MORNING REPORT

A Man with Increasing Abdominal Girth

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A 52-year-old man with a ten-year history of hepatitis C, acquired from intravenous heroin use, presents to the emergency room with increasing abdominal girth over the past two months. The swelling is worse whenever he eats or drinks. He has lost 32 pounds in the past three months and has had frequent drenching night sweats for the past two weeks. He denies fevers and chills. He has mild constipation, with bowel movements every three to four days, but otherwise his review of systems is negative for complaints. He has been incarcerated for the past ten years and was treated with isoniazid (INH) for latent tuberculosis.

Vital signs are a temperature of 97.7° F, heart rate of 108 beats per minute, respiratory rate of 26 breaths per minute, and a blood pressure of 143/89 mm Hg. His SaO_2 is 98% on room air. His physical exam is significant for scleral icterus but not sublingual or tympanic membrane jaundice. His abdomen is distended, firm, and diffusely tender. There is no rebound or guarding. He has shifting dullness to percussion and a fluid wave. Bowel sounds are hypoactive. The remainder of the physical exam is normal.

Initial laboratory studies show a white blood cell count (WBC) of 18,700 cells/mL, with a differential of 92% segmented neutrophils, 4% lymphocytes, and 4% monocytes. Hemoglobin is 12.7 g/dL. RBC count is 4.3 x 106 cells/mL. Platelets are 224,000 U/L. A basic metabolic panel is normal. Liver function testing shows total protein of 7.6 g/dL, albumin 2.8 U/L, total bilirubin 2.2 mg/dL, AST 77 U/L, ALT 21 U/L, and alkaline phosphatase 157 U/L. His INR is 1.3 and PTT 24.6 seconds.

Based upon his physical exam, his increasing abdominal girth is clearly due to the accumulation of fluid or ascites. The Starling equation illustrates the role of hydrostatic and oncotic forces in the accumulation of ascitic fluid in the peritoneum. In this patient, the most likely causes are increased capillary hydrostatic pressure (P_c) or increased interstitial oncotic pressure (π_i). Decreased interstitial hydrostatic pressure (P_i) has fewer etiologies (e.g. dehydration) and tends to result in subtle fluid shifts. This degree of fluid accumulation would be unusual. Decreased capillary oncotic pressure (π_c) is associated with other signs of fluid accumulation, such as pleural effusions, periorbital edema, and peripheral edema. Although he has a low serum albumin, he has likely arrived at 2.8 U/L over months to years, which allows for equilibration of oncotic pressures and a much lesser impact on fluid shifts. Acute albumin loss, such as nephrotic syndrome, is more typical of low capillary oncotic pressure resulting in ascites. The absence of peripheral edema makes low capillary oncotic pressure seem even less likely as the etiology. Finally, the filtration coefficient can change with systemic disease and inflammation, such as severe sepsis, pancreatitis, or shock. None of these appear to be the etiology at this point, although he does meet criteria for systemic inflammatory response syndrome (SIRS).

Distinguishing between increased capillary hydrostatic pressure and increased interstitial oncotic pressure can be accomplished by calculating the serum-ascites-albumin-gradient (SAAG) after paracentesis. A value greater than 1.1 suggests increased hydrostatic pressure and a value less than 1.1 suggests increased interstitial oncotic pressure.

Starting at the aortic root and working backwards through the heart into the lungs and then to the liver is an anatomic method for evaluating specific causes of increased capillary hydrostatic pressure. Aortic stenosis and mitral regurgitation can result in congestive heart failure and ascites but seem unlikely. His cardiopulmonary exam is normal. Pulmonary hypertension is possible, but the lack of increased jugular venous distention is a clue that this is not likely. This man's history of hepatitis C puts him at greatest risk for cirrhosis resulting in portal hypertension. A portal vein thrombosis is something that should also be considered.

Etiologies of increased interstitial oncotic pressure of the peritoneum include infection, malignancy, and autoimmune disease. It is the accumulation of inflammatory cells and protein that results in the increased oncotic force. The elevated serum WBC count and SIRS criteria is concerning for one of these possible etiologies. Particularly worrisome is bacterial peritonitis, which is not uncommon in patients with cirrhosis of the liver. A paracentesis with gram stain, cell count, cytology, and albumin (for SAAG) should be performed.

