Case Report

A rare cause of familial exogenous Cushing syndrome

Remya Rajan[1], Cijoy Kuriakose[1], Jinson Paul[1], Nitin Kapoor[1], Kripa Elizabeth Cherian[1], Thomas Vizhalil Paul[1]

[1]*Department of Endocrinology, Christian Medical College and Hospital, Vellore, Tamil Nadu, India*

Abstract

Exogenous steroid use is the most common cause of Cushing syndrome. With the use of glucocorticoids(GC) for a variety of diseases, the indiscriminate use of this group of drugs has increased. We present a family from which both children were brought with features suggestive of Cushing syndrome. On evaluation, they were found to have suppressed hypothalamic pituitary adrenal (HPA) axis, signifying steroid use from exogenous sources. On further evaluation by a psychiatrist, the mother who was on treatment for chronic depression confessed that she had bought dexamethasone tablets over the counter, and administered the same, mixed with fruit juices to her sons. The family was counselled regarding the consequences of chronic steroid abuse and the children were started on replacement doses of prednisolone. Certain features like posterior subcapsular cataract, glaucoma, avascular necrosis of femur and psychosis are specific to exogenous Cushing syndrome. Despite efforts to understand the effects of long-term steroid treatment on the HPA axis, it is not yet clear as to which patients will have prolonged HPA axis suppression. The time taken for the recovery of HPA axis remains variable. Also, HPA axis suppression due to exogenous steroids may present as acute adrenal crisis. Hence, it is important to start these patients on replacement dose of steroids and also educate them regarding the increased requirement of steroids during stress.

Keywords: Exogenous cushing syndrome, glucocorticoids, prednisolone

Introduction

Glucocorticoids are widely used for their anti-inflammatory action in variety of diseases (e.g. autoimmune, hematologic, and inflammatory diseases). The inadvertent and indiscriminate use of steroids for indistinct indications has increased. According to a 2011 report, 1% of the general population was on systemic glucocorticoids.[1] Among these, about two thirds exhibit iatrogenic manifestations related to excessive exposure to glucocorticoids.[2] This situation is further compounded by the irrational use of these drugs. Over the counter use of steroids and the use of indigenous medications adulterated with glucocorticoids are rampant in our country. It is important for physicians involved in primary care to be aware of this scenario. Though exogenous steroid use is the most common cause of Cushing syndrome, indiscriminate administration of exogenous steroids by a family member has not been reported so far.

Case Report

We present the story of an unusual family, from which both the children were brought with symptoms suggestive of Cushing syndrome at the same time. Two brothers from the same family of ages 16 and 18 years, respectively, presented with complaints of progressive weight gain of about 30 kg in the preceding 2 years. They also complained of proximal myopathy, progressive puffiness of face and pigmented striae over the abdomen, thighs and axillae which gradually worsened with time [Figure 1].

On examination, both brothers had features of florid Cushing syndrome. Though their mother was asymptomatic, she appeared Cushingoid with roundening of her face and facial plethora. She

Address for correspondence: Dr. Thomas Vizhalil Paul, Department of Endocrinology, Christian Medical College and Hospital, Vellore, Tamil Nadu, India.
E-mail: thomasvpaul@yahoo.com

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_294_19

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Rajan R, Kuriakose C, Paul J, Kapoor N, Cherian KE, Paul TV. A rare cause of familial exogenous Cushing syndrome. J Family Med Prim Care 2019;8:1798-800.

was known to have chronic depression and was on treatment for the same since past 10 years. Their father who was staying abroad returned home since his children were unwell. The family denied intake of indigenous or over the counter medications. The brothers were evaluated by at least five physicians elsewhere before presenting to us.

On evaluation, serum cortisol levels of both brothers were suppressed (<0.5 mcg/dL) confirming exogenous steroid source as the cause for Cushing syndrome. However, there were no signs of adrenal insufficiency. They also had impaired glucose tolerance, dyslipidemia, and low bone mass secondary to exogenous steroid use [Table 1]. The mother's investigation also revealed a low serum cortisol level (7 mcg/dL). A psychiatry opinion was taken and the family was counseled. After interrogation by the psychiatrist, the mother confessed that she had procured dexamethasone tablets over the counter, mixed them with fruit juices and administered the concoction to her sons. A diagnosis of Munchausen syndrome by proxy (MSBP) was made. The family was counseled regarding the consequences of steroid overuse. The children were started on replacement doses of steroids and were educated regarding additional steroid supplementation during periods of illness/stress.

Discussion

This MSBP was first described by the British pediatrician Roy Meadow in 1977.[3] MSBP occurs when a caregiver fabricates illness in a child to satisfy their desire for attention. Recently, MSBP has been replaced with the term "Factitious Disorder Imposed on Another."[4] The caregiver fabricating the disorder is known as "perpetrator." The most common psychiatric diagnoses recorded among the perpetrators were factitious disorder imposed on self (30.9%), personality disorder (18.6%), and depression (14.2%).[5] In the family reported, the mother was suffering from chronic depression and was on treatment for the same since past 10 years. When confronted, she confessed to her actions, and the family was explained about the consequences of exogenous steroid abuse.

