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A case report on topical steroids causing infantile iatrogenic cushing syndrome

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Abstract---Cushing Syndrome is characterised by raised levels of Glucocorticoids in free plasma. It is caused because of excess endogenous release of steroids or excess usage of exogenous steroids. The common form Cushing syndrome present in children is Iatrogenic Cushing syndrome. It is either due to excessive administration of parenteral or oral preparations of steroids which are used in treatment of pulmonary, renal, haematological and autoimmune diseases. Topical steroids rarely causes Cushing syndrome. In our case report, We will describe about a four month old girl child who developed Cushing syndrome (Iatrogenic) because of prolonged and excessive use of Topical preparations steroids Namely clobetasol for treatment of napkin (diaper) dermatitis.

Keywords---topical steroids, infantile iatrogenic, syndrome, case report.

Introduction

Cushing Syndrome is characterised by raised levels of Glucocorticoids in free plasma.¹ It is caused because of excess endogenous release of steroids or Exogenous administration of steroids.¹ The usual clinical presentation of Cushing syndrome is facial plethora and Oedema which gives an appearance of moon face, Buffalo hump Which is due to fat accumulation in the Supraclavicular region and in the trunk, Truncal obesity, which results in skin fragility which appears as purple Striae commonly seen in abdomen and limbs. Other clinical presentation include hirsutism, easily bruising skin which can lead to ecchymoses, delayed and prolonged wound healing process, muscle wasting involving proximal muscle groups, arterial hypertension, hypoglycaemia, retarded growth.²

Cushing syndrome is very rare in paediatric age group, with an incidence of 2–5/10,00,000 population per year.² Iatrogenic cause is the most commonly seen form. Where as, in under 5 children (Pre school age group) adrenal hyperplasia, adrenal adenoma, or adrenal carcinoma accounts for endogenous Cushing syndrome.² Pituitary and ectopic causes are not usual seen in Pre school children. High prevalence of chronic diseases like bronchial asthma, pulmonary pathologies, haematological pathologies, renal pathologies, or dermatological pathologies, which needs steroid therapy leads to iatrogenic Cushing syndrome.^{2,3}

There are various diagnostic modalities used in the diagnosis of Cushing syndrome. Midnight salivary cortisol test, urine free cortisol (UFC) and low-dose dexamethasone suppression test (LDDST) have been shown effective as a primary screening for endogenous Cushing syndrome, particularly of the endogenous type, with the confirmation by urine free cortisol (UFC), low-dose dexamethasone suppression test (LDDST), and dexamethasone/ corticotrophin-releasing hormone (DST-CRH) tests, a definitive criteria or a highly sensitive/specific diagnostic test for iatrogenic Cushing syndrome is still lacking in the literature.⁴

The diagnosis of exogenous Cushing syndrome can be made based on the clinical presentation and it is confirmed by a decrease of 8 AM basal corticosteroid levels.^{5,6} Chronic and prolonged usage of corticosteroids can present in systematic manifestations of Cushing syndrome. These patients are prone to Develop complications like tertiary Adrenal insufficiency following the reduction and elimination of the corticosteroid therapy due to the negative (inhibitory) feedback mechanism on the (HPA) hypothalamic-pituitary-adrenal axis, which mainly releases corticotropin hormone (CRH) and adrenocorticotrophic hormone (ACTH). The reactivation of CRH is required for the effective reactivation of the HPA axis post cessation of long term corticosteroid therapy.⁷ Oral and parental Corticosteroids are commonly to cause Iatrogenic Cushing syndrome, where as topical corticosteroids causing Cushing syndrome is rare.⁸ In this article, we present an infant with Iatrogenic Cushing syndrome post 2 months of topical corticosteroid therapy.

Case Report

A 4 and half month old female child was brought to our hospital with complaints of face puffiness along with generalised oedema (Anasarca) . On further questioning of the mother we came to an understanding that her condition had an insidious onset from 2 and half months of age, and gradually increased over time. There was no other significant history.

