

## Case Report

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## Usefulness of Low-Dose Olanzapine for Initial and Maintenance Treatments of Very-Late-Onset Schizophrenia-Like Psychosis: A Case Report

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### ABSTRACT

In pharmacotherapy for schizophrenia, it is recommended that antipsychotic medications should not be discontinued, and their dosage should not be reduced during the stabilization and maintenance phases. Nevertheless, these drugs also have side effects that can increase extrapyramidal symptoms and mortality in the elderly population. It is yet to be determined whether antipsychotics should be reduced or discontinued in patients with very-late-onset schizophrenia-like psychosis (VLOSLP) during the stabilization and maintenance stages. Therefore, we describe the case of an elderly woman for whom low-dose olanzapine was useful throughout the initial, stabilization, and maintenance phases of VLOSLP. The patient was a 70-year-old woman who had experienced persistent hallucinations and delusions for 3 years. Two years after her diagnosis, except for relapse due to self-discontinuation, she remained in remission of her psychotic symptoms by continuing olanzapine treatment (2.5 mg/day). The standard effective dose of olanzapine was 10 mg/day, and she was able to respond to therapy with a low dose of olanzapine in the initial and subsequent phases of stabilization and maintenance. It is suggested that the discontinuation of antipsychotics should be avoided to avoid recurrence, even if the dose is lower than the standard amount during the stabilization and maintenance phases. Additionally, if the patient progresses to dementia, the treatment approach may vary, and it is imperative to monitor cognitive decline and self-discontinuation of oral medications during the follow-up of VLOSLP.

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### Introduction

The primary treatment for schizophrenia is antipsychotics [1]. The management of schizophrenia can be divided into three phases: acute, stabilization, and maintenance [2]. In the stabilization and maintenance phases, it has been reported that the group that discontinued antipsychotic medications had an increased relapse rate and worsened psychological symptoms compared to the group that continued antipsychotic medications [3]. According to the Japanese guideline on the pharmacological treatment of schizophrenia, it is recommended to continue taking antipsychotics in the stabilization and maintenance phases of schizophrenia, considering effectiveness and safety [4]. A meta-analysis of predictive factors for successful dose reduction of antipsychotics in the stabilization and maintenance phases of schizophrenia showed that the risk of relapse increased when the post-reduction dosage was <200 mg daily in a chlorpromazine equivalent dose [5].

When a person aged 60 years or older develops symptoms of schizophrenia-like psychosis, it is classified as very-late-onset schizophrenia-like psychosis (VLOSLP) [6]. Treatment of VLOSLP follows the same principles as those used for treating non-late-onset schizophrenia and typically involves the use of antipsychotic medications [7]. A randomized controlled trial showed the efficacy and safety of amisulpride after 24 weeks in patients with VLOSLP [8]; however, its efficacy and safety beyond 24 weeks is still unknown. It is thought that the discontinuation or reduction of antipsychotic medications should not be recommended even if the symptoms have remitted with the administration of the antipsychotics; yet, there are few reports on the effectiveness and safety of long-term prescription of antipsychotics for VLOSLP in the stabilization and maintenance phases. Even if the dose of antipsychotic drugs in the stabilization and maintenance phases should be reduced, 200 mg/day equivalent to chlorpromazine is the minimum necessary dose to prevent recurrence, but it is still unclear whether this applies to elderly patients with VLOSLP [5].

We describe the case of an elderly woman whose symptoms remitted with low-dose olanzapine in the initial phase and the subsequent stabilization and maintenance phases of treatment for VLOSLP. We report this case because it has important implications for the dose adjustment of antipsychotic medications administered to patients with VLOSLP.

### Case Presentation

A 70-year-old, right-handed woman visited our psychiatric outpatient clinic. The patient's chief complaint was that she felt anxious about forgetting things and heard the voices of people she knew saying negative things about her. She was born as the third child among three brothers. After graduating from high school, she worked as an office worker and retired at 24 years of age after marriage. She had two children. She had been working as a food service provider for 15 years and currently lives with her husband and son. Three years ago, she had recognized auditory hallucinations of the voice of an acquaintance. She felt as if they were saying bad things about her, but she could not clearly understand the content; thus, she did not address the issue. Six months ago, she experienced insomnia due to auditory hallucinations and quit her job as a food service provider. She was affected by auditory hallucinations, became anxious, and stopped sleeping and eating approximately a week ago without any trigger; therefore, her husband took her to our clinic for an emergency visit.

During the initial consultation, the patient was observed to be sitting with an anxious facial expression. Auditory hallucinations were observed when she shouted in an empty corridor that she had not been drinking alcohol. Active auditory hallucinations prevented neurological and psychological examinations. The patient did not make any statements during the examination, suggesting the presence of a recent memory impairment. There were no remarkable findings on neurological examination, including hearing or brain magnetic resonance imaging. Blood tests revealed dehydration. There were no findings consistent with abnormal glucose metabolism.

Since delusional thoughts and hallucinations continued for 3 years without any association with mood disorders and her occupational functioning decreased to the point of unemployment in the past half year, a diagnosis of schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition was made. Schizophrenia was classified as VLOSLP, as it occurred in an elderly patient aged 60 years or older.

