clinical suspicion is warranted along with a systematic approach to diagnosis based on fulfillment of certain criteria.

The diagnostic criteria for HRS as defined by the International Ascites Club Consensus Workshop in 2007 include the following:

1. Cirrhosis with ascites
2. Serum creatinine level higher than 1.5 mg/dL (133 μmol/L)
3. Lack of improvement in the serum creatinine level (to ≤1.5 mg/dL or ≤133 μmol/L) after at least 2 days of diuretic withdrawal and volume expansion with albumin (1 g/kg of body weight per day, up to a maximum of 100 g/day)
4. Absence of shock
5. Lack of current or recent treatment with nephrotoxic drugs
6. Absence of parenchymal kidney disease as indicated by proteinuria of more than 500 mg/day, microhematuria (>50 red blood cells per high-power field), or abnormal renal ultrasonographic findings.

HRS has two types, type 1 and type 2. HRS type 1 is characterized by rapid deterioration of kidney function with doubling of the initial creatinine to greater than 2.5 mg/dL within 2 weeks or less. HRS type 2 produces a more moderate renal failure that is slowly progressive.

An Acute Kidney Injury Network criterion redefines acute renal failure and is generally recognized by criticare specialists and nephrologists. This criterion divides kidney injury into three stages. Stage I is defined as an increase in serum creatinine of more than or equal to 0.3 mg/dL (≥26.4 μmol/L) or urine output of less than 0.5 mL/kg/hour for longer than 6 hours. Stage II is an increase in serum creatinine of more than 2 to 3 folds from baseline or urine output of less than 0.5 mL/kg/hour for longer than 12 hours. Finally stage III is a rise in serum creatinine of more than 3 fold from baseline or serum creatinine of more than or equal to 4.0 mg/dL. This can also be characterized by either oliguria (output <0.3 ml/kg/hour) for 24 hours or anuria for 12 hours. The key is to detect renal failure early and start appropriate therapy promptly in order to prevent progression.

Typically, the kidneys are histologically normal and can regain normal function in the event of recovery of liver function (e.g., after liver transplantation). Severe cortical vasoconstriction has been demonstrated angiographically, and such vasoconstriction reverses when these kidneys are transplanted into patients who do not have cirrhosis.

Treatment and Prognosis

The mortality rate is high in HRS, and so prevention is important. In all patients with cirrhosis, precipitating factors (e.g., diuretics, lactulose, nonsteroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors) should be avoided if possible. Patients should be promptly diagnosed and treated for any signs of SBP, and colloid (albumin) should be administered if rising creatinine levels are observed. Prevention of variceal bleeding should also be optimized by primary and secondary prophylaxis.

Studies have shown an increased mortality rate with AKI among hospitalized cirrhotic patients. Several medical therapies are currently under review, including use of terlipressin, a vasopressin V_1 receptor analogue, in combination with albumin for type 1 HRS. Other studies have evaluated the combination of octreotide and midodrine (an α-adrenergic agonist) and intravenous albumin. Placement of TIPS has also been reported to stabilize or even improve renal function, mainly in patients with type 2 HRS. However, a significant limitation of TIPS is the possibility of worsening hepatic function in decompensated cirrhosis. Liver transplantation has become the accepted treatment for HRS because it is the only known therapeutic intervention that reverses the process. It is limited by rapid progression of HRS and lack of available organs.

HEPATIC ENCEPHALOPATHY

Definition

HE is a complex, reversible neuropsychiatric syndrome that occurs in patients with chronic liver disease, portal hypertension, or portosystemic shunting. HE is also seen in patients with acute liver failure. HE develops in about 30% to 45% of cirrhotic patients, and when it is present, the survival probability is approximately 23% at 3 years.

Pathophysiology

The pathogenesis of HE in the setting of cirrhosis is thought to be multifactorial and may differ in acute and chronic liver disease. Contributors include the inadequate hepatic removal of potential endogenous neurotoxins, altered permeability of the blood-brain barrier, and abnormal neurotransmission. Elevation of blood ammonia levels, derived from both amino acid deamination and bacterial hydrolysis of nitrogenous compounds in the gut, has been the best studied factor, but its specific role in the pathogenesis of HE remains uncertain. Many other potential contributors to HE have been investigated, including increased tone of the inhibitory GABAA/benzodiazepine neurotransmitter system, activation of the astrocytic 18-kDa translocator protein (PTBR), production of endogenous benzodiazepine-like compounds, altered cerebral metabolism, zinc deficiency, increase in serotonin levels, up regulation of H1 receptors, altered melatonin production, and deposition of manganese in the basal ganglia.

Clinical Presentation

The clinical features of HE include disturbances of higher neurologic function such as intellectual and personality disorders, dementia, inability to copy simple diagrams (constructional apraxia), disturbance of consciousness, disturbances of neuromuscular function (asterixis, hyperreflexia, myoclonus), and, rarely, a Parkinson-like syndrome and progressive paraplegia. One of the earliest manifestations of overt HE is alteration of the normal sleep-wake cycle

Diagnosis

There is no laboratory or imaging study that allows a specific diagnosis of HE. Rather, it is a clinical syndrome. Blood levels of ammonia are commonly measured, but elevated levels are neither sensitive nor specific for HE. Neuropsychometric and