# Catatonia in a patient with bipolar disorder type I

Sir,

Catatonic symptoms can be present in any severe phase of bipolar disorder (BD), when the specifier "with catatonic features" is applied to describe the particular episode (DSM-5).[1] There is a wide range of catatonic symptoms; manifestations can vary from negativism, withdrawal, staring, immobility/stupor, mutism, posturing, grimacing, stereotypies, and mannerisms to non-purposeful excitement, undirected combativeness, unexplained impulsive behavior, echopraxia and echolalia. Numerous motor abnormalities have been described in catatonia including such manifestations as rigidity, waxy flexibility (limbs staying in same position when moved), catalepsy (fixity of posture regardless of external stimuli), mitgehen (anglepoise lamp sign), gegenhalten (involuntary variable resistance during passive movement), etc., According to revised criteria in DSM-5, at least three of the above-mentioned manifestations must be present to specify that the patient is suffering from catatonia.[2] Abundant evidence suggests that patients with mood disorders regularly get afflicted with catatonia, but the syndrome may go unrecognized which complicates the management.[3] Here, the case of a patient with bipolar disorder type I is described who developed catatonia and showed steady and complete response to oral levetiracetam therapy. A 50-year-old post-menopausal patient with a thirty year history of BD was seen in the out-patients psychiatry department of Pakistan Railway Teaching Hospital, Rawalpindi, accompanied by her husband. The past history revealed that the first affective episode occurred in the post-partum period followed by recurrent exacerbations, which were manic, mixed and depressive in nature. Many of these were followed by partial remissions and the patient also had sub-threshold affective symptoms in between episodes. During the course of the illness, she had been treated by different psychiatrists who had

managed her at various points with lithium carbonate, carbamazepine, divalproex sodium, haloperidol, trifluoperazine, and diazepam. Most psychiatrists had avoided using antidepressants, although once she was prescribed amitriptyline in combination with mood stabilizers to treat a depressive episode. The mood episodes were only partially responsive to the above-mentioned psychotropic medications and her illness was characterized by rapid cycling.

Her present episode happened when she was already taking two mood stabilizers - namely carbamazepine in a dose of 600 mg/d and divalproex sodium 1500 mg/d. During this episode she gradually became lethargic, stopped doing her day-to-day household chores and started spending prolonged periods in bed. She did not properly look after her basic needs like eating and drinking, washing, changing clothes and grooming. She became socially withdrawn, stopped meeting friends and relatives and felt tired most of the time. She had a pervasive feeling of unhappiness and lowness of spirits and experienced loss of pleasure in day-to-day activities. These symptoms were present for the past eight to twelve weeks and were steadily increasing in severity.

In the clinic, mental state examination revealed psychomotor retardation with poor eye-to-eye contact, decreased blinking and prolonged staring. She was speaking in a low volume with greatly reduced verbal output and was incomprehensible at times. She showed moderate resistance to instructions and motiveless contrary behavior (negativism), accompanied with ambivalence and hesitant body movements (ambitendency). On examination, she had posturing with catalepsy and waxy flexibility. The patient was 5 ft. and 7 inches tall and weighed 150 lbs. She had mild essential hypertension and acid peptic disease, and was taking amlodipine 5 mg/d and omeprazole 20 mg/d. Apart from these conditions, there was no past history of major medical disorders. Laboratory tests which included complete blood count, erythrocyte sedimentation rate, liver function tests, serum electrolytes, urea and creatinine, thyroid function tests, and urinalysis were all normal. Serum carbamazepine and valproate levels were not part of the laboratory work-up. The patient was diagnosed as suffering from bipolar disorder Type I, current episode depressed with catatonic features.

It was noted that the patient's condition was progressively getting worse with increased self-neglect and poor food intake. The signs and symptoms noted above were also exacerbating, indicating an aggravation of the catatonic state. As such electro-convulsive therapy was suggested but she and her husband refused to give permission for ECT, although it must be acknowledged that the patient probably could not give informed consent. Lorazepam was considered, but it was only available as an oral formulation, as the parenteral form was not manufactured in this country. Further, psychiatrists in the treatment team were not experienced in the use of Lorazepam in catatonic patients.

In view of the fact that the patient was showing refractoriness to conventional mood stabilizers, it was decided to treat her with a novel anticonvulsant, levetiracetam. It was introduced as 125 mg once daily orally and by the end of the first week, the dose had been gradually increased to 1500 mg/day, administered in two divided doses. At the end of the first week of levetiracetam therapy, the patient showed some response with decrease in staring, increased verbal output and improved social interaction. The progress continued during the second week with better eye-to-eye contact, conversation that was appropriate and coherent, social interaction regulated by gesture, and greater spontaneity in behavior. In the third week, the patient's lethargy decreased and she started taking interest in day-to-day chores. By the end of fourth week, she was no longer lying in bed, had resumed doing some of her household duties and started having more conversation and social interaction with family members. Her hesitation and indecisiveness decreased; she also started paying more attention to personal hygiene and self-grooming. Her condition continued to improve on levetiracetam 750 mg twice daily until no sign or symptom of catatonic behavior was evident by the end of 6 weeks.

Once the catatonic state resolved, the patient was found to be suffering from lingering affective symptoms of low mood, anhedonia, anorexia, insomnia and lack of energy. Atypical antipsychotics which were withheld up to now to avoid the risk of the development of neuroleptic malignant syndrome were introduced. Aripiprazole was given in a dose of 15 mg/d and quetiapine 100 mg nightly while levetiracetam was continued as 1500 mg/d. This regime resulted in the complete remission of the depressive episode after another 8 weeks or so. The follow-up period was increased to once every four weeks and the patient was advised to continue taking the above-mentioned medications to maintain the remission phase of the bipolar affective disorder. Extended review of the patient for the next six months revealed that she continued to be free of psychiatric symptoms with the medication schedule remaining unchanged.

