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CASE REPORT

Mutism and rigidity due to antipsychotic-induced catatonia improved by hemodialysis: A case report

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Abstract

Background: Catatonia is a psychomotor syndrome linked to various medical conditions. Among these, several reports have described antipsychotic-induced catatonia (AIC). Treatment typically includes benzodiazepines and electroconvulsive therapy. Here, we report a rare case of AIC that showed an improvement in symptoms under hemodialysis.

Case Presentation: A 79-year-old man with diabetic nephropathy was admitted with acute renal failure and metabolic acidosis. Hemodialysis was initiated, and his acute renal failure and metabolic acidosis were mild. On Day 11, following an intramuscular injection of haloperidol (2.5 mg) for agitation the previous day, he developed mutism, rigidity, and resistance to mouth-opening, leading to a diagnosis of AIC. His symptoms improved dramatically during the course of hemodialysis, with no recurrence after seven sessions. He was discharged after 49 days and did not experience recurrence of catatonia in the following 12 months.

Conclusion: While this case showed a rapid improvement in AIC following hemodialysis, no robust evidence implicating AIC and hemodialysis has been reported to date. This case suggests the potential role of hemodialysis in improving AIC symptoms. Further research to better understand the relationship between AIC and hemodialysis and the underlying mechanisms of catatonia is required.

KEYWORDS
antipsychotics, antipsychotics-induced catatonia, catatonia, hemodialysis

BACKGROUND

Catatonia is a psychomotor syndrome associated with a variety of psychiatric and other medical conditions.[1] Various medical diseases and substances are associated with catatonia and antipsychotic-induced catatonia (AIC) occurs infrequently.[2,3] AIC has been reported to occur within hours after the first dose of both first-generation antipsychotics (FGAs) and second-generation antipsychotics (SGAs),[4] although the risk of incident AIC is higher with FGAs than with SGAs.[5] Among FGAs, many reports have described AIC due to haloperidol.[5,6] Treatment of catatonia includes conservative treatment, benzodiazepines, and electroconvulsive therapy, in addition to eliminating or improving the cause, such as antipsychotics. In contrast, hemodialysis is not typically categorized as a treatment for catatonia.

Here, however, we report a case of AIC induced by intramuscular injection of haloperidol that was promptly improved by hemodialysis.

