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Acute Psychosis and Suicide Attempt As Manifestations of Severe Endogenous Hypercortisolism: A Case Report of Adrenocorticotropic Hormone (ACTH)-Independent Cushing Syndrome

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Abstract

Cushing syndrome is an endocrine disorder caused by chronic exposure to excess cortisol. Although neuropsychiatric manifestations are common, progression to acute psychosis with a suicide attempt is exceptionally rare. We present the case of a patient with adrenocorticotropic hormone (ACTH)-independent Cushing syndrome secondary to a cortisol-secreting adrenocortical carcinoma, whose predominant neuropsychiatric manifestation was an acute psychotic episode with a suicide attempt. The patient had a five-month history of Cushingoid signs and symptoms, followed by one week of emotional lability that rapidly progressed to an acute psychotic episode with a suicide attempt prior to surgical resection, requiring hospitalization and psychiatric evaluation. Open adrenalectomy was performed, and histopathological examination confirmed a cortisol-secreting adrenocortical carcinoma. Subsequently, the patient experienced rapid resolution of psychiatric symptoms and a favorable clinical course following tumor resection. This case highlights the importance of considering hypercortisolism as a potentially reversible cause of acute psychosis and suicidal behavior. It also underscores the need to include endocrine disorders in the differential diagnosis of de novo psychosis and to incorporate early psychiatric evaluation into the multidisciplinary management of patients with Cushing syndrome, particularly in the presence of severe neuropsychiatric manifestations.

Categories: Psychiatry, Endocrinology/Diabetes/Metabolism
Keywords: adrenocortical carcinoma, cushing syndrome, hypercortisolism, psychotic disorders, suicide attempt

Introduction

Cushing syndrome is a clinical disorder caused by chronic exposure to excessive cortisol levels, resulting in harmful effects on multiple organs and tissues. Under physiological conditions, adrenocorticotropic hormone (ACTH), secreted by the anterior pituitary gland, acts on the zona fasciculata of the adrenal cortex to stimulate cortisol synthesis and secretion. Under pathological conditions, certain tumors can produce cortisol autonomously, releasing large amounts of the hormone into the bloodstream. This results in ACTH-independent Cushing syndrome, in which hypercortisolism occurs independently of pituitary stimulation [1-3]. Cushing syndrome encompasses the clinical manifestations resulting from prolonged exposure to excessive glucocorticoids, whether due to exogenous glucocorticoid use or endogenous cortisol overproduction. In contrast, Cushing disease refers specifically to the ACTH-dependent form of Cushing syndrome caused by an ACTH-secreting pituitary adenoma. The present case corresponds to ACTH-independent Cushing syndrome.

Neuropsychiatric manifestations are among the most frequent complications of Cushing syndrome, with depression and anxiety representing the most common presentations, reported in up to 50-80% of patients. In contrast, psychosis is considerably less frequent. In a retrospective cohort of 238 patients with Cushing syndrome, psychosis was reported in 7% and suicidal tendencies in 1%, although the frequency of suicide attempts specifically was not reported separately [4]. Given this rarity, clinicians may not initially consider hypercortisolism when a patient presents with acute psychosis or suicidal behavior. Although uncommon, acute psychosis accompanied by a suicide attempt requires immediate psychiatric assessment; the Endocrine Society clinical practice guideline likewise recommends urgent treatment of hypercortisolism in the presence of acute psychosis [5].

At the hippocampal level, markedly elevated cortisol levels reduce neurogenesis and increase neuronal degeneration, resulting in impaired emotional regulation and decreased cognitive function. Furthermore, hypercortisolemia disrupts serotonergic and dopaminergic neurotransmission, which has been described in

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multiple studies as a pathophysiological mechanism contributing to psychotic disorders, depression, and a reduced capacity to experience pleasure [1,6,7].

This report describes a severe and uncommon case of acute psychosis with a suicide attempt associated with ACTH-independent Cushing syndrome secondary to a cortisol-secreting adrenocortical carcinoma.

Case Presentation

A 33-year-old man with no significant past medical or family history and no history of exogenous corticosteroid use presented to the outpatient clinic with a five-month history of facial flushing, weight gain, muscle fatigue, and diaphoresis. One week before admission, the patient began experiencing alternating episodes of emotional lability, described by family members as abrupt shifts between irritability, intense sadness with a tendency to cry, feelings of worthlessness, and periods of social withdrawal. During these episodes, depressive symptoms were observed, including markedly decreased energy, hypersomnia, and loss of interest in usual activities.

