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Reversible Adrenal Hyperplasia Associated with Chronic Etomidate Use: A Case Report with 3-Year Radiological Follow-Up

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Case Report

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Abstract

Background: Etomidate, a commonly used intravenous anesthetic, is known to reversibly inhibit adrenal 11β-hydroxylase (CYP11B1). Illicit electronic cigarettes containing etomidate have emerged in some regions, and chronic inhalation has been associated with acquired adrenal hyperplasia. However, the long-term reversibility of etomidate-induced adrenal hyperplasia after drug cessation has not been documented in the literature.

Case presentation: We report a 33-year-old male patient who presented with recurrent fatigue, after approximately 10 years of 4-5 times per week etomidate-containing e-cigarette use. Laboratory evaluation revealed hypokalemia (serum K^+ 3.37 mmol/L), normal morning cortisol (9.66 μg/dL), elevated adrenocorticotropic hormone (ACTH) (322.00 pg/mL), and normal aldosterone-to-renin ratio. Computed tomography demonstrated bilateral adrenal thickening (9.3mm on the right, 9.5 mm on the left). Genetic testing excluded *CYP11B1* and *CYP21A2* mutations, supporting an acquired etiology. The patient was advised to discontinue etomidate use. At the 3-year follow-up, the patient remained abstinent. Repeat CT imaging showed largely resolution of adrenal hyperplasia, with adrenal thickness reduced to 3.9-4.3 mm bilaterally, and biochemical parameters returned to normal range.

Conclusion: This case provides the first imaging evidence that etomidate-induced adrenal hyperplasia is reversible upon drug cessation, with largely radiological resolution documented at 3-year follow-up. The diagnosis of drug-induced adrenal hyperplasia can be established through a combination of exposure history, biochemical profile, and imaging findings, even in the absence of genetic testing. Early recognition is crucial to avoid unnecessary invasive investigations or genetic workup. A conservative "watch-and-wait" approach after drug withdrawal appears to be appropriate for similar cases.

1. Background

Etomidate is a rapid-acting intravenous anesthetic that acts on the GABAA receptor. Beyond its anesthetic properties, it inhibits adrenal 11β-hydroxylase (CYP11B1), thereby impairing cortisol and aldosterone synthesis and causing transient adrenal dysfunction [1]. In recent years, illicit electronic cigarettes containing etomidate—commonly referred to as "heady e-cigarettes"—have emerged in some regions. Chronic inhalation of these products can lead to sustained suppression of adrenal CYP11B1, resulting in acquired bilateral adrenal hyperplasia accompanied by biochemical features such as hypokalemia and hypertension, which phenotypically mimic congenital adrenal hyperplasia (CAH) due to 11β-hydroxylase deficiency(11β-OHD) [2, 3].

Several cases of etomidate-induced adrenal dysfunction have been reported, documenting the acute-phase clinical and biochemical manifestations [2, 3]. However, a critical unanswered question remains: whether etomidate-induced adrenal hyperplasia is reversible after long-term drug cessation, particularly from a radiological perspective. To date, no published case has provided imaging follow-up data demonstrating resolution of adrenal hyperplasia following discontinuation of etomidate.

We report a case of a patient with chronic etomidate-containing e-cigarette use who presented with bilateral adrenal hyperplasia and biochemical features consistent with11β-OHD. Crucially, follow-up CT imaging at 3 years after drug cessation demonstrated largely resolution of adrenal hyperplasia. This case provides, for the first time, imaging evidence that this condition is reversible and carries important clinical implications for the diagnosis and conservative management of similar cases.

Case Presentation

A 33-year-old man presented to our hospital with a 2-month history of recurrent limb weakness, on a background of similar episodic weakness over the preceding 10 years. Previous evaluations had consistently demonstrated hypokalemia, with symptoms responding to potassium supplementation; however, the underlying etiology remained unidentified, and the episodes recurred every 2 to 3 months.

