Journal of Clinical Neuroscience 22 (2015) 6–13

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Review

Inclusion body myositis: A review of clinical and genetic aspects, diagnostic criteria and therapeutic approaches

Frank L. Mastaglia *, Merrilee Needham

Institute of Immunology and Infectious Diseases, Murdoch University, Murdoch, WA, Australia
Western Australian Neuroscience Research Institute, Queen Elizabeth II Medical Centre, Verdun Street, Nedlands, WA 6009, Australia

ARTICLE INFO

Article history:
Received 17 August 2014
Accepted 14 September 2014

Keywords:
Clinical phenotype
Diagnostic criteria
Genetics
Inclusion body myositis
Sporadic IBM
Treatment

ABSTRACT

Inclusion body myositis is the most common myopathy in patients over the age of 40 years encountered in neurological practice. Although it is usually sporadic, there is increasing awareness of the influence of genetic factors on disease susceptibility and clinical phenotype. The diagnosis is based on recognition of the distinctive pattern of muscle involvement and temporal profile of the disease, and the combination of inflammatory and myodegenerative changes and protein deposits in the muscle biopsy. The diagnostic importance of immunohistochemical staining for major histocompatibility complex I and II antigens, for the p62 protein, and of the recently identified anti-cN1A autoantibody in the serum, are discussed. The condition is generally poorly responsive to conventional immune therapies but there have been relatively few randomised controlled trials and most of these have been under-powered and of short duration. There is an urgent need for further well-designed multicentre trials of existing and novel therapies that may alter the natural history of the disease.

© 2014 Elsevier Ltd. All rights reserved.

1. Introduction

The first description in the literature of the condition now referred to as inclusion body myositis (IBM) appears to have been that of Adams, Kakulas and Samaha in 1965 [1], although the name was not suggested until 1971 [2]. It is now recognised that sporadic inclusion body myositis (sIBM) is the most common primary myopathy presenting after the age of 40 years and the form of inflammatory myopathy most likely to be encountered in adult neurological practice. The prevalence of IBM varies, being highest in Caucasian northern European, North American and Australian populations in which prevalence figures of 4.9–14.9 per million have been reported [3,4]. It is distinguished from other inflammatory myopathies by its insidious and progressive course and selective pattern of muscle involvement, and pathologically by the combination of inflammatory and myodegenerative features and abnormal protein aggregates in affected muscles. Because of this, and the fact that the condition is poorly responsive to conventional forms of immune therapy, there is still debate as to whether IBM is primarily autoimmune in origin or a degenerative myopathy with a secondary inflammatory/immune response.

2. Clinical aspects

Typically, the quadriceps femoris and long finger flexors are preferentially affected and there is progressive wasting of the thighs and forearms (Fig. 1). Other muscle groups such as the finger extensors, upper arm muscles and ankle dorsiflexors are often also affected to varying degrees in patients with more advanced disease, and some patients may also develop weakness of the paraspinal muscles resulting in dropped-head or camptocormia, and of the facial muscles (Fig. 2). Because of the insidious nature of the disease and nonspecific initial symptoms many patients only seek medical attention once they start to have falls, and by then the degree of weakness and atrophy of the quadriceps is already quite advanced. Early symptoms which should raise suspicion of the diagnosis include difficulty in climbing stairs or rising from a chair or squat, aching in the thighs and knees with exercise, weakness of grip and difficulty using spray cans or other utensils and tools. Dysphagia is occasionally an early symptom but more often develops later in the course of the disease [5,6]. Obstructive sleep apnoea due to weakness of the oropharyngeal muscles is also common [7]. Other clues to the diagnosis include the finding of selective weakness of the flexor digitorum profundus and flexor pollicis longus in the early stages with sparing of the flexor digitorum superficialis and intrinsic hand muscles, and an asymmetric pattern of muscle involvement with the weakness usually being more severe in the non-dominant arm and leg (Fig. 1).

* Corresponding author. Tel.: +61 8 9360 1350; fax: +61 8 9360 1388.
E-mail address: f.mastaglia@iiid.com.au (F.L. Mastaglia).

http://dx.doi.org/10.1016/j.jocn.2014.09.012
0967-5868/© 2014 Elsevier Ltd. All rights reserved.

Several studies have investigated the natural history of sIBM [8–12]. The rate of progression of weakness has been shown to be around 4% per year and is more rapid in the lower limbs, but varies from patient to patient. As the condition progresses, patients have increasing difficulty with everyday activities such as handwriting, cutting up food, dressing, personal hygiene and mobility and become increasingly dependent. Most patients need to use a walking stick or walker after 5–10 years, but only a minority become wheelchair-bound. A 10 point IBM functional rating scale has been developed to quantify and monitor the severity of these disabilities over time [13].

