

Case Report

Cushing's Syndrome Masquerading as Treatment Resistant Depression

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ABSTRACT

Treatment resistant depression (TRD) is a common clinical occurrence among patients treated for major depressive disorder. A significant proportion of patients remain significantly depressed in spite of aggressive pharmacological and psychotherapeutic approaches. Management of patient with treatment resistant depression requires thorough evaluation for physical causes. We report a case of recurrent depressive disorder, who presented with severe depressive episode without psychotic symptoms, not responding to multiple adequate trials of antidepressants, who on investigation was found to have Cushing's syndrome and responded well to Ketoconazole.

Key words: Antiglucocorticoid drugs, Cushing's syndrome, treatment-resistant depression

INTRODUCTION

The main aim of management of depression is remission of the episode. However, in a proportion of the patients with major depression, despite the use of adequate antidepressant doses for the adequate duration, clinical remission is not achieved. Although there is no consensus, but in general it is accepted that those patients with major depression who do not respond to 2-3 adequate trials of antidepressants are considered to have treatment-resistant depression (TRD).^[1] Some of the authors^[2] have suggested staging for TRD and based on the level of nonresponse the patient is allocated to different stages of TRD. The prevalence of TRD varies depending on the stage.^[1] It is suggested that whenever

a patient present's with TRD, a thorough evaluation needs to be done to evaluate the underlying organic and psychosocial causes.^[1] We here, report a case of recurrent depressive disorder, current episode severe depressive episode without psychotic symptoms, who did not respond to adequate trials of antidepressants and showed minimal response to electroconvulsive therapy (ECT). In view of the lack of remission, on investigation she was found to have adrenal adenoma and raised cortisol levels. She was managed with ketoconazole 400 mg/day along with the continuation of antidepressants with which she achieved remission.

CASE REPORT

Mrs. A, 40-year-old, known case of recurrent depressive disorder, with first episode occurring at the age of 36 years, with two episodes in the past which responded to antidepressant treatment, presented with severe depressive episode without psychotic symptoms of 18 months duration. For the current episode, the onset was insidious with the evolution of symptoms over the period of 1-month, without any precipitating event and the course was continuous for the current

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episode. Her clinical presentation was characterized by persistent sadness of mood with morning worsening, poor interaction, anhedonia, lethargy, psychomotor retardation, sleep disturbance in the form of difficulty in falling asleep with frequent midnight awakenings, reduced appetite associated with weight loss of 3 kg, reduced libido, ideas of guilt, suicidal ideations, suicidal planning with one unsuccessful attempt and off and on anxiety symptoms. Her treatment history revealed that during the current episode she was treated with tablet paroxetine 12.5-37.5 mg/day for 4 months, tablet mirtazapine 15-30 mg/day for 3 months, tablet imipramine up to 175 mg/day for 5 months, C. venlafaxine up to 300 mg/day for 2 months with no response. Later she was treated with C. venlafaxine 300 mg/day along with thyroxine 75 µg/day (for 2 months) and C. venlafaxine 300 mg/day and lithium 600 mg/day for a period of 2 months but with minimal improvement. Her compliance with the medication throughout was satisfactory.

Her general physical examination and systemic examination were normal. On mental status examination, she had sadness of mood, psychomotor retardation, ideas of hopelessness, worthlessness, guilt, and suicidal ideas. Investigations in the form of hemogram, liver function test, renal function test, serum electrolytes, thyroid function test, serum vitamin B12 levels were did not reveal any abnormality. Her magnetic resonance imaging (MRI) scan of the brain did not show any abnormality. Her psychosocial history did not reveal any evidence of chronic stressors and her family was very supportive. There was no history suggestive of mania, psychotic symptoms, alcohol or drug abuse, seizure, head injury, and cognitive decline. Her Hamilton Depression Rating scale (HDRS) score was 35.

She was continued on C. venlafaxine 300 mg/day along with tablet lithium carbonate 300 mg/day (with serum levels in the therapeutic range). In addition, due to lack of response to adequate doses of antidepressants she was treated with 14 sessions of modified ECT over the period of 6 weeks with minimal improvement (HDRS score reduced to 32). In view of the lack of response to ECT, further investigations were done for Cushing's syndrome although her physical examination was not suggestive of the same. Workup for Cushing's syndrome revealed raised plasma cortisol level (722.7 nmol/L [normal range 193-634 nmol/L]), dexamethasone nonsuppression and reduced plasma adreno corticotrophin hormone. MRI scan of the abdomen revealed small homogenous, well-defined lesion measuring 2 cm in the adrenal cortex with clear margins suggestive of an adrenal adenoma. She was advised surgical intervention for the same. However, she was reluctant for the same. As a result, she was started on tablet ketoconazole 200 mg/day and increased to 400

mg/day over next 15 days along with the continuation of C. venlafaxine 300 mg/day. Patient improvement was monitored clinically and using HAM-D score. Over a period of next 4 weeks, the patient showed significant improvement in her depressive symptoms with no associated side effects. Her HDRS score reduced from 32 to 5. After remission she was clinically monitored. She has been maintaining well on tablet ketoconazole 400 mg/day and of C. venlafaxine 225 mg/day for the last 4 years. Her adrenal mass has been monitored with no increase in the size of the tumor.

DISCUSSION

According to the staging of TRD by Thase and Rush,^[2] the index case can be considered as stage-5 TRD, that is, patient who has not responded to antidepressants of two different classes, tricyclic antidepressants and ECT. In addition, the patient had also not responded to augmentation with thyroxine and lithium. It is suggested that whenever a patient presents with TRD, first there is a need to evaluate the patient for pseudo-resistance. The factors that contribute to pseudo-resistance include poor compliance, inadequate dosing, and discontinuation of antidepressant before adequate duration.^[3] The history of the index case did not reveal the same. In view of the stage-5 nonresponse, she was empirically evaluated for Cushing's syndrome and was found to have positive evidence for the same. Addition of ketoconazole led to remission of the episode.

Due to the role of stress and involvement of cortisol in understanding the etiopathogenesis of depression, researchers have used antigluocorticoid drugs such as metyrapone, aminoglutethimide, ketoconazole, and Mifepristone in the management of TRD. In a review, which included 11 studies, authors reported that 67-77% of the patients show at least a partial antidepressant response and largest two series documenting response rates of 70-73%.^[4]

Our case highlights the fact that while dealing with patients with TRD, psychiatrists should look into all possible medical causes for depression. Further, our case suggests that antigluocorticoid medications can be considered in patients with TRD who do not respond to conventional treatments.

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