In the patient, this was the first time that a mood episode was complicated by catatonic features. She was very lethargic and could have become stuporous, developed

muteness or demonstrated increasing self-neglect and food refusal, the complications of severe catatonia.[4] In view of the clinical circumstances in this particular case, levetiracetam was used to treat catatonia, with the expectation that this agent would exert a mood stabilizing effect and be instrumental in treating the underlying depressive episode. The rationale to choose levetiracetam was manifold. This drug has a unique mechanism of action among anticonvulsants, namely specific binding to SV2A synaptic vesicle glycoprotein.[5] The resulting effect on glutamate and GABA neurotransmission appears crucial in therapeutic outcomes in a host of neuropsychiatric disorders.[6,7] Neurological conditions that show responsiveness to levetiracetam include simple partial and complex partial seizures with or without secondary generalization, migraine and neuropathic pain. It has been used with variable success in several psychiatric disorders including anxiety spectrum disorders, major depressive disorders and bipolar disorders.[8] A large number of studies showed that the neurobiology of catatonia involved abnormality of glutamate and GABA neurotransmission, in which case levetiracetam in theory would exert a beneficial effect.[9] It has a favorable pharmacokinetic profile with renal excretion being the major route of elimination, no adverse drug-drug interactions and low risk of side effects resulting in high patient tolerability and acceptability.

The informed decision to use levetiracetam had a successful outcome as the patient started a steady course of recovery from catatonic symptoms upon administration of this drug. It may have exerted a mood stabilizing effect, but the fact that affective symptoms persisted after the resolution of the catatonic state and required additional psychotropic agents indicates that the latter responded to levetiracetam alone. In order to objectively assess the progress of catatonic patients, the Bush-Francis Catatonia Rating Scale is a valuable instrument. In this patient, catatonia was discovered while conducting psychiatric assessment for determining the nature of the mood episode; in the busy clinical setting, repeated mental state examination was used to monitor both the catatonic and affective symptoms and psychometric scales were not employed. A thorough search of the literature was conducted, but no other example was found where a catatonic patient had such a marked response to levetiracetam. Interestingly, there was a case report where this drug induced catatonia like symptoms.[10] This case raised several issues – firstly, levetiracetam could be considered as a potential mood stabilizer in refractory bipolar affective disorder patients. Secondly, it could be tried in those bipolar patients who developed catatonia during the course of an episode. These matters could only be resolved through properly designed controlled trials in which each of these issues was examined meticulously. Levetiracetam could be an important addition in the armamentarium against bipolar affective disorder which remained a difficult to treat condition that had myriad manifestations, including catatonia. While there is no doubt that the patient showed a marked response with relief from catatonia, evidence-based treatments of Lorazepam and ECT were not used before trying levetiracetam. This is a limitation of the case report and the new finding must be interpreted in the light of the above-mentioned fact.

**Ather Muneer**

*Department of Psychiatry, Islamic International Medical College, Riphah International University, Rawalpindi, Pakistan*

**Address for correspondence:**
Dr. Ather Muneer,
House No. 1-A, Street No. 21, Chaklala,
Scheme III, Rawalpindi, Pakistan.
E-mail: muneerather2@gmail.com

## References

1. Carpenter WT, Tandon R. Psychotic disorders in DSM-5: Summary of changes. Asian J Psychiatr 2013;6:266-8.
2. Tandon R, Heckers S, Bustillo J, Barch DM, Gaebel W, Gur RE, *et al*. Catatonia in DSM-5. Schizophr Res 2013;150:26-30.
3. Fink M. Rediscovering catatonia: The biography of a treatable syndrome. Acta Psychiatr Scand Suppl 2013:1-47.
4. Weder ND, Muralee S, Penland H, Tampi RR. Catatonia: A review. Ann Clin Psychiatry 2008;20:97-107.
5. Vogl C, Mochida S, Wolff C, Whalley BJ, Stephens GJ. The synaptic vesicle glycoprotein 2A ligand levetiracetam inhibits presynaptic $Ca2^{+}$ channels through an intracellular pathway. Mol Pharmacol 2012;82:199-208.
6. Lee CY, Chen CC, Liou HH. Levetiracetam inhibits glutamate transmission through presynaptic P/Q-type calcium channels on the granule cells of the dentate gyrus. Br J Pharmacol 2009;158:1753-62.
7. Doelken MT, Hammen T, Bogner W, Mennecke A, Stadlbauer A, Boettcher U, *et al*. Alterations of intracerebral γ-aminobutyric acid (GABA) levels by titration with levetiracetam in patients with focal epilepsies. Epilepsia 2010;51:1477-82.
8. Reinares M, Rosa AR, Franco C, Goikolea JM, Fountoulakis K, Siamouli M, *et al*. A systematic review on the role of anticonvulsants in the treatment of acute bipolar depression. Int J Neuropsychopharmacol 2013;16:485-96.
9. Fornaro M. Catatonia: A narrative review. Cent Nerv Syst Agents Med Chem 2011;11:73-9.
10. Chouinard MJ, Nguyen DK, Clément JF, Bruneau MA. Catatonia induced by levetiracetam. Epilepsy Behav 2006;8:303-7.

| Access this article online | |
|---|---|
| Quick Response Code: | Website: www.ruralneuropractice.com |
| | DOI: 10.4103/0976-3147.133652 |