Agomelatine-Induced Akathisia in a 38-Year-Old Woman With Depression

To the Editor: Akathisia is linked to dopamine deficiency most often associated with antipsychotic medication. Newer antipsychotic medication is thought to reduce akathisia due to its serotonin (5-HT) 2(2A/2C) receptor blockade activity.[1] Akathisia may also be related to increased adrenergic neurotransmission.[2]

Mirtazapine in low doses (15 mg) is a 5-HT 2A/2C antagonist and is antiakathisic, while in higher doses (> 30 mg/d) it may induce akathisia due to stimulation of adrenergic neurotransmission via alpha2 autoreceptor blockade.[2]

Agomelatine is a novel antidepressant that is both a melatonergic agonist and a 5-HT 2C antagonist.[3] Agomelatine also enhances dopaminergic and adrenergic input to the frontal cortex.

There is 1 previous report of agomelatine-induced akathisia with concomitant duloxetine treatment.[4] That report suggested a pharmacodynamic drug-drug interaction causing noradrenergic overstimulation as an explanatory model.[4] We present a novel case of likely agomelatine-induced akathisia.

Case report. Ms A is a 38-year-old woman who presented with a several-month history of depression without anxiety or suicidal ideation. Many years previously, she had been prescribed sertraline without experiencing akathisia. There was no significant past medical history. Agomelatine was started at the first visit at a dose of 25 mg. Immediately after starting agomelatine, Ms A noticed an inability to sit still, restless movement of the legs, and a constant urge to move. Over the ensuing weeks, she became more significantly distressed and experienced insomnia, loss of appetite and weight, and suicidal ideation. After 5 weeks of taking agomelatine, a psychiatric consultation was sought and a provisional diagnosis of agomelatine-induced akathisia was made on the basis of a global Barnes Akathisia Scale[5] score of 4 (marked akathisia). Within 3 days of stopping agomelatine, Ms A noticed significant improvement; in 5 days, all symptoms of akathisia had ceased with no ongoing anxiety, insomnia, or suicidal ideation.

In this case, agomelatine was likely causing akathisia on the basis of a Naranjo Adverse Drug Reaction Probability Scale[6] score of 7 (probable adverse drug reaction). This case is the first report without a concomitant drug-drug interaction.

The induction of akathisia by agomelatine in this patient was somewhat unexpected, given that agomelatine is a 5-HT 2C antagonist and increases dopamine transmission in the frontal cortex. However, there is debate as to whether 5-HT 2A antagonism is more related to antiakathisic effect as opposed to 5-HT 2C antagonism. It may be that an increase in adrenergic stimulation induced by agomelatine may cause akathisia. However, akathisia is a complex phenomenon, and a clear explanatory model for what we observed is unknown. Clinicians should therefore be alert to the possibility of akathisia in patients prescribed agomelatine.

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