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## Evaluation of New-Onset Ascites

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A white woman in her 60s with undifferentiated connective tissue disease and longstanding pulmonary arterial hypertension presented for evaluation of new-onset ascites. The patient reported no alcohol or drug use and no personal or family history of liver disease.

Medications included diltiazem and furosemide. On physical examination, her blood pressure was 108/54 mm Hg and pulse was 64/min. She was anicteric with mild bilateral temporal wasting and jugular venous distension. Further pertinent findings included regular heart rate and rhythm with an accentuated P<sub>2</sub>, grade 1/6 holosystolic murmur in the left lower sternal border, full bulging abdomen with flank dullness, and scattered spider angiomata on her chest. Doppler ultrasound revealed an irregular liver echo pattern without lesions, normal common bile duct, patent portal and hepatic vasculature, splenomegaly, and ascites. Laboratory results including diagnostic paracentesis are shown in Table 1.

## Answer

**B.** Her ascites is primarily due to chronically elevated pressures on the right side of her heart.

## Test Characteristics

Ascites is the accumulation of fluid in the abdominal cavity. In the United States, the 3 main causes of ascites are cirrhosis ( $\approx 85\%$ ), peritoneal malignancy ( $\approx 7\%$ ), and heart failure ( $\approx 3\%$ ), with causes such as nephrotic syndrome and tuberculosis accounting for the remainder.<sup>1–4</sup> Approximately 5% of patients have more than 1 cause.<sup>2</sup> For evaluating new-onset ascites, diagnostic paracentesis is safe, cost effective, and recommended as the first-line evaluation by the American Association for the Study of Liver Diseases.<sup>3</sup> In patients with cirrhosis, the most common complication of paracentesis is ascites fluid leak ( $\approx 5\%$  of cirrhosis patients), and the complications of bleeding and infection occur in less than 2% of patients.<sup>5</sup> The initial laboratory investigation of ascites includes cell count and differential, total protein, and albumin for calculation of the serum-ascites albumin gradient (SAAG [calculation, serum albumin concentration minus ascitic albumin concentration]).<sup>3</sup> Based on

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clinical presentation and pretest probability, other ascites studies may be considered.<sup>3</sup> A SAAG level of 1.1 g/dL or greater indicates that ascites is due to portal hypertension, the pathologic increase of pressure in the portal venous system (97.0% sensitivity and 90.2% specificity).<sup>2</sup> In this context, an ascites protein level of 2.5 g/dL or greater suggests accumulation is due to heart failure.<sup>6</sup> A recent study noted a combined SAAG level of 1.1 g/dL or greater and an ascites protein level of 2.5 g/dL or greater in a validation cohort had a diagnostic accuracy of 78.3% for heart failure–related ascites, with 53.3% sensitivity (95% CI, 28.1%–78.6%), 86.7% specificity (95% CI, 76.7%–96.6%), a negative likelihood ratio of 0.54, and a positive likelihood ratio of 4.00.<sup>7</sup> Supplementation with intravenous albumin may confound test results. The Medicare midpoint reimbursement is \$10.31 for peritoneal fluid cell count with differential, \$6.75 for peritoneal fluid protein, and \$9.53 for peritoneal fluid albumin.<sup>8</sup>

## Application of Test Result to This Patient

This patient has multiple potential causes of ascites. Diagnostic paracentesis is the first step in investigation. The SAAG and ascites protein levels are most useful for distinguishing among the 3 main causes of ascites (Table 2). The patient has an elevated SAAG ( 1.1 g/dL), which is found in both heart failure and cirrhosis-related ascites. She has an ascites total protein level of 3.5 g/dL, which is greater than the 2.5- g/dL threshold and suggests her ascites is related to heart failure.<sup>5</sup> This pattern occurs because hepatic sinusoids are normally permeable in heart failure–related ascites, which allows for leakage of protein-rich lymph into the abdominal cavity.<sup>7,9</sup> In cirrhosis, hepatic sinusoids are less permeable due to fibrous tissue deposition, resulting in ascites with low protein content.<sup>7,9</sup> Nevertheless, this patient likely also has some liver fibrosis due to long-standing congestive hepatopathy. Her anemia and thrombocytopenia are predominantly due to splenomegaly. Her hypoalbuminemia is likely due to cardiac cachexia rather than liver synthetic dysfunction. Malignant ascites in patients without large liver masses typically has a fluid white blood cell count of 500/mm<sup>3</sup> or greater, SAAG of less than 1.1 g/dL, and total protein of 2.5 g/dL or greater, while spontaneous bacterial peritonitis is diagnosed by an elevated ascitic neutrophil count ( 250 cells/mm<sup>3</sup>) and when secondary causes of peritonitis are excluded.<sup>3</sup>

