CASE REPORT

Auditory hallucinations induced by trazodone

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SUMMARY

A 26-year-old female outpatient presenting with a depressive state suffered from auditory hallucinations at night. Her auditory hallucinations did not respond to blonanserin or paliperidone, but partially responded to risperidone. In view of the possibility that her auditory hallucinations began after starting trazodone, trazodone was discontinued, leading to a complete resolution of her auditory hallucinations. Furthermore, even after risperidone was decreased and discontinued, her auditory hallucinations did not recur. These findings suggest that trazodone may induce auditory hallucinations in some susceptible patients.

BACKGROUND

Auditory hallucinations are common in schizophrenic patients whereas a few case reports have described antidepressant-induced auditory hallucinations.^{1,2} To the best of our knowledge, this is the first report of trazodone-induced auditory hallucinations.

CASE PRESENTATION

In February 2006, an 18-year-old female patient was referred to the psychiatric outpatient department of our university hospital. She had been bullied at elementary school and junior high school, suffering from a chronic anxiety state and insomnia since then. She also suffered from nasal and paranasal papilloma to which several surgical operations were performed at the department of otolaryngology and she had lumbago which was treated at the department of orthopaedic surgery of our university. Her elder brother died in an accident (drowning in a pond) when he was 4 years old and her younger brother suffered from school phobia and had received psychiatric treatment. Her parents divorced when she was at junior high school.

The patient suffered from a depressive state consisting of depressed mood, guilty ideation, suicidal thoughts, insomnia, anxiety and general fatigue. She scored 19 points on the Hamilton Depression Rating Scale (HAM-D). According to the Diagnostic and Statistical Manual-IV (DSM-IV-TR), she met the criteria for major depressive disorder. Milnacipran (50 mg/day), mianserin (20 mg/day) and flunitrazepam (2 mg/day) were started, but she could not tolerate both milnacipran and mianserin due to nausea and so on. Thereafter, paroxetine and subsequently fluvoxamine were tried in small doses but she did not comply regularly and she eventually discontinued this treatment. She continued to take flunitrazepam, brotizolam and levomepromazine for several years. Several attempts were made to start antidepressants for her depression,

but she was very sensitive to them and quit them as soon as she experienced some side effects. Throughout these depressive states, she had never heard auditory hallucinations.

In January 2013, the patient reported sleepiness during daytime when she took flunitrazepam (2 mg/day), brotizolam (0.25 mg/day) and levomepromazine (15 mg/day) at night. Following a discussion, it was decided that levomepromazine be partially changed to trazodone. Following this, flunitrazepam (2 mg/day), brotizolam (0.25 mg/day), levomepromazine (5 mg/day) and trazodone (50 mg/day) were administered at night. In February 2013, her daytime sleepiness reduced and she could sleep better at night. At that time, trazodone was decreased to 25 mg/day and the other drugs were continued as they were. In April 2013, she reported hearing her younger brother's voice, her grandmother's voice and/or her divorced father's voice at home, all of who were living elsewhere. These auditory hallucinations were heard at night when she was going to bed. In response to these voices, she tried to find their source within the house, but she could not locate them. She clearly noticed these voices were not a part of her dream and clearly recollected them later.

In May–June 2013, blonanserin (4–8 mg/day) was added to the treatment regimen with no effect on her auditory hallucinations. Blonanserin was changed to paliperidone (6 mg/day), but she reported severe xerostomia and paliperidone was changed to risperidone (1 mg/day). From July to November 2013, risperidone was gradually increased to 4 mg/day and her auditory hallucinations gradually decreased. In November, however, she began to state that her auditory hallucinations had begun just after starting trazodone. Following a further discussion, it was decided that trazodone should be discontinued as the time course of its administration and the appearance of auditory hallucinations were very coincidental. As an alternative to trazodone, levomepromazine was increased to 25 mg/day with risperidone (4 mg/day), flunitrazepam (2 mg/day) and brotizolam (0.25 mg/day). Throughout the treatment, she had never experienced schizophrenic pathological experiences such as Schneider's first rank symptoms.

DIFFERENTIAL DIAGNOSIS

Schizophrenia.

TREATMENT

Just after trazodone discontinuation, the patient's auditory hallucinations were dramatically decreased. Owing to 25 mg/day of levomepromazine, she initially suffered from over-sedation, and

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so the dose was decreased to 10 mg/day. From December 2013 to January 2014, risperidone was gradually decreased and discontinued without the recurrence of auditory hallucinations.

OUTCOME AND FOLLOW-UP

When levomepromazine was further decreased to 5 mg/day, auditory hallucinations did not recur but insomnia worsened. Following the change in treatment regimen the patient was very well without any auditory hallucinations on flunitrazepam (2 mg/day), brotizolam (0.25 mg/day) and levomepromazine (10 mg/day) as before.

DISCUSSION

In the present case, auditory hallucinations began after starting trazodone and subsided after trazodone discontinuation. Although the hallucinations partially responded to risperidone, trazodone discontinuation reduced the patient's auditory hallucinations dramatically. She had never suffered from schizophrenic pathological experiences, such as Schneider's first rank symptoms, and never heard auditory hallucinations during depressive states before starting trazodone. Therefore, it seems likely that trazodone induced auditory hallucinations in this patient.

Low-dose trazodone has been widely used for insomnia. Similarly, in this case, trazodone was administered for insomnia which was not adequately treated with levomepromazine, but unexpectedly auditory hallucinations occurred. The auditory hallucinations were heard at night when the patient was going to bed. As such, it could be suggested that these hallucinations were hypnagogic. The fact, however, that she clearly noticed these voices as not a part of her dream and remembered them clearly suggests that these were not derived from dream or delirium.

Pierre³ reported non-antipsychotic therapy for monosymptomatic auditory hallucinations, where auditory hallucinations of three patients responded well to trazodone. Therefore, trazodone may ameliorate auditory hallucinations in some cases whereas it may cause them in others, such as the present case. It is likely that the appearance or subsidence of hallucinations may

depend on patients themselves when treated with trazodone. Yet, it is very difficult to speculate as to the pharmacodynamic mechanism(s) involved. Although we are not aware of trazodone-induced auditory hallucinations, there are case reports of paroxetine-induced visual and auditory hallucinations¹ and escitalopram-induced visual and auditory hallucinations,² providing a possibility of serotonergic involvement in hallucinations, which can also be applied to the present case.

In conclusion, the present findings suggest that trazodone may induce auditory hallucinations in some susceptible patients.

Learning points

- It is important to suspect trazodone as a cause of auditory hallucinations.
- It is important to discontinue trazodone to treat trazodone-induced auditory hallucinations.
- Antipsychotic drugs can partially ameliorate such antidepressant-induced hallucinations, but antidepressant discontinuation is essential.

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