Stanley Martin Cohen
Perica Davitkov *Editors*

Liver Disease
A Clinical Casebook

Springer

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Preface

The field of clinical hepatology has been rapidly advancing over the last several years. Much of this has been fueled by the extraordinary developments and treatments for viral hepatitis (especially hepatitis C). However, extensive research into all aspects of liver disease has provided significant insights and therapeutic developments and opportunities in a variety of liver-related conditions.

Liver disease is a common and often confusing medical issue that is frequently encountered in general clinical practice. There are a multitude of clinical manifestations seen with liver disease, especially in those patients with cirrhosis and portal hypertension. Because of this, caring for patients with liver disease can be somewhat overwhelming to the general care provider. Our goal with this book is to provide a systematic and logical approach to the diagnosis and treatment of patients with a variety of liver conditions.

In this clinical casebook, we have put together case-based presentations to go through a number of common clinical scenarios seen in patients with liver disease. The chapters each present a case and then pose a number of clinically relevant questions. The authors then answer the questions as a mechanism to describe the various liver conditions. Figures and tables have also been incorporated into the text to enhance the educational experience.

As the editors (as well as chapter authors) of this manuscript, we have had the honor and privilege of working with a large group of world-renowned authorities in the field of liver disease. Many of the chapter authors are leaders in their field and have been instrumental in developing the current, international diagnostic and

therapeutic guidelines. In addition, many of them are world-renowned researchers in the field of liver disease. We wish to acknowledge each and every one of the authors for their hard work. This book would not have been possible without their considerable time and effort.

We also wish to thank the publishers for their editorial and overall support.

Finally, we hope that this book provides the reader with a comprehensive review of liver disease and that it will serve as a valuable resource for providers caring for patients with liver disease.

Cleveland, OH, USA

Stanley Martin Cohen
Perica Davitkov

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Chapter 1
Drug-Induced Liver Injury

Dennis L. Shung and Joseph K. Lim

Introduction

Drug-induced liver injury (DILI) accounts for about 50% of acute liver failure cases in the United States. Diagnosis is challenging, especially due to the myriad combinations of potentially hepatotoxic medications and clinical presentations. Unexplained liver injury should prompt a thorough investigation of medication administration (e.g., for accidental or intentional overdose) and the use of herbal and dietary supplements. The framework for approaching DILI includes the following: (1) categorize the injury as either intrinsic or idiosyncratic, (2) establish time course and pattern of injury, and (3) triage effectively to minimize mortality risk.

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Clinical Case Scenario

A 75-year-old gentleman presented to his primary care physician with malaise and jaundice for several days. He has a history of hypertension, hyperlipidemia, and osteoarthritis. He had several joint surgeries in the past, primarily of the shoulder and knee. He takes atorvastatin, amlodipine, and as-needed Tylenol and ibuprofen. He had recently seen a homeopathic practitioner who had recommended taking silver therapy. Family history reveals no known history of liver disease or autoimmune disease. He denied tobacco, alcohol, or illicit drug use. He is married, is a retired former realtor, and has one adult son. His physical exam is notable for scleral icterus and mild tenderness in the right upper quadrant. He was alert and fully oriented, with no asterixis and no hyperreflexia. He has no stigmata of chronic liver disease. Initial labs revealed ALT 5169 U/L, AST 4494 U/L, alkaline phosphatase 70 U/L, total bilirubin 3.1 mg/dL, direct bilirubin 2.7 mg/dL, INR 1.4, and albumin 4.5 g/dL. CBC and kidney function were within normal limits.

Questions

1. What features would you use to triage the patient, and how would you risk stratify his liver injury?
2. Which medications are common culprits (especially in this case), and how do you differentiate DILI from other etiologies?
3. What are the patterns of liver injury and how do they relate to DILI?
4. What are the treatment options for this patient's presumed DILI?
5. When should a liver biopsy be obtained?

Discussion

Question 1. What features would you use to triage the patient, and how would you risk stratify his liver injury?

This patient presents with acute liver injury. It is important to differentiate acute liver injury from acute liver failure (ALF), since the latter requires emergent evaluation for transplantation. First determine if this is indeed a de novo liver injury with no previous signs of hepatic impairment (<26 weeks). Then, assess for signs of neurologic failure (asterixis, decreased mental status or confusion), multiorgan failure, and degree of coagulopathy (INR >1.5).

