Iatrogenic Cushing’s Syndrome Due to Intranasal Usage of Ophthalmic Dexamethasone: A Case Report

Sarah Orton, MD, Marisa Censani, MD

Iatrogenic Cushing’s syndrome (ICS) is caused by exogenous corticosteroid administration with suppression of the hypothalamic–pituitary–adrenal axis. It has been commonly described with oral and topical steroid use, but scarce reports have documented intranasal steroid usage as the etiology in infancy. In this article, we describe a case of a 4-month-old infant who developed ICS after 6 weeks of intranasal dexamethasone ophthalmic solution administration for nasal obstruction. To our knowledge, this is the youngest patient reported with ICS due to intranasal use of a prescribed dose of an ophthalmic steroid. His hypothalamic–pituitary–adrenal axis recovered fully 4.5 months after steroid discontinuation. Because of the small body surface area and supine position during administration, infants are particularly susceptible to ICS. Given that intranasal steroids are commonly prescribed to infants and children for a variety of diagnoses, this case highlights the risks inherent in the use of intranasal steroid drops, particularly in young infants, for both adrenal suppression and linear growth deceleration, even with short-term use. Close monitoring of these patients’ height and weight should occur while on steroid treatment, with every effort made to decrease or discontinue steroid use when possible.

CASE PRESENTATION

A 4-month-old male was admitted to the pediatric ICU for respiratory distress. He was a product of a twin pregnancy and was born prematurely at 26 weeks gestation. His medical history was complicated by chronic lung disease, retinopathy of prematurity, patent ductus arteriosus requiring indomethacin for closure, and a 3 month NICU admission. Nasal Ciprodex (ciprofloxacin/dexamethasone) was initiated 1 week after his initial NICU discharge when he was readmitted for an apparent life-threatening event secondary from the patient’s mother for publication of this case report and any accompanying images.

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Dr Orton diagnosed and treated the patient, contributed to the concept and design of the case report, drafted the manuscript, and critically revised the manuscript for important intellectual content; Dr Censani diagnosed and treated the patient, contributed to the concept and design of the case report, drafted the manuscript, and critically revised the manuscript for important intellectual content; and both authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

DOI: 10.1542/peds.2015-3845

Accepted for publication Feb 17, 2016

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest relevant to this article to disclose.
to severe nasal congestion. His congestion improved, but treatment was changed to dexamethasone ophthalmic solution after 1 week due to a rash that was thought to be caused by Ciprodex. The patient was readmitted to the hospital 4 weeks later for respiratory distress with a 1-week history of lethargy, decreased appetite, and increased facial swelling.

On initial presentation, the patient weighed 4.1 kg with a length of 49 cm (corrected for gestational age: 5% and 0% respectively). He had a normal, age-adjusted heart rate of 155 bpm and blood pressure of 86/40 mm Hg. Review of growth charts revealed he had gained 24 g per day since starting steroids, but his growth velocity had markedly decreased from 5 cm per month to 1 cm per month after steroid introduction (Fig 1). On exam, he was noted to have large, ruddy cheeks with moon facies (Fig 2). He did not have striae, edema, acanthosis nigricans, or hypertrichosis. Laboratory evaluation revealed a cortisol level of <0.4 μg/dL (reference range: 6.7–22.6 μg/dL) obtained at 6:30 AM, and the diagnosis of ICS was made.

At the time of the endocrinology consultation, the patient had been on intranasal steroids at an equivalent hydrocortisone dose of 28 mg/m² per day for 6 weeks (conversion used: 1 mg of dexamethasone equivalent to 40 mg hydrocortisone; this is based on the concentration of the ophthalmic dexamethasone of 1 mg/mL with 20 drops/mL and a total daily dose of 3 drops).

On hospital discharge, otolaryngology felt that the patient should continue with dexamethasone treatment because of continued respiratory distress and improvement of the patient’s respiratory status on treatment. At diagnosis, a dexamethasone taper was initiated with a decrease to 2 drops daily (18 mg/m² per day of hydrocortisone), followed by a decrease to 1 drop daily (8 mg/m² per day of hydrocortisone) by 3 months, and discontinuation by 4 months post–ophthalmic steroid initiation (Fig 1). During the dexamethasone taper, the patient received 1 2-day course of stress-dose hydrocortisone for an upper respiratory infection with fever, but otherwise remained off additional steroid use for the remainder of his clinical care. His mother was instructed on stress dosing and emergency Solu-Cortef administration. His growth improved once the dexamethasone dose was weaned to 1 drop (8 mg/m² per day of hydrocortisone) with a consistent velocity of 4 cm per month thereafter (Fig 1). One month post–steroid use, his morning cortisol level was
1.6 ug/dL. By 2.5 months post-steroid use, his Cushingoid facies resolved, and a low-dose, 1 mcg adrenocorticotropic hormone (ACTH) stimulation test was performed, revealing a baseline cortisol level of 6.2 ug/dL, with levels at 14.9 ug/dL and 15.7 ug/dL at 30 min and 60 min, respectively. At 4.5 months post-steroid use, a low-dose ACTH stimulation test showed a baseline cortisol level of 6.0 ug/dL, with levels at 17.9 ug/dL and 19.2 ug/dL at 30 min and 60 min, respectively.

