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Investigation and treatment of ascites

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Investigation and management of ascites

Ascites is defined as the pathological accumulation of fluid in the peritoneal cavity. It arises as a consequence of liver disease in over 80% of cases, of cancer in 10% and the remainder from conditions such as heart failure, constrictive pericarditis, tuberculosis or pancreatic disease[1]. Over 4,000 people died from cirrhosis in the UK in 1999, and ascites is the most common and serious complication of cirrhotic liver disease[2]. The development of ascites is a poor prognostic sign, with only 50% of cases remaining alive at two years[3], and it is an indication for considering evaluation for liver transplantation. The pathogenesis of ascites is complex, but portal hypertension and sodium retention are key to its development.

The treatment of ascites depends on the cause. This review focuses on the investigations and management of patients with ascites secondary to chronic liver disease.

Assessing patients with ascites

History

Treatment depends on accurate distinction of cirrhotic from non-cirrhotic ascites. Questions about risk factors for liver disease must therefore be asked and diagnostic tests for causes of chronic liver disease performed. Sudden development of ascites in patients with previously stable cirrhosis raises the suspicion of an underlying hepatocellular carcinoma (HCC).

Physical examination

Ascites can be detected clinically by the presence of shifting dullness which becomes clinically demonstrable when about 1,500 ml of fluid are present[4]. If the flanks are resonant, the probability of having ascites is less than 10%[4]. Ultrasound is useful if diagnostic doubt remains.

Diagnostic ascitic tap

The history, physical examination and ascitic fluid analysis will almost always reveal the cause of ascites[5]. Abdominal paracentesis with careful analysis of the ascitic fluid should be performed early in the evaluation of patients with ascites. This can be safely performed at the bedside even in the presence of deranged clotting or reduced platelet count[5].

For a diagnostic tap, 20–50 ml of ascitic fluid is taken for the following investigations:

- *Cell count:* usually in an ethylene diamine tetraacetic acid (EDTA) (purple top) tube to prevent clotting
- *Microscopy:* separate sterile container
- *Ascitic fluid total protein/albumin:* separate sterile container
- *Culture:* sterile container or blood culture bottles
- *Cytology:* separate sterile container.

Appearance

Ascitic fluid is usually straw coloured and clear. The presence of blood in a non-traumatic tap can indicate malignancy. Milky fluid (chylous ascites) is a feature of thoracic duct blockage or injury. Infected ascites can appear cloudy although it is frequently clear.

Cell count

The white cell count with differential is the single most helpful test and should be requested on every specimen. Specimens can be sent in a full blood

count (FBC) tube (EDTA tube to prevent clotting) and the cell count performed using a standard automated FBC machine. Alternatively, the cell count can be checked and calculated manually. An absolute neutrophil count above 250 cells/mm^3 is diagnostic of bacterial infection and warrants antibiotic treatment[6]. Spontaneous bacterial peritonitis is present in up to 30% of patients admitted with cirrhosis and ascites[7]. Prophylaxis against recurrence with an oral quinolone antibiotic is indicated[7].

Protein

The traditional concept of transudate/exudate based on absolute levels of albumin is not useful in ascites. However, the serum-ascites albumin gradient (SAAG), calculated by subtracting ascitic fluid albumin from the serum albumin, is useful in determining the presence of portal hypertension. A SAAG above 11 g/l indicates portal hypertension with 97% accuracy[8]. Portal hypertension can arise from conditions other that cirrhosis, including cardiac disease and metastases affecting portal venous flow[5] but a low gradient indicates an inflammatory or neoplastic non-liver cause of ascites (Table 1).

Culture

Culture in blood culture bottles is expensive but is indicated when initial analysis is abnormal. Conventional culture of ascitic fluid containing over 250 neutrophils/mm^3 demonstrated bacterial growth in only 50% compared with 80% when inoculated into blood culture bottles at the bedside[9]. Cytology can be requested depending on initial investigation.

