

Inclusion-body myositis

Clinical and pathologic aspects, and basic research potentially relevant to treatment

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Sporadic inclusion-body myositis (s-IBM) describes patients with chronic myositis whose biopsy specimens have, in addition to lymphocytic inflammation, abnormal muscle fibers containing characteristic filamentous inclusions in the cytoplasm and nuclei. Previously considered uncommon, s-IBM is now recognized as the most common muscle disease beginning over the age of 50 years. Its course is progressive, gradually leading to severe disability. Most disturbingly, there is no remarkably successful treatment available. Because clinical and pathologic diagnostic criteria of s-IBM are becoming better known, s-IBM is being identified more often by clinicians and pathologists.

s-IBM was first described about 30 years ago, and during the past three decades increasingly detailed observations have been reported regarding its clinical, pathologic and immunologic aspects. Recent interest in s-IBM has been generated by the identification of "degenerative" changes within s-IBM muscle fibers, for example, β -pleated-sheet amyloid and other striking pathologic features that were not believed to occur in diseased human muscle.

Two hypotheses predominate regarding the key pathogenic mechanisms involved in s-IBM: an amyloid- β -related degenerative process and an immune dysregulation. Ultimately, both may be considered important, and their possible interrelationship may be clarified. An intriguing feature is the accumulation within s-IBM muscle fibers of amyloid- β (A β), phosphorylated tau, and at least 20 other proteins that are also accumulated in Alzheimer brain. In the s-IBM muscle fibers, there is evidence of mis-

folding of proteins, pathologic proteinaceous inclusions including aggresomes, abnormalities of the two protein-disposal systems involving the ubiquitin-proteasome pathway and the lysosomes, mitochondrial dysfunctions, and oxidative stress. The pronounced T-cell inflammation can be striking, and it is characterized by activated, antigen-driven, cytotoxic CD8+ T-cells.

This supplement is based on a small "think-tank" conference that was organized to promote ideas regarding new treatments for s-IBM. We have obtained the participation of outstanding basic scientists from various fields not directly involving s-IBM but ones related to Alzheimer disease, the ubiquitin-proteasome system, virology, autoimmune cytotoxicity, RNA interference, protein misfolding, and intracellular cholesterol metabolism. They have enthusiastically contributed their knowledge and experience to the conference, and have also generously contributed their state-of-the-art chapters to facilitate the formulation of ideas concerning possibilities relevant to new treatments for s-IBM.

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Most importantly, we thank our esteemed colleagues whose gracious participation has made this conference a success and who, we hope, will continue to be involved in helping to achieve useful treatment for s-IBM.

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