ABC of diseases of liver, pancreas, and biliary system
Portal hypertension—2. Ascites, encephalopathy, and other conditions

J E J Krige, I J Beckingham

Ascites

Ascites is caused by cirrhosis in 75% of cases, malignancy in 10%, and cardiac failure in 5%; other causes account for the remaining 10%. In most patients the history and examination will give valuable clues to the cause of the ascites—for example, signs of chronic liver disease, evidence of cardiac failure, or a pelvic mass. The formation of ascites in cirrhosis is due to a combination of abnormalities in both renal function and portal and splanchnic circulation. The main pathogenic factor is sodium retention. About half of patients with cirrhosis develop ascites during 10 years of observation. The development of ascites is an important event in chronic liver disease as half of cirrhotic patients with ascites die within two years.

Causes of ascites

Portal hypertension
- Cirrhosis of liver
- Congestive heart failure
- Constrictive pericarditis
- Budd-Chiari syndrome
- Inferior vena cava obstruction

Hypoalbuminaemia
- Nephrotic syndrome
- Protein losing enteropathy

Neoplasms
- Peritoneal carcinomatosis
- Pseudomyxoma

Miscellaneous
- Pancreatic ascites
- Nephrogenic ascites (associated with maintenance haemodialysis)
- Myxoedema
- Meigs's syndrome

Diagnosis

Ascites may not be clinically detectable when present in small volumes. In larger volumes, the classic findings of ascites are a distended abdomen with a fluid thrill or shifting dullness. Ascites must be differentiated from abdominal distension due to other causes such as obesity, pregnancy, gaseous distension of bowel, bladder distension, cysts, and tumours. Tense ascites may cause appreciable discomfort, difficulty in breathing, eversion of the umbilicus, herniae, and scrotal oedema. Rapid onset of ascites in patients with cirrhosis may be due to gastrointestinal haemorrhage, infection, portal venous thrombosis, or the development of a hepatocellular carcinoma. Ascites can also develop during a period of heavy alcohol misuse or excessive sodium intake in food or drugs. Ultrasonography is used to confirm the presence of minimal ascites and guide diagnostic paracentesis.

Successful treatment depends on an accurate diagnosis of the cause of ascites. Paracentesis with analysis of ascitic fluid is the most rapid and cost effective method of diagnosis. It should be done in patients with ascites of recent onset, cirrhotic patients with ascites admitted to hospital, or those with clinical deterioration. The most important analyses are quantitative cell counts, fluid culture, and calculation of the serum:ascites albumin gradient, which reflects differences in oncotic pressures and correlates with portal venous pressure. Patients with normal portal pressures have a serum:ascites albumin gradient less than 11 g/l, whereas patients with ascites associated with portal hypertension usually have a gradient above 11 g/l.

The traditional classification of transudative and exudative ascites based on ascitic fluid protein concentrations below and above 25 g/l is less useful than the serum:ascites albumin gradient because diuresis can affect the total ascitic protein concentration.

Tense ascites with umbilical and left inguinal hernias

Analysis of ascitic fluid
- Evaluate macroscopic appearance (straw coloured, turbid, bloody, chylous)
- Cell count and differential
- Chemistry profile (protein, albumin, amylase)
- Cytology
- Gram stain and bacterial culture

Tests to consider ordering
- Adenosine deaminase (if tuberculosis is suspected)
- pH, lactate, lactate dehydrogenase (if bacterial peritonitis suspected)

Classification of ascites by serum:ascites albumin gradient

High gradient (≥ 11 g/l)
- Cirrhosis
- Alcoholic hepatitis
- Cardiac ascites
- Fulminant hepatic failure
- Budd-Chiari syndrome
- Portal vein thrombosis
- Veno-occlusive disease

Low gradient (<11g/l)
- Peritoneal carcinomatosis
- Tuberculous peritonitis
- Pancreatic ascites
- Biliary ascites
- Nephrotic syndrome
- Serositis of collagen, vascular disease

Treatment

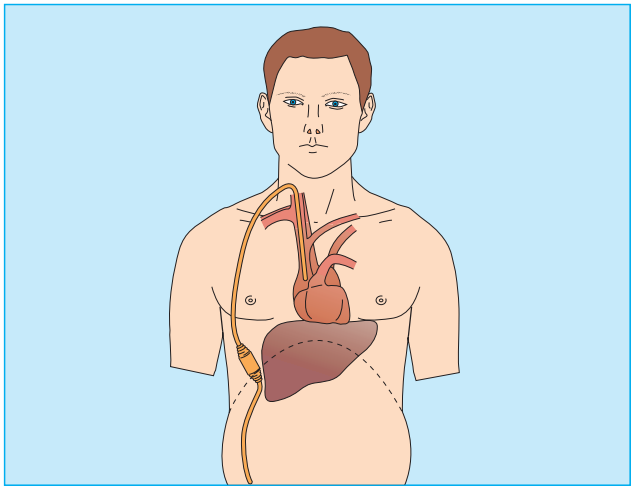
The principal aim of treatment of symptomatic ascites in cirrhotic patients is to improve general comfort and quality of life. Most patients will respond to dietary sodium restriction and diuretic induced excretion of sodium and water, but other treatments are available for those who do not. Treatment does not necessarily improve the prognosis for patients with cirrhosis and may cause complications. Small amounts of ascites that are asymptomatic should not be treated.