The patient had normal growth and developmental milestones, was married, and had healthy children. There was no family history of hypertension, hypokalemia, or adrenal disorders. Notably, he reported a 10-year history of daily inhalation of “heady e-cigarettes” (containing etomidate), approximately 4–5 times per week, with a reversed sleep-wake cycle.

Diagnostic Assessment

1.Physical examination: On admission, physical examination revealed blood pressure of 156/97 mmHg. The patient exhibited generalized skin hyperpigmentation but no central obesity, moon face, or abdominal striae. Secondary sexual characteristics were normally developed.

2.Laboratory testing

Laboratory investigations are summarized in Table 1–4. Key findings included:

· Hypokalemia with increased urinary potassium excretion

· Normal morning serum cortisol and elevated ACTH

· Suppressed plasma renin and aldosterone levels

· Increased levels of cortisol precursors

Table 1. Blood and urine electrolyte.

Value	Blood(mmol/L)	Urine (mmol/24h)
Potassium	3.37(3.5-5.5)	68.67
Sodium	141.0(137-147)	102.6
Chlorine	104.3(99-110)	118.4

Urine volume:3.1L

Table 2. Plasma Aldosterone and Renin Activity Test.

Value	Baseline	2 hours	4 hours
Aldosterone(ng/dL)	3.20(3.0-16.0)	1.31(7.0-30.0)	0.50(7.0-30.0)
Renin activity(ng/ml/h)	0.24(0.15-2.23)	0.11(0.10-6.56)	0.20(0.10-6.56)
ARR	13.33	11.91	2.50

Baseline: supine position. 2 hours: hold upright posture for 2 hours. 4 hours: hold upright posture for 4 hours. ARR: aldosterone-to-renin ratio.

Table 3. Cortisol and ACTH diurnal rhythm.

Value	8am	4pm	0am
Cortisol(ug/dL)（3.5-20）	9.66	7.56	3.29
ACTH(pg/ml)（7.20-63.6）	322.00	278.00	118.00

Table 4. Other steroid panel.

Value	Result	Reference
Estradiol(ng/L)	41.60	0-38.98
FSH(U/L)	2.13	1.27-19.26
LH(U/L)	1.38	1.24-8.26
Testosterone(μg/L)	3.160	1.75-7.18
Prolactin(μg/L)	10.31	2.64-13.13
Progesterone(μg/L)	2.9	0.1-0.84
17α-OHP(ng/ml)	14.70	0.29-2.06
ASD(ng/ml)	7.96	0.602-3.100
DHEA(μg/dL)	861.00	106.00-464.00

FSH: follicle-stimulating hormone. LH: luteinizing hormone.17α-OHP: 17-α-hydroxy pregnenolone. ASD: androstenedione. DHEA: dehydroepiandrosterone.

3.Imaging studies and gene test

Adrenal CT imaging demonstrated bilateral adrenal hyperplasia (Figure 1). Pituitary MRI showed no abnormalities, and whole-exome sequencing revealed no pathogenic variants, effectively excluding CAH and other genetic causes.

4.Diagnose

Based on the constellation of hypokalemia with renal potassium wasting, relatively low cortisol and aldosterone levels, bilateral adrenal hyperplasia, and negative genetic testing, in the context of chronic etomidate exposure, the patient was diagnosed with acquired adrenal hyperplasia secondary to prolonged etomidate inhalation.

Treatment

Amlodipine 5 mg once daily was initiated for blood pressure control, and potassium chloride extended-release tablets 1 g twice daily were given for potassium supplementation. The patient's serum potassium normalized, and limb weakness resolved prior to discharge.

Follow-up and outcome

The patient was advised to discontinue all etomidate-containing e-cigarette use. At the 3-year follow-up, the patient reported sustained abstinence from etomidate and had voluntarily discontinued all antihypertensive and potassium supplements. He remained normotensive and asymptomatic.

Repeat laboratory evaluation demonstrated normal serum electrolytes and nearly restoration of adrenal hormone profiles (Table 5). Most importantly, follow-up adrenal CT imaging (Figure 2) documented largely resolution of bilateral adrenal hyperplasia, with adrenal thickness reduced to within normal limits.