Bedside ultrasound shows a large collection of peritoneal fluid. Diagnostic and therapeutic paracentesis are performed. The ascitic fluid is a dull red color, with a white cell count of

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Figure 1. Starling Equation

$$J_v = K_f ([P_c - P_i] - \sigma[\pi_c - \pi_i])$$

J_v = fluid flow
K_f = filtration coefficient
P_c = capillary hydrostatic pressure
P_i = interstitial hydrostatic pressure
σ = reflection coefficient
π_c = capillary oncotic pressure
π_l = interstitial oncotic pressure

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17,382 cells/mL (with differential of 96% segmented neutrophils and 4% lymphocytes) and a red blood cell count of 48,000 cells/mL. The fluid albumin is 1.2 U/L, LDH 2240 U/L, total protein 3.0 g/dL, and glucose 50 mg/dL. His SAAG is 1.6.

The SAAG is 1.6, which suggests that the main cause of the accumulation of ascites is due to increased capillary hydrostatic pressure. This is most likely due to cirrhosis, but there are a few things that suggest that there is more going on than simply ascites from cirrhosis. First, the ascitic fluid was noted to be bloody, which is always a red flag (no pun intended). It does not appear to be frank blood from a traumatic paracentesis considering that 27% of the cells counted are WBCs. In the serum, WBCs are closer to 1%. Clearly, something is promoting the deposition of WBCs in the peritoneal fluid. The LDH of 2240 U/L is highly elevated, which suggests extensive cell turnover. The LDH is too high for spontaneous bacterial peritonitis, but bacterial peritonitis remains a possibility. Empiric antibiotics would be prudent at this stage because cirrhosis and bacterial peritonitis are a bad combination that can have a poor prognosis if not treated early. Peritoneal infection with tuberculosis can be bloody. A peritoneal adenosine deaminase may be helpful because acid-fast analysis of peritoneal fluid is unreliable. Malignancy must be strongly considered, especially if gram stain of the peritoneal fluid and culture are negative. His history of weight loss and recent night sweats are concerning, especially for hepatocellular carcinoma or lymphoma. Chronic hepatitis is a clear and known risk factor for hepatocellular carcinoma, but it should be noted that patients with chronic hepatitis C infection are at a 20% to 30% greater risk of non-Hodgkin's lymphoma. If gram stain and culture are negative, cytology should be sent, and an abdominal and pelvic CT should be done.

The patient is started on empiric therapy for bacterial peritonitis, and the ascitic fluid is sent for cytology. Abdominal ultrasound with portal venous flow rules out a portal venous thrombus. Gram stain and acid-fast smears of the ascitic fluid are negative. Cultures are negative for bacteria or fungi. Cytology for the ascitic fluid shows atypical lymphoid cells concerning for malignancy. Both fluid samples are sent for flow cytometry.

The suspicion for malignancy, especially lymphoma, is even greater. An abdominal CT is warranted.

He undergoes CT scan of the abdomen, which finds a large retroperitoneal soft-tissue mass in the left upper quadrant displacing the kidney inferiorly and a large heterogenous spleen. This mass is biopsied by interventional radiology and sent for cytology and flow cytometry. Results are consistent with a large B-cell lymphoma.

Hepatitis C (HCV) has been shown to be associated with a number of B-cell clonal disorders, including mixed cryoglobulinemia, Waldenstrom's Macroglobulinemia, and non-Hodgkin's lymphoma. The underlying mechanism is thought to be chronic stimulus of the immune system, which ultimately leads to the selection of abnormal B-cell clones. The HCV-E2 envelope glycoprotein is thought by some to be the potential antigen. Anti-viral therapy has shown striking results with remission rates up to 75% in some patients with HCV and lymphoproliferative diseases. Splenic lymphoma has shown an even more impressive response, with 89% of patients having a complete hematologic response after reduction of the HCV viral load.[1, 2]

Unfortunately, he does not respond to therapy and develops hepatorenal syndrome with severe delirium. Because of his poor prognosis and lack of response to therapy, his family decides to place him in hospice.

References

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2. Giordano TP, Henderson L, Landgren O, et al. Risk of non-Hodgkin lymphoma and lymphoproliferative precursor diseases in US veterans with hepatitis C virus. JAMA 2007; 297:2010-7.

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