On initial physical examination, the patient was in fair general condition, with the following vital signs: blood pressure, 130/90 mmHg; heart rate, 82 beats per minute. He weighed 195 lb and was 162 cm tall, with a body mass index (BMI) of 33.7 kg/m^2, consistent with class I obesity. Physical examination revealed a plethoric Cushingoid facies with facial acne and a buffalo hump over the posterior cervical region. Diffuse red striae were also observed over the abdomen, along with small telangiectasias. The remainder of the physical examination was unremarkable.

Laboratory studies were performed, with results consistent with ACTH-independent hypercortisolism (Table *1*). Other relevant biochemical parameters were also assessed, including serum potassium, which was low.

Parameter	Result	Reference range
Morning serum cortisol (AM)	583.51 nmol/L	151.58-793.38 nmol/L
24-hour urinary cortisol	416.14 µg/24 h	96.6-120.63 ug/24 h
ACTH	5.15 pg/mL	7.27-62.73 pg/mL
Potassium	3.2 mEq/L	3.5-5.1 mEq/L
Creatinine	0.9 mg/dl	0.6-1.2 mg/dl
Sodium	139.5 mEq/L	135-145 mEq/L

TABLE 1: Laboratory findings at initial evaluation.

ACTH: adrenocorticotropic hormone.

After reviewing the laboratory results, an abdominal computed tomography (CT) scan was obtained, revealing a right adrenal mass of undetermined etiology (Figure *1*). Based on the imaging and laboratory findings, a diagnosis of ACTH-independent Cushing syndrome secondary to a right adrenal mass was established. Given the size of the lesion, the patient was scheduled for open adrenalectomy.

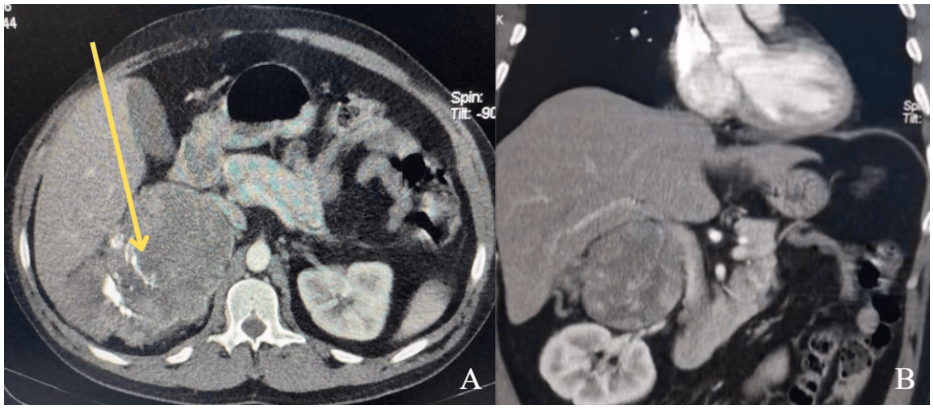


FIGURE 1: Abdominal CT showing a right adrenal mass.

Axial (A) and coronal (B) CT images demonstrating a large right adrenal mass (yellow arrow) measuring 12.7 × 11.9 × 12.7 cm. The lesion appears hypodense with multilobulated, irregular borders and is located adjacent to the upper pole of the right kidney, without evidence of local invasion.

Two days before surgery, the patient experienced an acute psychotic episode accompanied by a suicide attempt at home, requiring admission to the emergency department. According to family members, the episode was characterized by sudden behavioral changes, severe agitation, persecutory delusions, auditory hallucinations, and an acute loss of reality testing. The patient was evaluated by the Psychiatry team, who diagnosed an acute psychotic episode. Given the clinical context, the psychiatric manifestations were considered likely related to severe hypercortisolism. Due to the severity of the psychiatric emergency and the imminent risk to the patient's safety, the surgical intervention was urgently brought forward. Immediate management included strict hospital supervision for safety and emergency stabilization.

Before surgery, intravenous hydrocortisone (100 mg) was administered to prevent acute adrenal insufficiency. Following adrenalectomy, the patient showed steady improvement in his mental status, with no further documented psychotic episodes or suicide attempts during the available follow-up period.

Histopathological examination of the right adrenal gland following adrenalectomy (Figure *2*) confirmed the presence of adrenocortical carcinoma. The tumor exhibited a high mitotic rate, with 27 mitoses per 50 high-power fields, indicating marked proliferative activity. Tumor necrosis was also identified in 15% of the examined tissue. According to the Weiss scoring system, the tumor met more than three criteria for malignancy, supporting the diagnosis of adrenocortical carcinoma.