Dr. Hyman Zimmerman made the observation that patients with hepatocellular DILI and jaundice had high mortality of 10–40%. This has become known as "Hy's law." Furthermore, MELD score and coma grade on admission are the strong predictors of the need for liver transplantation, although prognostic scores are somewhat poor or rudimentary. Due to the extremely poor prognosis of ALF from DILI, liver transplantation may provide a rescue.

Question 2. Which medications are common culprits (especially in this case), and how do you differentiate DILI from other etiologies?

Exposure to known hepatotoxic medications should not preclude a thorough evaluation for other causes of acute liver injury since DILI remains a diagnosis of exclusion. These include acute ischemic hepatitis, malignancy with infiltration, Budd-Chiari syndrome, heatstroke, Wilson's disease (serum ceruloplasmin), acute hepatitis B (HBsAg and anti-HBcIgM), acute hepatitis A (HAV-IgM), and hemochromatosis (iron level, transferrin saturation, and

ferritin). If epidemiologically relevant, consider hepatitis E, hepatitis D coinfection, HSV, VZV, or EBV. Review for toxic exposures including Amanita mushroom poisoning. Less common but important diagnoses include autoimmune hepatitis and alpha-1-antitrypsin deficiency (ANA, anti-mitochondrial antibody, anti-LKM1, IgG levels, and alpha-1-antitrypsin phenotype).

When evaluating this patient, it is important to obtain a clear history of medication use including prescription medications, over-the-counter agents, and herbal supplements. In our patient, he is using acetaminophen as well as silver therapy, and he could be at risk for both intrinsic and idiosyncratic DILI. Intrinsic DILI is predictably dose-dependent and most commonly caused by acetaminophen, which our patient takes "as needed" for joint pain. With excessive acetaminophen use, labs would be expected to show extremely high aminotransferase elevation (>3500 IU/L). On biopsy, acetaminophen-induced liver injury would be expected to show a predominant centrilobular hepatocyte injury. As little as 3–4 gm/day of acetaminophen can cause acute liver injury (especially in patients using significant amounts of alcohol), although most ingestions have >10 gm/day. Idiosyncratic DILI has a less consistent relationship to dose and varies in its presentation depending on susceptibility of individuals. Other homeopathic remedies in this case are of particular concern, specifically silver, which in susceptible individuals can cause DILI.

Usually hepatotoxic drug reactions are characterized by rapid onset of malaise and jaundice, but each has its own pattern of injury (hepatocellular, cholestatic, or both). Allergic reaction are generally absent except in sulfa drugs (fever, rash, eosinophilia) and phenytoin (fever, lymphadenopathy, rash), and 20% of severe liver injury cases are idiosyncratic reactions.

Age and gender can also be associated with different susceptibility for DILI; in this patient's case, increased age can increase the risk of DILI from isoniazid, amoxicillin-clavulanate, and nitrofurantoin. For children, Reye's syndrome caused by aspirin-, valproate-, and propylthiouracil-induced liver injury is more common. Women appear to be at higher risk to have a DILI that appears as a chronic hepatitis resembling autoimmune hepatitis with minocy-

cline, methyldopa, diclofenac, nitrofurantoin, and nevirapine. Environmental (smoking, EtOH, infection/inflammation) and drug-related risk factors (dosage, metabolic profile, class effect/cross-sensitization, and polypharmacy) can also predispose a patient to idiosyncratic DILI.

A multitude of herbal remedies have been associated with DILI including germander, chaparral leaf, and usnic acid. Though statins have been associated with transient aminotransferase elevations, acute toxicity is rare. Livertox.nih.gov is a helpful website to look up the prevalence of drug-related liver injury for specific agents.

Question 3. What are the patterns of liver injury and how do they relate to DILI?

Usually, DILI occurs within the first 6 months of taking a new medication, although the latency can be variable. The R-value is the serum alanine aminotransferase/upper limit of normal (ULN) divided by alkaline phosphatase/ULN. $R > 5$ is considered hepatocellular, $R < 2$ cholestatic, and 2–5 "mixed." Hepatocellular liver injury refers to a predominant abnormality in aminotransferase levels. Aminotransferases include AST and ALT that are enzymes that transfer amino groups of aspartate and alanine to ketoglutaric acid. ALT is primarily present in the liver, while AST is present in cardiac and skeletal muscle, kidney, and brain tissue.

