CASE REPORT

Cushing’s syndrome presenting as treatment-resistant bipolar affective disorder: A step in understanding endocrine etiology of mood disorders

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ABSTRACT

Cushing’s syndrome (CS) is the multisystem disorder which is due to cortisol excess. It is very difficult to diagnose in early stages, especially when psychiatric manifestations are the predominant complaints. It could result in significant morbidity and mortality. We report a case of resistant bipolar affective disorder secondary to CS. Early diagnosis and treatment will lead to better functional outcome and prevention of neurocognitive side-effects of excessive cortisol.

Key words: Bipolar disorder, Cushing’s syndrome, treatment resistance

INTRODUCTION

Cushing’s syndrome (CS) affects most systems of the human body. The full-blown clinical picture is characterized by progressive specific site adiposity, myopathy, dermopathy, hirsutism, stress fractures, psychopathy, glucose intolerance, hypercholesterolemia, hypertension, atherosclerosis, and immunosuppression. The psychiatric manifestations include depression, mania or psychosis and can precede the onset of the classical physical signs by several years. [1] Although the classical syndrome is relatively easy to recognize in clinical practice, more subtle manifestations of CS are difficult to diagnose, particularly in the setting of concomitant psychiatric conditions. The recognition of CS by physicians is important for early diagnosis and treatment. The diagnosis of CS is often missed initially owing to its rarity and overlapping characteristics with common disorders like metabolic syndrome. It is generally diagnosed later in its full-blown state. Timely diagnosis and treatment of CS is important to decrease morbidity and mortality. [2]

CASE REPORT

A 20-year-old Muslim patient presented to the outpatient department (OPD) with complaints of increased speech, increased goal-directed activity, decreased sleep, irritability, and behavioral problems against family members. No psychotic symptoms. Patient also had increased blood pressure and dysglycemia. Patient had his first episode 3 years back with symptoms of low mood, motor retardation, tiredness, auditory hallucinations and was treated with 20 mg fluoxetine. One year later, he had another episode suggestive of mania with similar symptomatology like the current episode. He was treated with divalproex sodium up to 2 g in BD dose and olanzapine 20 mg at night, but he continued to have dysphoric mood and weight gain. He was started on lithium and dose was adjusted according to the serum level. At 1000 mg, level was 1 mEq/L. He had good symptomatic improvement and completed his higher secondary. Patient developed severe acne form eruptions while on Lithium. He was started on CBZ up to 800 mg. He had a relapse of a manic episode

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and was referred to our OPD. He had family history of colorectal malignancy.

During IP stay, lithium was gradually reintroduced, and he was also treated with quetiapine up to 600 mg. He was treated symptomatically for his metabolic syndrome. He had improvement in manic signs (YMRS 39 on admission to 16, after 2 weeks), but continued to have subsyndromal symptoms. He had another relapse after 5 months during which along with mood symptoms he had resistant hypertension, dysglycemia, central obesity, severe acne and abdominal striae.

We suspected CS and his serum cortisol and 24 h urinary cortisol was elevated. His adrenocorticotropic hormone (ACTH) level was also elevated. Low dose and high dose dexamethasone suppression were positive. We did corticotropin-releasing hormone (CRH) suppression test and was positive. Magnetic resonance imaging (MRI) pituitary was done, and he had a lesion in stalk. Diagnosis of pituitary dependent Cushing’s was made.

During the hospital stay, patient had a depressive syndrome with catatonic signs. His Hamilton Depression Rating Scale score was 30 and his Bush Francis Catatonia Rating scale was 29. He was treated with lorazepam up to 3 mg, divalproex sodium 2500 mg and quetiapine 600 mg. His catatonic signs improved significantly, and Bush Francis score was 3 after treatment, but continued to have depressive symptoms. Neurosurgical consultation was obtained for possible surgical removal, but in view of atypical finding in the MRI, medical management was considered. He was started on medical treatment for Cushing’s. Quetiapine was stopped in view of excessive drowsiness. Patient was started on lamotrigine 25 mg and dose was increased to 100 mg BD and he had reduction in HAM-D to 14 in 6 weeks time and 11 during follow-up for 6 months.

**DISCUSSION**

Cushing’s syndrome patients often suffer from major psychiatric syndromes, most often depression. However, patients with other psychiatric disorders such as bipolar affective disorder, personality disorders, and dementia can be manifestations of underlying CS when it is associated with clinical features, atypical presentation, and treatment resistance.

Patients with long-term cured CD show an increased prevalence of psychopathology and maladaptive personality traits. These observations suggest irreversible effects of previous glucocorticoid excess on the central nervous system rather than an effect of pituitary tumors and/or their treatment in general.

Cortisol is secreted by adrenal cortex in response to stimulation from ACTH and CRH from pituitary gland and hypothalamus respectively. This is called hypothalamus-pituitary axis (HPA axis). Cortisol secretion has normal diurnal fluctuations and physiological role. It is well-known fact that there is HPA axis dysfunction in mood disorders. HPA axis dysfunction and excess cortisol could lead to irreversible cognitive dysfunction secondary to damage of Cornu ammonis (CA3) of the hippocampus. When a person has significant stress in early life where maximum neurodevelopment happens, person is having increased chance of mood disorder later in the life. Cushing’s disease is also a condition where there is excess cortisol, which could be the cause of mood disorder.

There are case reports stating Cushing’s disease can present as manic episode and once the primary disorder is treated then there is good symptomatic recovery with maintenance treatment. It is reported that there are patients with recurrent mania without depressive episodes in a subsequently diagnosed as having an ACTH-producing basophil adenoma. There are difficulties involved in the clinical and laboratory diagnosis of CS, and the ramifications of neuroendocrinopathies’ ability to mimic symptoms of functional psychosis. Chronically elevated levels of cortisol have been associated with changes in cognitive functioning and brain morphology. Once treated there is a good improvement in the outcome of functional disorders.

Clinical decision making for patients with suspect hypercortisolism involves a complex diagnostic assessment. CS remains one of the most challenging endocrine pathologies. Most clinical features overlap with those of common diseases found in the general population, and some patients have an atypical clinical presentation with only isolated symptoms. Recently, several studies have suggested that the prevalence of CS is higher than previously thought. Therefore, efficient screening tests are needed to identify the few uncovered patients also among unselected high-risk ambulatory patients with disorders potentially related to cortisol excess.

When we come to the discussion of whether excess cortisol is cause or effect in the spectrum of mood disorders, our current case report supports the argument that the hypercortisolism could well be the cause of mood disorders.

**CONCLUSION**

From the above case report, proper identification and treatment of CS in the patient with bipolar affective disorder leads to improvement in the functional disorder with maintenance treatment. Hence, high index of suspicion is required to find out underlying endocrinological conditions.
presenting with functional disorders and proper diagnosis leads to good functional outcome and prevent long-term disability.

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