REVIEWS

Inclusion body myositis: clinical features and pathogenesis

Steven A. Greenberg^{1,2,8}

Abstract | Inclusion body myositis (IBM) is often viewed as an enigmatic disease with uncertain pathogenic mechanisms and confusion around diagnosis, classification and prospects for treatment. Its clinical features (finger flexor and quadriceps weakness) and pathological features (invesion of myofibres by cytotoxic T cells) are unique among muscle diseases. Although IBM T cell autoimmunity has long been recognized, enormous attention has been focused for decades on several biomarkers of myofibre protein aggregates, which are present in <1% of myofibres in patients with IBM. This focus has given rise, together with the relative treatment refractoriness of IBM, to a competing view that IBM is not an autoimmune disease. Findings from the past decade that implicate autoimmunity in IBM include the identification of a circulating autoantibody (anti-cN1A); the absence of any statistically significant genetic risk factor other than the common autoimmune disease 8.1 MHC haplotype in whole-genome sequencing studies; the presence of a marked cytotoxic T cell signature in gene expression studies; and the identification in muscle and blood of large populations of clonal highly differentiated cytotoxic CD8* T cells that are resistant to many immunotherapies. Mounting evidence that IBM is an autoimmune T cell-mediated disease provides hope that future therapies directed towards depleting these cells could be effective.

Inclusion body myositis (IBM) is a slowly progressive skeletal muscle disease with unique clinical and pathological features (including finger flexor and quadriceps weakness and the presence of infiltrating cytotoxic T cells in muscle). In patients with IBM, the onset of symptoms of muscle weakness typically occurs between 45 and 70 years of age, and progression is insidious. The combination of slow progression towards disability and the lack of any reliable treatment to reverse the disease course results in a substantial unmet medical need.

IBM lies within the category of inflammatory myopathies. This category started with the single member. polymyositis, in 1887 (FEFS) and has since undergone repeated subdivision (FIG. 1). Dermatomyositis was recognized as a separate entity early in 1891 (8EFS15). but it took almost a century before the next refinement, IBM, was adequately recognized in 1978 FHF 1. Immune-mediated necrotizing myopathy (IMNM) was distinguished in 1991 (HEFT). Advances continue to reduce the remaining category of polymyositis', splitting off non-specific myositis' (or unclassified myositis') and virtually eliminating the term polymyositis from what once constituted the entire category of inflammatory myopathies. The generally accepted scheme currently consists of five members (polymyositis, dermatomyositis, IBM, IMNM and non-specific myositis)(1) plus other rare entities (such as granulomatous myositis

and macrophagic myofasciitis). Further subdivision of dermatomyositis into distinct syndromes associated with specific autoantibodies is currently an active area of research".

Many excellent general IBM reviews have been published over the past 5 years and some have focused specifically on the pathogenesis. This Review discusses IBM generally, with a focus on some of the more confusing areas around nomenclature and clinical features, and addresses key questions regarding its pathogenesis.

History of IBM

A historical perspective provides some insight into what has shaped our current understanding of IBM #16 II. It was first viewed as a form of polymyositis resulting from chronic viral infection of muscle in 1967 #10 II. It leading to an ongoing line of research directed towards the identification of a persistent muscle viral infection. The mame inclusion body myositis is derived from a 1971 single case report entitled 'Inclusion body myositis' that described a 26-year-old patient with a limb-girdle pattern of weakness and quadriceps sparing with onset at age 18 years (which is not the disease we now call IRM).

The first IBM clinical case series was published in 1978 and described patients with a distinct form of inflammatory myopathy characterized by prominent

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<u>Inclusion Body Myositis</u> William Tillier,2022 *Inclusion-Body Myositis and Myopathies* Valerie Askanas, Georges Serratrice, W. King Engel, 1998-04-13 Inclusion body myositis IBM is now understood to be an important degenerative muscle disease The sporadic type s IBM is probably the most common muscle disease among those ailments that strike first in adulthood particularly people over 50 The hereditary type h IBM affects younger patients This book is devoted entirely to s IBM and h IBM Contributors discuss what is understood about the basic scientific foundations of IBMs the varied aspects of the pathology of IBMs and the application of clinical treatments One particular emphasis of the book is on the hereditary aspects of IBM and genetic predispositions to the disease **Inclusion Body Myositis** .2014 **Inclusion-body** myositis: clinical and pathologic aspects, and basic research potentially relevant to treatment American Academy of Neurology, 2006 Coping with a Myositis Disease James R. Kilpatrick, 2000-09-01 Patients with dermatomyositis DM polymyositis PM inclusion body myositis IBM and juvenile dermatomyositis JDM present a personal look at life with these Inclusion Body Myositis Umesh Arvind Badrising, 2006 Inclusion Body Myositis Marinos C. Dalakas, W. King diseases Myouclear Breakdown in Sporadic Inclusion Body Myositis Satoshi Nakano, 2011 Myouclear Breakdown in Engel,2006 The Official Patient's Sourcebook on Transverse Myelitis Icon Health Sporadic Inclusion Body Myositis Publications, 2002-10-01 This sourcebook has been created for patients who have decided to make education and Internet based research an integral part of the treatment process Although it gives information useful to doctors caregivers and other health professionals it also tells patients where and how to look for information covering virtually all topics related to transverse myelitis from the essentials to the most advanced areas of research The title of this book includes the word official This reflects the fact that the sourcebook draws from public academic government and peer reviewed research Selected readings from various agencies are reproduced to give you some of the latest official information available to date on transverse myelitis Following an introductory chapter the sourcebook is organized into three parts PART I THE ESSENTIALS Chapter 1 The Essentials on Transverse Myelitis Guidelines Chapter 2 Seeking Guidance Chapter 3 Clinical Trials and Transverse Myelitis PART II ADDITIONAL RESOURCES AND ADVANCED MATERIAL Chapter 4 Studies on Transverse Myelitis Chapter 5 Books on Transverse Myelitis Chapter 6 Multimedia on Transverse Myelitis Chapter 7 Physician Guidelines and Databases PART III APPENDICES Appendix A Researching Your Medications Appendix B Researching Alternative Medicine Appendix C Researching Nutrition Appendix D Finding Medical Libraries Appendix E Your Rights and Insurance ONLINE GLOSSARIES TRANSVERSE MYELITIS GLOSSARY INDEX Related topics include Transverse Myelitis

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