

CASE STUDY ON HEPATIC ENCEPHALOPATHY

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ABSTRACT

Hepatic Encephalopathy (HE) is broadly defined as a reversible and metabolically induces neuropsychiatric complication, often associated with cirrhosis. Manifestations mainly occur due to the accumulations of toxic substances in the liver, which are actively removed by the liver. The present case study deals with the study of a 70 years female patient, admitted with the complaints of confused and disoriented conditions. It was also accompanied by nausea, vomiting, low grade intermittent fever, pedal swelling, anorexia and also generalized weakness. Laboratory tests performed included complete sodium and potassium (serum), blood count, urea and creatinine tests, liver function tests, plasma ammonia and also the USG of whole abdomen. The reports investigated diffusely hyper echoic and coarse echo texture, thickened gall bladder and also splenomegaly. The final diagnosis reported was primary HE, along with esophageal candidiasis, hyperammonemia, hypothyroidism, hypernatremia, Parkinsonism and also lower respiratory tract infection.

KEYWORDS: HE, Hyper echoic, splenomegaly, hyperammonemia.

INTRODUCTION

The liver is the most important organ in the body, known for the well functioning and the active metabolism of all the active nutrients and its excretion from the body. Any disturbance in the homeostasis in liver, maybe termed as Acute Liver Failure (ALF) or chronic liver disease (cirrhosis), which may extensively lead to extra hepatic manifestations and where encephalopathy maybe ranked as one of the primary manifestations.

DEFINITION

Hepatic Encephalopathy (HE)^[1] is defined as a reversible and metabolically induced neuropsychiatric complication, most commonly associated with cirrhosis. The main reason for its manifestation is due to the accumulation of toxic substances in the blood stream, which are normally removed by the liver.

Attacks are often precipitated due to inter current problems, such as infections or constipations. HE is often reversible with treatment, often associated with suppressing the production of toxic substances in the intestine. This is commonly achieved by the administration of laxatives (e.g. Lactulose) or with certain non-absorbable antibiotics. The respective treatment procedure, may improve the underlying conditions and symptoms, but in case of ALF, the onset of encephalopathy may indicate the need for liver transplant.

CLASSIFICATION OF HE^[1,2]

According to veterinary means, the method for classification maybe given as follows:

- 1) **Acute encephalopathy:** It is generally rapidly progressive over a short course and is a complication of acute liver. This type of HE is a sign of terminal liver failure and often occurs in patients with acute fulminant viral hepatitis, toxic hepatitis etc.
- 2) **Chronic Encephalopathy:** It occurs multiple times and requires long-term treatment to minimize and prevent symptoms during intervening periods. Cirrhosis patients having extensive portal collateral circulation, typically experience such type of HE. Chronic HE is a sign of deterioration caused by cirrhosis, typically resulting due to alcoholism or hepatitis.
- 3) **Chronic cerebral degeneration and myelopathy:** It maybe characterized by permanent neurological abnormalities that don't respond well to treatment. It can affect a person's ability to walk or stay balanced. Tremors maybe present, similar to that of Parkinson's disease.

STAGES OF HE

There are 4 dominant stages described in HE. They maybe elucidated as follows:

- 1) **Stage 1:** Symptoms in this stage affect sleep pattern and may include anxiety, depression and restlessness.
- 2) **Stage 2:** It is often marked by personality changes and the ability to complete mental tasks is often impaired and disorientation may occur.

3) **Stage 3:** In this stage the behavior is observed to become bizarre. Aggression and rage are associated as common problems. Speech becomes difficult to understand.

4) **Stage 4:** During this stage the patient leads to coma and also becomes unresponsive to pain stimuli.

