A case of methamphetamine use disorder presenting a condition of ultra-rapid cycler bipolar disorder

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Abstract
Methamphetamine, a potent psychostimulant, may cause a condition of mood disorder among users. However, arguments concerning methamphetamine-induced mood disorder remain insufficient. This case study describes a male with methamphetamine-induced bipolar disorder not accompanied by psychotic symptoms, who twice in an 11-year treatment period, manifested an ultra-rapid cycler condition alternating between manic and depressive mood states with 3- to 7-day durations for each. The conditions ensued after a bout of high-dose methamphetamine use and shifted to a moderately depressive condition within 1 month after the use under a treatment regimen of aripiprazole and mood stabilizers. The cycler condition may be characteristic of a type of the bipolar disorder and a sign usable for characterization. Further efforts are needed to seek distinctive features and to improve diagnostic assessment of methamphetamine-induced mood disorders.

Keywords
Methamphetamine, substance-induced bipolar disorder, rapid cycler, manic switch, substance use disorder

Date received: 22 February 2018; accepted: 10 January 2019

Introduction
Methamphetamine (MAP) is a potent addictive psychostimulant that causes a wide range of psychiatric disorders among users.1,2 In particular, the psychotic disorder (MAP psychosis) is regarded as representative of MAP-induced disorders.3,4 In contrast, much less arguments have been made concerning MAP-induced mood disorders. Two studies in an early stage of research4,5 reported that the percentages of those who exhibited a typical bipolar picture were 5% and 24% among inpatients with MAP-induced disorders, and that a few of them presented a “pure (unaccompanied by psychotic symptoms)” bipolar picture. Indicating a close relationship with mood disorders, studies in emergency settings have reported considerable comorbidity rates among MAP users, including 16%–26% for bipolar disorder and 10%–48% for major depressive disorder.6–8 As for mood symptoms among MAP users, several studies have stressed the relevance of depressive symptoms (e.g. Iwanami et al.*). Longitudinal studies10,11 have shown a prolonged influence of MAP use on severity of depressive symptoms along with an influence on the severity of psychotic symptoms. A study12 also indicated that recent MAP use might increase mood symptoms such as racing thoughts, dysphoria, and anhedonia of persons with schizophrenia. In spite of the significance of mood symptoms counted above, a number of questions concerning the clinical appraisal of MAP-induced mood disorders remain unanswered.

The case presented here has two rare but important clinical features. First, the patient exhibited a “pure” bipolar picture during a long treatment course. Over the presence of the “pure” mood disorder, controversies are still continuing. Some authors have cast doubt on the presence of “pure” MAP-induced mood disorder, contending that the picture was no more than a secondary phenomenon of the underlying MAP psychosis.13,14 The second is that there were two periods of ultra-rapid cycling, that is, very brief mood cycles lasting for days15,16 in the treatment course. To our knowledge, this unusual mood cycling has been reported solely in
some studies of bipolar disorder15–18 and not in those of other mental disorders. This case report discusses the relevance of these features in diagnostic assessment of MAP-induced mood disorders.

Ethics

The patient described in this report provided written informed consent to publish the anonymized case details. Our institution did not require ethical approval for reporting individual cases.

Case presentation

The patient, a married man with robust build in his mid-40s, after 8 years of outpatient treatment for anxiety and depressive mood, fell into a condition of ultra-rapid cycling, that is, frequent alternations between manic and depressive states with 3- to 7-day durations for each. He was hospitalized 2 weeks after the start of this condition.

In his developmental period, no abnormalities had been reported. He had shown defiant and delinquent behavior in his youth, while he had no interaction with the juvenile legal system. After withdrawing from high school, he began to work, but frequently changed jobs. Around 30 years old, he had been a drug (MAP) supplier and tattooist for a crime syndicate for several years. During these years, he had several 1- to 2-month periods in which he used MAP 1–2 times a week by intravenous self-injection. In his mid-30s, he was seriously injured in a violent assault by syndicate members. After 1 month in hospital for the injury, he had returned to an honest living, that is, engaged in a construction job and making a living for his family. Complaining of flashbacks to the assault, diffuse anxiety, and depressive mood, he started to receive psychiatric treatment including medication with selective serotonin reuptake inhibitors and benzodiazepines. Thereafter, he had regularly been attending an outpatient clinic. In his early 40s, however, as depression and anxiety worsened due to a traffic accident he had caused, he became unable to work. Outpatient treatment including antidepressant regimens did not ameliorate symptoms. Finally, a condition of mood alternations emerged. However, he had not divulged any recent MAP use at that time. The patient and his family consistently reported that he had no history of habitual alcohol drinking or using illicit drugs other than MAP. In addition, they stated that he had experienced no depressive or manic episode resulting in a long absence from work prior to the start of psychiatric treatment. Likewise, clinically relevant psychotic symptoms such as hallucinations and delusions had not been reported by him, or recognized by his family and treatment staff.

