Myotonic Dystrophy

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Editors

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Disease Mechanism, Current Management and Therapeutic Development

Springer

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ISBN 978-981-13-0507-8 ISBN 978-981-13-0508-5 (eBook)
https://doi.org/10.1007/978-981-13-0508-5

Library of Congress Control Number: 2018957705

Printed on acid-free paper

This Springer imprint is published by the registered company Springer Nature Singapore Pte Ltd.
The registered company address is: 152 Beach Road, #21-01/04 Gateway East, Singapore 189721, Singapore

Preface

Myotonic dystrophy (DM) is an uncharacteristic form of muscular dystrophy. Despite being a type of muscular dystrophy, the distribution of the affected muscles in DM greatly differs from that of general muscle disorders, which usually affect proximal muscles. The myotonic phenomenon, from which the disease's name is derived, is another cardinal feature. In addition, this condition not only involves the skeletal muscles, but also affects various organs throughout the body. This makes the overall clinical features of individual patients difficult to detect even for neuromuscular specialists. However, the multi-organ nature of the condition means that clinicians from various medical specialties may encounter it. Furthermore, patients are sometimes unaware of their symptoms and problems, which may prevent them from receiving appropriate care and lead to unexpected complications.

Along with other forms of muscular dystrophy, the understanding of DM pathology has greatly advanced since the discovery of its responsible genes. In 1992, the first genetic cause was identified as an abnormal expansion of CTG repeats located at the 3′-untranslated region of the *DMPK* gene. It was subsequently revealed that the second type of DM, DM2, is caused by the similar abnormal expansion of CCTG repeats located in intron 1 of the *CNBP* gene. The finding that similar clinical feature was caused by abnormal repeats in the untranslated region of two different genes, and also observed in experimental animals that expressed expanded repeats, has led to the notion that DM is caused by abnormal RNA. It was further shown that disruption of normal RNA regulation (splicing) in various genes occurs in DM, leading to the failure of multiple organs, even though the disease is caused by only one gene. Such deeper understanding of the underlying disease mechanisms prompted the therapeutic development and clinical trials that are currently being planned and implemented.

In the era of translational medicine, awareness of the importance of understanding DM and establishing a standardized approach to medical care has increased. It is essential to understand the burden and natural history of the disease and to accurately evaluate the effects of intervention. Furthermore, a comprehensive evaluation of therapeutic efficacy and adverse effects would become considerably difficult if the complications are not accurately recognized and addressed during routine

clinical practice. An accurate understanding of the overall picture of DM is required for both determining what is the optimal current strategy and how we can expand the therapeutic armamentarium in the future.

In Japan, a multidisciplinary approach to muscular dystrophy management has been in place for more than half a century. Clinical research has been extensively carried out at a specialized ward established at the National Hospitals with central involvement of the research consortium supported by the Ministry of Health, Labour and Welfare. As a result of this multidisciplinary approach, which includes respiratory and myocardial protection therapy, patients with Duchenne muscular dystrophy have experienced a marked improvement in their survival prognoses and ability to carry out their daily activities. While extensive clinical research on DM has also been conducted, awareness of its results by overseas audiences is low since most of them are reported in Japanese.

We believe that it is timely that a book by 13 Japanese experts that covers the results of clinical research on DM in Japan and the latest insights regarding disease mechanism, functional impairment, and disorders of various organs be published. We would like to express our deep appreciation of the authors as well as other colleagues and collaborators who contributed to the publishing of this book and hope that it will help clinicians and researchers to acquire a more comprehensive understanding of DM.

Finally, we would like to mention that many of the authors of this book have been mentored by the late Dr. Mitsuru Kawai, the former director of NHO Higashisaitama National Hospital, via the aforementioned research groups and similar academic activities. He was a great clinician and also an excellent mentor of ours. He translated *Myotonic Dystrophy* by Professor Peter Harper for Japanese patients and their families. He always taught us to keep exploring what we can do for patients as clinicians. Dr. Kawai's passing in 2016 was a huge loss to the Japanese muscular dystrophy healthcare community. It is our mission to continue his work through our consistent efforts, and it is in Dr. Kawai's memory that we would like to offer this book with our thoughts and gratitude.

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February 2018

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