Switching to aripiprazole for the treatment of residual mutism resulted in distinct clinical courses in two catatonic schizophrenia cases

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Abstract
Objectives: The efficacy of a partial agonist for the dopamine D2 receptor, aripiprazole, for catatonia in schizophrenia has been reported.
Methods: We report distinct clinical courses in challenging aripiprazole to treat residual mutism after severe catatonic symptoms improved.
Results: In the first case, mutism was successfully treated when the patient was switched from olanzapine to aripiprazole. In contrast, switching to aripiprazole from risperidone aggravated auditory hallucinations in the second case.
Conclusions: We will discuss the benefits and risks of using aripiprazole for the treatment of catatonic schizophrenia and the possibility of dopamine supersensitivity psychosis.

Keywords
Mutism, catatonia, aripiprazole, dopamine supersensitivity psychosis

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Introduction
Mutism is defined as a functional inhibition of speech and vocalization. This symptom has been reported in various neuropsychiatric illnesses, including catatonic and paranoid schizophrenia, though the exact neurological mechanism is unknown. The efficacy of electroconvulsive therapy in mutism has been reported in case reports, which suggest that activation of the mesolimbic dopamine system is involved in the therapeutic outcomes. Case reports have shown that a partial agonist for the dopamine D2 receptor, aripiprazole, improves catatonia with or without other additional medication. Therefore, aripiprazole is expected to improve catatonic mutism due to its pharmacological property of partially activating dopaminergic neurotransmission. This report presents two schizophrenia cases with mutism as a residual symptom after severe catatonic symptoms were improved. They had distinct clinical outcomes after their pharmacotherapy was changed to the medication with aripiprazole. We will discuss the benefits and risks of using aripiprazole for the treatment of catatonic schizophrenia. In addition, we discuss the results from the perspective of a recent theory of drug-induced dopaminergic supersensitivity psychosis (DSP) because the recognition of DSP is useful to prevent the acquisition of treatment resistance in schizophrenia when prescribing antipsychotics parallel to the prevention of a well-known type of dopaminergic supersensitivity, tardive dyskinesia.

Case reports
Case 1 was a 55-year-old woman with 14 years of education. She was married at 22 years of age and lived with her husband and three daughters. At the age of 47, she began to have persecutory delusions, and she stopped talking with her family and withdrew to her room. At 48 years of age, she visited a hospital, accompanied by her family, and was admitted. She did not speak with anyone, but she indicated her intentions nonverbally. Organic brain disease, neurodegenerative disease, and psychosis due to systemic disease were excluded by a computerized tomography scan of the brain and a blood...
test. Her mutism and refusal to communicate were diagnosed as a symptom of schizophrenia, and she was successfully treated with olanzapine. After discharge, at 49 years of age, she lived with her family and started to work part-time. However, at 51 years of age, when the dosage of olanzapine was tapered down, due to overweight status, her mutism and refusal to communicate re-emerged. She was admitted to a hospital with a score of 18 on the Bush–Francis catatonia rating scale (BFCRS; 14 items). She was treated by increasing the dose of olanzapine to the original level. Abnormal symptoms improved within 3 months, and she was discharged with a BFCRS score of 7. She continued treatment as an outpatient with daily doses of 20 mg olanzapine, 1.5 mg lorazepam, and 150 mg amantadine. However, her mutism did not improve. In addition, she was overweight (161 cm, 84.9 kg). She agreed in writing to change treatment from olanzapine to aripiprazole. Thus, at 53 years of age, she started treatment with 24 mg aripiprazole daily. Shortly after adding the aripiprazole, she experienced a reduction in appetite and reduced her excessive eating. One month after starting aripiprazole, she reported difficulty urinating, and the daily dose of aripiprazole was reduced to 12 mg. Olanzapine was tapered off gradually, and aripiprazole was maintained at a daily dose of 15 mg. The patient began to speak vocally after 3 months of starting aripiprazole. Then, she began to take part in housekeeping when her BFCRS score dropped to 3. Finally, olanzapine was stopped at 8 months after introducing aripiprazole. Case 2 was a 55-year-old woman with 14 years of education. She was not married. She was diagnosed with schizophrenia when she began to exhibit catatonic symptoms, including immobility and mutism, at 32 years of age. She was treated with bromperidol, followed by risperidone. However, her catatonic symptoms recurred at 46 years of age when she learned that her mother had cancer, and then again at 48 years of age when her mother’s cancer relapsed. After treatment in a hospital, the next relapse of her mutism occurred at 53 years of age when her benzodiazepines were tapered without other severe symptoms. She was maintained without hospitalization, but her catatonic symptoms deteriorated at 55 years of age, when her mother’s dementia became severe in addition to her cancer. She was admitted to a hospital with catatonic symptoms, including immobility, mutism, and refusal to consume food and water when her mother moved to a care unit, and the patient was left alone at home. She scored 20 points on the BFCRS. She was treated with daily doses of 2 mg risperidone, 3 mg lorazepam, and 200 mg amantadine. Her catatonic symptoms gradually improved, except mutism. She communicated with gestures or writing on paper without vocalizing. To treat the mutism, aripiprazole was prescribed. Aripiprazole was started at a daily dose of 12 mg and then it was increased to 24 mg and maintained at that dose. Risperidone was tapered off and completely stopped at 4 weeks after starting aripiprazole. However, soon after the cessation of risperidone, the patient began to walk around the ward, attempting to leave the hospital; she told us (in writing) that she heard her mother’s voice calling her. We recognized this as an auditory hallucination, and we replaced aripiprazole with a dopamine D2 receptor antagonist, perospirone. After that replacement, the patient’s abnormal behavior stopped, but mutism was not cured.