Cholestatic liver injury is characterized by a predominant abnormality in alkaline phosphatase and total and direct bilirubin. Alkaline phosphatase is a zinc metalloproteinase enzyme that catalyzes phosphate ester hydrolysis and is found in the canalicular membrane of the hepatocyte (not bile duct) as well as the bone, placenta, intestine, and kidney. It increases when bile ducts are obstructed due to increased canalicular synthesis and translocation to the sinusoid, but the other canalicular enzyme GGT can be used to confirm that the elevation is from the liver. Bilirubin is predominantly in its unconjugated form (indirect) and becomes

conjugated by UDP-glucuronosyltransferase to direct bilirubin that allows excretion into bile. Conjugated bilirubin elevations are present in both hepatocellular and cholestatic disorders due to impairment in bile flow but can be helpful for diagnosing significant obstruction. Elevation in indirect bilirubin is likely from another process, most commonly hemolysis.

See Table 1.1 for several medications and herbal products that can cause DILI, their latency period, and their typical pattern of liver injury.

Table 1.1 from Chalasani et al. AJG 2014 provides a breakdown of typical liver injury patterns

Medication	Latency	Typical pattern of injury/identifying features
Antibiotics		
Amoxicillin/clavulanate	Short to moderate	Cholestatic injury (but can be hepatocellular), DILI onset frequently detected after cessation
Isoniazid	Moderate to long	Acute hepatocellular injury (similar to viral hepatitis)
Trimethoprim/sulfamethoxazole	Short to moderate	Cholestatic injury (but can be hepatocellular)
Fluoroquinolones	Short	Variable
Macrolides	Short	Hepatocellular (but can be cholestatic)
Nitrofurantoin		
Acute form (rare)	Short	Hepatocellular
Chronic form	Moderate to long	Typical hepatocellular; resembles idiopathic autoimmune hepatitis
Minocycline	Moderate to long	Hepatocellular
Anti-epileptics		
Phenytoin	Short to moderate	Variable with immune-allergic features (fever, eosinophilia)
Carbamazepine	Moderate	Variable with immune-allergic features
Lamotrigine	Moderate	Hepatocellular with immune-allergic features
Valproate		
Hyperammonemia	Moderate to long	Elevated blood ammonia, encephalopathy

Table 1.1 (continued)

Hepatocellular	Moderate to long	Hepatocellular
Reyes-like syndrome	Moderate	Hepatocellular, acidosis
Analgesics		
Nonsteroidal anti-inflammatory agents	Moderate to long	Hepatocellular
Immune modulators		
Interferon-beta	Moderate to long	Hepatocellular
Interferon-alpha	Moderate	Hepatocellular; resembles autoimmune hepatitis
Anti-TNF agents	Moderate to long	Hepatocellular; resembles autoimmune hepatitis
Azathioprine	Moderate to long	Variable, can have portal hypertension due to VOD and NRH
Herbals and dietary supplements		
Green tea extract (catechin)	Short to moderate	Hepatocellular
Anabolic steroids	Moderate to long	Cholestatic
Pyrrolizidine alkaloids	Moderate to long	SOS/VOD
Flavocoxid	Short to moderate	Mixed
Miscellaneous		
Methotrexate (oral)	Long	Fatty liver, fibrosis
Allopurinol	Short to moderate	Variable, granulomas with immune-allergic features
Androgen-containing steroids	Moderate to long	Variable
Inhaled anesthetics	Moderate to long	Cholestatic
Inhaled anesthetics	Short	Hepatocellular
Sulfasalazine	Short to moderate	Variable
Proton pump inhibitors	Short	Hepatocellular; very rare

Question 4. What are the treatment options for this patient's presumed DILI?

There are no specific therapies or antidotes for the majority of drug-induced liver injury cases; the cornerstone is withdrawal of the offending medication. For acetaminophen, N-acetylcysteine (NAC) repletes glutathione, which is depleted after lipophilic drugs have been conjugated to glutathione and excreted into the kidney or GI tract. It is most effective within 1 h of ingestion, can be beneficial 3–4 h after ingestion, and can even be considered up to 48 h after ingestion. For non-acetaminophen early-stage ALF, NAC should be considered due to some evidence for improved transplant-free survival in early coma grade patients (52% with NAC vs 30% with placebo). Surprisingly, children should not receive NAC due to one trial demonstrating a lower rate of 1-year survival.

Overall, supportive care with antihistamines for symptomatic pruritus while undergoing a "washout" or "de-challenge" period can help elucidate the diagnosis. Typically, cholestatic DILI patterns usually take longer (up to 180 days) than hepatocellular DILI (60 days) to resolve.

Afterward, monitoring for chronic DILI (15–20% of cases) should be pursued to document complete resolution, particularly for patients with cholestatic liver injury.

