

Case Reports

Methamphetamine Intoxication Encephalopathy Associated With Hyperammonemia



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Introduction

Ammonia (NH_3) is derived from amino acid metabolism in the liver via the urea cycle. It is routinely measured in cases of unexplained lethargy and vomiting, or encephalopathy. It is most useful when checked in encephalopathies of unknown cause.¹ Methamphetamine is an addictive psychostimulant drug, which is chemically related to amphetamine.² Elevated NH_3 has not been reported in cases of encephalopathy in humans due to methamphetamine toxicity. The authors report 3 cases of elevated NH_3 associated with methamphetamine toxicity in human subjects, and discuss the possible etiologies of this relationship.

Case Series

Case 1

Mr. A, a 27-year-old Hispanic male with a history of methamphetamine and marijuana abuse, hepatitis C (unknown duration), pathologic gambling, and antisocial personality disorder with multiple past suicide attempts was brought to a psychiatric emergency department at a tertiary academic medical center by police after a failed suicide attempt (he stood on freeway bridge and threatened to jump in a suicide attempt).

The precipitating event was his wife leaving him and taking their children.

On arrival, he was found to be agitated, hostile, and screaming, and was sedated with intramuscular medications (haloperidol, 5 mg). He was admitted with the

following target signs and symptoms: paranoid delusions, agitation, aggression, and suicidal ideation.

Objectively, he had stable vital signs (no tachycardia, and blood pressure within normal limits).

Physical examination manifested unsteady gait and dry cracked lips with blood present. Neurologic and mental status examination showed an unkempt, uncooperative, Hispanic male. His thought process was disorganized and illogical. Thought content was as follows: denying suicide ideations, denying homicidal ideations, and denying auditory/visual hallucinations. Paranoid delusions were elicited. Insight and judgment were poor. The rest of his physical examination was within normal limits. He admitted that he uses methamphetamine, and his laboratory investigations showed urine toxicology screening result as positive for methamphetamine and Tetrahydrocannabinol. His ethanol level was not detected, and he denied using alcohol. There was no urinary tract infection, no gastrointestinal bleeding, no recent surgery, and he was not on any medication that could cause elevated NH_3 (Table).

A serum NH_3 level was checked out of concern for encephalopathy with the history of hepatitis C and was found to be elevated at 91 (Ref range less than 33 $\mu\text{mol/L}$).

Hepatitis panel showed positive result for Hepatitis C antibodies with normal prothrombin time,

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Case Reports

TABLE. Methamphetamine Intoxication Encephalopathy Associated with Hyperammonemia

	Patient 1: Mr. A	Patient 2: Mr. B	Patient 3: Ms. C
Age	27	27	23
Psychiatric and medical conditions related	HCV, substance abuse	Schizophrenia, substance abuse	Substance abuse, psychosis
Substance abuse	METH, THC	METH	METH, THC
Ammonia level on admission	91 umol/L	123 umol/L	38 umol/L
Did the ammonia level normalize?	Yes	Yes	Yes
Time of encephalopathy resolution	After 4 days from admission	After 4 days from admission	After 2 days from admission
Hospital length of stay	7 days	25 days	11 days
Final primary discharge diagnosis	Amphetamine-induced psychosis	Chronic paranoid schizophrenia, Amphetamine abuse	Substance-induced, psychosis, psychosis
Discharge medications	Multivitamins	Risperidone 3 mg BID	Olanzapine 15 mg QHS

HCV = hepatitis C virus; METH = methamphetamine; THC = tetrahydrocannabinol.

aspartate transaminase 132 (Ref range 6–58 unit/L), alanine transaminase 132 (Ref range 14–67 unit/L). The rest of his laboratory investigations were unremarkable. No blood gases were drawn.

He was started on lactulose for his elevated NH_3 and confusional state. He experienced significant improvement in his mental status after having 2 bowel movements, and became fully oriented; he was able to tell us more about his history, and his thoughts were more organized without delusions. Serum NH_3 levels normalized after 4 days, whereas transaminases remained elevated.

He was discharged only on multivitamins. A week later, he re-presented to the psychiatric emergency department with agitation and physical aggression in the context of methamphetamine intoxication; no test for the detection of NH_3 level was done at that time.

Case 2

Mr. B, a 27-year-old man with a history of schizophrenia and methamphetamine abuse and without a history of liver disease was brought to the psychiatric emergency department due to worsening behavior and nonadherence with his psychotropic medication (olanzapine 20 mg/d). He was admitted for treatment of suicidal ideation, homicidal ideation, psychotic delusions, and agitation.

He admitted to using methamphetamine nearly every day, he denied any complaints, he denied alcohol, there was no recent surgery, and he was not on any medication that could cause an elevated NH_3 .

His family reported that he was evicted from his apartment after an argument with the landlord where he became aggressive. Family also reported chronic history of methamphetamine abuse.

He was noted to be disheveled, disoriented, and inattentive (failed serial sevens and could not spell a 5-letter word world backwards on mental status examination). His cardiac, respiratory, and abdominal examinations were unremarkable and his vital signs were stable (no tachycardia, and blood pressure within normal limits).

His laboratory workup revealed significant hyperammonemia of 123 umol/L. Liver function tests were normal, so no hepatitis testing were done. There was no urinary tract infection. His electrocardiogram showed a new left bundle branch block, and he was transferred to the cardiology department for 2 days, where he had an echocardiogram that did not show a cardiomyopathy. He was put on a statin and aspirin. The cardiology team thought his cardiac problem may be caused by an electrical disturbance due to his drug abuse, especially methamphetamines.

After transfer back to the psychiatric department, he was less disoriented and less disorganized. An NH_3 level was re-ordered and found to be decreased to 73 umol/L. Communication, mental status, and orientation gradually improved over the next several days with resolution of the hyperammonemia; his agitation resolved, his attention was good, and he was able to provide his history in detail.

He had chronic delusions that did not improve with treatment, so he was discharged to a state psychiatric

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