7) Ascites – Dr. Muhammad Omar

Ascites refers to the accumulation of free fluid in the peritoneal cavity and is usually due to malignant disease, cirrhosis or heart failure; however, many primary disorders of the peritoneum and visceral organs can produce ascites, and these need to be considered even in a patient with chronic liver disease.

Causes of ascites

Common causes

- Malignant disease
- Hepatic
- Peritoneal
- Cardiac failure
- Hepatic cirrhosis

Other causes

- Hypoproteinaemia
  - Nephrotic syndrome
  - Protein-losing enteropathy
  - Malnutrition
- Hepatic venous occlusion
  - Budd-Chiari syndrome
  - Veno-occlusive disease
- Pancreatitis
- Lymphatic obstruction
- Infection
  - Tuberculosis
  - Spontaneous bacterial peritonitis
- Rare
  - Meigs' syndrome
  - Vasculitis
  - Hypothyroidism
  - Renal dialysis

Pathogenesis of ascites

Ascites causes abdominal distension with fullness in the flanks, shifting dullness on percussion and, when the ascites is marked, a fluid thrill. These signs do not appear until the ascites volume exceeds 1 liter, even in thin patients, and much larger volumes can be hard to detect in the obese. Associated features of ascites include distortion or eversion of the umbilicus, hernia, abdominal striae, divarication of the recti and scrotal edema. Pleural effusions are found in about 10% of patients, usually on the right side (hepatic hydrothorax); most are small and only identified on chest X-ray, but occasionally a massive hydrothorax occurs. Pleural effusions, particularly those on the left side, should not be assumed to be due to the ascites.

Pathogenesis of ascites in cirrhosis

Splanchnic vasodilatation is thought to be the main factor leading to ascites in cirrhosis. This is mediated by vasodilators (mainly nitric oxide) that are released when portal hypertension causes shunting of blood into the systemic circulation. Systemic arterial pressure falls due to pronounced splanchnic vasodilatation as cirrhosis advances. This leads to activation of the renin-angiotensin system with secondary aldosteronism, increased sympathetic nervous activity, increased atrial natriuretic hormone secretion and altered activity of the kallikrein-kinin system. These systems tend to normalize arterial pressure but produce salt and water retention. In this setting, the combination of splanchnic arterial vasodilatation and portal hypertension alter intestinal capillary permeability, promoting accumulation of fluid within the peritoneum.

Ascitic fluid: appearance and analysis

Cause/appearance

- Cirrhosis: clear, straw-colored or light green
- Malignant disease: bloody
- Infection: cloudy
- Biliary communication: heavy bile staining
- Lymphatic obstruction: milky-white (chylous)

Useful investigations

- Total albumin (plus serum albumin)
- Amylase
- White cell count
- Cytology
- Microscopy and culture

Ultrasonography is the best means of confirming ascites, particularly in the obese and those with small volumes of fluid. Paracentesis (if necessary under ultrasonic guidance) can also be used to confirm the presence of ascites but is most useful for obtaining ascitic fluid for analysis. The appearance of the ascites may point to the underlying cause. The ascites protein concentration and the serum-ascites albumin gradient are used to distinguish ascites due to transudation from ascites due to exudation.

Cirrhotic patients typically develop a transudate with a total protein concentration below 25 g/l and relatively few cells. However, in up to 30% of patients, the total protein concentration is more than 30 g/l. In these cases it is useful to calculate the serum-ascites albumin gradient by subtracting the concentration of the ascites fluid albumin from the serum albumin. A gradient of more than 11 g/l is strongly suggestive of portal hypertension and cirrhosis.

Exudative ascites (ascites protein concentration above 25 g/l or a serum-ascites albumin gradient of less than 11 g/l) raises the possibility of infection (especially tuberculosis), malignancy, hepatic venous obstruction, pancreatic ascites or, rarely, hypothyroidism. Ascites amylase activity above 1000 U/l identifies pancreatic ascites, and low ascites glucose concentrations suggest malignant disease or tuberculosis. Cytological examination may reveal malignant cells (one-third of cirrhotic patients with a bloody tap have a hepatoma). Polymorphonuclear leucocyte counts above 250 × 106/l strongly suggest infection (spontaneous bacterial peritonitis, see below). Laparoscopy can be valuable in detecting peritoneal disease.

Management

Successful treatment of ascites relieves discomfort but does not prolong life, and if over-vigorous, can produce serious disorders of fluid and electrolyte balance and precipitate hepatic encephalopathy. Conventional treatment aims to reduce body sodium and water by restricting intake, promoting urine output and, if necessary, removing ascites directly by paracentesis. The rate of loss of sodium and water is most easily measured by regular weighing. No more than 900 ml can be mobilized from the peritoneum daily so the body weight should not fall by more than 1 kg daily if fluid depletion in the rest of the body is to be avoided.

Some drugs containing relatively large amounts of sodium or causing sodium retention

High sodium content

- Antacids
- Alginates
- Antibiotics
- Phenytoin
- Sodium valproate
- Effervescent preps, e.g. aspirin, calcium, paracetamol

Sodium retention

- Carbenoxolone
- Corticosteroids
- Diazoxide
- Metoclopramide
- NSAIDs
- Estrogens

Some antibiotics with a high sodium content

- Amoxicillin
- Ampicillin
- Benzylpenicillin
- Cefotaxime
- Cefoxitin
- Cefradine
- Ceftazidime
- Cefuroxime
- Chloramphenicol
- Flucloxacillin
- Piperacillin
- Ticarcillin

Note: Significant increases of sodium intake due to antibacterial therapy usually occur only during parenteral therapy when large (gram) amounts of drug are used. Maximum parenteral doses of the above drugs increase daily sodium intake by about 20-50 mmol. Drugs that do not themselves contain sodium increase sodium intake if they are infused in sodium-containing fluids.

