

# Idiopathic intracranial hypertension as a presenting sign of adrenal insufficiency

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## Abstract

Idiopathic intracranial hypertension is a diagnosis of exclusion defined by elevated intracranial pressure without mass lesions or hydrocephalus. Causes of idiopathic intracranial hypertension include obesity, vitamin derangements, antibiotics, corticosteroids, and autoimmune disorders. Cushing's disease and Addison's disease have been associated with idiopathic intracranial hypertension. Secondary adrenal insufficiency following withdrawal of inhaled corticosteroids has been found to be a relatively common phenomenon. This case describes an 11-year-old boy who was previously on inhaled corticosteroids for severe asthma who presented with secondary adrenal insufficiency after withdrawal of steroids. The adrenal insufficiency presented as idiopathic intracranial hypertension. We described the hospital course and process of diagnosis for this child with secondary adrenal insufficiency following withdrawal of inhaled corticosteroids. The association between the discontinuation of this patient's corticosteroids and his onset of headache suggests secondary adrenal insufficiency as the most likely cause of his idiopathic intracranial hypertension. The gradual improvement in his symptoms after steroid replacement further supports this. Due to the significant prevalence of children using inhaled corticosteroids, it is important for clinicians to be aware of the potential for the withdrawal of these drugs to induce hypothalamic–pituitary–adrenal axis suppression.

## Keywords

Diabetes/endocrinology, neurology, respiratory medicine, pediatrics adrenal insufficiency

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## Introduction

Idiopathic intracranial hypertension is a diagnosis of exclusion defined by elevated intracranial pressure in the absence of any evidence of mass lesions or hydrocephalus. Persistent headaches, nausea, vomiting, and papilledema are the characteristic signs and symptoms of this condition. It is classically associated with obese females of reproductive age but is also known to occur in children.<sup>1</sup> In addition to obesity, known causes of idiopathic intracranial hypertension include vitamin derangements, certain antibiotics, corticosteroids, and autoimmune disorders. Certain endocrine disorders, namely Cushing's disease and Addison's disease, have also been associated with idiopathic intracranial hypertension.<sup>2</sup>

Secondary adrenal insufficiency following withdrawal of inhaled corticosteroids has been found to be relatively common. In a retrospective study, 20.5% of patients on inhaled corticosteroids were found to have failed their adrenocorticotropic hormone (ACTH) stimulation test after stopping

steroids. The association is highest with higher doses and duration of treatment.<sup>3</sup> The temporal association between the cessation of this patient's corticosteroids and his onset of headache suggests secondary adrenal insufficiency as the cause of his intracranial hypertension. The gradual improvement in this patient's symptoms following steroid replacement further supports this. However, this improvement may not be solely attributed to the steroid replacement as acetazolamide was also given.

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## Case report

No approval from an ethical committee or institutional review board is necessary in our institution for documentation of a case study. Guidelines on patient consent have been met by obtaining written informed consent from the family.

An 11-year-old Caucasian boy with a past medical history of severe asthma diagnosed at 7 months of age was admitted to the pediatric service due to severe, persistent headaches. The headaches had been frequent and severe for the past 2 months, with the most significant worsening occurring over the 2 weeks prior to admission. The headaches were described as achy and bimodal and associated with nausea and mild photophobia. He reported minimal relief with sleep. Attempts at pharmacologically treating his headaches as acute migraines had proved unsuccessful. Review of the patient's medical records revealed chronic use of multiple inhaled corticosteroids for his severe asthma. The patient has been using a fluticasone inhaler for 5 years and was started on an additional steroid inhaler, beclomethasone dipropionate, 7 months prior to admission. The patient also has a history of frequent asthma exacerbations requiring hospitalization and oral steroids, with the most recent episode occurring 3 months prior to the current admission. Two months prior to the current admission, the patient was started on a tiotropium bromide inhaler in an effort to discontinue use of his inhaled corticosteroids due to the mother's concern about the patient's growth.

His brain magnetic resonance imaging showed a pineal cyst and Chiari type I malformation, which were incidental and non-contributory. A lumbar puncture was performed and revealed an opening pressure greater than 55 cm of cerebrospinal fluid (CSF). CSF studies were within normal limits. 35 mL of CSF were removed during the lumbar puncture, and closing pressure was recorded to be 15 cm of CSF. The patient briefly experienced some relief of his headaches after the lumbar puncture, but he soon began to experience worsening of the headaches on standing with associated dizziness and vomiting. The patient was started on acetazolamide as well as topiramate to help relieve the patient's migrainous symptoms. On ophthalmology consultation, the patient was also found to have mild to moderate disc edema.