This case provides a complete clinico-radiological trajectory: chronic etomidate exposure → acquired adrenal hyperplasia → drug cessation → largely radiological and biochemical resolution at 3 years.

Table 5-1. Blood and urine electrolyte (3-year-follow-up after etomidate withdrawal).

Value	Blood(mmol/L)
Potassium	4.01(3.5-5.5)
Sodium	139.6(137-147)
Chlorine	104.0(99-110)

Table 5-2. Cortisol and ACTH diurnal rhythm (3-year-follow-up after etomidate withdrawal).

Value	8am	4pm	0am
Cortisol(ug/dL)（3.5-20）	13.70	13.51	2.41
ACTH(pg/ml)（7.20-63.6）	53.00	71.90	12.50

Table 5-3. Cortisol precursors (3-year-follow-up after etomidate withdrawal).

Value	Result	Reference
17α-OHP(ng/ml)	1.74	0.29-2.06
ASD(ng/ml)	4.730	0.602-3.100
DHEA(μg/dL)	413.00	106.00-464.00

Discussion and conclusion

We report a case of chronic etomidate inhalation presenting with hypokalemia, hypertension, bilateral adrenal hyperplasia, and biochemical features consistent with 11β-OHD, which resolved largely after 3 years of drug cessation. To our knowledge, this is the first case to provide imaging evidence of radiological reversal of etomidate-induced adrenal hyperplasia following long-term abstinence. This discussion focuses on three aspects: the pathophysiological basis of etomidate-induced adrenal dysfunction, the distinction from CAH, and the clinical implications of our long-term follow-up findings.

Pathophysiological basis of etomidate-induced adrenal dysfunction

Etomidate is a rapid-acting intravenous anesthetic that exerts its sedative effects via GABAA receptor agonism. However, it also reversibly inhibits CYP11B1, a key enzyme in the adrenal steroidogenic pathway, thereby impairing the conversion of 11-deoxycortisol to cortisol in a dose-dependent manner [1]. Studies have shown that a single intravenous dose can suppress cortisol synthesis for at least 24 hours, far exceeding its sedative duration [4]. Indeed, this effect has been therapeutically exploited to rapidly lower cortisol levels in severe Cushing syndrome [5].

In illicit “heady e-cigarettes,” the etomidate content varies widely. After inhalation, etomidate is rapidly absorbed and, due to its high lipophilicity, distributes preferentially into adipose-rich tissues—including the adrenal gland. Because its central nervous system effects are short-lived, users may unconsciously escalate the frequency of use, leading to sustained adrenal suppression [6]. In our patient, 4-5 times weekly inhalation over 10 years resulted in chronic CYP11B1 inhibition, leading to cortisol deficiency, ACTH-driven bilateral adrenal hyperplasia, and mineralocorticoid-related hypertension with hypokalemia —a clinical picture closely resembling 11β-OHD.

Distinction from CAH

CAH due to 11β-OHD is an autosomal recessive disorder caused by *CYP11B1* gene mutations, accounting for approximately 5–8% of all CAH cases [7,8]. The enzymatic block leads to cortisol and aldosterone deficiency, ACTH feedback-driven adrenal hyperplasia, and accumulation of 11-deoxycortisol and deoxycorticosterone (DOC). The latter, a potent mineralocorticoid precursor, causes hypertension and hypokalemia via sodium retention and potassium wasting. Additionally, androgen excess may cause virilization in females and sexual precocity in males [9].

Although our patient's biochemical and imaging phenotype mimicked 11β-OHD, several key features supported an acquired etiology:

· Onset in adulthood without prior growth abnormalities or ambiguous genitalia, arguing against a congenital enzyme defect

· Normal whole-exome sequencing excluding pathogenic variants in *CYP11B1*, *CYP21A2*, and other CAH-related genes

· Largely clinical and biochemical resolution after drug cessation, which would not occur in genetic CAH

These distinctions underscore the importance of obtaining a thorough substance use history in adults presenting with a CAH-like phenotype. In cases without genetic confirmation, acquired causes—including drug-induced adrenal dysfunction—should be actively considered.