## What Are Alternative Diagnostic Testing Approaches?

Though diagnostic paracentesis is the standard first step for evaluating new-onset ascites, serum brain natriuretic peptide (BNP) of greater than 364 pg/mL has been demonstrated to diagnose heart failure–related ascites with 99.1% accuracy.<sup>7</sup> Serum BNP may be useful if ascites results are inconclusive for diagnosis.

## Patient Outcome

The patient managed her heart failure–related ascites successfully with sodium restriction, diuretics, and pulmonary hypertension therapies including treprostинil and sildenafil.

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**HOW DO YOU INTERPRET THESE TEST RESULTS?**

- A. Her ascites is primarily due to cirrhosis.
- B. Her ascites is primarily due to chronically elevated pressures on the right side of the heart.
- C. Her ascites is primarily due to abdominal malignancy.
- D. Her ascites is primarily due to spontaneous bacterial peritonitis.

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**Clinical Bottom Line**

- In the United States, the 3 main causes of ascites are cirrhosis, malignancy, and heart failure.
- Diagnostic paracentesis is recommended as first-line evaluation for new-onset ascites.
- Initial laboratory investigation of ascites includes cell count and differential, total protein, and serum and peritoneal fluid albumin.
- In a patient with an elevated SAAG ( $1.1 \text{ g/dL}$ ), a fluid total protein of  $2.5 \text{ g/dL}$  or greater suggests ascites is due to heart failure.

**Table 1**

## Test Results

| Test  | Patient's Laboratory Values | Reference Range |
|---|-----------------------------|-----------------|
| Serum                                       |                             |                 |
| Aspartate aminotransferase, U/L             | 37                          | 15–41           |
| Alanine aminotransferase, U/L               | 9                           | 14–54           |
| Alkaline phosphatase, U/L                   | 42                          | 24–110          |
| Total bilirubin, mg/dL                      | 0.6                         | 0.4–1.5         |
| Albumin, g/dL                               | 2.5                         | 3.5–4.8         |
| White blood cell count, /µL                 | 4300                        | 3200–9800       |
| Hemoglobin, g/dL                            | 9.6                         | 12.0–15.5       |
| Platelets, × 10 <sup>3</sup> /µL            | 110                         | 150–450         |
| International normalized ratio              | 1.1                         | 0.9–1.1         |
| Ascites                                     |                             |                 |
| Appearance                                  | Yellow                      |                 |
| Albumin, g/dL                               | 1                           |                 |
| Protein, g/dL                               | 3.5                         |                 |
| Red blood cell count, × 10 <sup>6</sup> /µL | 258                         |                 |
| White blood cells, /mm <sup>3</sup>         | 145                         |                 |
| % Neutrophils                               | 2                           |                 |
| % Lymphocytes                               | 55                          |                 |

SI conversion factors: to convert alanine aminotransferase, alkaline phosphatase, and aspartate aminotransferase, to µkat/L, multiply by 0.0167; total bilirubin to µmol/L, multiply by 17.104.

**Table 2**

Typical Ascites Test Results Among the 3 Most Common Causes of Ascites

|                       | <b>SAAG<br/>(Threshold 1.1 g/dL)<sup>a</sup></b> | <b>Ascites Protein<br/>(Threshold 2.5 g/dL)<sup>a</sup></b> |
|-----------------------|--|---|
| Cirrhosis             | High   | Low   |
| Heart failure         | High   | High  |
| Peritoneal malignancy | Low  | High  |

Abbreviation: SAAG, serum-ascites albumin gradient.

<sup>a</sup>High indicates above threshold and low indicates below threshold.