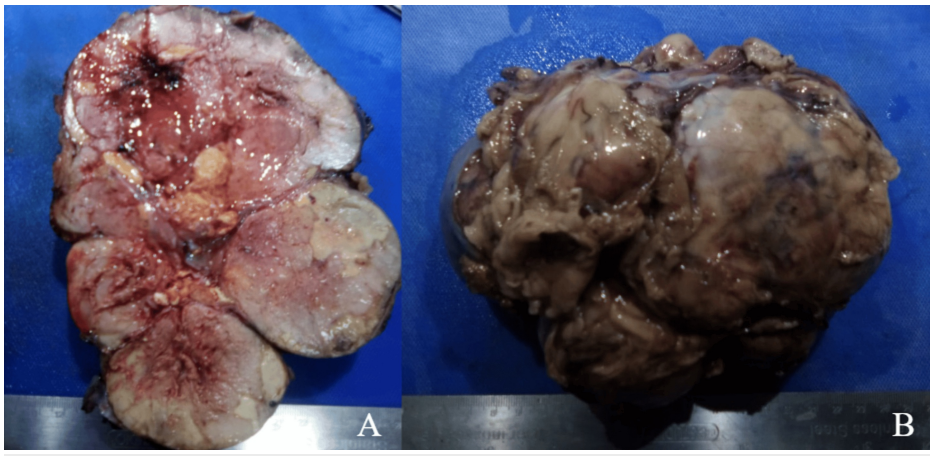


FIGURE 2: Gross pathological features of the right adrenal mass.

(A) A large adrenal mass with an irregular surface. (B) The cut surface reveals a heterogeneous lesion with areas of ochre-yellow tissue, hemorrhage, and necrosis, highly suggestive of malignancy.

The patient had a favorable postoperative course, with steady improvement in his mental status, no further episodes of hypokalemia, and no psychiatric relapses. Postoperatively, the patient received intravenous hydrocortisone replacement with a tapering regimen over the first 48 hours, followed by oral hydrocortisone

at a dose of 30 mg per day, divided into morning and afternoon doses. Oral hydrocortisone was subsequently gradually tapered and discontinued. He was subsequently referred to the oncology department at another hospital.

Differential diagnosis

The differential diagnosis of ACTH-independent Cushing syndrome included exogenous hypercortisolism, functioning adrenal adenoma, adrenocortical carcinoma, bilateral macronodular adrenal hyperplasia, and primary pigmented nodular adrenocortical disease (PPNAD). Laboratory results demonstrated suppressed ACTH levels with elevated urinary cortisol, confirming an ACTH-independent source of hypercortisolism and making ACTH-dependent causes, including Cushing disease and ectopic ACTH secretion, unlikely. Exogenous hypercortisolism was also excluded based on the absence of corticosteroid or other exogenous steroid use.

Bilateral adrenal disorders, including bilateral macronodular adrenal hyperplasia and PPNAD, were considered less likely because abdominal imaging revealed a solitary unilateral adrenal mass rather than bilateral adrenal involvement. The principal diagnostic consideration was therefore between a functioning adrenal adenoma and adrenocortical carcinoma, as both may present with ACTH-independent hypercortisolism. However, the large size, heterogeneous appearance, and irregular margins observed on computed tomography favored adrenocortical carcinoma over a benign adenoma. The diagnosis was ultimately confirmed by histopathological examination, which demonstrated malignant features consistent with adrenocortical carcinoma.

Ethics statement

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Patient confidentiality and privacy were strictly maintained, and all identifying information was removed from the manuscript to ensure that the patient could not be identified. This case report was prepared in accordance with the ethical principles of the Declaration of Helsinki. According to institutional policy, formal ethics committee approval was not required for the publication of this single case report.

Discussion

Adrenocortical carcinoma is a rare and aggressive endocrine malignancy, with an estimated annual incidence of 0.5 to 2 cases per million population [8]. Approximately 50-60% of these tumors are hormonally functional, with cortisol being the most frequently secreted hormone, leading to ACTH-independent Cushing syndrome [9]. In this case, the diagnosis was established based on elevated 24-hour urinary free cortisol levels, suppressed ACTH levels (Table *1*), and the identification of an adrenal mass on computed tomography (Figure *1*). These findings were consistent with the patient's clinical presentation, which was characterized by facial plethora, central weight gain, a buffalo hump, and violaceous abdominal striae, classic manifestations of the Cushingoid phenotype.

Neuropsychiatric manifestations represent an important component of the clinical spectrum of Cushing syndrome, particularly affecting mood and cognitive function, and may persist even after remission [10]. The literature describes a wide range of psychiatric manifestations, including depression, anxiety, psychosis, and suicidal behavior. A recent systematic review reported psychiatric symptoms in 93% of patients with Cushing syndrome, with depression, psychosis, and suicidal ideation or attempts reported in 39.2%, 35.1%, and 20.3% of cases, respectively. However, complete resolution of these symptoms is not always achieved following treatment [11].