On hospital day 3, the patient began to complain of new-onset, generalized abdominal pain. Physical exam revealed diffuse abdominal tenderness without rebound or guarding. He was hemodynamically stable and heart rate and blood pressure were within normal limits. Initial labs, including electrolytes, amylase, and lipase, were found to be within normal limits. An abdominal computerized tomography (CT) was unremarkable, and an abdominal X-ray revealed mild constipation. Adrenal insufficiency related to withdrawal of inhaled steroids was suspected as a cause of this patient's increased intracranial pressure and abdominal pain. Because of this suspicion, an ACTH stimulation test was performed and showed blunted production of cortisol. An

8AM cortisol level prior to cosyntropin administration was found to be 3.5 µg/dL. A baseline ACTH level was also obtained prior to the study and found to be 14.4 pg/mL. Cortisol levels 30 and 60 min after administration of a standard high dose (250 µg IV) of cosyntropin was administered were found to be 7.9 and 8.4 µg/dL, respectively. The patient was subsequently started on a physiologic dose of hydrocortisone at 5 mg three times daily. The hydrocortisone dose was later increased to 10 mg three times daily due to continued stress from persistent vomiting.

A repeat lumbar puncture was performed 4 days after initiation of treatment and showed a markedly improved opening pressure at 29.8 cm of CSF. 20 mL of CSF were removed, and closing pressure was recorded to be 17 cm CSF.

The patient was transferred to a higher-level facility for more specialized care on hospital day 6. A repeat ophthalmological examination was normal and without any evidence of papilledema. Both high- and low-dose cosyntropin stimulation tests were repeated and found to be abnormal. He was started on a steroid taper after 2 days at the new facility and discharged home 2 days later.

## Discussion

Patients with asthma have been found to have adrenal insufficiency not only with high-dose inhaled corticosteroids but also with low- to medium-dose inhaled corticosteroids when the inhaled corticosteroids have been given over a long period.<sup>4</sup> One-third of patients on low- to medium-dose inhaled steroids for an average of 4.5 years showed adrenal insufficiency.<sup>5</sup> In our case, the patient had been on high-dose inhaled corticosteroids for 5 years, over the maximum dose recommended for age. He was first on fluticasone propionate (Advair 230-21, two puffs twice a day). Advair is actually not recommended for pediatric use at all. He was then on another brand of fluticasone propionate (Flovent HFA 220, two puffs twice a day). With Flovent, the maximum dose for 4 to 11 year olds is 176 mcg/day with the maximum dose for 12 years and older being 1760 mcg a day. Our patient was receiving 880 mcg of Flovent per day. Seven months prior to admission beclomethasone dipropionate (Qvar) 80 mcg one puff twice a day was also added. Qvar 80 mcg bid is the maximum dose for 5 to 11 year olds.

The occurrence of idiopathic intracranial hypertension has been reported to be associated with several endocrine conditions. These include primary adrenal insufficiency,<sup>6,7</sup> the medical or surgical treatment of Cushing's disease,<sup>8</sup> and the use of oral corticosteroids.<sup>9</sup> However, very few cases have been reported describing idiopathic intracranial hypertension resulting from withdrawal of inhaled corticosteroids.<sup>10,11</sup> The mechanism by which adrenal insufficiency induces increased intracranial pressure is not currently well-understood. It has been postulated, however, that acute corticosteroid withdrawal induces decreased absorption of CSF and increased resistance to the flow of CSF.<sup>12</sup> Furthermore,

11 $\beta$ -hydroxysteroid dehydrogenase type 1, an enzyme that converts inactive cortisone into active cortisol, has been found to be expressed in the choroid plexus, supporting a role for cortisol in CSF volume regulation.<sup>13</sup>

## Conclusion

Due to the significant prevalence of children using inhaled corticosteroids, it is important for clinicians to be aware of the potential for withdrawal of these drugs to induce hypothalamic–pituitary–adrenal axis suppression. One study suggests the routine performance of annual morning cortisol levels in asymptomatic patients chronically using inhaled corticosteroids as an efficient screening tool.<sup>3</sup> Furthermore, it is important for clinicians to recognize idiopathic intracranial hypertension as a rare presentation of adrenal insufficiency due to the damaging potential of this condition in causing irreversible blindness. When prescribing corticosteroids of any type, clinicians should carefully titrate their dosages to the minimum required to achieve adequate symptom control.

## Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

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## Informed consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

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