A Case-Based Guide to Neuromuscular Pathology

Lan Zhou
Dennis K. Burns
Chunyu Cai
Editors

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Editors
Lan Zhou
Departments of Neurology
and Pathology
Boston University Medical Center
Boston, MA
USA

Chunyu Cai
Department of Pathology
University of Texas Southwestern
Medical Center
Dallas, TX
USA

Dennis K. Burns
Department of Pathology
Neuropathology Section
University of Texas Southwestern
Medical Center
Dallas, TX
USA

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To my family members, husband Ming, and daughters Grace and Rebecca, for their love, encouragement, and support.

Lan Zhou, MD, PhD

To my wife Carol, my daughter Kelly, and my son Evan, for their enduring love and support.

Dennis K. Burns, MD

To Jade.

Chunyu Cai, MD, PhD

Preface

We present this book, *A Case-Based Guide to Neuromuscular Pathology*, to neurologists, pathologists, and other practitioners who take care of patients with neuromuscular diseases.

Biopsy of skeletal muscle and peripheral nerve with histopathological interpretation is frequently requested by neurologists to evaluate patients with myopathies and neuropathies as a part of the clinical workup and management. Muscle biopsy plays an important role in the diagnosis and classification of inflammatory myopathies, metabolic myopathies, congenital myopathies, muscular dystrophies, and toxic myopathies. Nerve biopsy is essential for diagnosing vasculitic neuropathy, amyloid neuropathy, infectious neuropathies, and neuropathies caused by malignant cellular infiltration of nerves. Although muscle and nerve biopsies are less frequently performed in the era of molecular testing, biopsies are still useful in many cases, as the sensitivity of many genetic tests in identifying pathological mutations in hereditary myopathies and neuropathies is not high. Moreover, biopsies can be extremely valuable in the initial characterization of some myopathies and neuropathies and can be used to direct subsequent genetic testing for specific hereditary myopathies and neuropathies. In addition, skin biopsy for the evaluation of intraepidermal nerve fiber density has emerged as the gold standard for diagnosing small fiber neuropathy and has been increasingly utilized by neuromuscular specialists.

This book covers the entire spectrum of neuromuscular pathology including skeletal muscle, peripheral nerve, and skin biopsies with biopsy interpretation. It comprises three parts. Part 1 uses three introductory chapters to review muscle, nerve, and skin biopsy indications and procedures, biopsy specimen handling and processing, utility of individual stains, normal muscle and nerve histology, and common muscle and nerve pathology. The 28 myopathy case chapters in Part 2 and 11 neuropathy case chapters in Part 3, collected from our practice over many years, illustrate the clinical and pathological features of these entities, demonstrate the indications and utilities of biopsies, discuss clinical and pathological differential diagnosis, update the individual disease management, and summarize pertinent clinical and pathology pearls for each case.

This book is intended to help neurologists understand the utility of muscle, nerve, and skin biopsies, correctly order these biopsies, become more familiar with neuromuscular pathology, perform clinical and pathological correlations, and make sound clinical decisions for management of patients with neuromuscular diseases based on biopsy findings. The book will help neurology residents and neuromuscular fellows answer questions related to the muscle and nerve pathology in their in-service and board exams. It is our hope that this book will also benefit neuromuscular pathologists and trainees as they correlate morphological alterations in muscle and nerve biopsies with clinical presentations and communicate their findings to clinical colleagues caring for patients with neuromuscular disorders.

We are enormously grateful to the authors of this book, who are experienced neuromuscular specialists and neuropathologists with sophisticated knowledge and expertise in neuromuscular medicine and pathology. We thank Springer for publishing this book, and thank Michael Wilt and other members in Springer for their excellent editorial support.