Question 5: When should a liver biopsy be obtained?

Overall, for drug-induced liver injury, liver biopsy has low diagnostic yield. If the etiology is unclear, a biopsy can be considered specifically if you suspect an acute episode of autoimmune hepatitis with negative autoantibodies or there is a

previous history of cancer. However, if aminotransferases are persistently elevated despite cessation of potential culprit medications, a biopsy would be more helpful. Reasonable timeframes to consider liver biopsy include 60 days for predominantly hepatocellular liver injury and 180 days for predominantly cholestatic injury. Of note, a biopsy can also differentiate between viral infection and metabolic disease (e.g., Wilson's disease).

Patient Treatment Course

After obtaining a thorough history, the patient reported starting the silver therapy but self-discontinuing after 2 to 3 days due to progressive symptoms. He was taking high doses of acetaminophen, up to 10 extra-strength (500 mg) tablets daily due to worsening joint pain. His last dose of acetaminophen was the day prior to his visit. He was admitted to the inpatient ward and received NAC. His AST and ALT normalized rapidly with no long-term sequelae.

Conclusions

Drug-induced liver injury is an uncommon but important cause of acute liver injury and can lead to acute liver failure requiring transplantation. The most important clinical tools are obtaining a thorough history, excluding other causes of liver injury, withdrawing the offending agent, and providing supportive care including N-acetylcysteine. While idiosyncratic drug-induced liver injury has a wide variation in its presentation and outcome, the majority improve with cessation of the offending agent.

Further Reading

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Chapter 2
Acute Alcoholic Hepatitis

Sasan Sakiani and Arthur McCullough

Introduction

Alcohol-induced liver disease is the leading cause of chronic liver disease worldwide and remains the second most common cause of cirrhosis in the United States. Heavy alcohol use, which is defined by more than three drinks per day for men and more than two drinks per day for women for over 5 years, can lead to a broad range of chronic liver diseases, including steatosis (60–100% of patients), steatohepatitis and fibrosis (20–40% of patients), and eventually cirrhosis (10–20% of patients) and hepatocellular carcinoma (3–10%). Acute alcoholic hepatitis (AH) is a clinical diagnosis that is based on the development of jaundice and hepatocellular injury that occurs in 35–40% of patients with heavy alcohol use and has been associated with 20–50% mortality in untreated patients. In this chapter, we describe a case of a patient presenting with severe AH. We discuss diagnosis, prognosis, treatment options, and outcomes.

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Clinical Case Scenario

A 54-year-old male presents to the emergency room with a 1-week history of progressive jaundice and abdominal distention. He has a history of hypertension and arthritis. He denied any history of surgery. He takes occasional naproxen for chronic low back pain; otherwise he is not taking any over-the-counter, herbal products or prescribed medications. He typically drinks four to five beers per day after work and occasionally more on the weekends. He smokes half a pack a day. He has never had a blood transfusion. He denies any tattoos. He did experiment with IV drugs 30 years ago. He is married with two children and works as an accountant. His vital signs are BP 110/57, HR 105, RR 15, and temperature 36.7. His physical exam reveals significant jaundice and scleral icterus. He has multiple spider angiomas on his upper chest and back and a distended abdomen with protruding flanks. Labs performed in the emergency room reveal:

- ALT: 60 U/L
- AST: 130 U/L
- Alkaline phosphatase: 150 U/L
- Total bilirubin: 12 mg/dL
- Albumin 3.4 g/dL
- INR: 1.8
- Platelets: 95
- Hemoglobin 11.2
- MCV: 105
- Creatinine: 1.1 mg/dL
- Sodium: 134 mmol/L
- Hepatitis C antibody: negative
- Hepatitis B surface antigen: negative
- Hepatitis B surface antibody: positive
- Hepatitis A surface antibody: negative
- Antinuclear antibody (ANA): negative
- Smooth muscle antibody (SMA): negative

A right upper quadrant ultrasound shows a slightly enlarged liver with coarsened echotexture. The gallbladder is unremark-

able and there is no biliary dilation. There is also moderate ascites present within the abdomen.

He is admitted to the hepatology service for further management.

Questions

1. How is the diagnosis of acute alcoholic hepatitis made?
2. What is the prognosis of this patient?
3. What are treatment options for this patient?
4. Is liver transplantation an option for this patient?

Discussion

Question 1. How is the diagnosis of acute alcoholic hepatitis made?

