Iatrogenic Cushing’s Syndrome After Topical Steroid Therapy for Psoriasis

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Abstract
Glucocorticoids are used for the treatment of many diseases, such as inflammatory, allergic, autoimmune, and neoplastic diseases. They can be used in the form of topical, oral, inhalable, rectal, and intra-articular agents. Many topical steroid-related iatrogenic Cushing’s syndrome cases affecting especially children have been reported in the literature. Topical steroid-related Cushing’s syndrome is rarely seen in adults. In this report, we present the case of a 32-year-old male patient with iatrogenic Cushing’s syndrome related to long-term clobetasol propionate treatment for psoriasis. In the context of such treatment, the glucocorticoid withdrawal problem has to be overcome. At present there is no consensus on steroid withdrawal. Patients on long-term glucocorticoid treatment must be evaluated for potential adverse effects and withdrawal symptoms by their physician and their endocrinologist.

Key Words: Iatrogenic Cushing’s syndrome, psoriasis, topical steroid

Introduction
Glucocorticoids are used in the treatment of endocrine and nonendocrine allergic, inflammatory, and immunological disorders. Long-term treatment has many adverse effects including the suppression of the hypothalamic-pituitary-adrenal (HPA) axis. Development of the features of Cushing’s syndrome depends on the dose, duration, and potency of the corticosteroids used in clinical practice. Iatrogenic Cushing’s syndrome is the most common clinical form of hypercortisolemia.[1] Compared to adults, the dermis layer of the skin is thinner and the surface/volume ratio is higher in children. Therefore, glucocorticoids are more easily absorbed from the skin and cause systemic adverse effects more commonly in children.[2] Most of the studies in the literature focus on the treatment of endogenous hypercortisolism, and there are only a few studies on the iatrogenic form of hypercortisolism. Treatment for HPA axis suppression secondary to long-term steroid treatment is rather difficult. In this report, we present an adult patient who developed Cushing’s syndrome after long-term use of a topical synthetic glucocorticoid in the treatment of psoriasis.

Case Report
A 32-year-old male patient was admitted to the outpatient clinic with complaints of weight gain, dry mouth, and fatigue. In 2002, some eruptions appeared on the skull. Two (2) years later, skin eruptions spread all over his body. At that time, he was diagnosed with psoriasis and prescribed topical clobetasol propionate. He had not been reexamined after that and has been using clobetasol propionate 0.005% routinely for 10 years. He has applied the drug to his arms, legs, and all over the trunk. Over the past year, he put on weight obviously (8 kg). He stopped the treatment 1 month ago, at the time of writing. He has been complaining of dry mouth and fatigue for the last month. On his physical examination, moon face, central adiposity, and purple-red striae on the abdomen under umbilicus were observed. There were scaly patches and erythematous plaques on the skull, interscapular area, sacrum, arms, legs, knees, and elbows [Figure 1]. Other systemic examinations were all normal. Blood pressure was 130/90 mmHg, pulse 75/min, height 1.76 m, weight 77 kg, and body mass index 24.8 kg/m². On laboratory examination, fasting blood glucose: 152 mg/dL (N: 70-105), creatinine: 1 mg/dL (N: 0.72-1.25), triglyceride: 160 mg/dL (N: 0-200), total cholesterol: 240 mg/dL (N: 0-200), high-density-lipoprotein (HDL)-cholesterol: 44 mg/dL (N: 45-55), low-density-lipoprotein (LDL)-cholesterol: 164 mg/dL (N: 0-130), ALT: 42 u/L (N: 0-55); AST: 27 u/L (N: 0-34); sodium: 140 mmol/L (N: 136-145); potassium: 4.6 mmol/L (N: 3.5-5.1); calcium: 9.9 mg/dL (N: 8.4-10.2); phosphorus: 3.5 mg/dL.
Cushing’s syndrome by suppressing the HPA axis. Some may reach the systemic circulation and cause iatrogenic Cushing’s syndrome as a result of topical steroid use. For adrenal insufficiency, 20 mg/day hydrocortisone treatment was commenced, and for vitamin D deficiency, vitamin D replacement. As the patient had high blood glucose levels, dyslipidemia, and large waist circumference (101 cm), he was diagnosed with metabolic syndrome, and a low-calorie diet and exercise were advised. Metformin treatment at a dose of 2000 mg/day was commenced for glucose regulation. The patient consulted at the dermatology department for his psoriasis, and calcipotriol pomade and emollients were prescribed. One (1) month after that, 1 μg tetracosactide i.v. was applied and cortisol levels were measured at 30 min and at 60 min. As both measured levels were below 3 μg/dL, glucocorticoid maintenance treatment was continued.

Discussion

Glucocorticoids were first introduced in 1948 for the treatment of severe rheumatoid arthritis. Although they have provided these patients with substantial benefit, potential adverse effects have also been proven. All forms of Cushing’s syndrome share the same clinical findings on inspectional examination. Development of the features of Cushing’s syndrome depends on the duration of treatment and the dose and potency of the corticosteroids used in clinical practice. In case of long-term use of inhalable, topical, and intra-articular steroids, they may reach the systemic circulation and cause iatrogenic Cushing’s syndrome by suppressing the HPA axis. Some authors suggest that glucocorticoid treatment shorter than 3 weeks may be stopped without gradually decreasing the dose and suppressing the HPA axis. In other studies, on the other hand, high-dose glucocorticoid treatment for 5-30 days was shown to suppress the HPA axis, and even a single dose of 40 mg intramuscular triamcinolone caused Cushing’s syndrome by suppressing the HPA axis. The functional evaluation of the HPA axis and arrangement of glucocorticoid treatment are especially important in iatrogenic Cushing’s syndrome. In a patient who took the last dose of glucocorticoid at least 24-48 h ago, a morning (8 AM) serum cortisol level below 3 μg/dL (85 nmol/L) means absolute glucocorticoid need, whereas levels above 20 μg/dL (550 nmol/L) may not need maintenance treatment. In case of a serum cortisol level in the range of 3-20 μg/dL, dynamic tests should be performed to evaluate the HPA axis. Insulin hypoglycemia test, metyrapone test, corticotropin-releasing hormone test, and tetracosactide test may be used to evaluate the HPA axis.

In our case, as the morning (8 AM) serum cortisol level was below 0.2 μg/dL, 20 mg/day hydrocortisone treatment was started without first performing a dynamic test. In some cases, especially in patients who have had long-term glucocorticoid treatment, suppression of the HPA axis may last for 1 year. Our patient also had long-term topical glucocorticoid treatment. At present, there is no consensus on the subject of steroid withdrawal. However, it is advised to decrease the dose gradually and apply the dose taken for glucocorticoid maintenance treatment in the morning to minimize the suppression of ACTH.

Conclusion

Iatrogenic (exogenous) Cushing’s syndrome is more common than the endogenous forms of hypercortisolemia. For this reason, patients on long-term glucocorticoid treatment must be evaluated for potential adverse effects and withdrawal symptoms by their physician and their endocrinologist.

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.

References

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Received: February, 2015. Accepted: May, 2015.

Source of support: Nil. Conflict of Interest: Nil.
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