A crucial first step in treating ascites is to convince patients with alcoholic cirrhosis to abstain from alcohol. Abstinence for a few months can substantially improve the reversible component of alcoholic liver disease. Dietary salt restriction is the most important initial treatment. A low sodium diet of 1-1.5 g of salt (40-60 mmol/day) usually produces a net sodium loss, which may be sufficient in patients with mild ascites but is unpalatable and virtually impossible to adhere to in the long term. In practical terms a "no added salt" diet with levels of 80 mmol/day is the lowest that is generally sustainable. Fluid restriction is not needed for patients with cirrhotic ascites unless they have severe hyponatraemia (serum sodium <120 mmol/l). Although conventional recommendations suggest bed rest, its value is not supported by controlled trials.

Most patients need dietary restrictions combined with diuretics. The usual diuretic regimen comprises single morning doses of oral spironolactone (an aldosterone antagonist), increasing the dose as necessary to a maximum of 400 mg/day. Dietary sodium restriction and dual diuretic therapy is effective in 90% of patients. The patient's weight, electrolyte concentrations, and renal function should be carefully monitored. Treatment should be cautious because of the dangers of iatrogenic complications from aggressive treatment. Patients with ascites and peripheral oedema may tolerate 1-2 kg loss per day, but loss of 0.5 kg should be the goal in patients without oedema. Potential complications during diuresis are encephalopathy, hypokalaemia, hyponatraemia, hypochloraemic alkalosis, and azotaemia.

Patients with tense ascites should have a total abdominal paracentesis, followed by a sodium restricted diet and oral diuretics. Options for patients who do not respond to routine medical treatment include serial therapeutic paracentesis, peritoneovenous shunt, transjugular intrahepatic portosystemic shunt, and liver transplantation. Serial therapeutic paracentesis should be performed as required, every two to three weeks. Albumin infusion is unnecessary if <5 litres of fluid is removed.

Peritoneovenous shunts are seldom used because of problems with blockage and infection. They are reserved for patients who are resistant to diuretics, are not transplant candidates, and are unsuitable for paracentesis because of abdominal scars.



Denver peritoneovenous shunt

Events precipitating hepatic encephalopathy in cirrhotic patients

Electrolyte imbalance
- Diuretics
- Vomiting
- Diarrhoea

Gastrointestinal bleeding
- Oesophageal and gastric varices
- Gastroduodenal erosions

Drugs
- Alcohol withdrawal
- Benzodiazepines

Infection
- Spontaneous bacterial peritonitis
- Urinary
- Chest

Constipation
- Dietary protein overload

Hepatic encephalopathy

Hepatic encephalopathy is a reversible state of impaired cognitive function or altered consciousness that occurs in patients with liver disease or portosystemic shunts. The typical features of hepatic encephalopathy include impaired consciousness (drowsiness), monotonous speech, flat affect, metabolic tremor, muscular incoordination, impaired handwriting, fetor hepaticus, upgoing plantar responses, hypoactive or hyperactive reflexes, and decerebrate posturing. Hepatic coma, especially in alcoholic patients, should be diagnosed only after coma due to intracranial space occupying and vascular lesions, trauma, infection, epilepsy, and metabolic, endocrine, and drug induced causes has been excluded. Hepatic encephalopathy is a hallmark of deteriorating liver function, and patients should be assessed early for liver transplantation.

Hepatocellular insufficiency and portosystemic shunting may act separately or in combination to cause encephalopathy. Almost all cases of clinically apparent hepatic encephalopathy occur in patients with cirrhosis. Less than 5% occur in patients with non-cirrhotic forms of portal hypertension. However, a disproportionately large proportion of patients with surgical and radiological portosystemic shunts develop severe, often intractable, hepatic encephalopathy. A combination of impaired

Drugs that can cause hepatic encephalopathy
- Barbiturates
- Analgesics
- Other sedatives

Treatment of hepatic encephalopathy
- Identify the precipitating factors
- Stop diuretics
- Check serum Na^+, K^+, and urea concentration
- Empty bowels of nitrogen containing content
  - Control bleeding
  - Protein-free diet
- Lactulose
- Neomycin (1 g four times a day by mouth for 1 week)
- Maintain energy, fluid, and electrolyte balance
- Increase dietary protein slowly with recovery

hepatic and renal function is often associated with hepatic encephalopathy. About half these patients have diuretic induced renal impairment and half have functional renal failure.