SYMPTOMS

The early stages of encephalopathy include the following symptoms:

- Musty or sweet odor breath (foetor hepaticus)
 - Changes in the sleep pattern
 - Changes in thinking
 - Mild confusion
 - Changes in mood and personality
 - Lack of concentration and fine motor skills are also impaired, especially writing
- Severe symptoms of HE includes:
- Abnormal movements of limbs
 - Agitation and excitement
 - Drowsiness or confusion
 - Dramatic changes to behavior and personality
 - Slow movements
- The final stage is often marked by the progression to coma

PATHOGENESIS^[4]

According to various studies as proposed by different investigators, it has been concluded that hyperammonemia, maybe regarded as the main factor responsible for HE. Ammonia is the main substrate that conducts a number of enzymatic reactions in the brain and is also a product for a number of reactions. Hyperammonemia often influences the normal regulation of the BBB, influencing the passage of various molecules through it (BBB). This often results in the impaired functioning of GABA-ergic, serotonergic, glutamatergic neurotransmission. Increased ammonia often causes cerebral edema, where massive amount of ammonia is delivered to astrocytes, resulting in the stockpiling of glutamine inside the cell bodies. The excess stockpile of intracellular glutamine causes massive osmotic drag and astrocytes begin to swell. The swelling often results in the increased distance between the capillaries and neurons resulting in nutrient deficient defect. This ultimately results in the impairment of acutely encephalopathy patients.

TREATMENT

There are a plethora of treatment regimens, in targeting the various severities of HE. The reduction of plasma ammonia remains as the primary objective, according to which several novel strategies have been introduced. The various postulates may be given as under:

- **Diet:** A diet with adequate consumption of protein is essential, in order to maintain a stable body weight. Branched chain ammonia acid are also included as

dietary supplements, they are useful in maintaining and restoring muscle mass in advanced liver disease.

- **Lactulose/Lactitol:** They are disaccharides that are not absorbed from the digestive tracts. They help in reducing the ammonia level by converting them into in absorbable ammonium ions and increase transit of bowel content through gut, in a way to relieve constipation, one of the prior reasons for encephalopathy.
- **Antibiotics:** Intestinal urease positive bacteria to gut ammonia production takes place mainly in the colon, which favors enhanced ammonia diffusion. Oral, non-absorbable, antibacterial agents like Neomycin, Rifampin have been popularly used to kill susceptible ammonia genic bacterial species. Rifampin is proven efficacious with a superior safety profile.
- **Lola:** Preparation of **L-ornithine and L-aspartate (Lola)** is used to increase the generation of urea cycle. This is a metabolic pathway that removes ammonia by turning it into neutral substance urea.

CASE STUDY

A 70 year female patient was admitted near Kolkata. She was experiencing generalized weakness and anorexia, shortness of breath for the past one week. She also had complaints of confusion and disorientation, nausea and low grade intermittent fever. Laboratory tests included complete blood count, liver function tests, plasma ammonia levels, the results of which came out to be significantly abnormal. Hence, complicating the respective case. The BP of the patient was reported to be 130/80 and the pulse rate was found to be 88 beats/minute.

Liver function tests revealed serum albumin 3gm/dl (normal range reported to be 3.50-5.00), AST was 37 U/L (reference range was reported to be 14-36), Creatinine (serum) was 1.23 mg/dl (normal range is 0.70-1.20), bilirubin content (total) was 2.70 mg/dl (reference range is 0.20-1.30), alkaline phosphatase (ALP) was reported to be 115 U/L (the reference of which is 38-126). The plasma ammonia was reportedly alarmingly high i.e. 112 μ mol/L (reference range of which is given as 9.00-30.00 respectively). Sodium level was reported as 130 (normal range is 135-148), potassium level was 4.20 (normal range was 3.50-5.30). Hematology reports suggested Hb level to be 10.3 gm/dl, platelet count was 0.95, neutrophil was 79%, lymphocyte was 16% and Eosinophil was 0.1.

Reduced level of serum albumin, abnormal elevation of liver enzymes (i.e. AST, ALP) and hyperammonemia, indicated H.E. So, she was recommended CT-scan and ultra sound. USG of the whole abdomen investigated diffusely hyper echoic^[8] and coarse echo texture of liver, indicating diffuse liver disease. It also reported diffusely thickened gall bladder and splenomegaly. Thus, hepatic encephalopathy and splenomegaly were reported.

