Clopidogrel-Induced Auditory and Visual Hallucinations

To the Editor: Clopidogrel is a thienopyridine derivative used for prevention of thrombotic events. We report a case of clopidogrel-induced auditory and visual hallucinations.

Case report. Ms A, an 83-year-old white woman, was admitted to the hospital for an angiogram and possible endovascular surgery due to complaints of claudication. She had a history of coronary artery disease, aortic stenosis, paroxysmal atrial fibrillation, hypertension, sick sinus syndrome, congestive heart failure, chronic obstructive pulmonary disease, and depression. Lung and cardiac examinations were unremarkable, and her vital signs were stable. Postsurgically, she was started on clopidogrel 75 mg daily and exhibited auditory and visual hallucinations within roughly 5 hours of starting the medication. She had no past history of visual or auditory hallucinations. Ms A stated that she was hearing voices of people on trains with guns who were telling her that they would kill her. The voices were said to be persistent while they lasted, culminating in her becoming distressed. She did not exhibit an altered sleep-wake cycle, fluctuating course, or change in cognition. Serum electrolyte tests revealed sodium: 147 mmol/L, potassium: 4.1 mmol/L, chloride: 114 mmol/L, bicarbonate: 28 mmol/L, blood urea nitrogen: 19 mmol/L, and creatinine: 0.8 µmol/L, while computed tomography revealed no acute abnormalities. Urinalysis and electroencephalography were also unremarkable. Ms A and her family members later stated that she had a previous experience with clopidogrel in which hallucinosis resolved with discontinuation of the drug. Clopidogrel was discontinued the next day, and Ms A reported that the symptoms had abated.

Clopidogrel prevents activation and aggregation of platelets through irreversible binding of adenosine diphosphate to its platelet P2Y12 receptor. This results in activation of the glycoprotein IIb/IIIa complex, thus inhibiting platelet aggregation.[1] Adverse effects associated with clopidogrel include hemorrhage, diarrhea, rash, neutropenia, and thrombotic thrombocytopenic purpura, while postmarketing reports[2] have reported occasional association with ageusia, confusion, and hallucinations. We are aware of one peer-reviewed account[3] attributing visual without auditory hallucinations to clopidogrel. The exact mechanism of clopidogrel-induced hallucinosis is unknown; common mechanisms of medication-induced hallucinations have been suggested.[4]

The P2Y12 receptor has a myriad of subtypes with pharmacologic effects involving adenosine and uridine nucleotides. Reduction in adenosine has been associated with increased activity of brain neurotransmitters like dopamine and glutamate. This unusual adverse effect of clopidogrel emphasizes the need for clinicians to be aware of clopidogrel-induced hallucinations when reviewing the potential side effects of clopidogrel with patients.

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