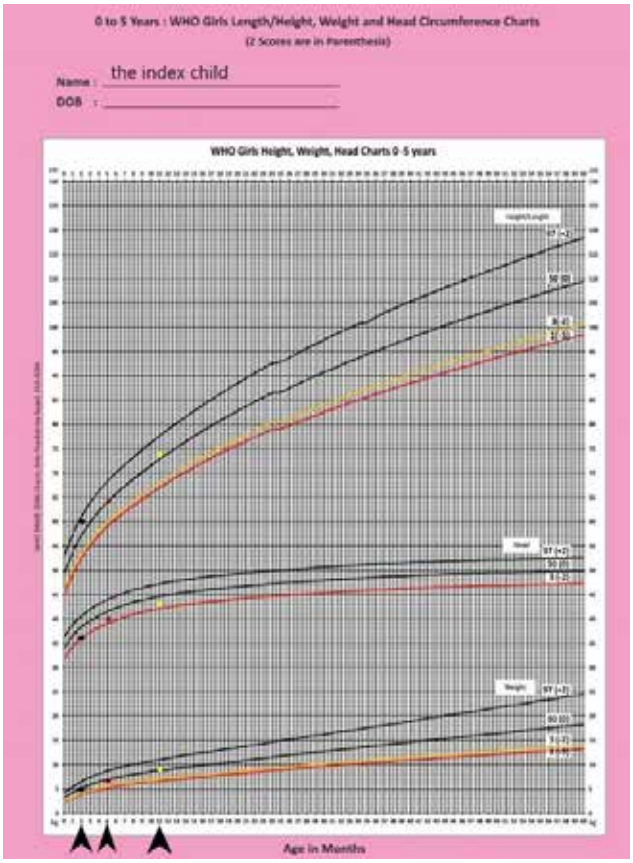
Case report

A 2-month-old baby girl was admitted to the hospital because of excessive growth noticed over the past month. She was born by cesarean section to non-consanguineously married parents and had a birth weight of 2700g. The child had no neonatal admissions and was discharged on the third day of life on exclusive breastfeeding. The baby appeared healthy until 15 days of age when she began to have loose stools for which a local practitioner prescribed antibiotics. Two days after onset, the child developed perianal dermatitis, and a cream containing clotrimazole, beclomethasone, and neomycin was prescribed. As the dermatitis worsened, another topical cream containing clobetasol, neomycin, and clotrimazole was prescribed, and the parents were instructed to discontinue the previous cream. However, they continued to apply both creams inappropriately. Over the next three weeks, the child was observed to gain weight, particularly in the face, with no other associated symptoms. Eventually, the child developed oral lesions, possibly candidiasis, and the parents began using another oral preparation containing triamcinolone for treatment. At admission, child was active and feeding well. She exhibited a characteristic Cushingoid facial appearance, with fat accumulating under the skin of the abdomen, shoulders, genitals, and thighs (as seen in the figure 1a).The child was developmentally appropriate for age. The child's growth parameters were as shown in the figure-2.

The child's blood pressure readings were above the 99th percentile (124/74 mm Hg in the right upper limb, 120/70 mm Hg in the left upper limb, 117/70 mm Hg in the right lower limb, and 118/74 mm Hg in the left lower limb). This hypertension persisted throughout the hospital stay and follow-up visits one week later. Perianal

Figure 1: a: appearance of the child at the time of admission; 1 b appearance at the age of 11

Figure 2: Growth chart



excoriation was noted upon examination, but there were no signs of muscle weakness. Based on the presence of Cushingoid facies and hypertension, Cushing's disease/Cushing's syndrome was considered as a possible diagnosis.

Laboratory evaluation revealed a random blood glucose level of 117 mg/dl (Normal: 70-120 mg/dl); hemoglobin of 11.9 g/dl, white blood cell count 12,350/mm3, platelet count 248,000/mm3, blood urea nitrogen 8 mg/dl, creatinine 0.3 mg/dl; sodium 136 mEq/l, potassium 4.2 mEq/l, chloride 109 mEq/l. Serum cortisol and ACTH levels at 8.00 AM were 0.6 mcg/dl and <5 pg/ml, respectively. Secondary adrenal insufficiency was diagnosed performing a 1mcg ACTH stimulation test and the peak cortisol level was<1mcg/dl. Ultrasonography of whole abdomen showed no demonstrable abnormalities.

Topical and oral corticosteroid were immediately discontinued. Hypertension was controlled with amlodipine (0.1 mg/kg/day). Intravenous hydrocortisone of 50 mg/m^2/day was prescribed for 5 days and tapered to 10 mg/m2/day over a week and discontinued.

During the 3-month follow-up period, the child did not experience any intercurrent illnesses. The child's weight stabilized while her length and head circumference increased appropriately (as shown in figure 2). Morning serum cortisol and ACTH levels returned to normal levels of 13.1 mcg/dl and 56 pg/ml, respectively. The hypertension also subsided and antihypertensive medication was stopped. The features associated with Cushing's syndrome had resolved, and at the age of 11 months, as demonstrated in the figure 1b, all features were within normal ranges.

