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Review

Sporadic inclusion body myositis: A review of recent clinical advances and current approaches to diagnosis and treatment

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HIGHLIGHTS

- Recent cohort studies have defined more fully the clinical phenotype and natural history of sporadic inclusion body myositis (IBM) and genetic susceptibility.
- Electrophysiology and muscle imaging can contribute to the diagnostic process in IBM and may be potential biomarkers for clinical trials.
- Novel disease-modifying therapies for IBM are under investigation.

ABSTRACT

Sporadic inclusion body myositis is the most frequent acquired myopathy of middle and later life and is distinguished from other inflammatory myopathies by its selective pattern of muscle involvement and slowly progressive course, and by the combination of inflammatory and degenerative muscle pathology and multi-protein deposits in muscle tissue. This review summarises the findings of recent studies that provide a more complete picture of the clinical phenotype and natural history of the disease and its global prevalence and genetic predisposition. Current diagnostic criteria, including the role of electrophysiological and muscle imaging studies and the recently identified anti-5′-nucleotidase (anti-cN1A) antibody in diagnosis are also discussed as well as current trends in the treatment of the disease.

Contents

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1. Introduction

Since it was first described in 1971 (Yunis and Samaha, 1971) inclusion body myositis (IBM) has come to be recognised as the most common acquired myopathy presenting over the age of 45 years and is the type of inflammatory myopathy most likely to be encountered in adult neurological practice. It is distinguished from other inflammatory myopathies clinically by its selective pattern of muscle weakness and wasting and progressive clinical course, and pathologically by the combination of inflammatory and myodegenerative features with multi-protein aggregates in muscle tissue. Because of these unique phenotypic characteristics, and the fact that the condition responds poorly to conventional forms of immune therapy, there is still debate as to whether IBM is a primary autoimmune disease of muscle or a degenerative myopathy with an associated vigorous immune response and secondary inflammatory component (Needham and Mastaglia, 2007, 2008; Askanas et al., 2015).

As a result of studies over the past decade the clinical and pathological phenotype and natural history of the disease have been more clearly defined, and diagnostic criteria have been proposed for use in cohort studies and selection of patients for clinical trials. There has also been further recognition of racial and ethnic differences in the prevalence of the disease and of the importance of genetic factors in determining disease susceptibility. In addition, there have been advances in the search for disease biomarkers, such as the identification of the anti-cNA1 antibody (Larman et al., 2013; Pluk et al., 2013) and in the application of muscle imaging techniques such as MRI and ultrasound as tools for diagnosis and monitoring outcomes in trials of new therapies (Amato et al., 2014).

The present review summarises these recent advances and discusses the current approach to the diagnosis of IBM, including the role of electrophysiological and imaging studies, as well as current approaches to treatment.

2. Prevalence of IBM

There have been relatively few studies of the prevalence of IBM, but recent studies have shown that there is considerable global variability in prevalence. In Europe, the reported prevalence ranges from 4.3×10^{-6} per million in the Netherlands, with a prevalence of 22 per million for men >50 years of age (Badrising et al., 2000), to 33×10^{-6} in South-East Norway (Dobloug et al., 2015), while in the United States, a prevalence of 71×10^{-6} was reported in Olmsted County (Wilson et al., 2008). There is little published data on the prevalence of the disease in Asian countries, but the condition is thought to be increasing in frequency in Japan (Suzuki et al., 2012; Nakanishi et al., 2013) and to be rare in India and Turkey (Khadilkar et al., 2008; Oflazer et al., 2011). In the Southern Hemisphere, the prevalence in Western Australia was found to have risen to 14.9×10^{-6} in 2008, (with an age-adjusted prevalence of 51.3 per million over 50 years of age), compared to 4.3×10^{-6} in an earlier survey, probably as a result of improved case ascertainment (Needham et al., 2008a), whereas a much higher prevalence of 50.5×10^{-6} was reported in the neighbouring State of South Australia (Tan et al., 2013). However, it is likely that these prevalence figures are still an under-estimate of the true frequency of the disease in view of its insidious nature and delays in diagnosis as well as a high rate of initial misdiagnosis (Needham et al., 2008a). It has been proposed that variations in prevalence may reflect differences in population frequencies of the *HLA-DRB1* * 03:01 risk allele which is known to be strongly associated with the disease in European, North American and Australian populations, but could also reflect variable case ascertainment in different studies (Mastaglia, 2009; Mastaglia et al., 2009; Rojana-udomsart et al., 2012).

3. Clinical phenotype

Detailed analysis of several large patient cohorts has provided a clearer appreciation of the typical patterns of muscle involvement and degree of variability in the clinical phenotype, as well as atypical presentations and other disease manifestations (Needham et al., 2008c; Dimachkie and Barohn, 2013).

3.1. Patterns of muscle involvement

The majority of cases have the typical disease phenotype, with slowly progressive weakness and wasting of the quadriceps and forearm muscles (Fig. 1), and often present only when they start to have falls or difficulty walking or climbing stairs. Recent studies have looked at the frequency and circumstances of falls (Hiscock et al., 2014), and have analysed the abnormal gait patterns in patients with IBM (Bernhardt et al., 2011; Davenport et al., 2015) finding that there is a good correlation between knee extensor strength and functional lower limb measures such as the 2-min and 6-min walk tests (Lowes et al., 2012; Alfano et al., 2014). A smaller group of patients present initially because of weakness of the long finger flexor muscles, which is usually more severe in the non-dominant hand, or bulbar weakness, with lower limb weakness occurring at a later stage.

Distinctive features which are helpful in the differentiating IBM from amyotrophic lateral sclerosis and other forms of distal myopathy are the selective pattern of weakness of the flexors of the distal phalanges of the fingers and thumb in the early stages, with sparing of the intrinsic hand muscles, and the asymmetric pattern of weakness. A systematic study of hand function in a cohort of 45 IBM patients showed that whilst hand-grip and pinch strength were markedly impaired, compensatory strategies were commonly employed, and fine motor abilities were relatively well preserved (Eriksson and Lindberg, 2012). In one series, 24% of cases were considered to have atypical phenotypes, such as a limb-girdle pattern of weakness, scapular winging, foot-drop, or prominent forearm weakness with sparing of the quadriceps (Dimachkie and Barohn, 2013). Mild to moderate weakness of the facial muscles is common and in occasional cases it may precede other manifestations (Needham et al., 2008c; Dimachkie and Barohn, 2013; Ghosh et al., 2014; Mastaglia and Needham, 2015). Weakness of the paraspinal muscles may develop as the disease progresses, resulting in dropped head or camptocormia, and is the presenting feature in some cases (Goodman et al., 2012; Ma et al., 2013).

3.2. Swallowing

Dysphagia occurs at some stage of the disease in 51–65% of cases (Needham et al., 2008c; Cox et al., 2009; Dimachkie and Barohn, 2013). In one series dysphagia was the presenting symp-