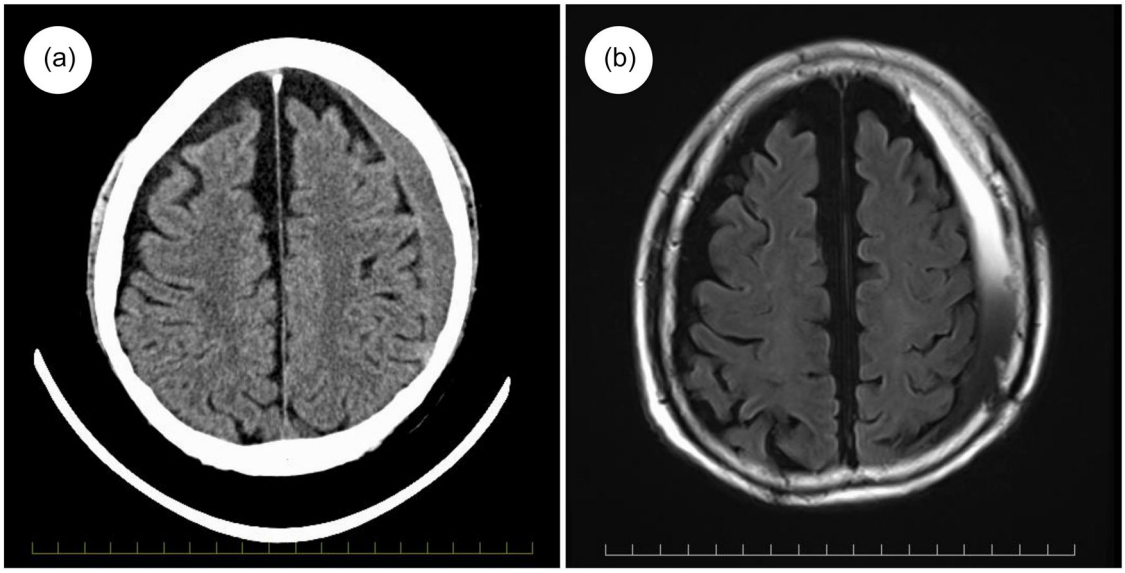

FIGURE 1 Brain images of the patient's left chronic subdural hematoma (CSDH). (a) CT on admission. (b) FLAIR MRI on Day 15 after admission. On the scale at the bottom, one division represents 10 mm. Both images show a CSDH with no change in volume.

CASE PRESENTATION

A 79-year-old Japanese man admitted to our hospital's nephrology department was seen by a psychiatrist at the psychiatry department. He had no history of thyroid dysfunction but had experienced diabetic nephropathy for the past year. He also had an asymptomatic chronic subdural hematoma (CSDH) on the left side that had been present and kept under observation without surgery or other treatment for 10 years. The CSDH was likewise noted on a head CT just before the present admission (Figure 1a). There was no history or family history of psychiatric disorders. Before this admission, he had normal cognitive function and was independent in daily activities. He was admitted due to renal failure with metabolic acidosis and hyponatremia. There was no motor dysfunction but mild impaired consciousness with some distraction was noted. His blood tests showed Na 113 mEq/L, Cre 7.91 mg/dL, pH 7.17, PCO2 18.1 Torr, and HCO_3− 6.3 mEq/L (Table 1). Treatment was initiated with Na correction from the day of admission and hemodialysis three times a week from Day 4 of admission. His mildly impaired consciousness improved on Day 5 of admission, his hyponatremia and renal failure were relieved, and hemodialysis was continued after evaluation of efficacy. On Day 9 of admission, the third hemodialysis session was performed during the daytime, and he had no disorientation. He experienced agitation during the night on Day 10 of admission and was given an intramuscular administration of 2.5 mg of haloperidol. On the morning of the following day, he was noted to have mutism and to be motionless, even though his eyes were open. After a further 4 h, he developed severe rigidity of the extremities and refused to open his mouth. The same day, he was seen by the psychiatrist before the fourth dialysis. He was right-handed, 158.3 cm tall, and weighed 44.8 kg. He showed mild fever (body temperature of 37.5°C), tachycardia (pulse of 115/min), and blood pressure of 128/79 mmHg.

TABLE 1 Main blood test findings from admission to discharge. The patient's catatonia occurred on Day 11 (d11).

	d1	d5	d9	d11	d14	d47
pH	7.17	–	–	7.42	–	7.40
PCO2 (Torr)	18.1	–	–	46.0	–	46.4
HCO3- (mEq/L)	6.3	–	–	28.9	–	28.5
Cre (mg/dL)	7.91	4.97	1.84	1.68	1.56	0.91
Na (mEq/L)	113	139	142	151	143	139
Cl (mEq/L)	85	106	108	107	113	104
cCa (mg/dL)	8.70	8.64	8.68	8.44	8.18	9.06
CK (U/L)	335	148	97	169	136	25

Abbreviations: d, days since admission; cCa, corrected Ca.

His extremities were rigid, and waxy flexibility was noted in both lower extremities. Attempts to open his mouth with force were firmly refused. Blood tests on the same day showed no worsening of renal function or metabolic acidosis, but Na had increased to 151 mEq/L compared with 142 mEq/L 2 days previously. Serum albumin was 2.7 g/dL and measured Ca was 7.4 mg/dL (corrected Ca 8.44 mg/dL). There was no myoglobinuria or elevated CK (169 U/L). He had severe rigidity and resistance to mouth-opening but no features such as hyperthermia, severe autonomic neuropathy, or elevated CK, which ruled out neuroleptic malignant syndrome (NMS) as a differential disease. Based on the psychomotor disturbances of mutism, rigidity of the extremities, waxy flexibility, and resistance to mouth-opening, he was diagnosed with catatonia. Given his medical history, the catatonia was considered to be due to the administration of haloperidol.