3. Immunological associations

In some cases sIBM is associated with another autoimmune disease such as Sjögren's syndrome [14], systemic lupus erythematosus, scleroderma, rheumatoid arthritis or thrombocytopenic purpura [15]. In addition, the frequency of non-organ specific autoantibodies such as antinuclear antibody, anti-Ro 52/60 and anti-ribonucleoprotein, and monoclonal gammopathy is increased [16,17]. sIBM has also been reported to occur in association with retroviral infections (human immunodeficiency virus or human T-cell lymphotropic virus I), chronic lymphocytic leukaemia [18] and immunodeficiency states [19,20]. These findings are all suggestive of an underlying disturbance of immune control and support the hypothesis of an immune basis for the myopathy. The recent demonstration of serum antibodies to cytosolic 5-nucleotidase (anti-cN1A) with a high specificity for sIBM provides further evidence of an underlying immunological process and a possible link between the autoimmune and myodegenerative components of the disease [21,22].

4. Genetics

Most cases of IBM are sporadic, but there are rare reports of familial cases with a recessive or dominant pattern of inheritance [23–26]. In Caucasian populations there is a strong association with the HLA-DRB1*0301 allele and 8.1 major histocompatibility complex (MHC) ancestral haplotype (HLA-A1, B8, DR3) in sporadic cases, and HLA-DRB1*0301 carriers have more severe muscle weakness [17,27–30]. It has been estimated that in Western Australia, carriers of HLA-DRB1*0301 have a 10-fold higher risk of developing sIBM [3]. Carriers of the HLA-DRB1*0301/*0101 diplotype were found to have the highest disease risk and more severe muscle weakness [30,31]. In contrast, carriage of the secondary HLA-DRB loci DRB4 and DRB5 is protective and is associated with a reduced risk of developing IBM [32]. Although apolipoprotein E (APOE) alleles do not influence the risk of developing sIBM [33], the rs10524523 polymorphism in the *TOMM40* gene, which is in linkage disequilibrium with APOE and encodes an outer mitochondrial membrane translocase, has recently been shown to be protective and is associated with a reduced disease risk and a later age at the onset of symptoms [34].

5. Electrophysiological studies

Electromyography (EMG) can provide a clue to the diagnosis of sIBM, and typically shows a mixture of low amplitude short duration and large longer duration motor unit potentials, as well as spontaneous fibrillations and positive sharp waves in affected muscles such as the flexor digitorum profundus [35]. In some patients these findings may lead to a mistaken diagnosis of a neurogenic disorder such as amyotrophic lateral sclerosis [36]. While large polyphasic potentials can also be seen in other chronic myopathic conditions, this "mixed" EMG pattern with myopathic and neuropathic-appearing motor unit potentials is very typical of sIBM. A neurogenic component has in fact been excluded by quantitative EMG and single fibre EMG studies [37–39]. However, some patients may develop a mild peripheral neuropathy and electrophysiological evidence of a subclinical neuropathy may be found in some cases [40,41].

6. Muscle imaging

Muscle MRI can provide useful information that may help in the diagnosis of sIBM, particularly in cases in which the muscle biopsy is

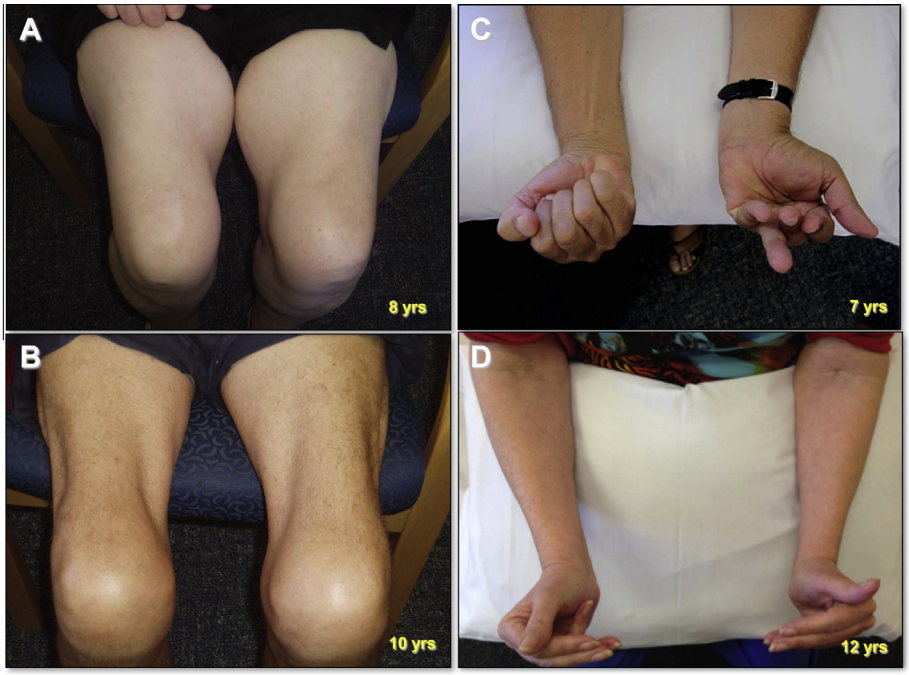

Fig. 1. Typical pattern of atrophy of the quadriceps femoris (A, B) and more severe impairment of hand closure on the non-dominant left side (C, D) in right-handed patients with sporadic inclusion body myositis of different durations as shown.

Download English Version:

https://daneshyari.com/en/article/3058955

Download Persian Version:

https://daneshyari.com/article/3058955

Daneshyari.com