Drugs are implicated in one quarter of patients with hepatic encephalopathy. Another quarter of cases are precipitated by haemorrhage in the gastrointestinal tract. This is often associated with deep and prolonged coma. The combination of gastrointestinal haemorrhage and hepatic encephalopathy indicates a poor prognosis. A small proportion of cases are precipitated by excess dietary protein, hypokalaemic alkalosis, constipation, and deterioration of liver function secondary to drugs, toxins, viruses, or hepatocellular carcinoma.

The treatment of hepatic encephalopathy is empirical and relies largely on establishing the correct diagnosis, identifying and treating precipitating factors, emptying the bowels of blood, protein, and stool, attending to electrolyte and acid-base imbalance, and the selective use of benzodiazepine antagonists. Non-absorbable disaccharides, such as lactulose or lactitol, are the mainstay of treatment. Antibiotics and protein restriction (40 g/day) can be used if there is no response. In intractable cases, closure of surgical shunts should be considered.

Hepatorenal syndrome

Hepatorenal syndrome is an acute oliguric renal failure resulting from intense intrarenal vasoconstriction in otherwise normal kidneys. It occurs in patients with chronic liver disease (usually cirrhosis, portal hypertension, or ascites) or acute liver failure; a clinical cause is often not found, treatment is often ineffective, and prognosis is poor. Hepatorenal syndrome is prevented by avoiding excessive diuresis and by early recognition of electrolyte imbalance, bleeding, or infection. Potentially nephrotoxic drugs such as aminoglycosides and non-steroidal anti-inflammatories should be avoided.

Patients with hepatorenal syndrome should have blood cultures taken and any bacteraemia treated. Most patients with liver disease who develop azotaemia will have prerenal failure or acute tubular necrosis. The diagnosis of hepatorenal syndrome is one of exclusion, and it should not be diagnosed until all potentially reversible causes of renal failure have been excluded. The common potentially reversible causes are sepsis, excessive diuresis or paracentesis, and nephrotoxic drugs. All patients suspected to have hepatorenal syndrome should be given an intravenous colloid infusion to exclude intravascular hypovolaemia as a cause of prerenal azotaemia. Liver transplantation, if otherwise appropriate and feasible, is the only truly effective treatment, and patients have a poor prognosis.

Spontaneous bacterial peritonitis

Spontaneous bacterial peritonitis is usually the consequence of bacteraemia due to defects in the hepatic reticuloendothelial system and in the peripheral destruction of bacteria by neutrophils. This allows secondary seeding of bacteria in the ascitic fluid, which is deficient in antibacterial activity.

Clinical signs may be minimal, and a diagnostic paracentesis should be performed in any cirrhotic patient who suddenly deteriorates or presents with fever or abdominal pain. A polymorphonuclear neutrophil count $>500\times10^6$/l is indicative of spontaneous bacterial peritonitis. Treatment with intravenous broad spectrum antibiotics should be started while awaiting the results of culture of ascitic fluid. Although the mortality associated with acute spontaneous bacterial peritonitis decreases with early treatment, it is still high (about 50%) and is related to the severity of the underlying liver disease.

In patients with cirrhosis and ascites spontaneous bacterial peritonitis is a common cause of sudden deterioration and may be present without any abdominal symptoms or signs

Characteristic findings associated with hepatorenal syndrome

- Ascites (but not necessarily jaundice) is usually present
- Hyponatraemia is usual
- Hepatic encephalopathy is commonly present
- Blood pressure is reduced compared with previous pressures recorded in patient
- Pronounced oliguria
- Low renal sodium concentration (<10mmol/l)
- Urinary protein and casts are minimal or absent

Summary points

- Cirrhosis is the commonest cause of ascites (90%)
- Ninety per cent of cases can be managed by sodium restriction and diuretics
- Hepatic encephalopathy is most commonly precipitated by drugs or gastrointestinal haemorrhage
- Non-steroidal anti-inflammatory drugs should be avoided in cirrhotic patients as they can cause renal failure

Further reading

Sherlock S, Dooley J. Diseases of the liver and biliary system. Oxford: Blackwell Scientific, 1996

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Spontaneous bacterial peritonitis

- An infection of ascites that occurs in the absence of a local infectious source
- Mainly a complication of cirrhotic ascites
- Prevalence is 15% to 20% (including culture negative cases)
- Caused by Gram negative enteric bacteria in $>$ 70% of cases

J E J Krige is associate professor of surgery, Groote Schuur Hospital and University of Cape Town, South Africa.

The ABC of diseases of liver, pancreas, and biliary system is edited by I J Beckingham, consultant hepatobiliary and laparoscopic surgeon, department of surgery, Queen's Medical Centre, Nottingham (Ian.Beckingham@nottingham.ac.uk). The series will be published as a book later this year.

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