Exogenous Cushing’s Syndrome with Secondary Adrenal Insufficiency in an Asthmatic Infant: “Healing Evil with Evil”

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Abstract
Exogenous Cushing’s syndrome is an ACTH-independent endocrine disorder, characterized by specific signs resulting from excessive glucocorticoid intake. This is mainly the case in the course of management of corticotherapy-necessitating chronic diseases such as asthma. It may occasionally lead to secondary Adrenal insufficiency, which is the inability of the adrenal glands to produce hormones, precisely cortisol and aldosterone, due to lack of secretion of ACTH from a suppressed pituitary gland. The clinical presentation of adrenal insufficiency may be gradual and nonspecific, depending on the degree of insufficiency and precipitating stress event. Symptoms may include fatigue, nausea, muscle weakness, and headache. We here present the case of an asthmatic infant treated with glucocorticoids, who came presenting with some of the above symptoms after the interruption of his medication, with onset of exogenous Cushing’s syndrome. The particularity of this case report is the association of iatrogenic Cushing’s syndrome with secondary adrenal insufficiency in an asthmatic infant. This is rare and very less reported in the pediatric population. Yet, it was effectively managed with a salt restriction diet and the re-administration of hydrocortisone, which is a glucocorticoid too. As such, a disorder caused by the intake of glucocorticoid had definitely found its solution in a treatment with glucocorticoids. Somewhat-“healing evil with evil” or a “hair of the dog that bit you”.

Keywords: Cushing’s syndrome; Adrenal insufficiency; Asthma

Introduction
Asthma is the most common chronic disease of childhood, with an estimated prevalence ranging from 5% to 30% in some countries [1]. Glucocorticoids are used in the management of moderate to severe cases of asthma. They are routinely administered as aerosols and offer control of the respiratory symptoms. Despite this advantage, exogenous administration of glucocorticoids might lead to the suppression of the hypothalamic-pituitary-adrenal axis for months [2]. Up to 6.8% of adrenal insufficiency are found in asthmatic infants secondary to the use of corticosteroids [3]. There are two types of adrenal insufficiency: primary and secondary, and these may be of acute or chronic onset. Chronic primary adrenal insufficiency has the highest prevalence in overall population [4]. Therapeutic glucocorticoid administration is thought to be the most common cause of secondary adrenal insufficiency. In effect, the chronic administration exogenous glucocorticoids may induce atrophy of pituitary corticotrophic cells [5]. As a matter of fact, it is estimated that induced linear growth impairment as a complication of hypothalamic–pituitary–adrenal axis suppression occurs with glucocorticoid doses ≤400 μg/day on biochemical testing. In addition, a Cushingoid appearance with central obesity and fatigue has been reported with higher doses [5,6]. Apart from common symptoms such as fatigue, nausea, muscle weakness, and headache, other features of adrenal insufficiency including hypoglycemia and weight loss, may occur as well on withdrawal
of an exogenous corticosteroid treatment [6]. However, adrenal glands and corticosteroid hormones they produce (cortisol and aldosterone) are so vital that the mainstay of the treatment in adrenal insufficiency can only be a replacement therapy with another synthetic corticosteroid. This may last from months to a year before remission [2-5].

