Case Report

Non-cirrhotic Hyperammonemia: A Risk Factor for Altered Mental Status

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ABSTRACT

Hyperammonemia refers to a rise in the level of ammonia in the blood. Ammonia is a normal component of all body fluids and the body excretes excess ammonia as urea after synthesis in the liver by enzymes commonly called urea cycle enzymes. If ammonia builds up in the blood, it can cross the blood brain barrier and cause neurological disorders associated with hyperammonemia. Altered mental state is a medical term that describes any change in mental functioning that involves consciousness or cognition or both. Elderly patients are more likely to experience an altered mental state, mainly because they have multiple vulnerability factors, such as old age, dementia, comorbidity and functional dependence. A 64 years Indian male patient was admitted to hospital with the complaints of deterioration in mental status, aggressive behavior for about 1 week. His home medications include olanzapine 10 mg po BD, senna lax 8.6 mg 2 tablets before bed, docusate sodium 100 mg po 2 tablets before bed and sucralfate. The serum ammonia was 92 mmol/l on first day. Liver function tests were normal. He was treated with lactulose enema and halodol. The high level of ammonia in the blood and the rapid resolution of symptoms along with the reduction of its ammonia level in the blood lead us to suspect that hyperammonemia may have explained its presentation.

Key words: Hyperammonia, Neurological disorders, Altered mental state, Non-cirrhotic, Halodol, Lactulose.

INTRODUCTION

Hyperammonemia refers to a rise in the level of ammonia in the blood. Ammonia is a normal component of all body fluids and the body excretes excess ammonia as urea after synthesis in the liver by enzymes commonly called urea cycle enzymes. Ammonia in humans is generated by the bacterial hydrolysis of urea and other nitrogen compounds in the intestine, by the nucleotide cycle of purines and by the transamination of amino acids in skeletal muscles and other metabolic processes in the kidneys and liver. If ammonia builds up in the blood, it can cross the blood brain barrier and cause neurological disorders associated with hyperammonemia.[1] Altered Mental State (AMS) is a medical term that describes any change in mental functioning that involves consciousness or cognition or both. Clinically, patients can present a spectrum from lack of attention, confusion, impaired behavior, agitation, to coma. Elderly patients are more likely to experience an altered mental state, mainly because they have multiple vulnerability factors, such as old age, dementia, comorbidity and functional dependence.[2] The vulnerabilities of these patients can help change the mental state with some triggering factors, including infection, electrolyte abnormalities, organ failure, intoxication, thyroid dysfunction, dehydration, central nerve damage, trauma and drugs. The etiologies of primary hyperammonemia include enzymatic defects in the urea cycle, organic acidemias, fatty acid oxidation defects and transport defects of dibasic amino acids, which are commonly observed in children.[3] In adults, secondary hyperammonemia is more common, especially in the presence of liver disorders. It can also occur with normal liver function when Reye's syndrome disrupts the mitochondrial pathways.[4] Drugs such as valproic acid,[5] carbamazepine,[6] salicylate,[7] topiramate,[8] or cytotoxic agents.[9] In addition, renal tubular acidosis,[10] dilation

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of the urinary tract or infection of the urinary tract,[11] pregnancy and hypoglycine,[3] can contribute to non-hepatic hyperammonemia.

CASE PRESENTATION

A 64 years Indian male patient was admitted to geriatric department at Sagar Multispecialty Hospital, Jayanagar, Bangalore with the complaints of deterioration in mental status, aggressive behavior for about 1 week. He had difficulty in finding appropriate words and he had suicide ideation before admission. He scolded and tried to harm hospital staff during shifting to psychiatry male ward. He was severely anxious and was asking to go to bathroom several times per hour. He had no history of headache, head injury, chest pain, seizure, muscle pain, dyspnea, numbness or tingling. He was admitted previously for anxiety, depression and chronic constipation.

His home medications include olanzapine 10 mg p.o BD, senna lax 8.6 mg 2 tablets before bed, docusate sodium 100 mg p.o 2 tablets before bed and sucralfate. He had no known drug and food allergies. He lived at home with his wife and had a support network of 2 sons and children. His blood pressure was 136/72 mmhg; heart rate was 70 bpm, oral temperature was 97.2-degree F, oxygen saturation was 99% on air room and respiratory rate was 18 breaths per minute. His BMI was 22.3 kg/m^2. He was alert to name and was able to follow simple commands. His physical examination revealed that he was confused. Pin prick sensation was normal on both upper and lower extremities. His muscle strength was 3/5 on upper and lower extremities. He had no gaze palsies and his speech was not slurred. He had no joint swelling, pale sclera or tenderness.

