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Inclusion Body Myositis : Clinical Features and Electrophysiological Findings

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Sporadic inclusion body myositis (s-IBM) is an aquired slowly progressive inflammatory myopathy with unknown etiology. Although light microscopic abnormalities and characteristic histopathology on muscle biopsy distinguishes from other inflammatory myopathies, vacuolated muscle fibers, intracellular amyloid deposits or tubulofilaments in electromicroscopic findings are not definite in some patients. This review shows the prominently involved muscles in s-IBM and specific or nonspecific electrophysiologic manifestations from reported data for helping the diagnosis of definite- or probable-IBM patients. In lower limbs, the quadriceps is predominantly involved, as is iliopsoas, and tibialis anterior is common. In the upper limbs, the greatest weakness is in forearm finger flexors. Finger extensors, biceps and triceps also are moderately to prominently involved. The majority of patients demonstrate polyphasic MUAPs that are short in duration. An additional striking feature is the concomitant documentation of long-duration, large-amplitude, polyphasic MUAPs. In spite of the frequent mixed myopathic-neurogenic electromyographic findings of IBM, just like that of chronic myositis, asymmetric, slowly progressive weakness of flexor digitorum profundus or quadriceps femoris muscles after age of 50 is very necessary condition for the diagnosis of IBM.

Key Words: Electromyography, Inclusion body myositis, Flexor digitorum profundus, Quadriceps femoris.

Introduction

Muscle biopsy of sporadic inclusion body myositis (s-IBM) combines features of inflammation and vacuolar degeneration with accumulation of pathological proteins, which exhibit many similarities to changes in the brain of Alzheimer's disease. Diagnosis of s-IBM is usually based on combined clinical and histopathological features including electromicroscopic and immunohistochemical studies (Table 1). For a definite diagnosis of s-IBM, certain morphological features should be present. Atypical cases or cases in which the muscle biopsy does not show all of the expected changes are diagnostic problems. In probable s-IBM[1] clinical features, electrophysiologic and laboratory findings also are very important for precise diagnosis of s-IBM.

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Clinical features

In nearly all cases, IBM is a sporadic disease, but a few familial cases have also been reported.[2,3] It is considered to be the most common aquired muscle disease after age of 50. There is a 3:1 male

predominance and the age-adjusted prevalence over the age of 50 years was 35 per million.[4] The age at onset of symptoms ranges from 16 to 81 years, with 20 percent between 10 and 30 years, and 50 percent between 50 and 70 years,[5] and typical s-IBM usually begins after age 50 years predominantly in men.[6-8] The onset is the slowest in s-IBM, in which muscle weakness develops insidiously and the diagnosis may not be made for several years. There is an overall quantifiable decline in 4 percent of predicted muscle strength from baseline in a 6-month period, but one-third of patients show no change or even slight improvement in strength.[9]

The clinical phenotype is variable and, in some patients with s-IBM, there is a more proximal pattern of muscle involvement in both the upper and lower limbs from the outset, or purely upper or lower limb involvement.[10-12] Infrequently, scapuloperoneal or postpolio syndrome-like presentations have been described.[13] Scapular, cervical, and even facial muscles are occasionally involved, but considerable bulbar weakness was noted in only four patients.[14] Spinal, respiratory, and abdominal muscles are also affected. The extraocular muscles are spared.

The most frequent symptom is difficulty with ambulation and frequent falls due to weakened knee extensors. The weakness can be more proximal than distal or more distal than proximal, or it may involve proximal and distal muscles more or less equally.[5] Early involvement of forearm flexor muscle compartment and the quadriceps is typical for s-IBM in contrast to polymyositis (PM) and

Table 1. IBM Diagnostic Criteria[1]

I. Diagnostic Classification
- A. Definite inclusion body myositis
  Patients must exhibit all muscle biopsy features including invasion of nonnecrotic fibers by mononuclear cells, vacuolated mucle fibers, and intracellular (within muscle fibers) amyloid deposits or 15~18 nm tubulofilaments. None of the other clinical or laboratory features are mandatory if muscle biopsy features are diagnostic
- B. Probable inclusion body myositis
  If the muscle shows inflammation (invasion of non-necrotic muscle fibers by mononuclear cells) and Vacuolated fibers but without other pathological features of inclusion body myositis, then a diagnosis of probable inclusion body myositis can be given if the patient exhibits the characteristic clinical (A1, 2, 3) and laboratory (B1,3) features

II. Characteristic features
- A. Clinical features
  1. Duration of illness > 6 months
  2. Age of onset > 30 years of age
  3. Muscle weakness
     Must affect proximal and distal muscles of arms and leg and Patient must exhibit at least one of the followings
     a. Finger flexor weakness
     b. Wrist flexor > wrist extensor weakness
     c. Quadriceps muscle weakness (> MRC grade 4)
- B. Laboratory features
  1. Serum Creatinine kinase < 12 times upper limit of normal
  2. Muscle Biopsy
     a. Inflammatory myopathy characterized by mononuclear cell invasion of nonnecrotic muscle fibers
     b. Vacuolated muscle fibers
     c. Either
  (I) Intracellular amyloid deposits (must use fluorescent method of identification before excluding the presence of amyloid) or
  (II) 15-18 nm tubulofilaments by electron microscopy
  3. Electromyography must be consistent with features of an inflammatory myopathy (however, long-duration potentials and do not exlude diagnosis of sporadic inclusion body myositis

dermatomyositis (DM) where more proximal shoulder and hip girdle muscles are typically involved early stage.