Although suicidal behavior has been associated with Cushing syndrome, the clinical sequence observed in this patient-characterized by emotional lability and depression, followed by a suicide attempt within one week and marked improvement in mental status after surgical resection-represents an uncommon presentation. Although an association between adrenocortical carcinoma and psychiatric manifestations such as panic attacks and psychosis has previously been reported [12], the striking temporal association observed in our patient is particularly noteworthy.

First-line treatment for endogenous Cushing syndrome is surgical resection of the causative tissue, whether the condition is ACTH-dependent or of adrenal origin [13]. In patients with an adrenal mass, unilateral adrenalectomy is the preferred surgical approach and is usually performed laparoscopically. In the present case, open adrenalectomy was planned because of the size of the lesion. Following tumor resection, suppression of the hypothalamic-pituitary-adrenal axis and possible atrophy of the contralateral adrenal gland should be considered; therefore, postoperative glucocorticoid replacement should be initiated to prevent adrenal crisis [14]. In this patient, postoperative glucocorticoid replacement was administered as described in the Case Presentation, and subsequent management was transferred to the oncology department. However, detailed information regarding the frequency of follow-up, postoperative hormonal assessment, imaging surveillance, adjuvant treatment, and long-term oncological outcomes was not available.

Cushing syndrome, regardless of its underlying cause, can be associated with various comorbidities and complications, including an increased risk of cardiovascular events, cerebrovascular events, sepsis, and thromboembolism, resulting in a 3.5- to 5-fold higher risk of mortality compared with the general population [15]. In the present case, the patient showed clinical improvement following surgery, with no further psychotic episodes. Although neuropsychiatric symptoms generally improve after correction of glucocorticoid excess, some patients may experience persistent cognitive or neuropsychiatric impairment despite remission [16]. Therefore, continued endocrinological and psychiatric follow-up is warranted to monitor recovery from hypercortisolism, assess for persistent or recurrent neuropsychiatric manifestations, and manage comorbidities associated with cortisol excess.

Furthermore, despite normalization of hormone levels, certain comorbidities may require prolonged treatment and may persist even after successful management, thereby affecting the patient's quality of life [16]. In patients with adrenocortical carcinoma, postoperative surveillance is important because of the risk of recurrence and generally includes clinical assessment, evaluation of hormone secretion, and periodic imaging. The need for adjuvant therapy should be determined according to pathological findings, tumor stage, and individual risk of recurrence. In the present case, the tumor met more than three criteria of the Weiss scoring system, supporting the diagnosis of adrenocortical carcinoma; however, detailed information regarding postoperative oncological surveillance and the use of adjuvant therapy was not available.

This case highlights the importance of considering endogenous hypercortisolism as a potentially reversible cause of acute psychiatric manifestations, including severe mood disturbances and psychosis. In patients presenting with new-onset psychiatric symptoms accompanied by clinical features suggestive of cortisol excess, recognition of an underlying endocrine disorder may allow timely treatment of the primary cause and potentially substantial improvement in neuropsychiatric outcomes.

Limitations

This case has several limitations. First, although the patient was evaluated by the Psychiatry team and diagnosed with an acute psychotic episode, a structured psychiatric assessment was not documented, limiting a more detailed characterization of the neuropsychiatric manifestations and their evolution. Second, serial postoperative cortisol measurements were unavailable, limiting biochemical assessment of postoperative hypothalamic-pituitary-adrenal axis recovery. Third, psychiatric follow-up after hospitalization was limited, precluding a detailed assessment of long-term psychiatric outcomes or residual symptoms. Finally, additional functional testing, such as a dexamethasone suppression test, was not performed, which limited further biochemical characterization of the cortisol excess.

Conclusions

This case highlights severe endogenous hypercortisolism as an important and potentially reversible contributor to acute psychosis and a suicide attempt. Although a direct causal relationship cannot be definitively established, the close temporal association between tumor resection and the patient's marked psychiatric improvement supports a possible link between cortisol excess and the neuropsychiatric manifestations observed. Acute psychosis with a suicide attempt as an initial manifestation of hypercortisolism represents an uncommon and potentially life-threatening presentation that should prompt consideration of an underlying endocrine disorder, particularly when accompanied by clinical features suggestive of Cushing syndrome. This case underscores the importance of early multidisciplinary management, including psychiatric evaluation, to facilitate timely diagnosis and treatment. Further studies are needed to better characterize the relationship between hypercortisolism and severe psychiatric symptoms and to define optimal long-term follow-up strategies.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Nicole Martel, Carlos Rojas, Yajaira Acosta Crousset, Daniel Ibanez Vasquez, Eugenio Ortiz

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Disclosures

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organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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