The laboratory results of the patient are listed in Table 1. The serum ammonia was 92 mmol/l on first day. Liver function tests were normal. He doesn't have any history of taking habit forming drugs as informed by his family members. He is vegetarian, non-smoker and non-alcoholic. He was treated with lactulose enema and halodol. He experienced gradual improvement over 12 hr of admission but still had aggressive behavior. Repeat serum ammonia estimation after 24 hr was 52μmol/L. His body temperature was in the range of 97-99 degree F and he had no oxygen desaturation during hospitalization. On the third day of admission, the repeat serum ammonia estimation was 40μmol/L and the patient became more calm, alert and cooperative. The doctor confirmed that patient has come back to his baseline mental status and was discharged home with the addition of lactulose (30 ml orally twice daily) to his home medication. He followed up with his primary care doctor within one week after discharge.

Table 1: The laboratory results of the patient.

Tests	Day 1	Day 2	Day 3	Normal range
WBC	4.9	-	7.1	4.8-10.8 10^3 μL
RBC	5.01	-	5.04	4.4-5.9 10^6 μL
Hemoglobin	13.0	-	13.02	14-18 gm/dl
Platelet	140	-	144	130-400 10^3 μL
Ammonia*	92	52	40	9-33 μmol/L
Sodium	138	-	140	137-145 mmol/L
Potassium	3.8	-	4.0	3.5-5.0 mmol/L
Chloride	107	-	111	98-107 mmol/L
Glucose	108	-	96	75-110 mg/dL
BUN	15	-	19	9-21 mg/dL
ALP	52	-	55	38-126 IU/L
T. bilirubin	0.3	-	0.5	0.2-1.3 mg/dL
D. bilirubin	0.1	-	0.2	0.0-0.4 mg/dL
Uric acid	4.2	-	4.4	3.5-3.8 mg/dL
GFR	91	-	92	>90 ml/min
TSH	-	-	1.430	0.38-6.15 mIU/mL
Urine pH	7	-	-	4.6-8 pH units
Urine gravity	1.013	-	-	1.001-1.035
Urine Protein	Negative	-	-	>30 mg/Dl
WBC in urine	1	-	-	0-2/HPF
RBC in urine	1	-	-	0-1/HPF
Epithelial cell	2	-	-	0-3/HPF

DISCUSSION

In this study, the etiology was unknown. The high level of ammonia in the blood and the rapid resolution of symptoms along with the reduction of ammonia level in the blood lead us to suspect that the hyperammonemia may have explained his presentation. The patient had no anemia (13g/dl), his liver enzymes, blood urea nitrogen (BUN), creatinine were in the normal range. The filtration rate of the glomerula (GFR) has found greater than 91. The patient did not take any drugs that could contribute to hyperammonemia according to previous reports. His constipation was resolved with more stool softeners. There was no any problems with nausea, vomiting or urination were found. The patient had no drug-drug interactions and drug-food interactions which would have increased the level of ammonia in the blood. This implied that hyperammonemia in this patient was not hepatic. Patient has a history of anxiety, depression, dementia and chronic constipation.

In dementia, the alteration of the mental state is mainly irreversible and progresses slowly (months or years). Patients with dementia may have impaired cognition involving language, memory, learning, social cognition, executive functions or attention.[12]

CONCLUSION

In this case, the patient has presented confusion, but can answer the questions logically. He clearly knew he could not control his aggressive behavior. His agitation and aggressive behavior has occurred in the past two days, compared to her basic mental state. The patient received Haldol (haloperidol) to control aggressive behavior and lactulose to reduce serum ammonia. The patient's mental state improved significantly when the serum ammonia level returned to the normal range, even when Haldol was used less frequently. These suggested that hyperammonemia could be the cause of a severely altered mental state in this case and that the treatment of hyperammonemia may promote improvement in the altered mental state, especially when patients have hyperammonemia.

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CONFLICT OF INTEREST

All authors have declared that there are no conflicts of interest in relation to the subject of this study.

ABBREVIATIONS

AMS: Altered mental status; **BMI:** Body mass index; **BUN:** Blood urea nitrogen; **WBC:** White blood cells; **RBC:** Red blood cells; **TSH:** Thyroid stimulating agent; **GFR:** Glomerular filtration rate.

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