All that is Ammonia is not Cirrhosis: A Case of Hyperammonemic Encephalopathy and Anchoring Bias.

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BACKGROUND

Ammonia is a potent neurotoxin which is most implicated the development of Hepatic Encephalopathy in decompensated cirrhosis.

The incidence of hyperammonia in hepatic encephalopathy or fulminant hepatitis is estimated to be as high as 90%.

Anchoring bias is a cognitive bias that results from relying heavily in the first piece of information that one in provided about in a topic.

To educate about non-cirrhotic hyperammonemia and resultant anchoring bias.

CASE PRESENTATION

20-year-old Caucasian male presents as a transfer secondary to refractory seizures and PEA arrest.

- **Past medical history:** Cerebral Palsy, Cognitive Dysfunction, Lennox-Gastaut Syndrome, Pancreatic Insufficiency.
- **Labs on presentation: Ammonia 174 µmol/L**. Alkaline Phosphatase (Alk Phos) 594 IU/L, AST 35 IU/L, ALT 39 IU/L, Total Bilirubin (T bili) 1.5, INR 1.4.
- **Intervention:** L-ornithine-L-Asparagine → **Ammonia 311 µmol/L**
- **MRI/MRCP:** Moderate to severe hepatic steatosis, no splenomegaly, no presence of shunts.
- **Initial Evaluation** was negative for Hepatitis A, B and C, CMV, EBV, HSV, AIH, PBC, Wilson's Disease, A1AT deficiency.
  Plasma Amino acids: ↑ Glutamine & Ornithine.
  Urinary Amino acids: ↑ Orotic acid

  Ornithine Aminotransferase deficiency
- **Intervention:**
  - Dialysis initiated for rapid reduction in hyperammonemia.
  - Low protein tube feeds + L-carnitine supplementation.

CAUSES OF NON-CIRRHOTIC HYPERAMMONEMIC ENCEPHALOPATHY

Decreased ammonia elimination	Increased Ammonia Production
Inborn errors of metabolism • Urea cycle defects (OTC deficiency, OAT deficiency) • Organic aciduria • Carnitine deficiency	Increase muscle catabolism • Seizures • Starvation • Trauma
Spontaneous portosystemic shunt	Total Parenteral Nutrition
Portal venous thrombosis	Multiple Myeloma
Medications • Valproic acid • Glycine • Carbamazepine • Ribavirin • Sulfadiazine	Chemotherapeutic Agents • Cytarabine • Vincristine • Etoposide • L-Asparaginase • Cyclophosphamide 5 - Fluorouracil
	Infections • *Proteus mirabilis* • *Escherichia coli* • *Klebsiella*

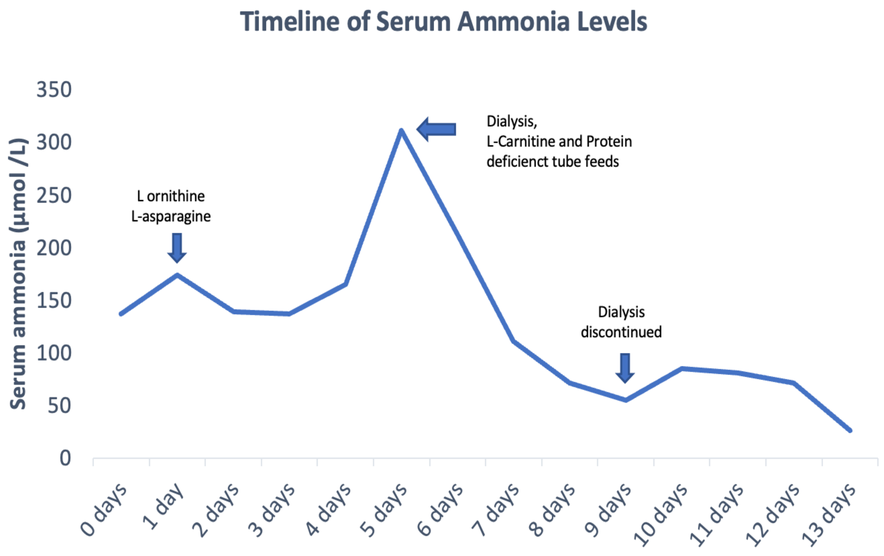

Figure 1: Timeline of Serum Ammonia Levels, and interventions.

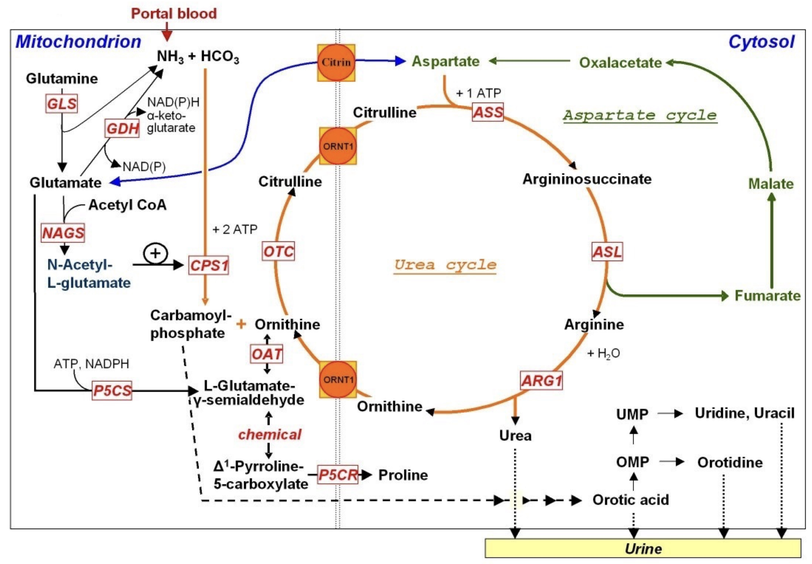

Figure 1: Schematic of the Urea cycle with rate limiting steps
GDH: Glutamate dehydrogenase, GLS: Glutaminase, NAD(P): nicotinamide adenine dinucleotide (phosphate), OAT: ornithine aminotransferase, OMP: orotidine monophosphate, P5CR: pyrroline-5-carbosylate reductase, P5CS – δ pyrroline-5-carboxylate synthetase, UMP: uridine monophosphate

DISCUSSION

- Ammonia levels by themselves hold no value in diagnosis, staging or prognosis for patients with chronic liver disease.
- Non-cirrhotic causes represent approximately 10% of the causes of Hyperammonemic Encephalopathy
- Hyperammonemia in an otherwise healthy individual should warrant investigation for non-cirrhotic etiologies.
- Urea cycle disorders are rare causes of non-cirrhotic hyperammonemia and usually present in childhood. However, some patients can be asymptomatic until a precipitating event such as infection, protein intake, or a medication unmasks the disorder.
- Although OTC deficiency in the most common urea cycle disorder, our patient had OAT deficiency which was likely unmasked by a recent change in tube feeds.

REFERENCES

- **The urea cycle and associated pathways.** Non-standard abbreviations include: GDH, glutamate dehydrogenase; GLS, glutaminase; NAD(P), nicotinamide adenine dinucleotide (phosphate); OAT, ornithine aminotransferase; OMP, orotidine monophosphate; P5CR, pyrroline-5-carboxylate reductase; P5CS, Δ¹-pyrroline-5-carboxylate synthetase; UMP, uridine monophosphate.
- Kalra, A. and Norvell, J.P. (2020), Cause for Confusion: Noncirrhotic Hyperammonemic Encephalopathy. Clinical Liver Disease, 15: 223-227. https://doi.org/10.1002/cld.929