A descriptive table presents a summary of Iatrogenic Cushing's syndrome caused by topical steroid use in infants below six months of age (2-8). The affected cases were all infants who were suspected to have diaper dermatitis, and the most commonly used steroid was clobetasol. All cases presented with typical symptoms of Cushing's syndrome and had suppressed cortisol and ACTH levels. The median duration of topical steroid application was 2 months, ranging from 1 to 4.5 months. After discontinuation of topical steroid, the median recovery time for the hypothalamic-pituitary-adrenal (HPA) axis was 3 months, ranging from 1 to 12 months. Two infants reported (case 4 and 5) died from severe disseminated Cytomegalovirus (CMV) infection (5,6).

Discussion

Cushing's syndrome (CS) is characterized by excessive cortisol levels resulting from a variety of causes. Under normal conditions, the pituitary gland secretes ACTH, which stimulates the adrenal glands to produce cortisol. However, exogenous administration of corticosteroids can suppress the hypothalamic-pituitary-adrenal

Table 1: Characteristics of children (< 6 months) with exogenous CS from Steroid application

	Age (months)	Age at start of steroid cream (months)	Duration of usage(months)	Steroid used	Cortisol (mcg/dl)	ACTH (pg/ml)	Recovery time (months)	Disease	Reference
1	4.5	2.5	2	Clobetasol	0.5	NA	6	Diaper dermatitis	2
2	4	2	2	0.1% Hydrocortisone butyrate + Clobetasol	1	<5	2	Diaper dermatitis	3
3	3	1.5	1.5	Clobetasol	<1	<5	1	Diaper dermatitis	4
4	3	1	2	Clobetasol	5.2	<5	Death	Diaper dermatitis	5
5	5	1.5	4.5	Clobetasol	<1	6.4	Death	Diaper dermatitis	6
6	4	2.5	1.5	Clobetasol	<1	<5	6	Diaper dermatitis	4
7	2	0.5	1.5	Clobetasol + beclomethasone + oral triamcinolone	<1	<5	3	Diaper dermatitis	Our case
8	3	Birth	2.5	Clobetasol + prednicarbate	<1	<5	12	Diaper dermatitis	7
9	3.5	2.5	1	Clobetasol	<1	<5	2	Diaper dermatitis	7
10	6	3	3	Clobetasol	0.66	7.1	NA	Dry Skin	8

(HPA) axis. While prolonged use of oral or parenteral steroids commonly leads to iatrogenic CS, some cases have reported the development of this condition due to prolonged use of topical steroids. In some instances, severe immunosuppression and fatal secondary infections have occurred in such cases (9).

The infant discussed in this article developed iatrogenic CS due to the excessive and prolonged use of a potent topical steroid i.e., clobetasol propionate, for the treatment of perianal dermatitis. The parents had inadvertently and inappropriately applied high doses of the topical corticosteroid continuously for a period of two months resulting in the absorption of clobetasol through the skin and into the systemic circulation. This resulted in the development of CS.

The child exhibited typical clinical features of Cushing's syndrome, such as moon face and generalized weight gain. Laboratory investigations revealed significant suppression of both cortisol and ACTH levels due to the administration of exogenous steroids. It is noteworthy that the child did not experience life-threatening adrenal insufficiency, which is a known risk associated with the use of various forms of glucocorticoids, including topical creams (10)]. There have been reports of routine doses of corticosteroid creams leading to adrenal insufficiency, with nonspecific symptoms (11). Therefore, it is crucial to maintain a high level of suspicion for iatrogenic causes of adrenal insufficiency and be able to identify such cases. As illustrated in the table, cases have been reported in which iatrogenic Cushing's syndrome developed due to the prolonged use of clobetasol for the management of napkin dermatitis. Nevertheless, our case stands out as it involves a diagnosis of Cushing's syndrome in a very young infant with a significantly elevated blood pressure (>99th centile), accompanied by other typical signs of the condition. Additionally, the infant had extensive perineal dermatitis with inflamed skin, which likely contributed to greater permeation and penetration of the topical medication.

Using a low-potency topical steroid may be sufficient to treat conditions like napkin dermatitis, as opposed to a high-potency steroid such as clobetasol. The use of other screening methods like midnight salivary cortisol may aid in the early detection of potential iatrogenic Cushing's syndrome while using topical steroids. The management of iatrogenic Cushing's syndrome includes discontinuation of the causative medication, close monitoring, administration of physiologic doses of steroids, and gradual tapering them over time (10).

Conclusion

Our case and others published in the literature emphasize the importance of educating patients about proper instructions for the use of topical or oral steroid preparations. High potency steroid applications in infants should be avoided whenever possible, and parents should be strictly instructed to use them only for a short duration. This study was ethically approved by the Institution Review Board.

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Conflict of interest

The authors have no conflict of interest to declare with regard to the subject discussed in this manuscript.

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