Radiology

Ultrasound and Doppler studies can confirm the appearances of chronic liver disease, reveal features of portal hypertension (eg splenomegaly) and other pathologies such as HCC or other tumours. There should be a special request to look for patency of portal and hepatic veins.

Computed tomography. This can be used where doubt remains about the underlying aetiology. Biphasic imaging can give further information on vascular anatomy and the presence of hepatoma[10].

Treatment

The mainstay of treatment for cirrhotic ascites is salt restriction and diuretics, to which 90% of cases will respond. Patients without liver disease and a low SAAG will not respond to these measures. Therapeutic paracentesis should be performed in those with tense, large volume ascites.

Salt restriction

Fluid loss and weight change are directly related to the sodium balance. A net loss of sodium (and hence water) can usually be achieved by restricting dietary intake to about 2 g sodium (or 88 mmol). Stricter diets are generally poorly tolerated. Education of the patient and their carer/cook is essential.

Table 1. Classification of ascites by serum-ascites albumin gradient.

High gradient (>11 g/l)	Low gradient (>1.1 g/dl)
Cirrhosis	Peritoneal carcinomatosis
Alcoholic hepatitis	Tuberculous peritonitis
Cardiac ascites	Pancreatic ascites
Constrictive pericarditis	Bowel obstruction/infarction
Massive liver metastasis	Biliary ascites
Fulminant hepatic failure	Nephrotic syndrome
Budd-Chiari syndrome	Postoperative lymphatic leak
Veno-occlusive diseases	Serositis
Myxoedema	

Key Points

- **Ascites is the commonest complication of portal hypertension and indicates poor prognosis**
- **Survival at two years is only 40–50%**
- **The mainstay of treatment is dietary restriction of sodium and diuretics**
- **The first–line treatment in refractory ascites is large volume paracentesis with albumin infusion**
- **Ascites can be an indication for liver transplantation in patients with irreversible liver disease**

KEY WORDS: ascites, CPD, investigations, liver disease, treatment

Diuretics

Inappropriate sodium retention distal to the loop of Henle is a feature of cirrhotic ascites. Spironolactone is the first-choice diuretic, usually at a starting dose of 100 mg/day. Amiloride is less effective[11], but can be used in patients who develop painful gynaecomastia. In those who do not respond to increasing doses of spironolactone, loop diuretics can be combined with spironolactone. A ratio of 100:40 spironolactone:frusemide is preferred, with a maximum dose of 400 mg spironolactone and 160 mg frusemide.

Overdiuresis, with weight loss of above 0.5 kg per day should be avoided, particularly in the absence of peripheral oedema with ascites[12], as hepatic encephalopathy and renal dysfunction can ensue.

Therapeutic paracentesis

The drainage of a large volume of ascitic fluid provides rapid relief of discomfort and respiratory embarrassment from a

tense abdomen. It is important to avoid introducing infection whilst performing this procedure. Rapid protein and fluid shifts can result in renal impairment, and adequate colloid fluid replacement is essential. Paracentesis should be performed prior to the introduction of diuretics and sodium restriction in patients presenting with tense ascites[5].

Practical management aspects. A suitable drain (eg suprapubic catheter) is inserted under aseptic precautions into the peritoneal cavity at the point of maximum dullness along the flanks. The abdomen is rapidly drained and the catheter removed within 4–6 hours to minimise the risk of introducing infection.

This author's current practice is to replace each two litres of ascitic fluid drained with one unit of 4.5% human albumin solution. Alternative fluid replacement includes high molecular weight dextrans. Although non-albumin colloid is cheaper, it results in a greater incidence of renal dysfunction[13]. Mild coagulopathy and thrombocytopenia do not preclude paracentesis, and prophylactic transfusion of platelets or fresh frozen plasma prior to paracentesis is not necessary.

Bed rest

There is no convincing evidence for or against this traditional aspect of treating ascites, although it frequently becomes a part of inpatient stay for investigations.