Figure 1: Siblings with features of Cushing syndrome

Table 1: Adrenal hormone profile and metabolic parameters of two siblings

Parameters	Elder brother	Younger brother
8 am cortisol (8-28 μg/dL)	<0.5	<0.5
24 hour urine cortisol (10-100 μg/24 hrs)	7	6
8 am ACTH (10-50 pg/mL)	<5	<5
HbA1C (<5.7%)	5.7	6.5
LDL (<130 mg/dL)	170	150

Cushing syndrome presents with weight gain, manifesting as central obesity, redistribution of body fat to truncal areas and the subsequent appearance of dorsocervical and supraclavicular fat pads and the classic "moon facies." Other features include facial plethora, easy bruising, thin skin, purple striae, myopathy, and proximal muscle weakness. The psychological adverse effects of steroid treatment can be quite severe and include depression and psychosis. Cortisol excess also leads to hyperglycemia, hypertension, dyslipidemia, and decrease in bone mineral density due to accelerated bone resorption. There are certain features specific to exogenous Cushing syndrome such as posterior subcapsular cataract, glaucoma, avascular necrosis of femur, psychosis and very rarely, spinal epidural lipomatosis. However, these features are not present in all patients with exogenous steroid use.[6]

Despite efforts to understand the effects of long-term and high-dose steroid treatment on the hypothalamic pituitary adrenal (HPA) axis, it is not yet clear as to which patients will have prolonged HPA axis suppression.[7] For patients who have been on long-term glucocorticoid therapy, the risk for adrenal insufficiency can continue for months to years. Therefore, the patient and the physician must discuss the potentially prolonged nature of steroid therapy withdrawal and approach the problem with patience.

Longer-acting glucocorticoids (GC) is associated with a higher risk of adrenal suppression. The timing of GC administration may also influence the development of adrenal suppression, with morning administration being potentially less suppressive than evening doses. Alternate day therapy is thought to be less suppressive than daily GCs based on the physiology of the HPA axis.[8] However, further clinical evidence is required to prove it. Although there are no evidence-based guidelines for tapering of GCs, gradual GC tapering is frequently a part of treatment protocols to reduce the risk of relapse. Recovery of endogenous cortisol production is expected after stopping the exogenous GCs, though the time to recovery can vary.

In our patients, replacement dose of GC (prednisolone 2.5 mg once daily) was started and they were asked to review after 3 months. The treatment plan made, was to taper steroids gradually, attempting to stop them over a period of 6 months. They were also advised to double the dose of prednisolone during illness and to take hydrocortisone/dexamethasone injections in case of symptoms suggestive of adrenal crisis.

This condition is of utmost importance to primary care and family physicians. The easy availability of glucocorticoids over the counter and its indiscriminate use leads to the development of exogenous Cushing syndrome. However, the administration of steroids by a family member as in this report is an extreme form of MSBP. It is absolutely essential that general practitioners and family physicians involved in primary care be aware of the possibility of exogenous Cushing syndrome and rule out this condition through careful history taking and evaluation of indigenous and native medication intake. It is also necessary that primary care physicians be informed of managing acute adrenal crises secondary to withdrawal of steroids.

Conclusion

The two brothers presenting with features of exogenous Cushing syndrome is an extreme form of MSBP. Although the motives behind the same are often not clear, it requires a patient and detailed evaluation of the scenario, a thorough knowledge of the psychosocial background of the family, and a pursuit of potential psychiatric illness in the family members. A multidisciplinary effort involving endocrinology and psychiatry may be required to tackle the many facets of this condition, particularly in the clinical and the psychological realms. Also, primary care physicians ought to be aware of the possibility of exogenous Cushing syndrome and be equipped to recognize and handle cases of acute adrenal crises, should they encounter them.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Fardet L, Petersen I, Nazareth I. Prevalence of long-term oral glucocorticoid prescriptions in the UK over the past 20 years. Rheumatology (Oxford) 2011;50:1982-90.
2. Fardet L, Flahault A, Kettaneh A, Tiev KP, Généreau T, Tolédano C, *et al.* Corticosteroid-induced clinical adverse events: Frequency, risk factors and patient's opinion. Br J Dermatol 2007;157:142-8.
3. Meadow R. Munchausen syndrome by proxy the hinterland of child abuse. Lancet 1977;2:343-5.
4. Faedda N, Baglioni V, Natalucci G, Ardizzone I, Camuffo M, Cerutti R, *et al.* Don't judge a book by its cover: Factitious disorder imposed on children-report on 2 cases. Front Pediatr 2018;6:110.
5. Yates G, Bass C. The perpetrators of medical child abuse (Munchausen syndrome by proxy)–A systematic review of 796 cases. Child Abuse Negl 2017;72:45-53.
6. Hopkins RL, Leinung MC. Exogenous Cushing's syndrome and glucocorticoid withdrawal. Endocrinol Metab Clin North Am 2005;34:371-84.
7. Christy NP. Pituitary-adrenal function during corticosteroid therapy. Learning to live with uncertainty. N Engl J Med 1992;326:266-7.
8. Lansang MC, Hustak LK. Glucocorticoid-induced diabetes and adrenal suppression: How to detect and manage them. Cleve Clin J Med 2011;78:748-56.