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A CASE REPORT OF CUSHING SYNDROME IN A CHILD INDUCED BY TOPICAL CLOBETASOL APPLICATION

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Annotation: Chronic low-dose steroid therapy in children can result in dysfunction of hypothalamic-pituitary-adrenal axis. However, the development of Cushing syndrome from topical steroid therapy is unusual. Long-term topical Clobetasol propionate application resulting in Cushing syndrome in a 7-month old male was evaluated. The patient was found to have severe adrenal suppression. Limiting the use of steroid-containing drugs, prescription of less potent topical agents, especially during infancy, and warning of parents about potential side effects are very important.

Keywords: Cushing Syndrome, Topical, Clobetasol, Steroid

Introduction:

Cushing syndrome refers to the clinical consequences of chronic exposure to excessive glucocorticoids, regardless of source. According to Harrison's Principles of Internal Medicine (21st edition), the most frequent overall cause is iatrogenic, resulting from prolonged glucocorticoid therapy for inflammatory or autoimmune conditions [1]. Endogenous Cushing syndrome is less common and is classified as either ACTH-dependent or ACTH-independent. ACTH-dependent causes include Cushing disease, due to a pituitary corticotroph adenoma, and ectopic ACTH secretion from neuroendocrine tumors, whereas ACTH-independent forms are usually due to adrenal adenomas, carcinomas, or bilateral adrenal hyperplasia [1].

The disorder is rare, with an estimated incidence of 2–3 cases per million population annually, and occurs more often in women between 20 and 50 years of age [1]. The clinical manifestations evolve gradually and are diverse, but certain features are characteristic. These include centripetal obesity, rounded plethoric face, dorsocervical fat pad, wide violaceous striae, thin skin with easy bruising, and proximal muscle weakness. Metabolic disturbances such as glucose intolerance, diabetes mellitus, hypertension, dyslipidemia, and osteoporosis are common. Additional features may include menstrual irregularities, psychiatric disturbances, increased infection risk, and thromboembolic events [1]. Because many of these features overlap with common disorders like obesity and metabolic syndrome, diagnosis is often delayed. Such delays contribute to increased morbidity and premature mortality, mainly from cardiovascular and infectious complications, underscoring the importance of early recognition and treatment [1].

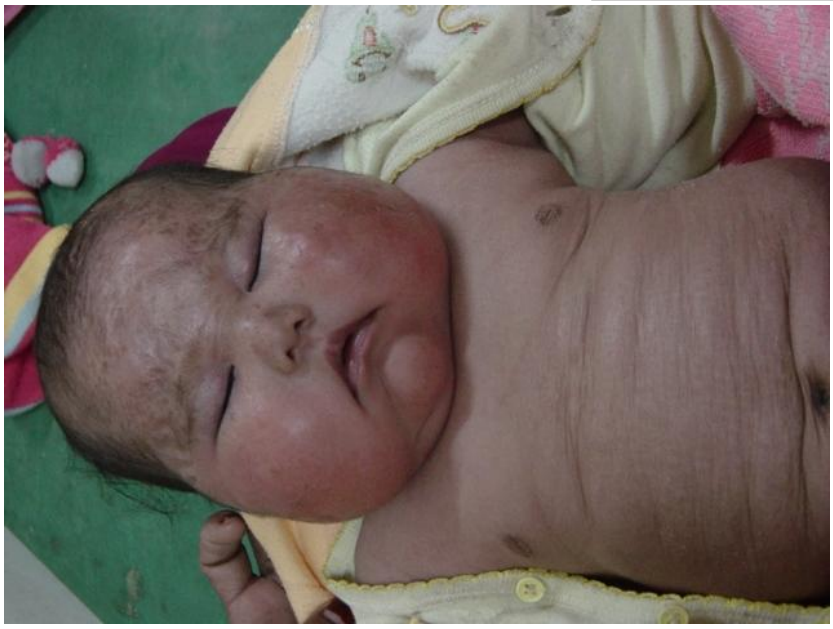
Cushing syndrome is exceptionally rare in infancy. However, potent topical corticosteroids may induce iatrogenic Cushing syndrome and suppression of the hypothalamo–pituitary–adrenal axis through systemic absorption [2–4]. Clobetasol propionate (0.05%) is the most potent topical corticosteroid available, and several reports have documented adrenal suppression and Cushingoid features following its prolonged or inappropriate use [2,3]. Lack of awareness of the

adverse effects of topical steroids may result in cumulative toxicity and serious systemic complications. We report an infant with Cushing syndrome caused by misuse and overuse of topical clobetasol prescribed for ichthyosis.