Her mother stated, she had using topical corticosteroid (clobetasol) in view of napkin dermatitis in a dose frequency of 4 -9 times a day for the past 2 and half months. The rash usually subsides in 3 to 4 days and then it flares up. Hence she ended up using clobetasol for 2 and half months. Her prenatal, antenatal and post natal period was uneventful.No NICU stay post delivery. She on exclusive breastfeeding , all vaccinations required were given at proper time.No significant family history. The infant's physical examination showed facial puffiness and anasarca. Sign like abdominal purple stria was absent. On the examination of skin it revealed napkin rash, no other skin findings were present. The infant's vitals were stable. Dysmorphic features and skeletal deformities were not present. Her growth and development were appropriate for age, and the examination of other systems was normal. On blood Investigations it revealed that the adrenocorticotrophic hormone (ACTH) 0.4pg/mL (interpretation- very low) , and S.cortisol level - 17µg/dl. The USG abdomen revealed no abnormality.

Initially treatment with Hydrocortisone (12mg/m²) for 6 weeks , and then every week 25 % of the dose was tapered. ACTH stimulation test done at 5th week revealed the following, ACTH - 5.9 pg/mL and cortisol - 28µg/dl. Treatment with Hydrocortisone terminated as the levels of ACTH and cortisol were within normal limits. Facial puffiness and oedema reduced over this period in a significant way.

Discussions

Normally, Secretion of the cortisol by adrenal gland is stimulated by ACTH which is secreted by the pituitary gland. Exogenously administration of corticosteroids leads to decreased activity of this hypothalamic-pituitary-adrenal (HPA) axis.³ Iatrogenic type of Cushing syndrome is commonly due to prolonged Oral and Parenteral Corticosteroids therapy, rarely seen in topical steroid therapy.⁹⁻¹² They are prone to immunosuppression in a sever way and secondary infections which are fatal.¹³

The child discussed in our article was diagnosed with iatrogenic type of Cushing syndrome after excessive and longer duration of therapy with a topical steroid - clobetasol propionate in view of diaper dermatitis .¹⁴ Higher dose of corticosteroid was consistently used for a period of 2 months which lead to absorption of clobetasol via the dermal route,and there by entering the systemic circulation which lead to occurrence of Cushing syndrome (Iatrogenic) .¹⁵ The clinical manifestations of the infant was typical in relation with Cushing syndrome and signs such as moon face, anasarca , and increased weight gain, the diagnosis was confirmed by the lab investigations . Suppression of ACTH was caused by the exogenous administration of steroids, nonetheless S.cortisol was still within the normal limit . Providentially, adrenal insufficiency which is a life threatening

complication wasn't seen in our patient. The risk of developing complications like adrenal insufficiency in individuals on any form of steroids is evident lately. Even prescribed doses of glucocorticoid topical creams can cause adrenal insufficiency.¹⁶

The infant's height, blood pressure, skin, immune system, and blood glucose levels were not involved. Similar to our case, Siklar et al.¹⁵, Sahip et al.¹¹, Guven et al.¹³, and Tempark et al.¹² reported similar cases of iatrogenic Cushing syndrome after prolonged use of clobetasol for the treatment of diaper dermatitis. However, in our case the diagnosis was made early in time as only facial puffiness and generalised oedema was observed with the suppression of ACTH level.

In this child, Clobetasol (Highly potent topical Steroid) is not recommended as the choice of treatment for diaper rash. Because the rash is extensive, and there is inflammation of the skin. This would allow for easy permeation and penetration of the clobetasol. Thus, it would be better to choose hydrocortisone (lowly potent topical Steroid) than clobetasol.¹⁷ Midnight salivary cortisol helps in early detection of iatrogenic Cushing syndrome while on topical steroids.¹⁸ Iatrogenic Cushing syndrome is managed by cessation of the drug causing it, use of exogenous steroids at physiological doses, and tapering them slowly over a period of time.²

The case as an example should imply the need of adequate and timely health education of the parents about the usage of any topical steroid preparation. Physicians should always advise the parents to apply the topical cream in thin layers only in the affected areas and should not exceed the limit of daily dose, and should only be used as short-term.

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