Mood alternations continued after admission, despite starting treatment regimens of aripiprazole (12 mg/day) and lithium carbonate (600–1000 mg/day). In a depressive state, he showed prominent hypersomnia and did not get out of bed, while complaining of anxiety, depressive mood, and pessimistic recognition. In a manic state, he showed extreme irritability, listlessness, pressured speech, racing thoughts, and stereotypic behavior (punding). He had to make much effort not to become aggressive to others around him. Both mood conditions fulfilled DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition) symptomatic criteria for major depressive or manic episodes. Routine admission laboratory testing including thyroid function tests gave no abnormal results. Brain magnetic resonance imaging and electroencephalogram did not indicate any sign of organic disorder. The blood lithium level checked at the time of 1 week after the start of a regimen including lithium carbonate 1000 mg/day was 0.52 mEq/L.

In the third week of hospital stay, an abnormal upsurge in blood creatine phosphokinase (CPK) level (10,241 U/L at peak; normal range, 59–248 U/L) was recognized, while there was no abnormality of vital signs or neurological symptoms, which reduced much the probability of neuroleptic malignant syndrome.19 When inquired about recent MAP use, which could have caused CPK elevation by inducing rhabdomyolysis,20 the patient denied any such drug use. Inspection conducted with his permission did not find any injection trace in his arms or drug paraphernalia among his belongings. MAP screening (urine) test was not performed, since this was available only in the emergency department then. While both aripiprazole and lithium carbonate could be assumed as the cause of abnormal blood CPK,20 a tentative action taken was to replace lithium carbonate with sodium valproate (600–1200 mg/day) and to continue aripiprazole. The level of CPK normalized within 10 days. The mood alternation continued for 8 weeks and shifted to a moderately depressive condition. A total of distinct six mood cycles were observed during this episode. The blood valproate concentration checked at discharge 2 weeks after the start of a regimen including sodium valproate 1200 mg/day was 63.8 µg/mL.

The patient was readmitted 6 months after discharge because of acute recurrence of the mood alternation. An abnormal finding of blood CPK (417 U/L) was recognized again on readmission and disappeared after 2 weeks. Confronted with the fact that emergence of the mood alternations and the temporal course of CPK levels could reasonably be explained by binge use of MAP, the patient confessed that he had self-injected MAP several times before the first appearance of these mood alternations, once during the first admission and once before the second admission. The patient also reported using a high-dose (1000 mg at a time) and high-purity (> 90%) of MAP hydrochloride. Medication had immediately been changed to a regimen of lithium carbonate (600–800 mg/day) and aripiprazole (12 mg/day), which had appeared to decrease mood symptoms more than the previous one that had included sodium valproate instead of lithium carbonate. The blood lithium level at discharge 1 week after the start of lithium carbonate 800 mg/day was
0.67 mEq/L. The duration of the second cycling series was 4 weeks, in which three distinct mood cycles were observed. During a 2-year outpatient follow-up period after hospitalization, under a regimen of aripiprazole and lithium carbonate, he predominantly remained in a moderately depressive condition, and intermittently engaged in employment. CPK tests conducted at regular intervals during this period found no abnormalities.

Discussion

The case presented in this report was a man diagnosed with DSM-5 MAP use disorder and MAP-induced bipolar disorder. One of its prominent features was that he showed a bipolar picture not accompanied by psychotic symptoms. It indicates that in diagnostic assessment of such cases, the possibility of MAP-induced bipolar disorder should not be discarded, though it might be very small.

The other feature is a condition of ultra-rapid cycling that started after a bout of high-dose MAP use and subsided principally within 1 month, which appeared to be clearly separated from other conditions in the clinical course. This ultra-rapid cycling is distinctive from the ones previously described in cases of bipolar disorder, which usually develop as a result of gradual worsening of the disorder. Thus, the ultra-rapid cycling of this case may be characteristic of a specific type of disorder and a sign usable for characterization. It would provide support for this finding that Tatetsu et al. reported an abrupt mood change between manic and depressive states as a characteristic of the mood disorder among MAP users, and reported four highly rapid cyclers (more than 8 episodes/year) patients.

Relevant to the ultra-rapid cycling are studies of manic switch phenomena. Manic switch is putatively involved with sudden elevation of monoamine levels, which can be caused by MAP and other amphetamines. Their administration has also been reported to cause a manic switch from a depressive state. On the contrary, occurrence of depressive conditions may be explained by the neurotoxic actions of chronic MAP use on central dopaminergic and serotonergic systems. Taken together, one possible explanation for the ultra-rapid cycling of MAP-induced bipolar disorder would be that the condition is a result of monoamine-system instability engendered by a combination of enduring monoamine depletion following chronic MAP use and acute elevation of monoamines induced by high-dose MAP intake.

However, particular care is needed in interpreting the findings of this report due to the limitation that they heavily depend on statements by the patient, even though he and his family had been maintaining a good relationship with treatment staff for years.

To conclude, although the neurobiological bases underlying the link between mood disorders and MAP use remain largely unknown, this report highlights an ultra-rapid cycler condition as a potentially distinctive feature of a type of MAP-induced bipolar disorder. It is also pointed out that MAP-induced mood disorders should not be ruled out in diagnostic assessment of MAP users just because no psychotic symptoms are recognized, though they are quite common among patients with the disorders. In addition, it should be stressed that treatment regimens applied for the case represent a building block for the development of more appropriate treatment protocols. Further efforts are needed to improve diagnostic assessment and to develop effective treatment approaches for patients with MAP-induced mood disorder.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Informed consent

Written informed consent was obtained from the patient for his anonymized information to be published in this article.

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