Case report:

A 7-month-old male was admitted in Kanti Children's hospital, Kathmandu for evaluation of swelling of face (Figs.1). The patient had a history of rough and scaly lesion on the skin since birth and for that the parents were applying clobetasol propionate (0.05%) ointment, obtained without prescription, four to five times a day for the last 7 months, starting from the first week of life, without medical supervision, until his presentation to hospital. His weight was 7000g (82% of expected), length 63 cm (90% of expected), and head circumference 41 cm (10^{th} percentile). He had pulse rate of 100/min, blood pressure 130/80 mm of Hg on right upper arm and respiratory rate of 38/min. Physical examination found a plethoric moon facies, plump looking body, buffalo hump and generalized scaly skin lesion consistent with lamellar ichthyosis. There were no striae and examination of abdomen revealed no masses. The genitalia were normal. Other examination was unremarkable. The application of this steroid was stopped and replaced by hydrocortisone parenterally and certain laboratory studies were performed. The results were the following: hemoglobin 12.8 g/dl, white blood cell count 5900/mm3, platelet count 200,000/mm3, ESR 5 mm at one hour, serum glucose level 103 mg/dl, serum creatinine 0.3 mg/dl, cholesterol 4.1 mmol/l, triglyceride 1 mmol/l, high-density lipoprotein cholesterol 1.3 mmol/l, low-density lipoprotein cholesterol 2.3 mmol/l, SGOT 23 IU/L, SGPT 16 IU/L, total protein 6 gm/dl, sodium 148 mEq/L, potassium 4.9 mEq/L. Urine examination was normal. The bone age, determined by radiographic examination of the left hand was 8 months. There was no cataract on opthalmological evaluation.

Serum cortisol levels were very low both in the morning (10 ng/ml; normal 68–213 ng/ml) and the evening (17.3 ng/ml; normal 19–115 ng/ml). ACTH stimulation test couldn't be performed due to the unavailability of the medicine.



(Photograph 1: Child at the time of admission)

Discussion:

Uncontrolled topical steroid treatment can cause potentially harmful effects. Long-term exogenous glucocorticoid therapy can suppress ACTH synthesis and reduce the need for endogenous cortisol production (6). Our patient presented with Cushing syndrome after long-term topical clobetasol propionate application. It is known that HPA axis suppression is seen in patients receiving potent topical glucocorticoid preparations (2, 5, and 6). Clobetasol seems to have a stronger systemic effect than any other topical steroid and this may be the result of increased percutaneous absorption, slow elimination from the body or the intrinsic potency of the clobetasol molecule (3). Several studies have shown that therapy with inhaled corticosteroids can cause detectable reductions in the normal physiologic secretion of cortisol (7). However, there are no reports of Cushing syndrome after inhaled corticosteroid treatment. Perry et al reported nine patients, four of whom presented with Cushing syndrome and showed various clinical findings of adrenal suppression caused by intranasal steroids (7). Ocular and intranasal steroid treatment can also affect the hypothalamo-hypophyseal-adrenal axis (8). It is also seen in cases where prescription of double or triple preparation of a corticosteroid with an antifungal and/or an antibiotics(9). The risk of systemic side effects from topical steroid therapy depends on the dose applied, the area of skin exposed to treatment and the degree of skin inflammation(4,10).

In conclusion, misuse or extensive use of topical steroids can cause Cushing syndrome. Awareness of the side effects, including Cushing syndrome, is important when prescribing steroid-containing medication. Such medications should be prescribed in small amounts and treatment should be limited to a short period. Warning parents about potential hazardous effects of steroids, limiting steroid-containing medications, and use of low-dose ointments for infants are some of the preventive measures that may be taken. Furthermore, the parents of Cushing syndrome patients should be asked whether they have applied any topical steroids or other steroid-containing drugs to their child.

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