Cyclobenzaprine-Induced Hallucinosis

To the Editor: Cyclobenzaprine has a cyclic structure similar to amitriptyline, which is a tricyclic antidepressant and a centrally acting skeletal muscle relaxant.[1,2] The drug is highly metabolized in the liver and has a long elimination half-life and can produce psychiatric symptoms as effect of its toxicity.[3] We describe a case of a patient with hepatitis C on citalopram treatment who developed psychotic symptoms after being started on cyclobenzaprine.

Case report. Ms A is a 51-year-old woman with a history of hepatitis C, back pain, and major depressive disorder that was precipitated by the death of her husband 5 years ago. She had no prior psychiatric hospitalizations. Ms A was being followed at the outpatient mental health clinic; her depression was stable on citalopram 20 mg daily. During a clinic visit, she reported a new onset of auditory hallucinations around the time of the anniversary of her husband's death. She described the voices as distressing episodic voices commenting that she was not doing well. Her urine toxicology screen was negative for illicit substances of abuse. Her routine laboratory test results were significant only for mildly elevated liver function tests (aspartate aminotransferase: 46 U/L, alanine aminotransferase: 53 U/L), which were consistent with her hepatitis C infection. Her HIV antibody test was negative. Olanzapine 5 mg by mouth daily was prescribed to treat the auditory hallucinations. After a month of treatment, Ms A reported that her hallucinations appeared at the same time she was started on cyclobenzaprine for her back pain. On her own, Ms A decided to discontinue both medications. This discontinuation resulted in complete resolution of her psychotic symptoms, and she has been asymptomatic since then.

A pharmacokinetic interaction between citalopram and cyclobenzaprine explain the hallucinations experienced by Ms A. She has a history of hepatitis C with mildly elevated liver function tests. Cyclobenzaprine is extensively metabolized in the liver by cytochrome P450 3A4 (CYP3A4) and has a long elimination half-life of 1–3 days. Ms A was also taking citalopram, a CYP3A4 mild inhibitor, which most likely increased the bioavailability of cyclobenzaprine and the risks for drug accumulation and toxicity resulting in hallucinatory symptoms. In this case, Ms A has organic hallucinosis (*ICD-10* code F06.0), as the disturbances were caused by a specific organic factor and appeared in clear consciousness, retaining her insight without any intellectual impairment or prominent delusions.

Cyclobenzaprine is a widely prescribed muscle relaxant that has many interactions due to metabolism through CYP3A4, 1A2, and 2D6. A reduction in dose should be considered in patients taking other medications as well as in those with liver disease. Our case highlights the importance of prescribing cyclobenzaprine with caution in such patients, and when prescribed, the patient should be monitored for psychiatric symptoms.

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