

Acute Exacerbation of Chronic Hepatitis B

Volume 2. Diagnosis
and Management

Qin Ning
Editor

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Foreword

Acute-on-chronic liver failure (ACLF) secondary to hepatitis B virus infection is now recognized as an important worldwide life-threatening disease with a high mortality. The work described in this book by experts in the field provides important information to the reader on its pathogenesis, clinical manifestations and current and future management strategies.

The work provides important new advances in the science of HBV replication and the host response. With major advances in our understanding of the virology and immunology of HBV infection, this book gives reason for cautious optimism that we will soon be able to provide exciting new therapies for this disorder.

To date, with the exception of liver replacement therapy (transplantation), there are few therapeutic options for patients who develop ACLF secondary to HBV. However, advances in diagnosis as well as management strategies including introduction of antiviral agents and inhibitors of pro-inflammatory cytokines offer the hope of better short- and long-term outcomes.

The advances in the basic science of ACLF and the development of small animal models outlined in this book give hope that new therapeutic approaches will lead to the control or eradication of HBV and amelioration of inflammatory disease lessening the need for liver transplantation.

The work described in this book strongly supports that clinical research in ACLF should build on the findings of basic science research and be directed to carefully controlled studies with well-characterized cohorts of patients so that we can evaluate the potential of new therapeutic approaches. The use of exciting new approaches detailed here will not only provide important new therapeutics but also insights into the mechanism of disease. The findings described in this book strongly support that we are approaching an exciting new era for therapy for patients with ACLF.

Toronto, ON

Gary Levy



Preface

It is now recognized that as a consequence of chronic HBV infection, many patients with or without established cirrhosis will develop acute decompensation and multi-organ failure, a syndrome known as acute-on-chronic liver failure (ACLF). Once patients develop ACLF, they are at high risk of death. A number of triggers including reactivation of HBV, coinfection of hepatitis A or E virus, onset of bacterial infection, gastrointestinal bleeding and development of renal dysfunction can precipitate the development of ACLF in patients who have been previously stable. ACLF is prevalent in Asia where many patients have incubative chronic hepatitis B virus (HBV) infection.

For the past decade, with an increasing understanding of the disease mechanisms and improved general internal medications, the overall mortality has significantly decreased due to HBV infection-related ACLF (HBV-ACLF) in Chinese patients. Here we have assembled a group of hepatologists and scientists from academic hospitals and universities to explore the current understanding of the clinical, genetic, virologic and immunologic factors that contribute to ACLF. In this book of 12 chapters, we have explored the current state of knowledge of HBV infection with a specific focus on the natural history and the clinical course to define important host and viral factors to the development of ACLF, sharing our profound experience and clinical procedures in early diagnosis and treatment of HBV-ACLF patients and its complications. All together about 2649 references have been cited, of which 754 were since 2012. At the beginning of the book, there is a complete table of contents, which together with the general index makes it possible for the reader to find specific topics easily. In each chapter, there is an abstract for the reader to gain a quick information of the chapter. We have also used 55 coloured figures to make the illustrations even more visual.

We enlisted the helpful advice of friends, colleagues and senior experts to supplement or confirm our own interpretations. The contacts arising from these discussions have been immensely benignant to me. Here my special thanks to Prof. Gary Levy, Prof. Didier Samuel, Prof. Gyongyi Szabo, Prof. Lanjuan Li, Prof. Zhimeng Lu, Prof. Shiv Kumar Sarin, Prof. Stephen Locarnini, Prof. Xinhua Weng, Prof. Yuquan Wei and Prof. Hui Zhuang.

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Wuhan, China

Qin Ning

A handwritten signature in black ink, consisting of stylized Chinese characters, likely 'Qin Ning'.

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Introduction

This book assembles recent achievements in both basic research and clinical management in the field of hepatology, virology, and immunology. It provides up-to-date information for clinicians who can apply the relevant knowledge to their daily clinical practice and for researchers who are interested in clinically orientated studies. The updated and detailed technology and state-of-the-art treatment strategies provided in this book serve as references for clinicians and resident physicians in the daily management of ACLF. The rationality and strategies for basic research as well as patient management in this book can also be a valuable reference for other fatal and end-stage liver diseases than HBV-induced ACLF.

This Volume 2 has six chapters and focuses on its diagnosis and management.



Clinical Manifestations and Laboratory Tests of AECHB and Severe Hepatitis (Liver Failure)

1

Liang Peng, Zhi-Liang Gao, Yu-Ming Wang, Deng-Ming He, Jin-Ming Zhao, Xue-Fan Bai, and Xiao-Jing Wang

Abstract

This chapter describes the clinical symptoms and signs of AECHB and HBV ACLF, classification, grading of HBV ACLF and their features, diagnostic principles and standards in liver pathology, biochemistry, and virology of HBV ACLF.

1. Liver failure is defined as serious damage to the liver cause by a variety of etiologies, leading to liver function disorder or even decompensation, and clinical syndromes with coagulopathy, jaundice, hepatic encephalopathy, and ascites.
2. Severe hepatitis B can be indicated pathologically by apparent hepatocellular necrosis, including extensive multifocal, confluent, bridging, sub-massive or massive necrosis.
3. Laboratory tests during the course of severe exacerbation of chronic hepatitis B can reflect pathological changes and liver function in a timely manner, providing objective and informative reference data for evaluation of disease severity and

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treatment efficacy. Among the most important laboratory tests are those for prothrombin activity, international normalized ratio, and increases in total bilirubin concentration.

4. Severe hepatitis B is associated with interactions between the virus and host factors. Detection of HBV DNA, HBV genotype, quasispecies and HBV mutation can provide important theoretical bases for the prevention, control or mitigation of the progress of severe hepatitis B.
5. Noninvasive imaging modalities can be used to visualize the entire liver and parts of it. Measuring liver volume to evaluate liver size and liver reserve capacity is regarded as important in diagnosis, surgical approach and prognostic evaluation of patients with severe exacerbation of chronic hepatitis B and liver failure.
6. Model for End-Stage Liver Disease (MELD) is the first quantitative method developed to assess whether a patient with liver failure requires a liver transplant. The predictive value of the MELD model has been improved by the MELD-Na, iMELD, and MESO models. Several other valuable prognostic models have been developed. For example, for patients with HBV-ACLF, the established TPPM scoring system was found to be more predictive than MELD score.

1.1 Clinical Manifestations of Hepatitis B Aggravation and Severe Hepatitis (Liver Failure)

Liang Peng, ZL Huang, YY Mei and Zhi-Liang Gao

1.1.1 Definitions and Clinical Classifications of Severe Hepatitis and Liver Failure

Currently, both clinical and pathophysiological diagnoses are made of severe hepatitis (liver failure) in China. According to the Guideline for the Prevention and Treatment of Viral Hepatitis (2000), severe hepatitis is classified as acute severe hepatitis, subacute severe hepatitis, and chronic severe hepatitis.

Acute severe hepatitis is initially diagnosed due to acute jaundice that rapidly progresses to liver failure within 2 weeks. Subacute severe hepatitis can be identified in patients with acute jaundice hepatitis that progresses to liver failure anywhere from 15 days to 24 weeks. Chronic severe hepatitis often develops with pre-existing chronic liver diseases. The clinical manifestations of chronic severe hepatitis are similar to those of subacute severe hepatitis in some patients, or, in some patients, appear similar to decompensated cirrhosis at disease onset. The diagnostic criteria for severe hepatitis in China remain to be fully developed and hence have not been introduced internationally.

To meet the clinical requirements and standardize the diagnosis and therapy of liver failure, the Branch of Infectious Diseases and the Branch of Hepatology of