The diagnosis of AH is mainly based on clinical presentation. Patients typically present with new or worsening jaundice in the setting of chronic, heavy alcohol use up to 8 weeks prior to presentation. This should not be confused with alcoholic steatohepatitis, which is the presence of fatty liver plus hepatic inflammation and fibrosis seen in patients with chronic excessive alcohol intake. However, AH can occur in any stage of alcoholic liver disease and 80% of patients presenting with AH may have underlying cirrhosis and thus can present with other complications of cirrhosis and sepsis.

Patients often present with non-specific symptoms such as fatigue, right upper quadrant abdominal pain, or loss of appetite along with new or worsening jaundice (see Table 2.1). Patients are often malnourished and may have evidence of sarcopenia. Other signs of chronic alcohol use and underlying advanced liver disease and portal hypertension may also be present, including spider angiomas, palmar erythema, splenomegaly, ascites, and hepatic encephalopathy. Hepatic encephalopathy should not be confused with alcohol withdrawal, which usually

Table 2.1 Signs and symptoms of alcoholic hepatitis

Nausea/vomiting
Abdominal pain (usually right upper quadrant and/or midepigastric)
Weakness
Anorexia
Malnourishment
Jaundice
Fatigue
Fever
Increased abdominal girth with ascites
Tender hepatomegaly
Hepatic encephalopathy
Bruit heard over the liver
Variceal bleeding
Stigmata of chronic liver disease Spider angiomata Palmar erythema Gynecomastia Parotid enlargement Increased venous collaterals across the anterior abdominal wall Dupuytren's contractures

involves more agitation, tremors, tachycardia, and even seizures. The presence of systemic inflammatory response syndrome (SIRS) features is also common and warrants investigation for potential sources of infection.

Laboratory findings in patients with AH include serum total bilirubin of greater than 3 mg/dL along with transaminases elevated greater than 1.5 times the upper limit of normal but usually less than 400 U/L. The AST to ALT ratio of greater than 1.5 helps differentiate this from other causes of hepatitis, although other causes of liver disease including biliary disease and drug-induced liver injury need to be ruled out. Although patients with AH often present with leukocytosis in the absence of infection, it is important to investigate all potential infectious etiologies. Serum albumin is often low and can be due to malnutrition, inflammation, or the severity of the underlying liver disease. The INR can be elevated on presentation for similar reasons. BUN can also be low in

patients with chronic alcohol use but can be elevated in patients presenting with renal failure or GI bleed. Other laboratory abnormalities include elevated serum creatinine, hyponatremia, hypokalemia, and hypomagnesemia.

The 2018 guidelines by the American College of Gastroenterology (ACG) have proposed three definitions and subtypes of AH:

1. *Definite* AH, in which there is histological confirmation of features of AH in a patient with a compatible clinical diagnosis
2. *Probable* AH, which is a clinical diagnosis based on heavy alcohol use for more than 5 years along with active alcohol use until 4 weeks prior to presentation, sudden onset or worsening of jaundice, AST/ALT ratio more than 1.5:1 with levels <400 IU/L, and the absence of other causes of liver disease
3. *Possible* AH, where the clinical diagnosis is uncertain due to another confounding etiology or unclear history of alcohol use

Patients presenting with possible AH may benefit from a liver biopsy to confirm the diagnosis. The characteristic histologic findings on a liver biopsy include macro-vesicular steatosis, ballooned hepatocytes, Mallory-Denk bodies, lobular infiltration of neutrophils, cholestasis, and fibrosis, which is often pericellular and sinusoidal. It is important to note that these findings are similar to those in nonalcoholic steatohepatitis (NASH), and thus the patient's history and other laboratory findings, such as those listed previously, may be helpful in distinguishing between the two. Also, as mentioned previously, many patients with AH may have underlying advanced liver disease or cirrhosis, and in these cases some of the features such as steatosis may not be prominent. When performing a liver biopsy, the transjugular approach is preferred given the increased risk of bleeding as well as the inability of patients to comply during a percutaneous liver biopsy.

Our patient has a clinical history and presentation that is typical for AH and thus he has probable AH. The ultrasound

does not show any evidence of biliary disease, although it does show some evidence of underlying cirrhosis. Other common causes of liver disease such as viral hepatitis, autoimmune hepatitis, and drug-induced liver injury have been ruled out as well. Therefore, a decision was made that he does not require a liver biopsy.

Question 2. What is the prognosis of this patient?