The key finding: radiological reversibility after 3-year follow-up

The most important contribution of this case is its long-term follow-up data. While several recent case reports have documented etomidate-induced adrenal hyperplasia in the acute phase [2,3], none have provided imaging evidence of adrenal regression after drug cessation. Our patient's follow-up CT at 3 years demonstrated largely resolution of bilateral adrenal hyperplasia, with normalization of adrenal thickness.

This finding has two critical implications.

First, it confirms the reversible nature of etomidate-induced adrenal hyperplasia. The pathophysiological sequence can be summarized as: chronic etomidate exposure → CYP11B1 inhibition → reduced cortisol synthesis → loss of feedback suppression on ACTH → ACTH-driven adrenal hyperplasia → drug cessation → restoration of hypothalamic-pituitary-adrenal axis → normalization of adrenal morphology. Our case provides the missing "final step" in this chain, strengthening the causal relationship between etomidate exposure and adrenal enlargement.

Second, it supports a conservative "watch-and-wait" management strategy for patients with suspected etomidate-induced adrenal hyperplasia. Once the offending agent is discontinued, adrenal function can

recover without the need for surgical intervention, long-term steroid replacement, or extensive genetic workup beyond targeted testing. This is particularly relevant given the rising prevalence of etomidate-containing e-cigarette use and the increasing detection of adrenal incidentalomas on routine imaging. Clinicians should be aware that drug-induced adrenal hyperplasia is a reversible mimicker of CAH, and careful follow-up may avoid unnecessary procedures.

Limitations

We acknowledge several limitations. First, DOC and 11-deoxycortisol levels, which would have provided direct biochemical evidence of CYP11B1 inhibition, were not measured because these assays were unavailable through multiple commercial laboratories we contacted. Despite this limitation, the clinical, biochemical, and imaging findings, together with negative genetic testing and the robust response to drug cessation, collectively support the diagnosis. Second, this is a single case report, and the findings require confirmation in larger cohorts. Third, the possibility of other undisclosed substance use cannot be entirely excluded, though the clinical course strongly correlated with etomidate exposure.

Conclusion

In summary, we report a case of chronic etomidate inhalation causing acquired adrenal hyperplasia with biochemical features mimicking 11β-OHD. Crucially, 3-year follow-up imaging demonstrated largely radiological resolution after drug cessation, providing the first evidence that this condition is reversible. This case highlights the importance of recognizing drug-induced adrenal dysfunction as a differential diagnosis in adult patients with bilateral adrenal hyperplasia and hypokalemia. Early identification and etomidate cessation, with regular follow-up, constitute a safe and effective management strategy.

Abbreviations

CYP11B1
11β-hydroxylase
CAH
congenital adrenal hyperplasia
ACTH
adrenocorticotropic hormone
11β-OHD
11β-hydroxylase deficiency
GABAA
gamma absorptiometry aminobutyric acid
ARR
aldosterone-to-renin ratio
FSH
follicle-stimulating hormone
LH

luteinizing hormone
17α-OHP
17-α-hydroxy pregnenolone
ASD
androstenedione
DHEA
dehydroepiandrosterone
DOC
deoxycorticosterone

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Availability of data and materials

All data generated or analysed during this study are included in this published article. The whole-exome sequencing data have been deposited in the NCBI Sequence Read Archive (SRA) under BioProject accession number PRJNA1514059 and are publicly available at: https://www.ncbi.nlm.nih.gov/bioproject/PRJNA1514059. The original CT images and laboratory records are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors made individual contributions to authorship. Shuhua Yuan was involved in the diagnosis of the patient and wrote the paper. Zhihua Sun was involved in the diagnosis and treatment of the patient. Yinghe Lin participate in the management of the patient.

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Not applicable.

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Figures



Figure 1

Adrenal CT scans.

