Stanley Martin Cohen
Perica Davitkov *Editors*

Liver Disease
A Clinical Casebook

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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

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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