Musical Hallucinations Induced by Conventional Doses of Paroxetine

Haruka Muraosa
Akihito Suzuki
Keisuke Noto
Koichi Otani

Corresponding Author: Akihito Suzuki, e-mail: a-suzuki@med.id.yamagata-u.ac.jp
Conflict of interest: None declared

Patient: Female, 22-year-old
Final Diagnosis: Depression • panic disorder
Symptoms: Musical hallucinations
Medication: —
Clinical Procedure: —
Specialty: Pharmacology and Pharmacy • Psychiatry

Objective: Unusual or unexpected effect of treatment

Background: A musical hallucination (MH) is a type of auditory hallucination, and is defined as hearing music, sounds, or songs in the absence of external auditory stimuli. There are several case reports of conventional doses of tri- or tetracyclic antidepressants inducing MHs, but no such report for selective serotonin reuptake inhibitors. Here we report a case of a patient with MHs induced by conventional doses of paroxetine.

Case Report: The patient was a 22-year-old woman with panic disorder (PD) and major depressive disorder (MDD). On the 10th day of treatment with paroxetine 20 mg/d, olanzapine 5 mg/d, and lorazepam 1.5 mg/d, she developed MHs such as “an opera song sung by a female singer.” The MHs occurred several times a day, and once continued for 5 to 10 min. Because of a suspicion of paroxetine-induced MHs and poor clinical improvement, paroxetine was reduced and discontinued on the 31st day, whereas venlafaxine was started and increased to 75 mg/d. Two days after the discontinuation of paroxetine, the MHs disappeared and symptoms of PD and MDD were much improved. Several weeks later, in response to a negative life event, her symptoms of PD and MDD returned to the original levels, but MHs were not observed.

Conclusions: The present report suggests that conventional doses of paroxetine can induce MHs, which are most likely ascribable to the anticholinergic effects of the drug. This adverse effect should be differentially diagnosed from psychotic symptoms arising from psychiatric disorders, especially MDD.

MeSH Keywords: Depressive Disorder • Hallucinations • Panic Disorder • Paroxetine

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/926735

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]
This work is licensed under Creative Common Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0)
Background

A musical hallucination (MH) is a type of auditory hallucination and is defined as hearing music, sounds, or songs in the absence of external auditory stimuli [1]. Compared with other types of auditory hallucinations, MHS are less common [1], but are likely to have a distinct pathophysiology as reflected in a specific brain activation pattern in a single-photon emission computed tomography [2]. Thus, it is important for clinicians to differentiate MHSs from other types of auditory hallucinations. It is suggested that MHSs are related to several factors such as drug effects, psychiatric and neurologic diseases, brain lesions, and hearing impairment [1]. Regarding drug effects, there are several case reports of conventional doses of tricyclic antidepressants [3,4] and tetracyclic antidepressants [5,6] inducing this adverse effect. As to selective serotonin reuptake inhibitors, there is a case report of paroxetine causing MHSs, but this was at an excessive dose of 120 mg/d [7]. In this report, we present the case of a patient who developed MHSs during treatment with conventional doses of paroxetine.

Case Report

The patient was a 22-year-old woman. She gave written informed consent for reporting her clinical course, and the Ethics Committee of Yamagata University School of Medicine approved this report. Her older brother had a history of depression, but there were no other family histories. She had no histories of psychiatric or neurologic diseases, hearing difficulties, usage of illegal drugs, or excessive alcohol intake.

Two months before admission to our hospital, she exhibited panic attacks, e.g., palpitations, shortness of breath, trembling, fear of dying, and worry about additional panic attacks. At a psychiatric clinic, under a diagnosis of panic disorder (PD), sulpiride 100 mg/d and alprazolam 0.8 mg/d were given, with no apparent improvement. Depressive symptoms including depressed mood, diminished interest, psychomotor retardation, insomnia, and decreased appetite emerged, and she was referred to our hospital to be admitted.

On admission, she had no psychotic symptoms such as hallucinations, delusions, disorganized speech, or disorganized or catatonic behaviors. Her laboratory blood tests, brain magnetic resonance imaging, and electroencephalogram were unremarkable. Diagnoses of PD and major depressive disorder (MDD) [8] were made. She scored 23/28 on the Panic Disorder Severity Scale (PDSS) [9] and 38/60 on the Montgomery-Asberg Depression Rating Scale (MADRS) [10]. Drug treatment using paroxetine 20 mg/d, olanzapine 5 mg/d, and lorazepam 1.5 mg/d was started. In light of the previous treatment failure and strong proposals for early recovery, olanzapine was coadministered, expecting its augmentation effect on paroxetine [11] and its efficacy for bipolarity [12] that might underly her major depressive episode. Several days after the initiation of treatment, dry mouth and constipation emerged. On the 10th day of the treatment, in the absence of external auditory stimuli she heard “an opera song sung by a female singer,” “a video game background music,” and “a recorder melody played by a strange face.” These MHSs occurred several times a day, and once continued for 5 to 10 min. Her symptoms of PD and MDD did not change. Because of a suspicion of paroxetine-induced MHSs and poor clinical improvement, on the 17th day paroxetine was reduced to 10 mg/d and venlafaxine 37.5 mg/d was started. On the 31st day, paroxetine was discontinued and venlafaxine was increased to 75 mg/d. On the 33rd day, the MHSs disappeared and her dry mouth and constipation were improved. Her symptoms of PD and MDD were also much improved (PDSS: 13/28, MADRS: 12/60). On the 35th day, she was discharged.

