Pathology of the Bile Duct
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About two to three decades ago, the diseases of the bile ducts, particularly the intrahepatic large bile duct and extrahepatic bile ducts, were mainly caused by infectious agents, gallstones, and malignancies, frequently associated with biliary obstruction, and these diseases were mainly dealt by surgeons therapeutically. However, in the recent two decades, the medical and pathological scopes of nonneoplastic and neoplastic diseases of these bile ducts have been much expanded and are now vigorously expanding. Particularly, imaging modalities and interventional and medical approaches to these biliary diseases have explosively advanced in these fields. In addition, with the emergence of several novel diseases such as IgG4-related sclerosing cholangitis and the discovery of preinvasive lesions of cholangiocarcinoma, new clinical and research approaches in biliary diseases have been explored. In addition, the discovery of peribiliary glands along the biliary tree and subsequent studies have caused diverse and exciting studies in this new field. Furthermore, several basic pathophysiologies of the biliary tree such as defense mechanisms, cellular senescence, innate immunity, and autophagy have been advanced and are actively being applied to the evaluation of the pathophysiologies of the bile ducts.

Accordingly, the roles of pathologists for diagnosis of these biliary diseases and for the evaluation of their pathogenesis have increased rapidly, and pathological knowledge and experiences are accumulating extensively. Many excellent clinical and basic research papers have been published and are being published in this field. So currently, the need for a comprehensive and concise pathology book covering recently accumulated pathological knowledge and experiences written in English is urgent and mandatory for pathologists and clinicians and basic scientists. There are a considerable number of excellent and concise pathology books of the liver and also of the pancreas available in bookshops, universities and hospital libraries, laboratories, and your room. However, there have been no pathology textbooks of bile ducts available at any place. At this most important and urgent time, Pathology of the Bile Duct has been just published.

This book is composed of 16 chapters, and these chapters are divided into two parts: basic understanding of bile duct pathology and practical understanding of biliary diseases. The former are composed of five chapters. In Chap. 1, recent
Preface

progress of bile duct embryology and anatomy including peribiliary glands is concisely described. This chapter is very important for understanding the other chapters. The biliary tree is constantly exposed to the bile containing many diverse and potentially toxic materials secreted from the hepatocytes and is also potentially exposed to the contents of the intestine which is continuous with the external world. So, the biliary tree is equipped with many elaborate defense mechanisms against toxic bile acids and other constituents and also possibly regurgitates hostile materials from the intestine. First, the bile ducts have a unique bicarbonate umbrella system against toxic bile acids and also an innate immune system to biliary constituents and also possibly regurgitate pathogens and antigenic materials. These defense issues are precisely described in Chaps. 2 and 3. Disturbances of these defense systems can also be involved in many biliary diseases. In Chap. 4, basic aspects of cell injuries of bile duct epithelia, particularly cellular senescence and cell death, are described, and the participation of the role of autophagy in these cell injuries is also referred. Autophagy is a topic of science at present, and in 2016, a Japanese researcher of autophagy, Dr. Osumi, got a Nobel Prize. In Chap. 5, the blood supply to the biliary system and its disturbance are described. The biliary tree is equipped with a characteristic blood supply, and this is a reason why several unique biliary diseases with ischemic change develop, and the pathologies of bile ducts and accompanying blood vessels are described in these diseases.

From Chaps. 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and 16, practical pathologies of biliary diseases are described. First, pathologies and pathogeneses of three representative immune-related biliary diseases such as primary biliary cholangitis, primary sclerosing cholangitis, and IgG4-related sclerosing cholangitis are described. These three types of biliary diseases have been much studied in these two decades, and particularly, IgG4-related sclerosing cholangitis is a newly discovered biliary disease. Primary biliary cholangitis has been extensively studied by immunopathologists, and Dr. Tsuneyama is one of the most diligent and productive persons in this field and has contributed much to the understanding of immune-mediated destruction of the bile duct in primary biliary cholangitis. The discovery of peribiliary glands along the biliary tree was a historic event, and subsequent studies have contributed much to the novel pathophysiological world of the biliary tree. The discovery of the relation between peribiliary cysts and peribiliary glands is one of the most fruitful products, and this field is described by referring to radiological findings in Chap. 9. Roles of innate immunity and viral infection have been reported to be important in the development of biliary atresia, and these are described with reference to peribiliary glands by Dr. Harada in Chap. 10. The role of epithelial-mesenchymal transition in the biliary fibrosis in biliary atresia is also explained with reference to the disordered innate biliary immunity.

From Chaps. 11, 12, 13, 14, 15 and 16, biliary neoplasms, which have been recently studied and discussed actively, are concisely and precisely described. Among them, cholangiocellular carcinoma is a difficult neoplasm which at one time belonged to intrahepatic cholangiocarcinoma and at other times belonged to combined hepatocellular cholangiocarcinoma. Many years ago, this carcinoma was an independent biliary neoplasm different from cholangiocarcinoma or hepatocellular
cancer. Dr. Kondo described its history and present and future in Chap. 11. So, readers will understand this puzzling neoplasm. Recent reclassification of cholangiocarcinoma into intrahepatic, perihilar, and distal cholangiocarcinoma is now accepted worldwide. However, it remains uncertain for many pathologists how to diagnose cholangiocarcinoma arising in the intrahepatic large bile ducts, and its relation to perihilar cholangiocarcinoma and peripheral intrahepatic cholangiocarcinoma is a dilemma. In Chap. 12, Dr. Aishima gave clear guidance for these questions which many pathologists have. Intraductal papillary neoplasm of bile duct, hepatic mucinous cystic neoplasm, biliary intraepithelial neoplasm, and intraductal papillary cystic neoplasm of the gallbladder and ampulla of Vater were introduced by the 2010 WHO Classification of Tumours of the Digestive System as a preinvasive neoplastic lesion of the bile duct, gallbladder, and ampulla of Vater, and these preinvasive lesions are eventually followed by invasive carcinomas. These preinvasive neoplasms are conceptually very new and very important and also useful for practical clinical and pathological fields, and the pathologies of these preinvasive lesions are very clearly described in these four chapters. Particularly, recent clinical progresses make it possible to discover these preinvasive neoplastic lesions preoperatively. As the invasive biliary cancers are still an intractable malignant disease with high mortality, it is urgent to discover these neoplasms at the preinvasive stage, and in this context, these chapters are mandatory for clinicians and pathologists dealing with these malignant disorders.

Biliary pathophysiologies including pathologies of the bile ducts are one of the rapidly growing clinical and pathological and research fields, and we are delighted to compile a current collection of the knowledge and experience pertaining to this field in this book Pathology of the Bile Duct. We anticipate the next decade to be as exciting and productive as the past two decades. In this context, we hope this book may contribute much to the progress of biliary pathophysiology in the next decades.

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Acknowledgment

Although the limitation of space prevents us from thanking individually our collaborators and also other many pathologists, clinicians, and researchers who have contributed much in various ways to the progresses of the pathology of bile ducts, we would like to gratefully acknowledge the works of all these persons. Their discoveries, experiences, and practices are crystallized in this book Pathology of the Bile Duct. We also appreciate all editors who made possible the completion of the English version of this book. We strongly hope that this book will be useful and important and deliver numerous and latest informations on pathologies of bile ducts to the world.
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