

SHORT COMMUNICATION

Cushing's Syndrome in a 6-month-old Boy: A Rare Side-effect due to Inadequate Use of Topical Corticosteroids

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Topical corticosteroids (TC) are used in several fields of medicine with universally recognized acceptable effectiveness and safety. TC are classified according to their potency, leading to different effectiveness, but also to different local and systemic side-effects. Iatrogenic Cushing's syndrome (CS) and concomitant hypothalamic-pituitary-adrenal (HPA) suppression are potential systemic adverse effects caused by the improper use of TC. We report here a case of a 6-month-old boy who developed CS after treatment with a TC prescribed for dermatitis. This case is compared with previously reported cases.

CASE REPORT

An Indian 6-month-old boy was admitted to our hospital with failure to thrive since 2–3 months of age, poor appetite, and growth of hair on the face, neck and shoulders. He was born at term, birth weight 3,240 g (25–50th percentile).

On presentation his body weight was 6,580 g (<3rd percentile), height 66 cm (3rd–10th percentile) and head circumference 43 cm (25–50th percentile). His heart rate was 118 bpm, blood pressure 104/53 mmHg (above 97th percentile for age and height), respiratory rate 30/min, and body temperature was normal. Physical examination revealed truncal obesity with a “moon face” appearance, facial and truncal hirsutism (Fig. 1), and erythematous papules in the skin folds of the neck.

The patient had a history of neck dermatitis, which had been treated since 2 months of life with a topical combination drug containing fusidic acid 2% and betamethasone valerate 0.1%. The topical steroid was used 2–3 times daily in 7–14-day cycles, despite the fact that it had been prescribed by a community paediatrician for a total of 6 days only. A total of 2 tubes of betamethasone valerate (30 g/tube) had been used within 4 months. Due to language difficulties the parents were unaware of the possible side-effects of the product.

Laboratory evaluation revealed a decrease in both morning adrenocorticotropic hormone (ACTH) (7.39 pg/ml; normal 10–60 pg/ml) and cortisol levels (1.17 µg/dl; normal 7–20 µg/dl). Fasting plasma glucose was 59 mg/dl (normal 60–100 mg/dl), sodium 140 mEq/l, potassium 5.8 mEq/l, alanine transaminase 89 U/l, and aspartate transaminase 76 U/l. White blood cell count (WBC) was slightly elevated. Other laboratory data, including haemoglobin and platelet count, blood urea nitrogen, creatinine, and bilirubin, were normal. Abdominal ultrasonography was unremarkable. Based on the history, physical and laboratory signs, iatrogenic Cushing's syndrome with HPA axis suppression was diagnosed. Application of the topical corticosteroid was stopped and a topical antiseptic (solution of eosin 2%) and hypoallergenic moisturizing cream were started.

Due to the complete adrenal suppression a substitutive dose of 10 mg/m² per day of oral hydrocortisone was started and then slowly tapered off, with instructions to double the dose during



Fig. 1. Cushingoid appearance. Typical “moon face” and facial hirsutism at admission (photograph reproduced with parental consent).

acute infections. Five weeks after stopping the topical steroid the HPA axis appeared to be persistently suppressed (peak cortisol after ACTH-stimulation test: 4.53 µg/dl). The hydrocortisone treatment was finally stopped approximately 2 months after admission. At 3 months follow-up the infant had fully recovered, with no further signs of hypercorticism. His weight was 9,750 g (50–75th percentile) and height 73.50 cm (25–50th percentile) (Fig. S1¹). The dermatitis had resolved; morning serum cortisol and ACTH levels were in the normal range.

DISCUSSION

Development of iatrogenic CS is not uncommon after systemic corticosteroid therapy. In 1986 Turpeinen et al. (1) reported that CS, together with HPA suppression, was produced by the long-term application of TC especially in infancy and childhood, due to systemic absorption of the potent TC used at that time.

TC have been used for decades as effective drugs for many mucocutaneous disorders. In paediatrics, TC combined with emollients remain the mainstay

¹<http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-2151>

of treatment of eczema. Therefore, it is important to avoid “corticophobia”, a phenomenon observed in some health practitioners and in many patients, as it causes more TC side-effects, poor therapeutic adherence and, consequently, poor treatment response (2). However, in chronic skin disorders such as eczema, the family’s perception of the disease should be taken into account. International directives underline the importance of the development of a personalized therapeutic education plan (3). Therefore, in many dermatological diseases TC must be used, but in the correct way, including verifying that the patient and/or parents, have correctly understood the therapeutic indications.

The efficacy and adverse effects of TC are essentially due to their potency, their absorption and the adequacy of their modality of use. It has been demonstrated that application of small doses of a superpotent TC can cause a decreased level of morning cortisol (due to suppression of the HPA axis) after only a few days of use, even through healthy normal skin (4). The use of potent and superpotent TC should be avoided for patients under the age of 12 years (5).

Percutaneous absorption of TC is influenced by several factors: patient’s age; type and location of dermatological lesion; and dose and duration of treatment. Absorption is greater in children, and in particular in infants, because of their higher ratio of body surface area to body weight and because of their thin skin. Absorption is also determined by the quality of previous skin problems: damaged and/or inflamed skin is more absorbent. Furthermore, prolonged use of TC can cause atrophy, which makes the skin more permeable (6). Absorption also differs according to the site of application: the mucous membranes, scrotum and face are more absorptive, while nails, hands and feet are areas of low absorption. Occlusive dressings (including nappies), as well as long-term and/or frequent application, and/or the use of large amounts of TC increase the absorption of glucocorticoids. Finally, considering that glucocorticoids are metabolized mainly in the liver by Cytochrome P450 3A4 (CYP 3A4), patients with severe liver diseases or those using CYP 3A4 inhibitors are at higher risk of TC complications, as reported by Atabek et al. (7).

The patient reported here was at very high risk because a potent TC was used in an infant for months, on a relatively large skin area including the neck and jaw angle. The parents were not aware of the possible side-effects. Thus, in this case, the improper use of a necessary and effective drug led to an endocrine complication that could indirectly promote future corticophobia.

Infants are particularly at risk of TC side-effects. Tempark et al. (8) reviewed the literature on iatrogenic CS due to topical steroids in children and adults. Most affected children were infants (86%), and in these infants clobetasol (82%) or betamethasone (18%) were applied for a mean of 2.75 months.

The management of complete adrenal suppression consists of administering a substitutive dose of hydrocortisone, 10 mg/m² per day, which should then be tapered off slowly. Parents should be instructed to double the dose in case of acute infections. Morning serum cortisol, ACTH, and an ACTH-stimulation test will be performed to confirm recovery of the HPA axis (3).

In conclusion, health practitioners should prescribe TC when needed, giving instructions for its correct use (modality, quantity and duration) and avoiding, if possible, superpotent molecules, especially for very young children. Close follow-up by the referring physician is mandatory in order to verify the evolution of the disease and the understanding of the parents in handling it (efficacy of therapeutic education).

The authors declare no conflicts of interest.

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