Myoclonus Associated with Mirtazapine

To the Editor,

Mirtazapine is a nor-adrenergic specific serotonergic antidepressant having blocking action on α2 adrenoceptors and antagonizing action on 5HT2, 5 HT3, and H1 receptors.[1] It is considered safer than selective serotonin reuptake inhibitors or serotonin no epinephrine reuptake inhibitors due to its different receptor profiles.[2]

Many drugs other than neuroleptic agents have the propensity to cause drug-induced hyperkinetic movements.[3] There are few case reports describing different mirtazapine-induced movement disorders, most commonly akathisia, followed by dystonia, dyskinesia, and periodic limb movement disorders.[4]

The present case report describes a case of myoclonic jerks that developed after the administration of mirtazapine in a patient diagnosed with major depressive disorder. As per the best of our knowledge, Mirtazapine-induced Myoclonic jerks have not been reported till now.

Case Report

A middle-aged adult male presented with five months history of persistent and pervasive low mood, loss of interest in previously pleasurable activities, feeling of tiredness, reduced appetite, and disturbed sleep. He had asthma for which he was using Fluticasone 250 µg and Salmeterol 25 µg through inhalational route daily for the last 12 years without any observable side effects. No other significant past, family, or personal history was reported. His physical examination was within normal limits. He was diagnosed as a case of a moderate depressive episode as per ICD 10 criteria, for which he was started on escitalopram 5 mg per day, which was increased up to 20 mg per day over the next six weeks, along with clonazepam 1 mg per day for sleep disturbances which was tapered over next four weeks. There was a 40% reduction of symptoms on clinical as well as on objective assessment by HAM-D scale after 12 weeks of therapy, following which tablet mirtazapine 7.5 mg was added because of partial response.

After two days of starting mirtazapine, the patient presented with his wife, complaining of involuntary, non-rhythmic, asymmetric, jerky movements of the trunk and bilateral shoulder joints (axial distribution) with onset half an hour after going to sleep, with the frequency of 10–12 times per minute, lasting for around 3 minutes.[4] The patient had no memory of these movements after waking up. There was no associated sleep disturbance or daytime sleepiness. The patient was referred to a neurologist in view of abnormal movements, and no abnormality was detected on a detailed neurological examination. Awake EEG record, neuroimaging, and routine blood studies were within normal limits which suggested that the myoclonus could be sub-cortical in origin. The abnormal movements were classified as drug-induced myoclonic jerks provisionally, for which the Naranjo adverse drug reaction probability scale indicated a probable relationship with Mirtazapine (a score of 6).

Mirtazapine was stopped, and movements disappeared within three days of stopping the drug. The same dose was reintroduced after one week, and no abnormal movements were reported. The patient has been on regular follow up since the last six months with remission of the symptoms.

Discussion

Mirtazapine has been known to induce various hyperkinetic movement disorders such as akathisia if higher doses are administered because of its antagonistic action on α2 adrenoceptors but has a therapeutic effect at low doses as it acts as an antagonist on 5-HT 2A receptor.[5]

In our case, the abnormal involuntary movements started after the introduction of mirtazapine at low doses, along with ongoing treatment with escitalopram. They disappeared following discontinuation of the drug, suggesting that the abnormal movements could have been induced by mirtazapine. There are no reported specific drug-drug interactions of mirtazapine with SSRIs that could have caused it.[6]

The above finding is supported by a clinical analysis of case reports, showing use of Mirtazapine at low doses or for a short duration may lead to the emergence of various abnormal movement disorders such as akathisia, dystonia, dyskinesia, and periodic limb movement disorder in patients diagnosed with depressive disorder having a history of SSRI use. Similarly, a single dose of mirtazapine has also been reported to induce hyperkinetic movements.[7]

Other conditions that were ruled out in this patient were akathisia, tardive dyskinesia, drug-induced chorea, and restless leg syndrome (RLS). The flowing and continuous fashion of movement in myoclonus differentiated it from the simple and quick jerk of chorea.[8] Tardive dyskinesia was ruled out as there were no abnormal movements in the face or mouth like repetitive tongue protrusions or lip smacking.

The sense of inner restlessness, irritability, and tension with or without physical signs and typically improving at night associated with akathisia differentiates it from myoclonus.[9] In our case, other movement disorders known to be induced by mirtazapine, like akathisia and RLS, were ruled out as there were no daytime symptoms and feelings of subjective tension and restlessness. Although periodic limb movements of sleep (PLMS) have been reported previously in our case the myoclonic jerks were less likely to PLMS as only the trunk and upper limbs were involved without any sleep disturbance.[10]

While myoclonus as an adverse reaction occurs infrequently with the use of Mirtazapine but should be taken into consideration when initiating the drug.

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Morita Therapy By Shoma Morita for Fear of Blushing

To the editor,

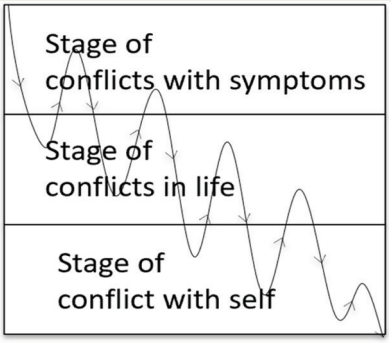
I read with interest Tanuja et al.'s paper about the first Taijin Kyofusho (TKS) case series from India.[1] TKS is originally a Japanese word, similar in meaning to social anxiety disorder, and characterized by intense fear from interpersonal situations related to thoughts, feelings, or the conviction that one's body parts or functions in social interactions are inadequate or offensive to others.[2] Although TKS has often been reported to have originated in Japan and is defined in the DSM-5 as a culture-based symptom, the case series from India indicates that it is found globally and may transcend cultures.

In Japan, Morita therapy, invented by Shoma Morita in 1919, is one of the leading psychotherapies for neuroses[3,4] and TKS has a long history of treatment with this type of method. Morita therapy had been considered a treatment specific to East Asian cultures; however, it has recently been widely applied in the West and is now considered a human nature-based treatment applicable worldwide.[3] In his own studies on TKS published a century ago, though the problem of diagnostic criteria validity is acknowledged, Shoma Morita discussed jiko-shisen-kyofu (18th case), fear of blushing (16th case), and olfactory reference syndrome.[5] Shoma Morita is particularly proud of his treatment method for fear of blushing[5] and has been known to have refined and perfected Morita therapy as an effective treatment method.[6]

Recently, a meta-analysis of treatment for fear of blushing has been published[7]; however, unfortunately, Morita therapy, which is widely and effectively used in Japan, was not included because of the lack of English case reports and quantitative efficacy evaluations. Quantitative studies of the effectiveness of Morita therapy have been limited to other conditions, not to fear of blushing.[9,10]

Based on Morita therapy, the classification of cases with fear of blushing is as follows: those who tend to pay more attention to their inner selves' experience

FIGURE 1.
Transition of Therapeutic Themes in Morita Therapy.



triggers, such as being accused of blushing in public. This will cause them to pay more attention to blushing, and a fixed symptom will appear.[3,4]

The course of treatment is generally the reverse of this process (symptom→how to live→self).[8] Morita explained to his patient that it is normal to turn red in tense situations and advised him to achieve his personal goals in his own way, thereby avoiding certain behavioural patterns that exacerbate the