

# Worsening mania while receiving low-dose quetiapine: A case report

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The second-generation antipsychotic quetiapine is commonly used to treat several psychiatric disorders, including bipolar disorder (BD) and insomnia. In this case report, we discuss a patient with a history of unipolar depression and initial signs of mania who experienced an exacerbation of manic symptoms following administration of low-dose quetiapine. This case underscores the need for careful monitoring of patients receiving quetiapine, especially at lower doses, and the potential limitations of its efficacy in controlling manic symptoms.

## Depressed with racing thoughts

Mr. X, age 58, is an Army veteran who lives with his wife of 29 years and works as a contractor. He has a history of depression and a suicide attempt 10 years ago by self-inflicted gunshot wound to the head, which left him with a bullet lodged in his sinus cavity and residual dysarthria after tongue surgery. After the suicide attempt, Mr. X was medically hospitalized, but not psychiatrically hospitalized. Shortly after, he self-discontinued all psychotropic medications and follow-up.

Mr. X has no other medical history and takes no other medications or supplements. His family history includes a

mother with schizoaffective disorder, 1 brother with BD, and another brother with developmental delay.

Mr. X remained euthymic until his brother died. Soon after, he began to experience low mood, heightened anxiety, racing thoughts, tearfulness, and mild insomnia. He was prescribed quetiapine 25 mg/d at bedtime and instructed to titrate up to 50 mg/d.

Ten days later, Mr. X was brought to the hospital by his wife, who reported that after starting quetiapine, her husband began to act erratically. He had disorganized and racing thoughts, loose associations, labile affect, hyperactivity/restlessness, and was not sleeping. In the morning before presenting to the hospital, Mr. X had gone to work, laid down on the floor, began mumbling to himself, and would not respond to coworkers. Upon evaluation, Mr. X was noted to have pressured speech, disorganized speech, delusions, anxiety, and hallucinations. A CT scan of his head was normal, and a complete blood count, comprehensive metabolic panel, thyroid-stimulating hormone, B12, folate, and hemoglobin A1c were within normal limits. Mr. X's vitamin D level was low at 22 ng/mL, and a syphilis screen was negative.

Mr. X was admitted to the hospital for his safety. The treatment team discontinued quetiapine and started risperidone 3 mg twice a day for psychotic symptoms and mood stabilization. At the time of discharge 7 days later, Mr. X was no longer experiencing any hallucinations or delusions, his thought process was linear and goal-directed, his mood was stable, and

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### Clinical Point

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his insomnia had improved. Based on the temporal relationship between the initiation of quetiapine and the onset of Mr. X's manic symptoms, along with an absence of organic causes, the treatment team suspected Mr. X had experienced a worsening of manic symptoms induced by quetiapine. Before starting quetiapine, he had presented with an initial manic symptom of racing thoughts.

At his next outpatient appointment, Mr. X exhibited significant akathisia. The treatment team initiated propranolol 20 mg twice a day but Mr. X did not experience much improvement. Risperidone was reduced to 1 mg twice a day and Mr. X was started on clonazepam 0.5 mg twice a day. The akathisia resolved. The treatment team decided to discontinue all medications and observe Mr. X for any recurrence of symptoms. One year after his manic episode, Mr. X remained euthymic. He was able to resume full-time work and began psychotherapy to process the grief over the loss of his brother.

### Quetiapine's unique profile

This case sheds light on the potential limitations of quetiapine, especially at lower doses, for managing manic symptoms. Quetiapine exhibits antidepressant effects, even at doses as low as 50 mg/d.<sup>1</sup> At higher doses, quetiapine acts as an antagonist at serotonin (5-HT<sub>1A</sub> and 5-HT<sub>2A</sub>), dopamine (D<sub>1</sub> and D<sub>2</sub>), histamine H<sub>1</sub>, and adrenergic receptors.<sup>2</sup> At doses <300 mg/d, there is an absence of dopamine receptor blockade and a higher affinity for 5-HT<sub>2A</sub> receptors, which could explain why higher doses are generally necessary for treating mania and psychotic symptoms.<sup>3-5</sup> High 5-HT<sub>2A</sub> antagonism may disinhibit the dopaminergic system and paradoxically increase dopaminergic activity, which could be the mechanism responsible for lack of control of manic symptoms with low doses of quetiapine.<sup>2</sup> Another possible explanation

is that the metabolite of quetiapine, N-desalkylquetiapine, acts as a norepinephrine reuptake blocker and partial 5-HT<sub>1A</sub> antagonist, which acts as an antidepressant, and antidepressants are known to induce mania in vulnerable patients.<sup>4</sup>

The antimanic property of most antipsychotics (except possibly clozapine) is attributed to their D<sub>2</sub> antagonistic potency. Because quetiapine is among the weaker D<sub>2</sub> antagonists, its inability to prevent the progression of mania, especially at 50 mg/d, is not unexpected. Mr. X's subsequent need for a stronger D<sub>2</sub> antagonist—risperidone—at a significant dose further supports this observation. A common misconception is that quetiapine's sedating effects make it effective for treating mania, but that is not the case. Clinicians should be cautious when prescribing quetiapine, especially at lower doses, to patients who exhibit signs of mania. Given the potential risk, clinicians should consider alternative treatments before resorting to low-dose quetiapine for insomnia. Regular monitoring for manic symptoms is crucial for all patients receiving quetiapine. If patients present with signs of mania or hypomania, a therapeutic dose range of 600 to 800 mg/d is recommended.<sup>6</sup>

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