Depending on the severity, AH can have a mortality as high as 65%. The severity and prognosis typically depend on the number of organs systems involved and the underlying degree of liver disease. In addition, the degree of malnutrition plays a very important role in prognosis, with one study demonstrating mortality rates up to 80% in veterans with severe malnutrition. Having other concomitant diseases such as hepatitis C (HCV) or obesity also affect the prognosis, with one study demonstrating 20–25% higher mortality in those with concomitant HCV. As previously mentioned, up to 80% of patients who present with AH already have underlying cirrhosis, and those who are obese are two times more likely to have cirrhosis than nonobese individuals.

Several scoring systems have been used to help predict AH mortality, and many of these have demonstrated good predictive values for 30-day mortality (see Table 2.2). Unfortunately, they are less accurate for predicting mortality at 90-days or longer, as abstinence from alcohol remains the key factor for long-term survival. The most commonly used scoring system is the Maddrey discriminant function (MDF), which involves a calculation involving prothrombin time (PT) and total bilirubin. A score of $\geq$32 is associated with a 30-day mortality of 20–50% and has thus been used for initiating treatment with corticosteroids in patients with severe AH. However, the MDF relies on PT, for which normal values vary across different laboratories and is thus not universally consistent. On the other hand, the

Table 2.2 Prognostic clinical scoring systems for alcoholic hepatitis

Scoring system	Calculation formula	Severe disease indicator
Maddrey discriminant function	4.6 × [patient's prothrombin time (seconds) – control prothrombin time (seconds)] + bilirubin (mg/dL)	≥ 32
MELD (model for end-stage liver disease)	3.8 × $\log_e$ bilirubin (mg/dL) + 11.2 × $\log_e$ INR + 9.6 × loge creatinine (mg/dL) + 6.4	≥ 20
Glasgow alcoholic hepatitis score	Age < 50–1 point Age ≥ 50–2 points	≥ 9
	WBC < 15 K – 1 point WBC ≥ 15 K – 2 points	
	Urea <5 mmol/L – 1 point Urea ≥5 mmol/L – 2 points	
	INR < 1.5–1 point INR 1.5–2 – 2 points INR > 2–3 points	
	Bilirubin <125 μmol/L – 1 point Bilirubin 125–250 μmol/L – 2 points Bilirubin >250 μmol/L – 3 points	
	The total score is the sum of the above factors	
ABIC (age, bilirubin, INR, creatinine)	Age (years) × 0.1 + bilirubin (mg/dL) × 0.08 + creatinine (mg/dL) × 0.3 + INR × 0.8	> 9
Lille score	Calculator available at www.lillemodel.com	> 0.45

model of end-stage liver disease score (MELD), which has been shown to be comparable to the MDF in predicting 30-day mortality, uses INR rather than PT, making it consistent across laboratories. A score ≥ 20 has been associated with 20% mortality at 90 days. The MELD score has the added benefit of being used for liver transplant listing and has become increasingly utilized in prognosticating AH.

Other scoring systems include the ABIC (age, bilirubin, INR, and creatinine) score, the Glasgow score, and the Lille

score. The ABIC score is similar to the MELD score with the addition of age as a variable and has been shown to be comparable to the MDF and MELD. The Glasgow score utilizes age, WBC, urea, INR, and bilirubin and may also be useful to determining which patients benefit from the use of corticosteroids, although it is not widely utilized in the United States. The Lille score, which uses age, albumin, creatinine, PT, and bilirubin at days 1 and 4 (originally day 7), has been shown to predict response to corticosteroids when the score is less than 0.45. In addition, the combination of MELD at baseline and Lille score has been shown to be the most effective for predicting 2-month and 6-month mortality.

In addition to these scoring systems, other biomarkers such as serum lipopolysaccharide levels and SIRS criteria are helpful in predicting mortality. In particular, the presence of SIRS criteria on admission predisposes to acute kidney injury and the development of hepatorenal syndrome, as well as multi-organ failure.

Our patient has a MELD score of 25 and an MDF greater than 32. Using these criteria, our patient has severe AH with at least 20% mortality at 30 and 90 days and may benefit from corticosteroids.

Question 3. What are treatment options for this patient?

While mild cases of AH often improve with supportive care, treatment options for AH remain limited, with long-term mortality in severe AH remaining as high as 30–40% despite treatment. Patients with severe AH should be admitted with the initiation of general supportive care measures as well as for the work-up for underlying infectious etiologies, particularly if SIRS criteria are present. For hypotensive patients, volume replacement with albumin is generally preferred over crystalloids.