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Case Report

Adrenal insufficiency and growth failure secondary to iatrogenic inhaled and intranasal corticosteroids – a case report

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Abstract

Introduction: Chronic glucocorticoid therapy by systemic and inhaled forms is the most common cause of adrenal insufficiency. There is no administrative form, dosing, duration or underlying disease for which it is more common, although higher dose and prolonged use have highest risk.

Clinical case characteristics: A 11-year-old girl was brought with cough and cold for a week, fever, vomiting and headache for one day.

She had been diagnosed to have asthma and allergic rhinitis 7 years ago. She was started on Mometasone 120mcg nasal spray OD, used for 4 years and Budesonide 64mcg nasal spray BD for 1 year. She was also put on Formoterol 6mcg + Mometasone 200mcg MDI, used for 4 years, and Formoterol 6mcg + Budesonide 200mcg MDI, used for 1 year. No significant birth or family history.

On examination, child was severely stunted and wasted, with height and weight below – 3 standard deviations on IAP growth chart. She was hemodynamically stable, head to toe and systemic examination was normal.

Outcome: She was found to have severe hyponatremia, which was corrected. Due to significant past history of chronic usage of intranasal and inhaled corticosteroids, adrenal insufficiency was suspected and serum cortisol levels done, which were low. ACTH stimulation test was administered and serum cortisol levels tested at 30 minutes and 60 minutes, remained below the reference range after the test. Hence the child was diagnosed to have adrenal insufficiency. Pediatric endocrinology reference taken and steroids tapered over several weeks. Serum cortisol levels monitored during follow up were normal.

Conclusion: Clinicians must have a high index of suspicion, especially in patients with nonspecific symptoms after cessation of high-dose or long-term steroids and consider testing for cortisol levels. Patient education, monitoring and regular follow up is a key feature of management of this condition.

Key words – 'Adrenal Insufficiency', 'Growth Failure', 'Inhaled and Intranasal Corticosteroids'

Introduction

The adrenal cortex secretes the steroid hormones, cortisol and aldosterone, under the control of pituitary adrenocorticotropic hormone and angiotensin II. Adrenal insufficiency is characterised by inadequate - glucocorticoid synthesis due to destruction of the adrenal cortex or lack of adrenocorticotropic hormone stimulation. The most common cause of adrenal insufficiency is exogenous steroid usage in the form of long-term therapy by systemic and inhaled forms. This inhibits the hypothalamic-pituitary-adrenal axis by negative feedback, which causes adrenal insufficiency after stopping the corticosteroid therapy. Patients can present with insidious onset of symptoms, or in acute adrenal crisis, which requires rapid diagnosis and treatment.

According to a meta-analysis, 4.2% patients on chronic intranasal steroid use (95% CI – 0.5 to 28.9) and 6.8% patients on chronic inhaled steroids (95% CI – 3.8 to 12.0) developed adrenal insufficiency.[1] There is no set

protocol regarding dosage and duration of treatment to prevent adrenal insufficiency, though higher doses and prolonged use have higher risk.

In a study done in 2012 on the effects of glucocorticoid therapy, follow-up of a cohort of 5 to 12-year-old children with childhood asthma treated for 4 to 6 years with inhaled corticosteroids showed a significant outcome on final adult height.[2]

In view of high numbers of children on long term corticosteroid use for multiple indications in clinical pediatrics, it is important to understand the risk of developing adrenal insufficiency, a grave and life-threatening adverse effect.

Case report

A 11-year-old girl was brought by her parents to the department of Pediatrics at our institution, on 16/01/2023, with cough and cold for a week, fever for one day with associated multiple episodes of vomiting and headache.

She had been diagnosed with asthma and allergic rhinitis 7 years ago, at 4 years of age. She was commenced on Mometasone 120 mcg (6mcg/kg/day) nasal spray once daily, which she used for 4 years and Budesonide 64 mcg (6.4 mg/kg/day) nasal spray twice daily for 1 year. She was also put on Formoterol 6 mcg + Mometasone 200 mcg MDI, used for 4 years, and Formoterol 6 mcg + Budesonide 200 mcg MDI, used for 1 year.

She was the second issue of a non-consanguineous marriage, born via term caesarian section with birth weight of 4 kg, a developmentally normal child with good scholastic performance and immunized appropriately for age.

Clinical findings:

On examination, child was found to be severely stunted and wasted, with height and weight below – 3 standard deviations on the IAP growth chart, with previously recorded anthropometric values also being below – 3 standard deviations, as shown in Table 1, with low BMI. She was hemodynamically stable on receiving. Head to toe and systemic examination was normal.

