Hepatic Encephalopathy (Portal-Systemic Encephalopathy)

Hepatic encephalopathy is a neuropsychiatric syndrome caused by liver disease.

It most often results from high gut protein or acute metabolic stress (eg, GI bleeding, infection, electrolyte abnormality) in a patient with portal-systemic shunting. As it progresses, confusion is followed by a coma.

Confusion needs to be differentiated from delirium tremens and Wernicke's encephalopathy, and coma from a subdural hematoma, which can occur in alcoholics after a fall

Features include :

- Changes of intellect,
- Personality,
- Emotions and
- Consciousness, with or without neurological signs

Classification of hepatic encephalopathy

Two broad categories of hepatic encephalopathy are
-Covert (Covert hepatic encephalopathy) and
*-Overt (Overt hepatic encephalopath*y

Covert Hepatic Encephalopathy is particularly associated with poor outcomes

Hepatic encephalopathy is also classified into three types based on the disease state of the liver, as follows:

Type A: Hepatic encephalopathy associated with acute liver failure
Type B: Hepatic encephalopathy associated with a portosystemic bypass with no intrinsic hepatocellular disease
Type C: Hepatic encephalopathy associated with cirrhosis and portal hypertension or portosystemic shunts.

Causes

Portal-systemic encephalopathy may occur in fulminant hepatitis caused by viruses, drugs, or toxins.

It most commonly occurs in cirrhosis or other chronic disorders when extensive portal-systemic collaterals have developed as a result of portal hypertension.

Encephalopathy also follows portal-systemic anastomoses, such as surgically created anastomoses connecting the portal vein and vena cava (portocaval shunts, transjugular intrahepatic portosystemic shunting [TIPS]).

Signs and symptoms

The degree of encephalopathy can be graded from 1 to 4, depending on these features, and this is useful in assessing response to therapy

When an episode develops acutely, a precipitating factor may be found.

The earliest features are very mild and easily overlooked but, as the condition becomes more severe, apathy, inability to concentrate, confusion, disorientation, drowsiness, slurring of speech and eventually coma develop.

Convulsions sometimes occur.

Clinical Examination findings

The examination usually shows a ?apping tremor (asterixis), inability to perform simple mental arithmetic tasks or to draw objects such as a star (constructional apraxia; and, as the condition progresses, hyper-re?exia and bilateral extensor plantar responses.

Hepatic encephalopathy rarely causes focal neurological signs; if these are present, other causes must be sought.

Fetorhepaticus, a sweet musty odor to the breath, is usually present but is more a sign of liver failure and portosystemic shunting than of hepatic encephalopathy.

Rarely, chronic hepatic encephalopathy (hepatocerebral degeneration) gives rise to variable combinations of cerebellar dysfunction, Parkinsonian syndromes, spastic paraplegia, and dementia.

West Haven Classification System Grading Of Symptoms

Grade 0

- Minimal hepatic encephalopathy,
- Lack of detectable changes in personality or behavior;
- Minimal changes in memory, concentration, intellectual function, and coordination;
- Asterixis is absent.

Grade 1

- Trivial lack of awareness,
- shortened attention span,
- Impaired addition or subtraction;
- Hypersomnia,
- Insomnia, or inversion of sleep pattern;
- Euphoria, depression, or irritability;
- Mild confusion;
- Slowing of the ability to perform mental tasks

Grade 2

- Lethargy or apathy;
- Disorientation;
- Inappropriate behavior,
- Slurred speech;
- Obvious asterixis
- Drowsiness, lethargy, gross deficits inability to perform mental tasks,
- Obvious personality changes,
- Inappropriate behavior, and intermittent disorientation, usually regarding time

Grade 3

- Somnolent but can be aroused,
- Unable to perform mental tasks,
- Disorientation about time and place,
- Marked confusion; amnesia,
- Occasional fits of rage,
- Present but incomprehensible speech

Grade 4

Coma with or without response to painful stimuli

Pathophysiology of hepatic encephalopathy

Hepatic encephalopathy is thought to be due to a disturbance of brain function provoked by circulating neurotoxins that are normally metabolized by the liver.

Accordingly, most affected patients have evidence of liver failure and portosystemic shunting of blood, but the balance between these varies from individual to individual.
Some degree of liver failure is a key factor, as portosystemic shunting of blood alone hardly ever causes encephalopathy.

The ‘neurotoxins’ causing encephalopathy is unknown, but they are thought to be mainly nitrogenous substances produced in the gut, at least in part by bacterial action.

These substances are normally metabolized by the healthy liver and excluded from the systemic circulation.
Ammonia has traditionally been considered an important factor.

Recent interest has focused on ?-aminobutyric acid (GABA) as a mediator, along with octopamine, amino acids, mercaptans and fatty acids that can act as neurotransmitters.

The brain in cirrhosis may also be sensitized to other factors such as drugs that can precipitate hepatic encephalopathy
Disruption of the function of the blood-brain barrier is a feature of acute hepatic failure and may lead to cerebral edema.

Precipitating Factors for hepatic encephalopathy

In patients with chronic liver disease, acute episodes of encephalopathy are usually precipitated by reversible causes.

The most common are the following:

- Metabolic stress (eg, infection; electrolyte imbalance, especially hypokalemia and dehydration)
- Use of diuretic drugs
- Disorders that increase gut protein (eg, GI bleeding, high-protein diet)
- Nonspecific cerebral depressants (eg, alcohol, sedatives, analgesics)

Diagnosis and Investigations

The diagnosis can usually be made clinically, but when doubt exists.

An electroencephalogram (EEG) shows diffuse slowing of the normal alpha waves with the eventual development of delta waves.

The arterial ammonia is usually increased in patients with hepatic encephalopathy. However, increased concentrations can occur in the absence of clinical encephalopathy, rendering this investigation of little diagnostic value.

Treatment

The principles are to treat or remove precipitating causes and to suppress the production of neurotoxins by bacteria in the bowel.

Dietary protein restriction is rarely needed and is no longer recommended as first-line treatment because it is unpalatable and can lead to a worsening nutritional state in already malnourished patients.

Lactulose (15–30 mL 3 times daily) is increased gradually until the bowels are moving twice daily. It produces an osmotic laxative effect, reduces the pH of the colonic content, thereby limiting colonic ammonia absorption, and promotes the incorporation of nitrogen into bacteria.

Rifaximin (400 mg 3 times daily) is a well-tolerated, non-absorbed antibiotic that acts by reducing the bacterial content of the bowel and has been shown to be effective.

Rifaximin is usually preferred because neomycin is an aminoglycoside, which can precipitate ototoxicity or nephrotoxicity.

It can be used in addition, or as an alternative, to lactulose if diarrhea becomes troublesome.

Sedation deepens encephalopathy and should be avoided whenever possible

Chronic or refractory encephalopathy is one of the main indications for liver transplantation

zinc supplementation is sometimes helpful.