A Mysterious Case Report of Acute Liver Failure: Possible Defect in Ammonia Metabolism

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Introduction

- Acute liver failure is defined as severe, acute liver injury causing with encephalopathy and impairment of synthetic function in a patient without cirrhosis or pre-existing liver disease.
- Acute liver failure may result from a wide variety of causes including infections, hepatotoxic drugs, hypoperfusion and autoimmune diseases. Less commonly, metabolic disorders may be the culprit. In some cases, however, the cause of acute liver failure remains unknown.
- We present the case of a young male with acute liver failure of unknown etiology, possibly resulting from a non-specific defect in ammonia metabolism.

Case Description

- 21-year-old male with no significant past medical history was admitted to our transplant liver center with acute liver failure
- The patient was visiting New Jersey from Ohio. Two days prior to admission, he ate at a restaurant and developed nausea the next morning. Later in the afternoon, he was found incoherent covered in coffee-ground emesis.
- In the hospital, he was found to have elevated AST/ALT 938/875 U/L, extremely elevated ammonia of 2000 µmol/L, elevated lactic acid, and an INR of 4.87.
- Hospital course was complicated by development of acute kidney injury and cerebral edema.
- He was started on continuous renal replacement therapy due to the hyperammonemia and metabolic acidosis and was intubated.
- Extensive work-up of his acute liver failure included viral panels to assess for hepatitis, CMV, EBV, and HSV which were all negative. Ceruloplasmin, alpha-1-antitrypsin, AMA, and ASMA testing were all unyielding.
- His notable hyperammonemia raised suspicion for urea cycle disorder.
- However, despite having an abnormal amino acid profile (see table 1), genetic testing showed no conclusive explanation.

Amino Acid	Value	Reference Range
Aspartate	2.2 umol/L	0.0 - 7.4 umol/L
Asparagine	**86.0 umol/L**	29.5 - 84.5 umol/L
Glutamate	47.1 umol/L	18.1 - 155.9 umol/L
Glutamine	**1021.9 umol/L**	372.8 - 701.4 umol/L
Proline	**543.9 umol/L**	84.8 - 352.5 umol/L
Glycine	337 umol/L	144.0 - 411.0 umol/L
Alanine	362.9 umol/L	209.2 - 515.5 umol/L
Citrulline	**52.2 umol/L**	15.6 - 46.9 umol/L
Cystine	22 umol/L	15.8 - 47.3 umol/L
Homocitrulline	<0.5 umol/L	0.0 - 1.7 umol/L
Cystathionine	**22.0 umol/L**	0.0 - 0.7 umol/L
Argininosuccinate	<0.1umol/L	0.0 - 3.0 umol/L
Beta-Alanine	4.1 umol/L	1.1 - 9.0 umol/L
Ornithine	**178.1 umol/L**	30.1 - 101.3 umol/L
Lysine	**424.7 umol/L**	94.0 - 278.0 umol/L
Histidine	**123.1 umol/L**	47.2 - 98.5 umol/L
Arginine	**210.0 umol/L**	36.3 - 119.2 umol/L

Table 1. Plasma Amino Acid Profile

Case Description

- The patient ultimately underwent an orthotopic liver transplantation which resulted in significant clinical improvement in his neurologic status and resolution of his hyperammonemia. He was discharged on post-transplant therapy.
- Liver biopsy pathology revealed extensive degenerative changes and confluent necrosis.

Discussion

- The etiology of ALF remains undiagnosed in approximately 20-40% of cases.
- Although the availability of liver transplantation has substantially advanced the management of ALF, identification of the underlying cause significantly influences determination of prognosis, management approach, and the likelihood of recurrent liver failure, especially in cases of suspected metabolic disorders.
- The continued pursuit of potential causes of ALF will aid in making life-saving decisions.

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