Case Presentation

A 3-year-old male infant presented with an insidious onset of puffiness of the face. The swelling progressed over a period of 4 months associated with non-quantified weight gain. Persistent fatigue, intermittent nausea and vomiting were noted as well, during the last 2 weeks prior to consultation. The infant’s perinatal and developmental history were insignificant. He was born full-term to non-consanguineous parents via a eutocic per vaginal delivery. After delivery, the birth weight was 3500g, and all other anthropometric and vital parameters were normal for age. The infant did not require neonatal intensive care and was discharged in good health. He presented with more than 3 repetitive episodes of lower respiratory tract infections with bronchiolitis as from 3 months of age and had been diagnosed with asthma. There was history of atopy manifesting with intermittent rhinitis and urticaria. The child had been treated with salbutamol and betamethasone sprays for over two years with improvement of the condition. However, recent arrest in the use of betamethasone 3 weeks before the visit was noted. There was no relapse of asthma crises in the meantime. The child was feeding with home meals and had received all the required vaccinations at their proper times. The psychomotor development was normal. There was a family history of asthma. As clinical findings, the physical examination of the infant revealed an overweight patient at the 93rd percentile and normal vital parameters. Facial puffiness could be observed with no body oedema. The patient had facio-truncular obesity with curly hair but no cutaneous abnormality. The rest of the physical assessment was unremarkable. Laboratory findings revealed low serum cortisol level of 2 ng/l and low ACTH at 10 pg/ml. Fasting blood sugar was normal at 1.1 g/l. The complete blood count and serum electrolytes performed were in their normal ranges. The patient was placed on a salt restriction diet. Oral hydrocortisone was given at 10 mg/m2 body surface area, and the parents were advised to administer double doses in case of illness or any other stress. The patient was seen 3 months later with regression of signs and symptoms of Cushing syndrome, and the prescription was halved to 5 mg/m2 body surface area. The next visit was scheduled 3 months thereafter, to check for blood ACTH and cortisol restitution in order to envisage hydrocortisone discontinuation.

Discussion

Cushing’s Syndrome (CS) is an endocrine disorder resulting from high glucocorticoid level in the blood. It is either categorized as ACTH-dependent CS (due to pituitary tumors or excess ACTH administration) or ACTH-independent CS (due to adrenal neoplasms or excessive glucocorticoid intake) [7]. Under normal circumstances, ACTH is secreted by the pituitary gland which in turn stimulates the secretion of cortisol by the adrenal glands [8]. Prolonged exogenous corticosteroid administration can lead to a number adverse effects based on the potency and duration of the treatment. This include secondary adrenal insufficiency marked with the suppression of the hypothalamic-pituitary-adrenal axis, iatrogenic Cushing’s syndrome with metabolic disorders, severe infections with immuno defciency, and failure to thrive due to epiphyseal fusion. Our case report further highlights the potential for the systemic activity of iatrogenic glucocorticoids to induce concomitant Cushing’s syndrome with adrenal insufficiency in an infant. In this patient, facio-truncular obesity with curly hairs were consistent with Cushing syndrome, while fatigue, nausea and vomiting characterizing adrenal insufficiency. Moreover, this child had biochemical evidence of adrenal insufficiency with low blood ACTH and cortisol levels, even though further complementary work-up was not conducted with blood aldosterone.

The low ACTH blood level indicated exogenous pituitary gland inhibition from betamethasone, which was originally meant for treating the child’s asthma [6-8]. While decreased blood cortisol was a repercussion of the insufficiently stimulated adrenal glands from low ACTH. Given the context and the clinical findings, all these factors oriented the diagnosis towards exogenous Cushing’s syndrome with secondary adrenal insufficiency. However, blood electrolytes’ levels were normal, with normal kaliemia and natrema. This seemed strange, as low cortisol and aldosterone blood levels in adrenal insufficiency is generally responsible for hyperkalemia and hyponatremia. Such a strange phenomenon had earlier been documented in secondary adrenal insufficiency and postulated to be the result of inappropriate vasopressin secretion [9].

Corticosteroids form a family of biochemically active substances, naturally synthesized in vivo as hormones and pharmacologically reproduced in vitro as drugs. They have functions in the regulation of overall metabolism, hydro-electrolytic balance and various stress. They are also immunosuppressant with anti-inflammatory activity [6-11]. With respect to the predominance of their individual functions, they may be subdivided into glucocorticoids and mineralocorticoids. Hydrocortisone is the recommended replacement therapy in case of adrenal insufficiency [6-11]. Although from the family of glucocorticoids as betamethasone (the causative drug in this case report) and cortisol (the main lacking hormone), it has some mineralocorticoid action in addition, making it similar to aldosterone (another lacking hormone in adrenal insufficiency). It is however closest in function with cortisol, which makes it even more suitable as a replacement therapy. Its use as sole replacement therapy is generally sufficient to restore carbohydrate, fat and amino-acids metabolism and
prevent electrolyte imbalances that may occur as well in adrenal insufficiency [6-12].

