A CASE REPORT OF NONCIRRHOTIC HYPERAMMONEMIC ENCEPHALOPATHY IN AN ADULT

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Significance

Noncirrhotic hyperammonemia is a rare cause of acute deterioration of mental status where a late-onset inborn error of metabolism (IEM) is an important consideration because therapeutic outcome is promising.

Clinical Presentation

We report a 68 year old male with ventricular tachycardia with an implantable cardioverter defibrillator, chronic kidney disease and subclinical hypothyroidism, with a 1 week history of acute mental status deterioration. His maintenance medications include amiodarone, furosemide, ketoanalogues, carvedilol, rivaroxaban, levothyroxine.

Patient had unsustained regard with no abdominal pathology nor stigmata of chronic liver disease.

Management

Baseline serum ammonia was 209 ug/dL (normal 30-122 ug/dL), seronegative for Hepatitis B, C with adequate synthetic liver function and unremarkable triphasic CT scan of the abdomen. CT scan of the Brain and EEG were compatible with metabolic encephalopathy. Patient slowly improved on hepatic encephalopathic management and upon starting L-ornithine-L-arginine (LOLA), he exhibited sustained wakefulness and sent home stable.

Patient was readmitted after a month due to cellulitis causing poor compliance to oral medications with relapse of altered sensorium and hyperammonemia at 190 ug/dL. Once LOLA was resumed and infection resolved, patient regained alertness at serum ammonia of 104 ug/dL and was discharged stable.

Recommendations

Primary causes of noncirrhotic hyperammonemia are aberrations in the urea cycle. Our patient showing a sustained response to ammonia lowering management and LOLA has led us to suspect that hyperammonemia may have accounted for his presentation. Plans for urea cycle enzyme deficiency evaluation is underway.

Keywords

Case report, noncirrhotic hyperammonemia, encephalopathy, inborn error of metabolism

1. Significance

Ammonia, as a potent neurotoxin, may cause an acute, fluctuating and or progressive deterioration of mental status where in the etiology of serum ammonia elevation must be determined for therapeutic guidance. Rarely, hyperammonemia occurs without severe liver disease and late-onset inborn error of metabolism (IEM) remains to be an important consideration because it is highly responsive to medical management.

We will discuss a case of noncirrhotic hyperammonemia, its management and our recommendations.

There is no locally published case report at the time of submission of this paper.

2. Clinical Presentation and Management

We present and novel case of a 68 year old male patient with ventricular tachycardia and paroxysmal atrial fibrillation with implantable cardioverter defibrillator on a 10-year use of amiodarone, chronic kidney disease not on dialysis and subclinical hypothyroidism, presenting with a 1 week history of progressive deterioration of mental status. Premorbidly, the patient was independent on all activities of daily living until there were bouts of disorientation to person, place and time, verbalization of incomprehensible words with gradual increasing in somnolence which brought about difficulty in coordination of his motor skills and made him bed bound. There was no history of head trauma or fall, nor preferential use of his extremities. Appetite was poor due to change in mentation, however he had good daily bowel movements. His maintenance medications includes furosemide, ketoanalogues, carvedilol, rivaroxaban, levothyroxine. He had stable vital signs with no febrile episodes. He was easily arousable with name calling, had regard and able to follow simple commands at times due to difficulty in maintaining his alertness. He had no tremors had slurred speech, with power of extremities 3-4/5, had no neurological localizing signs, abdominal pathology nor stigmata of chronic liver disease.

His initial laboratory values are in Table 1.

He was seronegative for Hepatitis B, C, with adequate synthetic liver function and no signs of chronic liver pathology on triphasic CT scan of the whole abdomen and Hepatic artery, portal vein, inferior vena cava and hepatic veins color doppler. Plain CT scan of the Brain and modified barium swallow were unremarkable and EEG was compatible with metabolic encephalopathy

Patient slowly improved on hepatic encephalopathic management but then deteriorated again becoming lethargic and was readmitted after a month due to lower extremity cellulitis causing poor compliance to liver medications causing metabolic encephalopathy and hyperammonemia at 190 ug/dL with poor access to oral medications. Once LOLA was resumed and cellulitis resolved, patient once again showed significant improvement of mental status at serum ammonia of 104ug/dL and was sent home alert with sustained wakefulness with no motor deficits.

3. Recommendations

Ammonia's main route for detoxification is via the urea-cycle or thru the synthesis of glutamine from NH3 and glutamate via glutamine synthetase wherein elevations of NH3 may result when production exceeds the metabolic capacity of the liver.

Primary causes of hyperammonemia include congenital aberrations in the urea cycle, such as deficiencies of ornithine transcarbamylase (OTC) and argininosuccinate lyase leads to different severities of altered sensorium. The prevalence of which is 1:30,000 live births which is likely an under estimation because of unreported cases and death before diagnosis. There were several case reports about acute onset hyperammonemia from late-onset inborn errors of metabolism in previously healthy adults.

All these enzyme disorders are transmitted as autosomal recessive except OTC which is an X-linked trait.

OCT deficiency is the most common among urea-cycle disorders which presents from a range of complete absence of symptoms to acute neonatal coma. The characteristic of having a wide range of heterogeneity is hypothesized to be from a combination of genetic and environmental factors. Its presentation is caused by the toxic effects of ammonia to the brain cells. It is important to note that those whole have mild molecular changes can lead a functional life until a stressor triggers a hyperammonemic crisis which is highly responsive to management, offering a good outcome. Many conditions may precipitate hyperammonemia and most commonly cause by an intercurrent infection.

Management of hyperammonemia encompasses limitation of endogenous ammonia production by lactulose, enteral antibiotics by use of rifaximin, protein diet and ammonia elimination by use of L-ornithine L- aspartate, both of which were applied to our patient who subsequently showed a dramatic improvement after a few days of this combination therapy. Other cited management is the supply of urea-cycle substrates by use of arginine hydrochloride and L-carnitine or liver transplantation.

In our patient showing a sustained response to ammonia lowering management, control of infection and L-o-L-a; concomitant reduction of serum ammonia levels has led us to suspect that hyperammonemia may have accounted for his presentation. Plans for further work up include evaluation for urea cycle enzyme deficiency for the patient and possibly for his family.

References

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Table. Initial laboratory values

Test	Results	Normal Ranges
Hemoglobin (g/dL)	12.9	14.0-17.5
Hematocrit (%)	37	41.5-50.4
White blood cell (x103/uL)	5.99	4.4-11.0
Platelet count (/uL)	134,000	150,000-450,000
Serum creatinine (mg/dL)	1.27	0.73-1.18
Blood urea nitrogen (mg/dL)	31.43	8.4-25.77
Sodium (mEq/L)	138	136-145
Potassium (mEq/L)	4.16	3.5-5.10
Anti-Smooth Muscle Ab	Negative	Negative
PT INR, % activity	1.54, 54.6%	
Ammonia (mg/dL)	209.91	30.68-122.62
Alpha-Feto Protein (ng/mL)	2.21	0.9-8.83
CA 19-9 (U/mL)	<2.00	0.00-37.00
Ceruloplasmin (mg/dL)	34.00	20.00-60.00
Albumin (g/dL)	3.21	3.5-5.00
AST (U/L)	38.98	5.00-34.00
ALT (U/L)	12.84	5.00-55.00
Alkaline phosphatase (U/L)	230.91	40.00-150.00
GGTP (U/L)	26.73	12.00-64.00
Total Bilirubin (mg/dL)	2.03	0.20-1.20
Direct Bilirubin (mg/dL)	1.37	0.00-0.50
Indirect Bilirubin (mg/dL)	0.66	0.20-0.70