**DISCUSSION**

To our knowledge, this is the youngest patient reported with ICS due to intranasal use of a prescribed dose of an ophthalmic steroid. Our patient was diagnosed after only a 6-week course of dexamethasone ocular drops compared with a previously prescribed 3-month course.6 Given that intranasal steroids are commonly prescribed to infants and children for a variety of diagnoses, this case highlights the risks inherent in the use, even short-term, of intranasal steroid drops, particularly in young infants, for both adrenal suppression and linear growth deceleration. Because oral and topical glucocorticoids are a more common cause of ICS, there are limited reports of intranasal steroids as the etiology,5–9 with patients being diagnosed with ICS anywhere from 2 to 4 months to several years after steroid initiation.

Infants given intranasal dexamethasone drops may be at higher risk for systemic absorption through the gastrointestinal tract because they are often supine during administration and may swallow a significant portion of each drop. They also have a smaller body surface area than older children and adults.1–5,9 Although some publications report ICS caused by prescription errors or parents using excessive doses and prolonged courses of therapy,6,7,10 our patient was receiving the appropriate prescribed dose for a short duration.

Patients with ICS due to various etiologies have presented with a spectrum of signs and symptoms ranging from excessive weight gain and growth delay to posterior cervical fat pad, hypertrichosis, and violaceous striae.1–10 Our patient presented with Cushingoid facies and poor growth. Once our patient was weaned to physiologic dosing of steroids, his growth improved dramatically and his Cushingoid features resolved.

Our patient was weaned to physiologic hydrocortisone dosing by 3 months post-steroid initiation, with discontinuation by 4 months. To determine hypothalamic–pituitary–adrenal axis recovery, a low-dose ACTH stimulation test with a goal peak cortisol level of 18–20 ug/dL was implemented.11,12 Our patient’s cortisol level of 19.2 ug/dL documented adrenal recovery from suppression 4.5 months after discontinuation of steroid treatment, with a noted improvement in height velocity and an appropriate weight gain and energy level.

There has been only 1 other documented case where physiologic dosing was not used during the recovery period for intranasal steroid–induced ICS.7 The patient was a 19-month-old male who developed ICS after 3 months of excessive intranasal betamethasone nasal drops for rhinorrhea and snoring. He was weaned off the steroid drops over 3 weeks and had a normal cortisol level 3 months later. He was not given physiologic dosing of glucocorticoids, but he did require 3 days of stress dosing for pharyngitis 2 weeks after discontinuing the intranasal steroids. Our patient was given instruction on stress dosing steroids during times of illness or surgery and received stress-dose steroids for an upper respiratory illness without issue. Our case supports the notion that it is safe and effective to supply steroids only at times of illness and stress during axis recovery. However, although it may not be necessary to supplement with physiologic hydrocortisone, close monitoring and clear stress-dosing instructions are required in these patients because ICS has been reported to result in death.6

In conclusion, this case presents the youngest patient to date who developed ICS through intranasal use of ophthalmic dexamethasone drops. The diagnosis of ICS in our patient was made after only 6 weeks of therapy, the shortest reported course of intranasal steroid treatment. This case emphasizes the potential risk of ICS for any infant with poor growth and Cushingoid features regardless of the duration of steroid use or the route of administration. Given the small body surface area and supine position during administration, infants are particularly susceptible to ICS. Close monitoring of these patients’ height and weight should occur while on steroid treatment, and every effort should be made to decrease or discontinue steroid use when possible. This case also suggests that physiologic dosing during the time of hypothalamic–pituitary–adrenal axis recovery may not be required and that patients can be safely monitored and provided with stress-dose steroids as long as appropriate education and management plans are provided to the patients’ families.

**ACKNOWLEDGMENTS**

We thank Dr. Oksana Lekarev for her expert review of and suggestions regarding this manuscript.

**ABBREVIATIONS**

ACTH: adrenocorticotropic hormone
ICS: iatrogenic Cushing’s syndrome
REFERENCES


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Dexamethasone: A Case Report
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*Pediatrics* 2016;137;; originally published online April 7, 2016;
DOI: 10.1542/peds.2015-3845

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