Metronidazole-Induced Mania

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Metronidazole, a 5-nitroimidazole antibiotic, is widely used for the treatment of bacterial vaginosis and trichomonas vaginalis.[1] It is also used in combination with a proton pump inhibitor and clarithromycin, the so-called "triple therapy," for the eradication of *Helicobacter pylori* in peptic ulcer disease.[2] Its common side effects include headache, diarrhea, nausea, and vomiting. Although rare, metronidazole can cause neuropsychiatric adverse effects such as encephalopathy, confusion, depression, and psychosis.[3] Here, a case of mania following metronidazole use in a patient with a provisional diagnosis of bipolar disorder is described. She had previously experienced a manic episode with the use of an antidepressant.

Case Report

Ms A was a 32-year-old woman with a past psychiatric diagnosis of seasonal affective disorder. She did not receive any antidepressant until the summer of 2021. Her family physician prescribed escitalopram 10 mg by mouth daily for depression. She was partially compliant with her medication; however, about 4–6 weeks into the treatment, Ms A experienced her first manic episode. For about a week, she had decreased need for sleep and increased energy. Her husband described her as "hyper" and impulsive with spending sprees. The manic symptoms subsided after she stopped taking escitalopram.

Two months later, Ms A received metronidazole 500 mg by mouth twice daily for bacterial vaginosis. Into the fifth day of treatment, she began to have difficulties falling asleep and to have increased goal-directing activities. She presented to the emergency department 2 days later with pressured speech, flight of ideas, and intrusive behaviors. She denied any hallucination, though she exhibited grandiose delusion, believing she had the ability to make the world a better place. Medical workup including comprehensive metabolic panel, complete blood count, thyroid-stimulating hormone, urine toxicology screen, and computed tomography scan of the head were all negative. She was admitted to the neuropsychiatric hospital. Olanzapine 5 mg by mouth at bedtime was initiated for her mania. On the second day of admission, she had improved sleep, normal rate and volume of speech, and minimal grandiosity. She continued to do well with euthymic mood and went home after 4 days of hospitalization. After a 4-week follow-up, Ms A stayed symptom free while she still took olanzapine 5 mg nightly.

Discussion

In an article reviewing cases of antibiotic-induced mania, Abouesh et al[4] coined the term *antibiomania* to describe the infrequent manic episodes as side effects of antimicrobial use. AlShakori et al[5] reported a case of exacerbation of mania with metronidazole use in a patient with bipolar disorder. Metronidazole crosses the blood-brain barrier in humans; it was speculated that metronidazole and its metabolite might bind to neuronal RNA, causing direct and indirect reversible central nervous system side effects.[6] The patient presented here was interesting and unusual in that she has a history of antidepressant-induced mania. The temporal relation between the acute onset of symptoms with the use of metronidazole and the remission of symptoms after cessation of the medication and the addition of a low dose of olanzapine use suggested a probable causality. Although there does not seem to be a significant risk correlation between antibiotic use and mania,[4] clinicians should be aware of the phenomenon, especially in patients with history of mania, to avoid unnecessary workup.

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