The patient was admitted to our hospital because of dehydration. After admission, she was given 2.5 mg/day of olanzapine, which led to a decrease in auditory hallucinations and improved her eating and sleeping habits, allowing her to be discharged within 2 weeks. After discharge, she continued to visit the outpatient department of the hospital while taking 2.5 mg/day of olanzapine. She stopped complaining of memory impairment and was able to resume her hobby playing tennis.

Six months after her initial consultation, the patient felt that her condition had improved, and she discontinued the medication on her own. However, she started to complain about hearing auditory hallucinations from her husband. Then, she heard a command to bake a cake in the middle of the night and stopped getting enough sleep; hence, she visited the hospital again. She was suspected to have relapsed into schizophrenia; therefore, the dose of olanzapine was increased to 5 mg/day. After 10 days, her condition did not improve. One month after increasing the dose of olanzapine to 5 mg/day, her auditory hallucinations were relieved.

Eight months after the initial consultation, the dose was decreased to 2.5 mg/day at the patient's request. Subsequently, she continued to attend our outpatient clinic for 2 years since the initial visit and continues to take olanzapine (2.5 mg/day). Her cognitive function has been maintained, and no recurrence of psychotic or extrapyramidal symptoms has been observed.

### Discussion

In this case, a patient with VLOSLP was treated with low-dose olanzapine and showed a rapid improvement in hallucinations. Self-discontinuation of low-dose olanzapine resulted in the worsening of symptoms, suggesting that olanzapine, even at low doses, was necessary to maintain remission. Olanzapine has been reported to be effective at a dose of approximately 10 mg/day in clinical trials for patients aged 18–60 year, but in the present case, a good response was obtained with a low dose (2.5 mg/day). When her symptoms worsened again, the dose was temporarily increased to 5 mg/day, but after the symptoms stabilized, remission was maintained at a dose of 2.5 mg/day. Reports have shown that olanzapine levels in the blood can increase in elderly and female patients and this may have been the case in the current patient too [9, 10]. Elderly patients generally have decreased metabolic and excretion functions, which may cause an increase in antipsychotic drug levels compared to younger patients. High doses of antipsychotics have been reported to be associated with an increased risk of delayed extrapyramidal side effects and cardiovascular side effects [11,12]. Based on these considerations, it is suggested that low doses should be attempted first for the acute-phase treatment of VLOSLP.

When the patient discontinued taking 2.5 mg/day of olanzapine, she experienced a relapse of psychotic symptoms. In the stabilization or maintenance phase after acute-phase treatment, the patient was able to maintain remission by taking 2.5 mg/day of olanzapine, indicating that this dose was necessary for her to maintain remission from psychotic symptoms. The 2.5-mg/day dose of olanzapine was equivalent to 100 mg of chlorpromazine. This value is lower than the chlorpromazine equivalent of 200 mg, which was reported to increase the risk of relapse in a meta-analysis by Tani et al. [5]. In the treatment of the acute phase of VLOSLP, even if the amount of antipsychotic was lower than the usual effective dose and symptoms were relieved, it was suggested that continuing the lower dose might be necessary for the maintenance of remission.

Initially, the present patient had subjective complaints of memory loss, but with improvement of the hallucinations, the complaints were alleviated, and social adaptation was eventually maintained. From the course of reversibility, it is possible that temporary attentional impairment due to actively manifested auditory hallucinations causes memory loss, rather than cognitive impairment due to the onset of psychosis [13]. However, it has been reported that patients with VLOSLP have a higher risk of transitioning to dementia than controls without a history of psychosis, and the current case may also have the potential to develop dementia in the future [14]. If this patient develops dementia, the treatment approach for maintaining remission could change. This is because the use of antipsychotics in elderly patients with dementia increases the mortality rate and anti-cholinesterase drugs are reported to be effective for the neuropsychiatric symptoms of Alzheimer's type dementia and Lewy body type dementia [15–18]. Therefore, the findings of this case may not be applicable if a patient is diagnosed with dementia.

This report has some limitations. First, this report describes a course of 2 years after the first visit, and it is unclear whether the findings apply to longer courses. Second, in this case, discontinuation of low-dose olanzapine caused relapse, but it is unclear whether dose reduction causes relapse. Therefore, further research is needed to determine whether dose reduction of antipsychotics is acceptable during the stable and maintenance phases of treatment for VLOSLP. Third, olanzapine, an antipsychotic approved in Japan, was prescribed in this case. It is not known whether the findings of this report are applicable to antipsychotics other than olanzapine.

The current case suggests that low-dose olanzapine is useful in the initial treatment of VLOSLP and in the stabilization and maintenance phases of treatment for VLOSLP. Additionally, this case suggests that treatment in the acute phase of VLOSLP should be initiated using low-dose antipsychotics. During the stabilization and maintenance phases of VLOSLP, it may be important to monitor the deterioration of cognitive dysfunction and self-discontinuation of oral medication.

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### Institutional Review Board and Informed Consent Statements

Written informed consent has been obtained from the patient for the publication of this case report.

### Conflicts of Interest

The authors declare that they have no competing interests.

### Abbreviation

Very-late-onset schizophrenia-like psychosis (VLOSLP)

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