At about the same time, 2 h after the start of the fourth hemodialysis session on the same day, his catatonic symptoms significantly resolved, and he was able to speak. His attention was directed to the

doctor, and there was no disorientation. He remained hospitalized with the prohibition of neuroleptic drugs, including antipsychotic drugs, and no benzodiazepines, dantrolene, bromocriptine, or amantadine were used. There were no confused verbal responses, but his mutism and rigidity of the extremities slowly reappeared after the fourth hemodialysis session. Nevertheless, these symptoms improved again following the fifth hemodialysis session on Day 14 of admission. Blood tests on the same day showed an improvement in the mild hypernatremia. Brain magnetic resonance imaging (MRI) performed on Day 15 of admission showed no worsening of the left CSDH and no other abnormalities, including the bilateral basal ganglia (Figure 1b). Electroencephalogram examination the same-day revealed no abnormalities other than low amplitudes (Figure 2). After the seventh hemodialysis session, there was no observation of catatonic symptoms and his renal dysfunction improved (Figure 3). Thus, he completed a total of seven sessions of hemodialysis on Day 21 of admission. After withdrawal from hemodialysis, he remained admitted for physical function rehabilitation, during which time he had no recurrence of acute renal dysfunction or catatonia, and was discharged on Day 49 of admission. No recurrence of catatonia has been seen in the more than 12 months since discharge.