Two weeks after the discharge, in response to a breakup with a boyfriend, her PD and MDD deteriorated and returned to the original levels (PDSS: 22/28, MADRS: 35/60). However, no psychotic symptoms including MHSs were observed. The dose of venlafaxine was increased to 112.5 mg/d, and 1 month later symptoms of PD and MDD were much improved (PDSS: 7/28, MADRS: 4/60). Throughout the paroxetine and venlafaxine treatments, olanzapine and lorazepam were continued at the same doses.

Discussion

In the present case, there was no evidence of psychotic disorders such as schizophrenia, neurologic diseases, brain lesions, hearing impairment, use of illegal drugs, or excessive alcohol intake, etiologic factors known to contribute to MHSs [1]. The possibility that the MHSs were psychotic features of MDD is low, as reflected in the lack of psychotic symptoms including MHSs in the relapse of MDD. On the other hand, the MHSs had a clear relationship with the time course of paroxetine treatment, i.e., they emerged after the initiation and disappeared upon the cessation of the treatment. According to the World Health Organization-Uppsala Monitoring Centre System for Standardised Case Causality Assessment [13], the causality between paroxetine treatment and the MHSs is “probable/likely,” since rechallenge was not performed.

The present report for the first time showed that conventional doses of paroxetine can induce MHSs. This means that MHSs emerging during usual paroxetine treatment of a psychiatric disorder may be arising from the targeted disorder or may be an adverse effect of the drug. The chance to encounter this complex situation may be especially high in MDD, which often
It accompanies psychotic features [8]. In that occasion, differential diagnosis between the two conditions should be carefully made, paying special attention to the time course of MHs in relation to paroxetine treatment.

In the present case, paroxetine but not venlafaxine caused MHs. Radioligand binding assays show that paroxetine has much higher affinity for serotonin transporters and muscarinic acetylcholine receptors compared with venlafaxine [14]. In our patient, the onset and disappearance of MHs were almost in parallel with those of dry mouth and constipation, well-known anticholinergic adverse effects of paroxetine [15]. This finding points to the possibility that the MHs developed as an anticholinergic effect of this drug. Terao [3] postulated a similar mechanism for imipramine-induced MHs. Alternatively, implications of excessive serotonergic neurotransmission or a hyperserotonergic/hypocholinergic imbalance suggested by Kumagai et al. [7] cannot be excluded entirely.

One may wonder if lorazepam, which is reported to induce MHs [16], or olanzapine, which has significant anticholinergic effects [17], was responsible for the development of these hallucinations in our case. However, this possibility is low in light of the constant doses of these drugs throughout the paroxetine and venlafaxine treatments.

References:

1. Golden EC, Josephs KA: Minds on replay: Musical hallucinations and their relationship to neurological disease. Brain, 2015; 138: 3793–802
2. Izumi Y, Terao T, Ishino Y et al: Differences in regional cerebral blood flow during musical and verbal hallucinations. Psychiatry Res, 2002; 116: 119–23
3. Terao T: Tricyclic-induced musical hallucinations and states of relative sensory deprivation. Biol Psychiatry, 1995; 38: 192–93
4. Shoyama M, Uki S, Kitabata Y et al: Evaluation of regional cerebral blood flow in a patient with musical hallucinations. Neurocase, 2010; 16: 1–6
5. Padala KP, Padala PR, Malloy T et al: New onset multimodal hallucinations associated with mirtazapine: A case report. Int Psychogeriatr, 2010; 22: 837–39
6. Lee GH, Stewart JT: A case of musical hallucinations related to mirtazapine. Clin Neuropharmacol, 2018; 41: 222–23
7. Kumagai R, Ohnuma T, Nagata T et al: Visual and auditory hallucinations with excessive intake of paroxetine. Psychiatry Clin Neurosci, 2003; 57: 548–49
8. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Washington DC, American Psychiatric Publishing, 2013
9. Shear MK, Brown TA, Barlow DH et al: Multicenter collaborative panic disorder severity scale. Am J Psychiatry, 1997; 154: 1571–75
10. Montgomery SA, Asberg M: A new depression scale designed to be sensitive to change. Br J Psychiatry, 1979; 134: 382–89
11. Yoshimura R, Hori H, Umene-Nakano W et al: Comparison of lithium, aripiprazole and olanzapine as augmentation to paroxetine for inpatients with major depressive disorder. Ther Adv Psychopharmacol, 2014; 4: 123–29
12. Tohen M, McDonnell DP, Case M et al: Randomised, double-blind, placebo-controlled study of olanzapine in patients with bipolar depression. Br J Psychiatry, 2012; 201: 376–82
13. Uppsala Monitoring Centre: The use of the WHO-UMC system for standardised case causality assessment. URL: https://www.who-umc.org/medi/164200/who-umc-causality-assessment_new-logo.pdf
14. Owens MJ, Morgan WN, Plott SJ et al: Neurotransmitter receptor and transporter binding profile of antidepressants and their metabolites. J Pharmaco Exp Ther, 1997; 283: 1305–22
15. Gunasekara NS, Noble S, Benfield P: Paroxetine. An update of its pharmacology and therapeutic use in depression and a review of its use in other disorders. Drugs, 1998; 55: 85–120
16. Coebergh IA, Lauw RF, Bots R et al: Musical hallucinations: Review of treatment effects. Front Psychol, 2015; 6: 814
17. Bymaster FP, Calligaro DO, Falcone JF et al: Radioreceptor binding profile of the atypical antipsychotic olanzapine. Neuropsychopharmacology, 1996; 14: 87–96

Conclusions

The present report suggests that conventional doses of paroxetine can induce MHs. This effect should be differentially diagnosed from psychotic symptoms arising from psychiatric disorders, especially MDD.

Conflict of interest

None.