

Question 20 – Week of December 17

You are asked to consult on a 40 year old man hospitalized for new onset of confusion. He was found to have venous ammonia level of 150 $\mu\text{mol/L}$ and responded to treatment with lactulose, a negative drug screen, vitamin B12 and folate and TSH, and a normal head CT. consultation EEG did not reveal focal activity and neurology consultation was unrevealing.

He has a long standing history of bipolar disorder that has been well controlled with valproic acid, diet controlled diabetes and hypertension treated with hydrochlorothiazide. On exam he appears well, he has a BMI of 34, his abdomen is non-distended, without hepatosplenomegally. His skin is warm and dry with the exception of mild palmar erythema.

Other laboratory studies available include: white blood cell 5.6, hemoglobin 13, platelet 160, sodium 135, potassium 3.1, creatinine 1.2, ALT 40, AST 45, Alkaline phosphate 98, total bilirubin 0.9, INR 1.1, vitamin D level was 14. An abdominal ultrasound revealed increased hepatic echogenicity, with spleen size at upper limits of normal and no ascites. The following clinical scenarios or factors could explain the hyperammonemia and encephalopathy in this case except?:

- A. He has undiagnosed cirrhosis due to non-alcoholic fatty liver disease
- B. He has an undiagnosed portal vein thrombosis
- C. Long-term treatment with valproic acid
- D. Undiagnosed urea cycle disorder
- E. He has undiagnosed zinc deficiency

Answer: E

Both cirrhotic and non-cirrhotic portal hypertension can be associated with hepatic encephalopathy. Valproic acid has been associated with hyperammonemia even after long-term treatment and in the absence of supra-therapeutic serum levels. (1)

Urea cycle disorders are increasingly diagnosed later in life and can present with hyperammonemia and encephalopathy often with a background history of neuropsychiatric disease. (2) Zinc deficiency has been associated with hyperammonemia, but only in patients with sickle cell anemia. (3)

References:

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2. Serrano M, Martins C, Pérez-Dueñas B, Gómez-López L, Murgui E, Fons C, García-Cazorla A, Artuch R, Jara F, Arranz JA, Häberle J, Briones P, Campistol J, Pineda M, Vilaseca MA. Neuropsychiatric manifestations in late-onset urea cycle disorder patients. *Journal of Child Neurology*. 2010 Mar;25(3):352-8.
3. Prasad AS, Rabbani P, Warth JA. Effect of zinc on hyperammonemia in sickle cell anemia subjects. *Am J Hematol*. 1979;7(4):323-7.