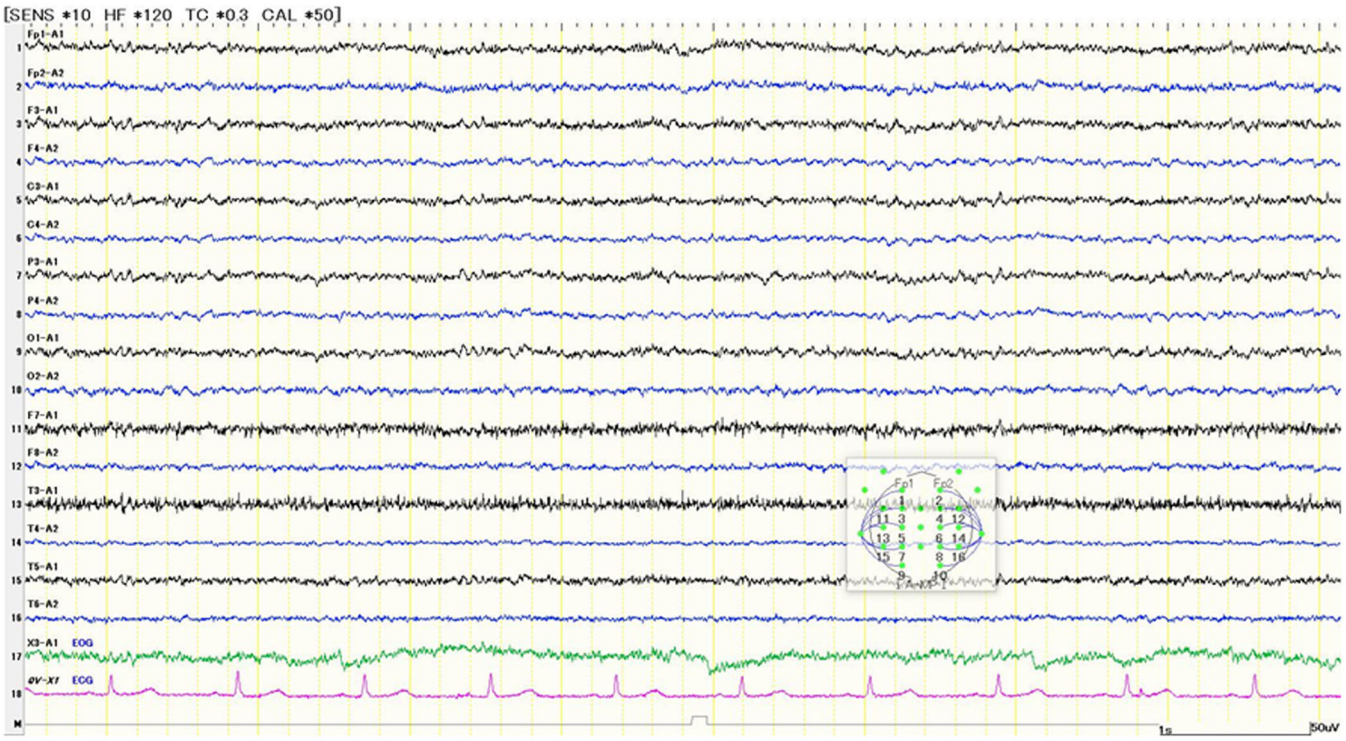

FIGURE 2 Findings of the patient's awake electroencephalogram on Day 15 after admission.

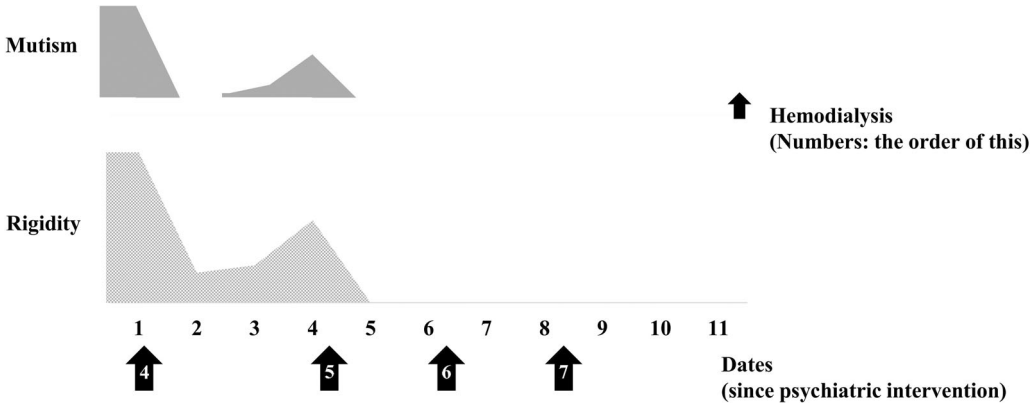

FIGURE 3 Course of treatment after the onset of antipsychotic-induced catatonia. Mutism and rigidity improved during the hemodialysis sessions.

DISCUSSION AND CONCLUSION

This report describes a case of catatonia following the use of a dopamine antagonist neuroleptic that rapidly improved with hemodialysis. Although the patient had other complications, namely acute renal failure and CSDH, the course of the disease led us to conclude that the main factor in the onset of catatonia was the administered haloperidol. While the pathological mechanisms of catatonia are not fully clear, dysfunction of γ-aminobutyric acid A and dopamine agonist transmission has been suggested.[7] Da Costa et al. found that antipsychotics, especially FGAs, are associated with higher risk of catatonia.[5] This suggests that haloperidol, which strongly binds to dopamine receptors, was a major risk factor for catatonia in this case. A previous report describes a case of uremia in which catatonia occurred after the first hemodialysis session.[8] However, we excluded the possibility that hemodialysis was a direct factor in the development of catatonia because the catatonia developed after several dialysis sessions, not the first, and because, in contrast to previous reports, the catatonia occurred during the improvement of renal dysfunction.

The other condition we initially suspected in this case was NMS. Although he did not have a fever over 38°C or severe autonomic symptoms, and accordingly did not fulfill the general diagnostic criteria for NMS, some patients with atypical NMS do not present with hyperthermia, as in this case. Indeed, a systematic review of cases of atypical NMS found 30% did not present with hyperthermia.[9] Although there is no typical order of appearance of symptoms in NMS, extrapyramidal symptoms often precede autonomic syndromes.[10] In an analysis of 340 cases of NMS, over 70% of patients had a course of mental status changes first, followed by extrapyramidal symptoms, hyperthermia, and autonomic dysfunction.[11] Our present case also followed this course. However, NMS is difficult to distinguish from AIC, and many case descriptions of catatonia signs arising in patients with NMS have been reported.[12] This case did not fulfill the diagnostic criteria for NMS, such as the Levenson criteria, Caroff criteria, or those of the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition. Nevertheless, it did fulfill the diagnostic criteria for catatonia, and therefore supported a diagnosis of AIC.

