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Cushing's syndrome and adrenal suppression following topical corticosteroid use

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CASE REPORT

ABSTRACT

The extended use of topical corticosteroids, particularly in young children, may cause suppression of the hypothalamo-pituitary-adrenal axis. Here, three cases of iatrogenic adrenal suppression resulting from topical corticosteroids are presented.

Key Words

Adrenal insufficiency, Corticosteroid, Iatrogenic cushing's syndrome.

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INTRODUCTION

Cushing syndrome, a systemic disorder, is the result of abnormally high blood level of cortisol or other glucocorticoids.[1] Iatrogenic cushing syndrome secondary to oral corticosteroids is a well-known entity. However cushing syndrome and adrenal suppression as a result of topical steroids is rarely described even after their wide spread use since they were first introduced.[2] Although the use of topical, intra-articular or aerosol therapy has the advantage of allowing more targeted therapy and therefore theoretically fewer systemic adverse effects, every mode of exogenous glucocorticoid delivery has been implicated in the development of Cushing's syndrome.[3]

CASE REPORT

Case 1

This baby was born at 37 weeks as second of twin, had a short stay in neonatal unit for transient hypoglycemia and hypothermia but otherwise no concerns. He was seen again at 6 weeks of age for feeding difficulties and noisy breathing and was treated as gastro oesophageal reflux. He was seen by the ENT team and was diagnosed as having laryngomalacia along with swelling of inferior turbinates, likely from reflux. A barium swallow was done which was normal and he was discharged on betamethasone nasal drops, 1drop twice daily for 2 weeks. He was seen again in paediatric clinic at 5 months of age, with continued feeding difficulties and poor growth.(length-0.4th centile, weight between 0.4-2nd centile) Clinically he was found to be floppy owing to which a battery of blood tests were done including genetic tests and his random cortisol turned up as 12 nmol/l which was very low. The low dose synacthen test showed a very low basal cortisol(<11nmol/l) and poor response to ACTH with peak levels of 149nmol/l.

He was started on replacement steroids for adrenal insufficiency and was seen in endocrine clinic. His length, by this time was falling way below 0.4th centile from an original length between 0.4-2nd centile. The only clinical finding of note was protuberant cheeks. His blood pressure was within normal limits. Parents denied the use of any medication including steroids. He had undetectable ACTH levels, normal thyroid function and a normal MRI. Clinically he was thought to be having ACTH deficiency. Further endocrine evaluation showed no evidence of congenital adrenal hyperplasia or other pituitary hormone deficiency.

In his next consultation at 7 months of age, parents brought up the fact that they were still using betamethasone nasal drops which was prescribed when he was 7 weeks old. Parents forgot to mention about nasal drops when asked about medications in general and they had no clue that this was steroid. His short stature and protuberant cheeks could now be emphatically attributed to iatrogenic cushing

syndrome, induced by long term use of betamethasone drops. This was stopped and steroid replacement was continued. He had short synacthen test repeated periodically which continued to be abnormal. His physical appearance started to normalize after 6 months, but the earliest sign of adrenal recovery was not seen till he was 30 months old. As his ACTH response continued to be sub optimal, his steroid replacement continued in a low dose until his 4th birthday when it was finally stopped.

Case 2

A 5 year old boy was referred to endocrine clinic for poor growth; his height was less than 0.4th centile and weight on 0.4th centile which had been so since 18 months of age. His parental heights were around 9th centile. He was thought to be having familial short stature. In the next follow up visit it was noted that his height dropped to well below o.4th centile. He had severe eczema and was treated with topical steroids on several occasions since the age of 4 months. He was treated with alclometasone and betamethasone in coal tar and was also started on beclomethasone inhalers for his asthma at 5 years of age. He had severe atopy evidenced by very high Ig E levels and mild iron deficiency anaemia. Clinically he did not have cushingoid features but in view of his prolonged steroid usage, we did a random cortisol which was low and the low dose synacthen test which followed, yielded sub optimal response to ACTH. He was started on steroid replacement; his inhaled steroid was stopped and was slowly weaned off his topical steroids. His adrenal response to ACTH normalized after 10 months and he showed good catch up growth after one year.

Case 3

A 10 year old boy was referred to endocrine clinic for faltering growth on the background of high dose inhaled steroids for 12 months. He was a known asthmatic and was started on inhaled beclomethasone when he was 3 years old. At 5 years of age he was started on salmeterol and at 6 years he received several short courses of oral steroids. His steroids were slowly escalated to bring a protracted cough under control but by now he was taking 1000 micrograms of inhaled budesonide daily. Diagnosed with a shield ulcer, he was also getting dexamethasone 0.1% eye drops with a drop on left eye 16 hours a day and four times a day on right eye for 6 weeks. He started to have increased appetite and apparent weight gain during this time. His height was on 50th centile and weight on 75th centile. Between 5 and 8 years, his height was on 91st centile. Clinically he was not cushingoid and had a normal blood pressure.

We requested a low dose synacthen test which could not be accomplished due to his severe needle phobia. He then had serial measurements of salivary cortisol which were low. His inhaled budesonide was initially reduced to 700 micrograms at which point he started getting muscular aches and pains which then stabilized with time. His eye drops were tapered to 1 drop a day and now he is on minimal dose of budesonide. After reduction of inhaled steroids he has shown a catch up growth to 75th centile. Since his faltering of growth happened before the use of eye drops, his toxicity was presumed to be due to inhaled steroids.

DISCUSSION

Cushing syndrome and adrenal suppression following topical steroids are rare in children. While the use of topical steroids is generally considered safe, its un regulated use can cause problems similar to systemic steroids as seen in this case series, as well as those reported recently.[4,5,6]

Inhaled corticosteroids are recommended for the treatment of persistent asthma but the lowest possible effective dose should be used. When high doses of inhaled corticosteroids are necessary, patient growth should be carefully monitored and the dose reduced according to symptom improvement.[7] There are recent reports that suggest inhaled steroids in conventional doses can cause symptomatic adrenal suppression due to a differential sensitivity to glucocorticoids.[8] In pediatric patients, large amounts of topical corticosteroids may be absorbed from the skin in a short period as the ratio of body surface area to the weight is greater than adult.[9]

Topical dexamethsone have also been implicated in adrenal suppression[6] although in our case it had a rather compounding effect. This potential toxicity need to be considered when such a treatment is prescribed to a child already on inhaled steroids.

When adrenal suppression from intranasal steroids is suspected, the most appropriate and widely available test is the low dose synthetic ACTH test. A non-invasive alternative is the measurement of cortisol in salivary profiles, but currently this assay is not routinely available.[5]

Growth and development as well as cortisol levels should be monitored in children on long-term topical corticosteroid treatment.[10]

CONCLUSION

Continuous use of moderate to high-potency topical corticosteroids over several months can contribute to adrenal suppression and Cushing's syndrome. When assessing children with short stature and growth failure, it is important to take a detailed history of medications.

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