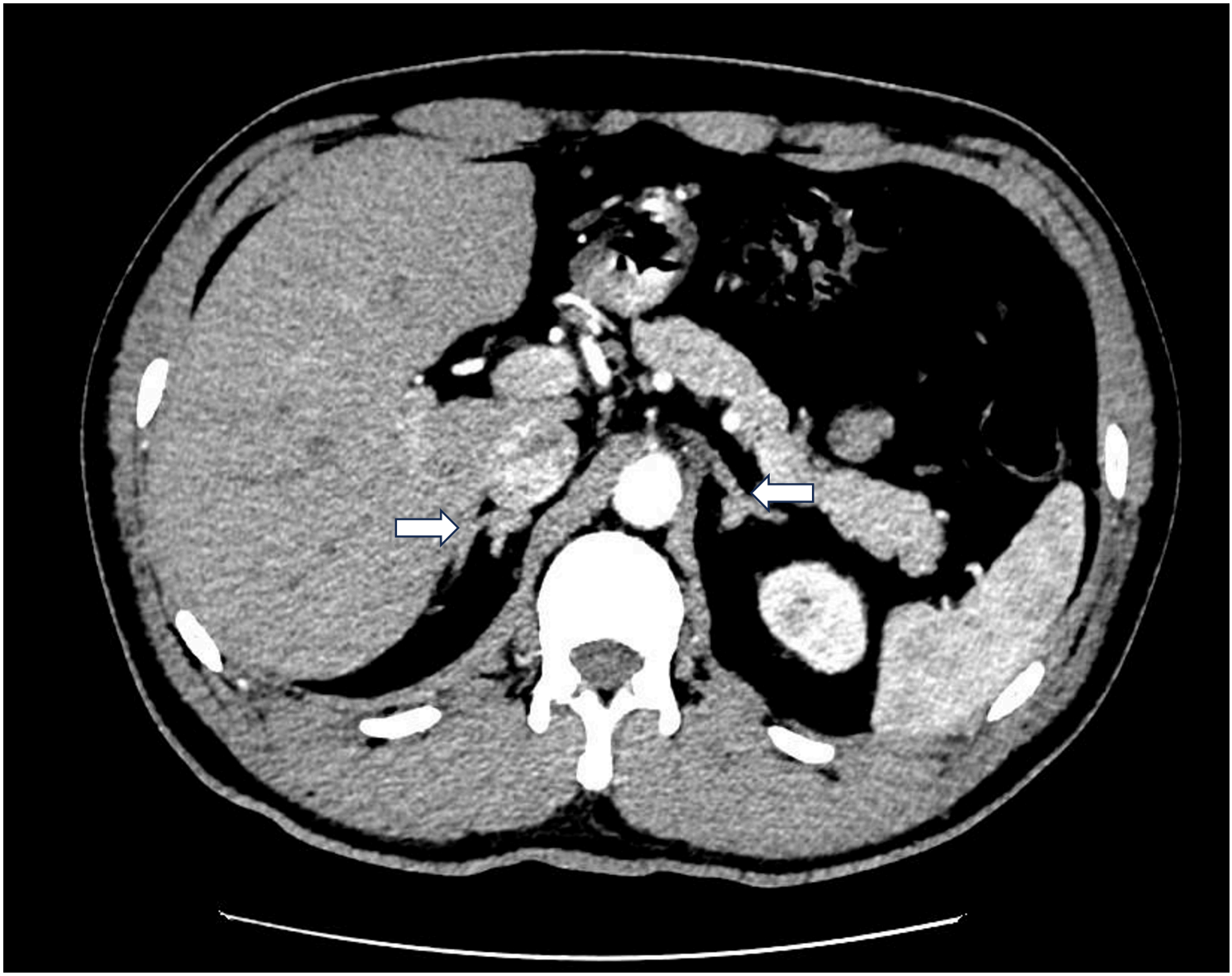


Figure 2

Adrenal CT scans (3-year-follow-up after etomidate withdrawal).