Diagnostic assessment and therapeutic intervention:

Relevant investigations were done, details of which are enclosed in Table 2. She was found to have hyponatremia, which was corrected. In view of significant past history of usage of intra nasal and inhaled corticosteroids, adrenal insufficiency was suspected and serum cortisol levels were done, which revealed low cortisol levels. ACTH stimulation test was administered and serum cortisol levels tested at 30 minutes and 60 minutes, were found to remain below the reference range after the test. Hence the child was diagnosed to have adrenal insufficiency. Parents counselled about the condition and danger signs explained. Pediatric endocrinology reference taken and the dosage of the intranasal and inhaled corticosteroids were tapered over several weeks. Serum cortisol levels monitored during follow up on out-patient basis and levels were found to normalize.

Table 1 - Height and weight monitoring during follow up:

Age	*8y 7m*	*9y*	*10y*	*11y 7m*	*12y*
Weight (kg)	16	18	19	21	23.5
Weight centile (IAP growth charts)	< 3rd	< 3rd	< 3rd	< 3rd	< 3rd
Height (cm)	102	115	120	124	128
Height centile (IAP growth charts)	< 3rd	< 3rd	< 3rd	< 3rd	< 3rd

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Table 2 – Investigations:

		16/01/23	*17/01/23*	*17/01/23*	*19/01/23*	*20/01/23*	*21/01/23*	*12/05/23*	*11/10/23*
Serum electrolytes (mmol/L)	*Na*	124	124	133	137				
	K	4.6	4.4	3.8	4.3				
	Cl	92	91	98	99				
S. Cortisol (mcg/dL)						2	8.8 -> 8.9	8.1	9.5

Discussion

The adrenal cortex comprises three zones: zona glomerulosa, fasciculata, and reticularis, which synthesize aldosterone, cortisol, and androgens, respectively. The synthesis of aldosterone is controlled by the renin-angiotensin system, and cortisol is regulated by the hypothalamic-pituitary-adrenal axis. Cortisol is secreted through a circadian rhythm according to different amplitudes of ACTH pulses, which occur every 30 to 120 minutes, highest in the morning, reduce through the day and reach a nadir at night. Secretions of corticosteroids can change in the presence of major illnesses, surgeries and sleep deprivation, where it can increase up to 10 times.

A side effect of glucocorticoid therapy is suppression of the hypothalamic-pituitary-adrenal axis which leads to adrenal insufficiency. This depends on duration of treatment, mode of administration, dosage form, potency, concomitant drug usage and individual susceptibility. Common symptoms are weight loss, failure to thrive, fatigue, headache, dizziness, recurrent infections, gastro intestinal disturbances, myalgia and arthralgia. Clinical signs include hypotension, tachycardia, dehydration, anemia, with hyponatremia, hyperkalemia, lymphocytosis and eosinophilia.

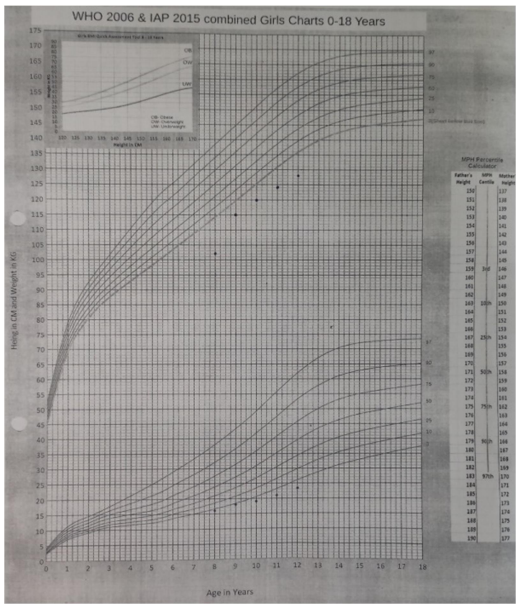
Adrenal insufficiency is diagnosed by the demonstration of low basal and/or stimulated serum cortisol. Clinicians must have a high index of suspicion, in patients with nonspecific symptoms while on high-dose or chronic therapy with inhaled or intra nasal corticosteroids and consider testing for cortisol levels. Patient education, monitoring anthropometric parameters, and regular follow up are key features of management of this condition.

Conclusion

1) Patient education about the risk and symptoms of adrenal insufficiency is essential;

2) Clinicians must display a low threshold for testing cortisol levels, in patients with nonspecific symptoms while on high-dose or chronic therapy with any dosage form of corticosteroids;

3) Regular monitoring and treatment of local and systemic adverse effects of corticosteroids is of paramount importance.



Anthropometric measurements on follow up on IAP growth charts

Clinical Photograph

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