CASE: 46 year old driver, previously healthy, presented to ED c/o 4 weeks of increasing abdominal girth and lower extremity swelling and 5 days of "yellow eyes." He smokes 1 pack/day and drinks "a case of beer sometimes, but not when I'm driving." Examination notable for a jaundiced man with scleral icterus, moderately tense ascites with fluid wave, bilateral lower extremity swelling; no asterixis. Laboratories: AST 456, ALT 122, Alkaline phosphatase 206, Total bilirubin 5.1, INR 1.6, albumin 3.6, creatinine 1.1. No prior labs are available.

What complications of end-stage liver disease does this patient have? What work-up would you do in the hospital? How would you manage his ascites?

Common Complications of End Stage Liver Disease - Ascites

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Ascites is the most common complication of ESLD; 80% with cirrhosis have ascites due to splanchnic dilatation. Ascites indicates poor prognosis and confers increased risk of infection and renal failure. One year survival is ~50%, and is >90% if no cirrhosis.

Physical Exam
Insensitive if <1-1.5 liters of ascites. Bulging flanks and shifting dullness are 60-90% sensitive, 40-70% specific. Fluid wave is 82-92% specific, 50-80% sensitive; LR 5.0.

Imaging
Ultrasound can detect 100 cc of abdominal fluid; use CT to evaluate for masses.

Management
- Bed rest increases GFR and Na excretion; low Na+ diet, 2 g/day, plus bed rest eliminates ascites in 10-20% if baseline urine Na excretion high (>50mEq/d) and moderate ascites.
- Diuretics: good evidence for starting with furosemide 40mg and spironolactone 100 mg daily. Goal weight loss of half-kg/day and up to 1kg/day if peripheral edema
  - Spironolactone, an aldosterone antagonist, has 3-4 day onset and 2 weeks to steady state.
  - Furosemide, a loop diuretic, can lead to azotemia, hypokalemia, and encephalopathy in 25%.
  - Complications include intravascular volume depletion/renal failure (25%), hyponatremia (28%), encephalopathy (26%). If renal dysfunction develops, hold diuretics, hydrate gently and resume diuretics at lower dose. Diuretics should never be initiated in patients with increasing creatinine, GI bleed or spontaneous bacterial peritonitis.
- Fluid restriction: Consider if serum Na<120-130 with ascites or edema; goal is <1L of fluid/day, try to minimize free water.
- Consider large volume paracentesis.
- Reduce risk of co-morbidities such as varices, with non-selective beta blockade.
- TIPS (Transcutaneous intrahepatic portosystemic shunt): Consider in refractory ascites.

In a hospitalized patient with moderate or tense ascites, first line therapy includes therapeutic paracentesis with albumin (see below) followed by diuretics and salt restriction. This regimen can accelerate recovery and hospital discharge; although there is no survival benefit, therapy improves quality of life and reduces incidence of SBP.

Diagnostic Paracentesis
Consider in new-onset ascites (if long-standing cirrhosis, rule out hepatocellular carcinoma); known ascites with new fever, abdominal pain, worse encephalopathy, or GI bleed; and worsened hepatic or renal function in known cirrhosis; any hospitalized patient. Consider repeat tap at 48 hours if no improvement and WBC still high as there may be secondary peritonitis or a resistant organism.

NOTE: Coagulopathy is NOT a contraindication to diagnostic paracentesis! Bleeding risk is <1% with a 22-gauge needle.

Ascitic Fluid Evaluation

- Spontaneous Bacterial Peritonitis (SBP): suggested by >250 PMNs and culture grows single organism. (see next chapter.)
- Secondary bacterial peritonitis: suggested by LDH > 225, glucose < 50, protein > 10 g/dL and polymicrobial growth on culture
- Obtain large volume of fluid for cytologic analysis and TB culture
- SAAG (serum ascites/albumin gradient) is 97% accurate in classifying etiology of ascites. A ratio ≥ 1.1 indicates portal hypertension associated with cirrhosis, alcoholic hepatitis, CHF, portal vein thrombosis, Budd-Chiari syndrome. A ratio < 1.1: TB, pancreatic ascites, nephrotic syndrome, perintoneal carcinomatosis.

"Therapeutic" or large-volume paracentesis: Fewer complications than diuretics (less azotemia, encephalopathy), faster ascites resolution. Fluid reaccumulates an average of 5-7% per day though sometimes faster. Infection and intestinal perforation are rare. Serious bleeding is rare but studies exclude pts with INR>1.6, platelets <50,000. Serious complications include dilutional hyponatremia in 20% and Hepatorenal Syndrome (HRS) in a few, which may confer shortened survival.

Albumin infusion: Controversial and expensive. Randomized studies have shown no consistent survival benefit except in SBP. Consider albumin if 5 liters or more of ascites is removed, since 15% of patients may develop hepatorenal syndrome (HRS); give 6-10g albumin/liter of ascites removed. May help with hyponatremia and transient electrolyte abnormalities. One multi-center randomized study of 126 patients showed decreased risk of HRS in patients who received albumin + antibiotics versus antibiotics alone (10% vs. 33%) and decreased in-hospital (10 vs. 29%) and 3-month mortality (22 vs. 41%). Infection resolution rate was the same. Highest benefit seems to be in patients with total bilirubin>4 mg/dL, baseline BUN>30 and/or creatinine >1.0. Albumin: use 1.5 g/kg within 6 hours of diagnosis and 1g/kg on day 3.

Refractory ascites is defined as resistant to diuretics and/or associated with encephalopathy, hyponatremia, and azotemia. Affects 5-10% of patients with ascites and confers increased risk of HRS with 1-year survival of 25-40%.

Treatment of refractory ascites: Perform large-volume paracentesis with albumin and initiate diuretics after tap. In a randomized, double-blind placebo-controlled trial, ascites recurred less frequently in four-week follow-up (18% vs. 93%) in patients on spironolactone. Restrict sodium. In 2 prospective randomized trials, TIPS is more effective than a large volume tap in controlling ascites, as partial response is 84% vs. 43%, but mortality data are mixed. 40-75% of TIPS are occluded at 1 year; TIPS may exacerbate encephalopathy.

Case Follow-up

The patient has ascites. A 6-liter diagnostic and therapeutic paracentesis with albumin was performed; the patient immediately felt more comfortable afterwards. Initial tap showed 80 WBCs, so he did not meet criteria for SBP. Furosemide 40 mg and spironolactone 100 mg daily were started and he received information about low sodium diet, and alcohol counseling.

Clinical Pearls

- Diagnostic paracentesis is indicated in new-onset ascites or known ascites with fever, abdominal pain, encephalopathy, or GI bleed. Consider paracentesis during hospitalization if there is significant change in clinical status.
- Albumin infusion probably benefits patients with SBP or undergoing large volume (>5L) paracentesis.
- First-line therapy for hospitalized patients with moderate-tense ascites is therapeutic paracentesis plus albumin (if >5L of fluid removed) followed by diuretics and salt restriction.
- Diuretics should never be initiated in patients with increasing creatinine, GI bleed or SBP.
- In patients with new ascites and known, compensated cirrhosis, rule-out hepatocellular carcinoma.

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