Neurologic Presentations of Hepatic Disease

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- Hepatic encephalopathy • ^{1}H-MR spectroscopy
- Hepatic cirrhosis • Hyperammonemia

Hepatic encephalopathy (HE) is a neuropsychiatric syndrome that develops in the context of portosystemic venous shunting, in the presence or absence of intrinsic hepatic disease.[1] HE is clinically characterized by altered sensorium and a spectrum of neuropsychiatric abnormalities. Several hypotheses have been proposed to explain the underlying pathogenic mechanisms of altered brain function associated with advanced hepatic disease and portosystemic shunting. HE may lead to coma and death; however, in many cases it is reversible. This article discusses the most recent developments in understanding the pathophysiology of HE and its diagnosis and management.

EPIDEMIOLOGY AND CLINICAL FEATURES

Amodio and colleagues[2] reported a 20% prevalence of cognitive abnormalities diagnosed by neuropsychological evaluation in patients with hepatic cirrhosis. Two other studies from the United Kingdom[3] and Japan[4] on the rate of development of HE in patients who underwent transjugular intrahepatic portosystemic shunts reported rates of 29.9% and 52%, respectively. HE is a frequent complication of advanced cirrhotic hepatic disease, and its development is often regarded as an indication for hepatic transplantation. Apart from neuropsychiatric abnormalities, other clinical manifestations of advanced hepatic disease that usually co-occur with HE include ascites, jaundice, and gastrointestinal (GI) variceal hemorrhage. Clinically, and based on the underlying hepatic pathology, HE is categorized into 3 major groups[5]: type A, encephalopathy from acute liver failure (ALF); type B, in which encephalopathy is caused by portosystemic shunting in the absence of intrinsic hepatic disease; and type C, in

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which HE occurs with hepatic cirrhosis and portal hypertension with portosystemic shunting. A list of potential precipitating factors of HE is given in **Box 1**.

Patients with HE present with a wide range of clinical manifestations ranging from subtle changes in mentation with memory dysfunction to confusion with somnolence and disorientation and, finally, to stupor and coma. Often patients may have minimal hepatic encephalopathy (MHE), which is characterized by normal neurologic findings except for mild cognitive difficulties usually associated with attention deficits detected only by neuropsychological testing.[1] Those with overt HE typically have symptoms that begin with mental confusion and decreased motor activity. Often within a few days, patients may progress to a comatose state. Patients with HE may demonstrate flapping tremor or asterixis, and the smell of fetor hepaticus may be detected in their exhaled breath. Extrapyramidal symptoms may develop, such as tremor and various movement disorders. Occasionally seizures and increased intracranial pressure (ICP), with corticospinal tract involvement, occur. In some patients, rigidity may be observed

Box 1
List of precipitating factors for development of HE

- Elevated nitrogen load due to
  - GI bleeding
  - Uremia
  - Excessive dietary protein intake
- Electrolyte abnormalities
  - Hypokalemia
  - Acidosis
  - Hyponatremia
- Infective processes
  - Urinary tract, skin, or respiratory infections
  - Spontaneous bacterial peritonitis
  - *Helicobacter pylori* infection
- Superimposed hepatic injury
  - Drug-induced liver disease
  - Viral hepatitis
- Drugs
  - Acetaminophen
  - Valproic acid
  - Benzodiazepines
  - Narcotics
  - Diuretics
  - Anesthetic agents (eg, halothane)
  - High-dose acetylsalicylic acid
  - Alcohol abuse
- Terminal hepatic disease and hepatocellular carcinoma