This report describes an unusual case in which improvement in mutism and rigidity was observed in association with the provision of hemodialysis. In this case, hemodialysis had been introduced before the onset of catatonia, which thus allowed the course of treatment to be observed from an early stage. The primary drugs used in pharmacotherapy for NMS and severe extrapyramidal symptoms were not used. In addition, no anticholinergics or other drugs that improve extrapyramidal symptoms or benzodiazepines were administered. Despite this, the patient's catatonia improved in a short period of time. Therefore, this report suggests that hemodialysis may benefit patients with AIC.

Nevertheless, no robust evidence implicating AIC and hemodialysis has been reported. A previous case report described how catatonia observed during ciprofloxacin administration improved with hemodialysis.[13] This course was mainly attributed to the characteristics of ciprofloxacin, which is not well excreted and accumulates due to renal dysfunction.[14] In contrast, lipophilic haloperidol, the suspected primary cause of AIC in our present case, is less affected by renal dysfunction due to its low urinary excretion rate.[15] Although haloperidol does not have a high molecular weight (375.86 g/mol), its protein binding is approximately 90% and its volume of distribution is 1000–3000 L.[16] Thus, hemodialysis generally does not remove haloperidol. Considering these characteristics, it is difficult to explain the course of catatonia induced by haloperidol and its resolution with dialysis. Another case report suggested that hemodialysis could filter out the neurotoxins associated with catatonia.[17] Nevertheless, the literature and reports on AIC remain limited,[18] and our present case of hemodialysis-induced improvement is remarkable given the still poorly understood pathogenesis of catatonia.

There are several limitations to this case. First, we describe the improvement of AIC symptoms in association with hemodialysis, but a single case report cannot prove whether an improvement in AIC is strongly related to hemodialysis. We hope to accumulate more case reports with a similar course. Second, serum haloperidol levels during this case were not obtained. Third, although this case did not fulfill the diagnostic criteria for NMS, the possibility of atypical NMS could not be completely ruled out. Fourth, the possibility that metabolic disturbances, especially hypernatremia, were related to the pathophysiology could similarly not be ruled out. Although extrapyramidal symptoms are atypical, the patient's hypernatremia may have influenced his psychiatric symptoms. Furthermore, this case may instead suggest that hemodialysis corrected metabolic disturbances, leading to the resolution of catatonia. Fifth, the possibility that the patient's CSDH was associated with the condition remains. Although the MRI showed no evidence of hematoma enlargement, thus suggesting little association with the acute onset of the catatonic symptoms, we cannot conclusively determine this.

This case report presents the course of a patient with mutism and rigidity due to AIC that improved with hemodialysis. Future research on how hemodialysis is associated with AIC is warranted.

AUTHOR CONTRIBUTIONS

Rintaro Fujii, Ryota Suga, Norihito Satoh, and Yasuo Watanabe treated the patient. Rintaro Fujii, Ryota Suga, and Reiji Yoshimura wrote the draft. All authors reviewed the draft and revised the manuscript.

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CONFLICT OF INTEREST STATEMENT

Reiji Yoshimura is an Editorial Board member of *Psychiatry and Clinical Neurosciences Reports* and a co-author of this article. To minimize bias, they were excluded from all editorial decision-making related to the acceptance of this article for publication.

DATA AVAILABILITY STATEMENT

N/A.

ETHICS APPROVAL STATEMENT

Ethics committee approval was not required for this case report.

PATIENT CONSENT STATEMENT

Written and verbal informed consent were obtained from the patient to publish this case report and any accompanying images.

CLINICAL TRIAL REGISTRATION

N/A.

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