Fluid restriction

Sodium balance is the most important determinant of net fluid loss and in most cases fluid restriction is not important. In cases with significant water excess and hyponatraemia (plasma sodium <130 mmol/l) fluid restriction to 1–1.5 litres/day can be useful.

Monitoring treatment response

Daily assessment of weight and close monitoring of electrolytes are vital. Urinary sodium loss (measured by 24-hour urine collection) should exceed daily sodium intake. Diuretic treatment should be stopped if there is worsening hyponatraemia, hyperkalaemia, renal impairment or hepatic encephalopathy developing without other precipitants.

Refractory ascites

About 10% of ascitic patients prove unresponsive to the standard medical treatment outlined above. Large volume paracentesis with albumin infusion is currently the first line of management in these refractory cases[5,6]. Peritoneovenous shunts have largely been abandoned as they offer no survival advantage, while incurring higher costs and longer inpatient stay. Transjugular intrahepatic portosystemic stent-shunting (TIPSS) is an effective way of reducing portal pressure and controls ascites in over 80% of cases[14]. It remains unclear whether improved control of ascites is associated with improved survival, but TIPSS may become first-line treatment for refractory ascites[15].

Liver transplantation

The prognosis is poor once cirrhosis is complicated by ascites and formal consideration for liver transplantation should be sought early in suitable cases.

Treatment of underlying liver disease

In addition to treating the ascites, it is always important to treat the underlying liver condition. In alcoholic liver disease, abstinence can result in dramatic reduction in portal pressure with resolution of ascites over several months. Treatment of severe autoimmune hepatitis can result in similar clinical improvement.

Conclusions

Ascites arises most frequently as a consequence of liver disease. Simple analysis of ascitic fluid will usually distinguish liver from non-liver causes. Most cases with liver disease-related ascites will have good control with dietary salt restriction together with diuretic treatment. Referral to a specialist centre should be considered for all cases potentially suitable for liver transplantation.

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Indication and assessment for liver transplantation

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Liver transplantation provides effective therapy for most forms of acute and chronic liver failure – one-year survival rates exceed 90%[1] – and the indications continue to expand. In general terms, the indications for liver transplantation are objective evidence of liver failure and subjective criteria such as poor quality of life due to liver disease and occasionally rare metabolic defects.

Chronic liver disease

In chronic liver disease the most important aspect of patient selection is timing. Transplantation should improve both quality and quantity of life. The procedure is optimally carried out when the patient is well enough to withstand the procedure, but ill enough to warrant it (ie predicted survival is about 1–2 years without a transplant).

Assessment for transplantation in chronic liver disease is difficult. Objective and subjective measures are used. The Child-Pugh classification[2] (Table 1) allows objective assessment of a patient's functional liver status and in the USA forms the basis for the criteria required to list patients. Those with Childs C grade have a 58%, 21% and 0% one-year, five-year and 10-year survival, respectively.

Subjective measures of liver disease may be more difficult to assess. Tools are available to document quality of life[3], and a full psychosocial assessment should be carried out.

Cholestatic liver disease

Primary biliary cirrhosis

Primary biliary cirrhosis (PBC) is a declining indication for liver transplantation, but still accounted for 7.8% of liver transplants in Europe in 1998–2000[1]. The disease has three stages:

- an initial asymptomatic stage
- a symptomatic stage with worsening cholestasis and declining synthetic function (falling albumin and increasing prothrombin time)
- a decompensating stage with severe jaundice and evidence of portal hypertension.

The natural history of PBC is well defined. Various prognostic models have been designed. The most commonly used is the Mayo Clinic model[4]; this has

Key Points

There are objective and subjective criteria for transplantation

Disease-specific criteria exist for different conditions

Certain indications are common to all conditions, for example:
- **failing synthetic function (serum albumin <25 g/l)**
- **complications of portal hypertension**
- **intolerable quality of life**

Discussion/referral should occur prior to end-stage disease

KEY WORDS: acute liver disease, chronic liver disease, CPD, liver transplantation