On the basis of medical investigation, she was advised to consume balanced diet, medication included thyrox 100 mcg: 1 tablet once daily before breakfast given to continue, tablet syndopa 110 mg: 1 tablet thrice daily, tablet deriphylline retard 300 mg: 1 tablet daily, tablet syscan 150 mg: 1 tablet twice a day for a period of 10 days, tablet Mucinac 600 mg: 1 tablet daily for a period of 7 days, Hepameraz sachet: 1 sachet twice a day for a period of 10 days, tablet Augmentin (1 gram): 1 tablet twice a day for a period of 5 days, Tablet rifagut 400 mg: 1 tablet thrice a day for a period of 5 days.

Syrup Duphalac 20 ml, twice a day. After a span of 10 days the medicines were reviewed and reduced accordingly.

After a period of 30 days, patient was observed to develop edema, as she was not responding to diuretic medication. Hepatologists recommended abdominal paracentesis, to draw out ascetic fluid. After a few episodes, conditions deteriorated, marked with low sensorium and hyperammonemia. Liver functioning tests were also abnormal. Being a geriatric patient, liver transplant was not advisable; hence Hepatologists recommended utmost clinical care as the only resort.

DISCUSSION

This is the case study of a geriatric patient, who was suffering from hepatic encephalopathy. The dose regimen was designed to prevent further manifestations to the liver.

Hepameraz sachet^[9] was given in order to metabolize the ammonia to urea, in a way of controlling hyper ammonia. Rifagut was given in order to kill susceptible ammonia genic species. Augmentin was introduced to treat the bacterial species. Deriphylline retard was administered to prevent buccal congestion and Mucinac was given mucolytic and also to prevent the infection of microbial contaminants. Duphalac was given for easy bowel transit and prevent constipation, which is regarded as the prior reason for encephalopathy.

Apart from these, patient was also treated with thyrox and syndopa respectively, due to reported complaints of hypothyroidism and Parkinsonism respectively.

CONCLUSION

The given study concluded the requirement for complete and conservative medical profile. Incomplete treatment maybe fatal as it causes severe exposure to the disease. HE as our study suggests precipitates due to the accumulation of toxic substances in the blood stream which are usually removed by the liver.

HE is reversible with treatment. It relies on suppressing the production of toxic substances in the intestine especially ammonia. It is commonly done using laxative or with non-absorbable antibiotics. The report mainly

emphasizes on the need of good clinical evaluation by qualified therapists and also the implementation of appropriate investigative studies.

RECOMMENDATION

Patients suffering from HE should receive prophylactic antibiotics and also have the essential investigative studies performed within 24 hrs. Hyperammonemia should be controlled via suitable medicaments and constipation should be strictly avoided using proper laxatives. Ascites should be treated with balanced diet and also with reduced amounts of salt, in case of fluid retention.

REFERENCES

1. Prakash R, Mullen K.D. *Nat. Rev. Gastroenterology, Hepatol*, 2010; 7: 515-525.
2. Andres T. Blei, Juan Cordoba. The Practice Parameters Committee of American College of Gastroenterology, "Hepatic Encephalopathy". *The American Journal of Gastroenterology*, Vol. 96(7): 2001.
3. R. Muhammad, A. Zubair, A. Hassan, Shanulqadir, U. Muhammad, Case Study of Patient With Liver Cirrhosis, 2016; 3: 13-16.
4. M. Irena Ciecko, S. Malgorzata, S.Agnieszka, M.Tomasz, Pathogenesis of Hepatic Encephalopathy, *Gastroenterology Research and Practice*, 2012.
5. G. Wright, A. Chatree, R. Jalan, Management of Hepatic Encephalopathy, *International Journal of Hepatology*, 2011.
6. S. Mina, C. William, Hepatic Encephalopathy, *Disease Management*.
7. Savlan I, L. Valentina, V. Jonas, Concise Review of current concepts on nomenclature and pathophysiology of Hepatic Encephalopathy, 50(2): 2014.
8. Dr. W. Yuranga, et al. Hyper echoic Liver Lesions, *Radiopaedia.org*
9. L- ornithine- L-aspartate granules (Hepameraz® Sachets) for Hepatic Encephalopathy, *Interface Pharmacist Network, Specialist Medicines*.
10. G. Matteo et al., Prevention and Treatment of Hepatic Encephalopathy: Focusing on gut micro biota, *World Journal of Gastroenterology*, 2012; 18(46): 6693-6700.