A Case of Cushing’s Disease Presenting with Isolated Suicidal Attempt

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ABSTRACT: Cushing’s disease is an abnormal secretion of ACTH from the pituitary that causes an increase in cortisol production from the adrenal glands. Resultant manifestations from this excess in cortisol include multiple metabolic as well as psychiatric disturbances which can lead to significant morbidity and mortality. In this report, 23-year-old woman presented to mental health facility with history of severe depression and suicidal ideations. During evaluation, she found to have Cushing’s disease, which is unusual presentation. She had significant improvement in her symptoms with reduction of antidepressant medications after achieving eucortisolism. Cushing syndrome can present with wide range of neuropsychiatric manifestations including major depression. Although presentation with suicidal depression is unusual. Early diagnosis and prompt management of hypercortisolism may aid in preventing or lessening of psychiatric symptoms. The psychiatric and neurocognitive disorders improve after disease remission (the normalization of cortisol secretion), but some studies showed that these disorders can partially improve, persist, or exacerbate, even long-term after the resolution of hypercortisolism. The variable response of neuropsychiatric disorders after Cushing syndrome remission necessitate long term follow up.

KEYWORDS: cushing syndrome, cushing disease, hypercortisolism

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Introduction

Endogenous Cushing syndrome is a complex disorder caused by chronic exposure to excess circulating glucocorticoids. It has a wide range of clinical signs and symptoms as a result of the multisystem effects caused by excess cortisol.1

The hypercortisolism results in several complications that include glucose intolerance, diabetes, hypertension, dyslipidemia, thromboembolism, osteoporosis, impaired immunity with increased susceptibility to infection as well as neuropsychiatric disorders.2,3

Cushing syndrome presents with a wide variety of neuropsychiatric manifestations like anxiety, major depression, mania, impairments of memory, sleep disturbance, and rarely, suicide attempt as seen in this case.2,4

The mechanism of neuropsychiatric symptoms in Cushing’s syndrome is not fully understood, but multiple proposed theories have been reported, one of which is the direct brain damage secondary to excess of glucocorticoids.5

Case Report

A 23-year-old female presented to Al-Amal complex of mental health in Riyadh, Saudi Arabia with history of suicidal tendencies and 1 episode of suicidal attempt which was aborted because of religious reasons. She reported history of low mood, having disturbed sleep, loss of interest, and persistent feeling of sadness for 4 months. She also reported history of weight gain, facial swelling, hirsutism, and irregular menstrual cycle with amenorrhea for 3 months. She was prescribed fluoxetine 40 mg and quetiapine 100 mg. She was referred to endocrinology clinic at King Fahad Medical City, Riyadh for evaluation and management of possible Cushing syndrome as the cause of her abnormal mental health.

She was seen in the endocrinology clinic where she reported symptoms as mentioned above in addition to headache, acne, and proximal muscle weakness.

On examination her vital signs were normal. She had depressed affect, rounded face with acne and hirsutism, striae in the upper limb, and abdomen with proximal muscle weakness (4/5).

Initial investigations showed that 24 hour urinary free cortisol was more than 633 µg which is more than 3 times upper limit of normal (this result was confirmed on second sample with level more than 633 µg/24 hour), cortisol level of 469 nmol/L after low dose 1 mg-dexamethasone suppression test and ACTH level of 9.8 pmol/L. Levels of other anterior pituitary hormones tested were within normal range. She also had prediabetes with Hba1c of 6.1 and dyslipidemia. Serum electrolytes, renal function and thyroid function tests were normal.

MRI pituitary showed left anterior microadenoma with a size of 6 mm × 5 mm.

MRI pituitary (Figure 1).

No further hormonal work up or inferior petrosal sinus sampling were done as the tumor size is 6 mm and ACTH level consistent with Cushing’s disease (pituitary source). She was referred to neurosurgery and underwent trans-sphenoidal resection of the tumor. Histopathology was consistent with pituitary adenoma and positive for ACTH. Her repeated cortisol level after tumor resection was less than 27 and ACTH 2.2 with indicated excellent response to surgery.
She was started on hydrocortisone until recovery of her hypothalamic pituitary adrenal axis documented by normal morning cortisol 3 months after surgery (Table 1).

During follow up with psychiatry her depressive symptoms improved but not resolved and she was able to stop fluoxetine 5 months post-surgery. Currently she is maintained on quetiapine 100 mg with significant improvement in her psychiatric symptoms.

Currently she is in remission from Cushing’s disease based on the normal level of repeated 24 hour urinary free cortisol and with an over-all improvement in her metabolic profile.

**Discussion**

Cushing syndrome is a state of chronic hypercortisolism due to either endogenous or exogenous sources. Glucocorticoid overproduction by adrenal gland can be adrenocorticotropic (ACTH) hormone dependent which represent most of the cases and ACTH independent. To the best of our knowledge this is the first case documented in Saudi Arabia.

There are multiple theories behind the neuropsychiatric manifestations in Cushing syndrome. These include increased stress response leading to behavioral changes, prolonged cortisol exposure leading to decreased brain volume especially in the hippocampus, reduced dendritic mass, decreased glial development, trans-cellular shift of water and synaptic loss, and excess glucocorticoid levels inhibiting neurogenesis and promoting neuronal tendency to toxic insult.

In this report, the patient presented with severe depression with suicidal attempt. She had significant improvement in her symptoms with reduction of antidepressant medications but her depression persisted despite remission of Cushing disease. A similar case has been reported by Mokta et al, about a young male who presented with suicidal depression as initial manifestation of Cushing disease. As opposed to the present case he had complete remission of depression within 1 month of resolution of hypercortisolism.

In general, psychiatric and neurocognitive disorders secondary to Cushing syndrome improves after normalization of cortisol secretion, but some studies showed that these disorders can partially improve, persist, or exacerbate, even long-term after the resolution of hypercortisolism. This may be due to persistence hypercortisolism creating toxic brain effects that occur during active disease. Similar patients need to be followed up for mental health long after Cushing syndrome has been resolved.

**Conclusion**

Depression is a primary psychiatric illness, that is, usually not examined for secondary causes. Symptoms of depression and Cushing syndrome overlap, so diagnosis and treatment of Cushing disease can be delayed. Early diagnosis and prompt management of hypercortisolism may aid in preventing or lessening psychiatric symptoms. The variable neuropsychiatric disorders associated with Cushing syndrome post-remission necessitates long term follow up.
Informed Consent
Written informed consent was obtained from the patient for the publication of this case and accompanying images.

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