Discussion

In both cases, mutism had continued for about 2 years. In Case 1, a successful course was achieved when the patient was switched from olanzapine to aripiprazole. Olanzapine targets multiple receptors, including dopamine D2 receptors, which it antagonizes with relatively low affinity. Classical antipsychotics with strong dopamine D2 antagonism have been known to exacerbate catatonic symptoms, due to excessive inhibition of dopaminergic activity.2 In accordance with previous reports that aripiprazole could successfully treat catatonia,6–9 the switch from olanzapine to aripiprazole had a favorable effect in Case 1, which suggested that the D2 partial agonist provided an advantage over the antagonist. Notably, the onset of psychosis occurred late in life in Case 1. Moreover, her social/occupational function recovered enough to work part-time during remission. Thus, paranoid schizophrenia or paranoia should be considered as a differential diagnosis. Mutism may emerge as a result of adaptive coping in the presence of a paranoid delusion.12 A catatonic state may emerge as an attempt to self-heal by escaping from a threatening psychiatric experience.2 A randomized study indicated that aripiprazole provided an advantage over a dopamine D2 antagonist, paliperidone, for improving subscale scores on the Quality of Life Scale; this improvement was associated with therapeutic efficacy for negative symptoms or cognitive function.13 Hence, in the present Case 1, the therapeutic effect might be attributed to an improvement in negative symptoms or cognitive function, which resulted in the normalization of excessive behavioral reactions associated with a psychiatric disturbance. In Case 2, switching to aripiprazole from risperidone aggravated the condition by causing auditory hallucinations. Risperidone is a potentially strong antagonist of dopamine D2 receptors. This finding supported the notion that dopamine D2 partial agonists can potentially exacerbate dopamine-related pathology, like hallucinations, as previously suggested, both theoretically10 and practically.14 In Case 2, the patient was vulnerable to stress, as indicated by the multiple episodes of deterioration after stressful life events and by the abrupt relapse triggered by the reduction or discontinuation of the usual medication. This vulnerability and the aggravation caused by switching antipsychotic treatments are proposed to be core elements in DSP.15 Furthermore, long-term treatment with a strong D2 receptor antagonist elevates the risk of DSP.14 Taken together, these considerations suggested that Case 2 represented a patient that had acquired DSP. This could explain why the partial agonist, aripiprazole, worsened the hallucinatory symptoms. This case study described two cases of mutism that persisted after treating catatonic schizophrenia. Although the application of aripiprazole is a valid choice for treating
catatonic schizophrenia, the clinician must monitor the course carefully because the outcome appears to depend on the patient’s history with pharmacotherapy.

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