Although growth suppression has been reported as being associated with chronic adrenal insufficiency in some studies, this was not a feature in our patient [10,13]. Perhaps the absence of this sign was indicative of acute adrenal insufficiency, meaning an onset induced by the withdrawal of betamethasone spray [6,10,11]. However, this may also imply that adrenal suppression may manifests differently, depending on patient susceptibility, glucocorticoid doses and duration.

Conclusion

Exogenous Cushing’s syndrome and secondary adrenal insufficiency can manifest conjointly in pediatric patients. Asthmatic children with moderate to severe symptoms are mostly at risk for developing these. The onset of Cushing’s syndrome and adrenal insufficiency which may lead to adrenal crisis in such children should perhaps encourage to investigate different algorithms for management of asthma. The insidious nature of adrenal insufficiency in infants is even more alarming as the imbalance can progress unnoticed if Cushingoid features are not present. A large number of patients with asthma might have adrenal insufficiency even with low- to medium-dose corticosteroids treatment when they are administered over a long period. Thus, it is essential that patients with asthma under this treatment be checked for adrenal insufficiency more frequently.

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References

1. Calpin C, Macarthur C, Stephens D, Feldman W, Parkin PC. (1997) Effectiveness of prophylactic inhaled steroids in childhood asthma: A systematic review of the literature. J Allergy Clin Immunol 100: 452-457.

2. Joshi RR, Maresh A. (2018) Iatrogenic Cushing’s syndrome and adrenal insufficiency in infants on intranasal dexamethasone drops for nasal obstruction – Case series and literature review. Int J of Pediatr Otorhinolaryngol. 105:123-126.

3. Broersen LHA, Pereira AM, Jørgensen JOL, Dekkers OM. (2015) Adrenal Insufficiency in Corticosteroids Use: Systematic Review and Meta-Analysis. J Clin Endocrinol Metab. 100: 2171-2180.

4. Spiegel RJ, Vigersky RA, Oliff AL, Echelberger CK, Bruton J, et al. (1979) Adrenal suppression after short-term corticosteroid therapy. The Lancet. 313: 630-633.

5. Art W, Alolio B. (2003) Adrenal insufficiency. The Lancet. 361:1881-1893.

6. Patel L, Wales Jk, Kibirige MS, Massarano AA, Couriel JM, et al. (2001) Symptomatic adrenal insufficiency during inhaled corticosteroid treatment. Arch Dis Child 2001; 85: 330-334.

7. Alkhuder L, Mawlawi H. (2019) Infantile Iatrogenic Cushing Syndrome due to Topical Steroids. Case Rep Pediatr 2019: 2652961.

8. Stratakis CA. (2016) Diagnosis and Clinical Genetics of Cushing Syndrome in Pediatrics. Endocrinol Metab Clin North Am 45: 311-328.

9. Oelkers W. (1989) Hyponatremia and inappropriate secretion of vasopressin (antidiuretic hormone) in patients with hypopituitarism. N Engl J Med 321: 492-496.

10. Wong JYW, Zacharin MR, Hocking N, Robinson PJ. (2002) Growth and adrenal suppression in asthmatic children on moderate to high doses of fluticasone propionate. J Paediatr Child Health 38: 59-62.

11. Todd GR, Acerini CL, BuckJJ, Murphy NP, Ross-Russel R, et al. (2002) Acute adrenal crisis in asthmatics treated with high-dose fluticasone propionate. Eur Respir J 19: 1207-1209.

12. Moyo GPK, Sobguemezing D, Adjifack HT. (2020) Neonatal Emergencies in Full-term Infants: A Seasonal Description in a Pediatric Referral Hospital of Yaoundé, Cameroon. Am J Pediatr. 6: 87-90.

13. Moyo GPK, Djomkam IFK. (2020) Factors Associated with Stunting in School Children of an Urban Community in Cameroon. Am J Pediatr. 6:121-124.