Restriction of dietary sodium intake is essential to achieving negative sodium balance in patients with ascites. Restriction to 100 mmol/day ('no added salt diet') may be adequate, but restriction to 40 mmol/day (which requires close dietetic supervision) is necessary in more severe ascites. Drugs containing relatively large amounts of sodium and those promoting sodium retention, such as non-steroidal analgesic agents, must be avoided. Restriction of water intake to 0.5-1.0 litre/day is necessary only if the plasma sodium falls below 125 mmol/l. A few patients can be managed satisfactorily on this treatment alone.

Diuretic drugs

Most patients require diuretic drugs in addition to sodium restriction. Spironolactone (100-400 mg/day) is the drug of choice for long-term therapy because it is a powerful aldosterone antagonist; unfortunately, it can cause painful gynecomastia and hyperkalemia. Some patients will also require powerful loop diuretics, e.g. furosemide, although these can cause fluid, electrolyte and renal function disorders. Diuresis is improved if patients are rested in bed while the diuretics are acting, perhaps because renal blood flow increases in the horizontal position. Patients who do not respond to doses of 400 mg spironolactone and 160 mg furosemide are considered to have refractory or diuretic-resistant ascites and should be treated by other therapeutic measures.

Paracentesis

The first-line treatment of refractory ascites is large-volume paracentesis with intravenous albumin. Paracentesis to dryness or the removal of 3-5 liters daily is safe, provided the circulation is supported by giving intravenous colloid such as human albumin (6-8 g per liter of ascites removed) or another plasma expander. Total paracentesis can therefore be used as an initial therapy or when other treatments fail.

Peritoneo-venous (LeVeen) shunt

The peritoneo-venous shunt is a long tube with a non-return valve running subcutaneously from the peritoneum to the internal jugular vein in the neck, which allows ascitic fluid to pass directly into the systemic circulation. It is effective in ascites resistant to conventional treatment but complications, including infection, superior vena caval thrombosis, pulmonary edema, bleeding from esophageal varices and disseminated intravascular coagulopathy, limit its use and insertion of these stents is now rare.

Transjugular intrahepatic portosystemic stent shunt (TIPSS)

TIPSS can relieve resistant ascites but does not prolong life. It can be used where liver function is reasonable or in patients awaiting liver transplantation, but should not be used in the terminally ill.

Prognosis

Ascites is a serious development in cirrhosis, as only 10-20% of patients survive 5 years from its appearance. The outlook is not universally poor, however, and is best in those with well-maintained liver function and where the response to therapy is good. The prognosis is also better when a treatable cause for the underlying cirrhosis is present or when a precipitating cause for ascites, such as excess salt intake, is found.

Complications

Ascites may be complicated by renal failure and also by infections which are spontaneous (see below) or, more commonly, precipitated by invasive investigations or treatment, such as upper gastrointestinal endoscopy and injection sclerotherapy. Both of these complications have adverse prognostic significance and may prompt referral for transplantation.

Hepatorenal syndrome

Ten per cent of patients with advanced cirrhosis and ascites develop the hepatorenal syndrome. There are two clinical types; both are mediated by severe renal vasoconstriction due to extreme underfilling of the arterial circulation.

Type 1 hepatorenal syndrome is characterized by progressive oliguria, a rapid rise of the serum creatinine and a very poor prognosis (without treatment median survival is less than 1 month). There is usually no proteinuria, a urine sodium excretion below 10 mmol/day and a urine/plasma osmolarity ratio of > 1.5. Other non-functional causes of renal failure must be excluded before the diagnosis is made. Treatment consists of albumin infusions in combination with terlipressin and is effective in about two-thirds of patients. Hemodialysis should not be used routinely because it does not improve the outcome. Patients who survive should be considered for liver transplantation.

Type 2 hepatorenal syndrome usually occurs in patients with refractory ascites, is characterized by a moderate and stable increase in serum creatinine, and has a better prognosis.

Spontaneous bacterial peritonitis (SBP)

Patients with cirrhosis are very susceptible to infection of ascitic fluid. SBP usually presents suddenly with abdominal pain, rebound tenderness, absent bowel sounds and fever in a patient with obvious features of cirrhosis and ascites. Abdominal signs are mild or absent in about one-third of patients, and in these patients hepatic encephalopathy and fever are the main features. Diagnostic paracentesis may show cloudy fluid, and an ascites neutrophil count above 250 × 106/l almost invariably indicates infection. The source of infection cannot usually be determined, but most organisms isolated from ascitic fluid or blood cultures are of enteric origin and Escherichia coli is the organism most frequently found. Ascitic culture in blood culture bottles gives the highest yield of organisms. SBP needs to be differentiated from other intra-abdominal emergencies, and the finding of multiple organisms on culture should arouse suspicion of a perforated viscus.

Treatment should be started immediately with broad-spectrum antibiotics, such as cefotaxime. Recurrence of SBP is common and may be reduced by prophylactic quinolones such as norfloxacin (400 mg daily) or ciprofloxacin (250 mg daily).

Antibiotics and spontaneous bacterial peritonitis (sbp)

'In patients with a previous episode of SBP and continued ascites norfloxacin 400 mg/day prevents recurrence (NNTB 4.5).'

'In patients with cirrhosis who have had a gastrointestinal haemorrhage prophylactic antibiotics reduce the risk of bacterial peritonitis (NNTB 12.5) and improve survival (NNTB 11).'