Boston, MA, USA — Lan Zhou
Dallas, TX, USA — Dennis K. Burns
Dallas, TX, USA — Chunyu Cai

Contents

Contributors

Rahul Abhyankar, MD Department of Neurology & Neurotherapeutics, University of Texas Southwestern Medical Center, Dallas, TX, USA

Dennis K. Burns, MD Departments of Pathology, Neuropathology Section, University of Texas Southwestern Medical Center, Dallas, TX, USA

Chunyu Cai, MD, PhD Department of Pathology, University of Texas Southwestern Medical Center, Dallas, TX, USA

Ryan Castoro, DO, MS Department of Physical Medicine and Rehabilitation, Vanderbilt University Medical Center, Nashville, TN, USA

Diana P. Castro, MD Department of Neurology and Neurotherapeutics, University of Texas Southwestern Medical Center, Children's Medical Center of Dallas, Dallas, TX, USA

Shan Chen, MD, PhD Peripheral Neuropathy Center, Rutgers University, Robert Wood Johnson Medical School, New Brunswick, NJ, USA

Jeffrey L. Elliott, MD Department of Neurology and Neurotherapeutics, University of Texas Southwestern Medical Center, Dallas, TX, USA

Partha S. Ghosh, MD Department of Neurology, Boston Children's Hospital, Boston, MA, USA

Elisabeth Golden, MD Department of Neurology and Neurotherapeutics, University of Texas Southwestern Medical Center, Dallas, TX, USA

Michelle Kaku, MD Department of Neurology, Boston University Medical Center, Boston, MA, USA

Shaida Khan, DO Department of Neurology and Neurotherapeutics, University of Texas Southwestern Medical Center, Dallas, TX, USA

Patrick Kwon, MD Department of Neurology, New York University Langone–Brooklyn, New York, NY, USA

Jun Li, MD, PhD Department of Neurology, Wayne State University School of Medicine and Detroit Medical Center, Detroit, MI, USA

Hart G. W. Lidov, MD, PhD Department of Pathology, Boston Children's Hospital, Boston, MA, USA

Lingchao Meng, MD Neuromuscular Division, Department of Neurology, Peking University First Hospital, Beijing, China

Susan Morgello, MD Departments of Neurology, Neuroscience, and Pathology, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Rajeev Motiwala, MD Department of Neurology, New York University, New York, NY, USA

Sharon P. Nations Department of Neurology & Neurotherapeutics, University of Texas Southwestern Medical Center, Dallas, TX, USA

Dustin Jacob Paul, DO, MA Department of Neurology and Neurotherapeutics, University of Texas Southwestern Medical Center, Dallas, TX, USA

Susan C. Shin, MD Department of Neurology, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Kara Stavros, MD Department of Neurology, Warren Alpert Medical School of Brown University, Rhode Island Hospital, Providence, RI, USA

Laura K. Stein, MD Department of Neurology, Ichan School of Medicine at Mount Sinai, New York, NY, USA

Jaya R. Trivedi, MD Department of Neurology & Neurotherapeutics, University of Texas Southwestern Medical Center, Dallas, TX, USA

Yun Yuan, MD Neuromuscular Division, Department of Neurology, Peking University First Hospital, Beijing, China

Lan Zhou, MD, PhD Departments of Neurology and Pathology, Boston University Medical Center, Boston, MA, USA

Part I
Introduction to Neuromuscular Pathology Evaluation

Chapter 1
Skeletal Muscle Biopsy Evaluation

Dennis K. Burns

Introduction

First introduced into clinical practice in the middle decades of the nineteenth century, muscle biopsies have played an integral role in the diagnosis and treatment of patients with neuromuscular diseases for well over a century. The interpretation of morphological changes in skeletal muscles, supplemented by enzyme histochemical and immunohistochemical stains are now regularly integrated with molecular analyses to provide physicians with an unprecedented understanding of the pathogenesis and phenotypic complexities of neuromuscular diseases. Although advances in molecular diagnoses have eliminated the need for muscle biopsies in some disorders, in many conditions, biopsies continue to provide information not readily obtainable by other methods.

Muscle Biopsy Acquisition

There are three important aspects of muscle biopsy acquisition: selecting the proper muscle, obtaining an adequate amount of tissue, and minimizing artifacts.

The importance of selecting the right muscle for biopsy cannot be overemphasized. Skeletal muscles are not equally affected by a given disease process. While the majority of myopathies predominantly affect proximal limb muscles, a few preferentially involve distal limb, trunk, or facial muscles. In order to maximize the diagnostic yield of a muscle biopsy, it is important to carefully select the biopsy site. Selection of the biopsy site can be challenging and should be done in close consultation with the

D. K. Burns (✉)
Department of Pathology, Neuropathology Section, University of Texas Southwestern Medical Center, Dallas, TX, USA
e-mail: dennis.burns@utsouthwestern.edu

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