In lower limbs, the quadriceps is predominantly involved, as is iliopsoas, and tibialis anterior is common.[7,15] In the upper limbs, the greatest weakness is in forearm finger flexors (Fig. 1); the findings are often asymmetric. Finger extensors, biceps and triceps also are moderately to prominently involved (Fig. 1); deltoid, pectoralis major, and interosseous muscles of the hand are less involved.[16,17] Early involvement of the flexor digitorum profundus muscles leads to a characteristic inability to maintain flexion of the distal phalanges when the patient is asked to grip the examiner's fingers. As the disease progresses, there is also involvement of the flexor digitorum superficialis and finger extensors, and a "swan-neck" deformity of the fingers and hyperextension of the thumb may develop. Difficulty with swallowing due to involvement of the pharyngeal and esophageal muscles is encountered by about 30~50% of the patients.[10] Dysphagia in some patients may respond to criticopharyngeal myotomy.[18] Subacute respiratory failure was reported in one patient with s-IBM who required mechanical ventilation.[19]

The weakness is generalized or localized to the limbs and with few exceptions, is usually symmetrical in the later stage of the disease. The progressive course of s-IBM leads slowly to severe disability. Finger functions can become very impaired. Arising from a chair becomes difficult. Walking becomes more precarious. Sudden falls, sometimes resulting in major injury to the skull or other bones, can occur due to weakness of quadriceps and gluteus muscles depriving the patient of autonomic posture maintenance. A foot-drop can increase the likelihood of tripping. The tendon reflexes are normally active or even brisk; eventually they diminish in at least 40 percent of cases.[5]

A diffuse subcutaneous edema in addition to edema in the vastus lateralis and medialis muscles, with sparing of rectus femoris were detected with whole body turbo STIR (short T1 inversion

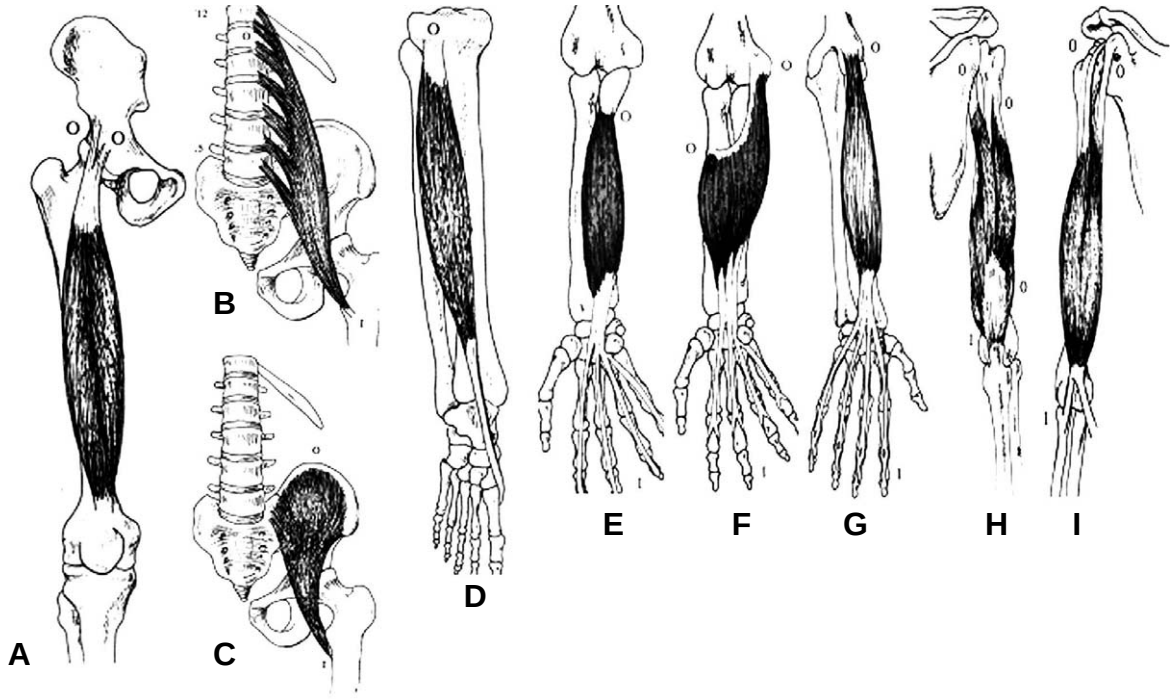

Figure 1. Predominantly involved muscles in sporadic inclusion body myositis.
A: Quadriceps femoris B: Psoas C: Iliacus D: Tibialis Anterior
E: Flexor digitorum profundus F: Flexor digitorum superficialis
G: Extensor digitorum H: Triceps I: Biceps

recovery) magnetic resonance imaging.[20]

Late-juvenile s-IBM. Late-juvenile s-IBM (LJ-sIBM) is a rare form of s-IBM recently described in three young unrelated males who have muscle-weakness distribution similar to that of a s-IBM, including prominent quadriceps weakness, but age at onset in two patients was in the late teens and at age 20 in one.[21] Their muscle biopsies had features of s-IBM, including vacuolated muscle fibers, lymphocytic infiltration and accumulations of IBM-characteristic proteins.[21] However, ther are also some pathologic aspects similar to hereditary-IBM; only infrequent congophilia (in intracellular plaquettes); and their phosphorylated-tau (p-tau) was mostly in straight tubulofilaments rather than in paired helical filaments configuration and it lacked some of the p-tau epitopes typical of s-IBM.[21] One patient biopsed at age 30 had muscle blood-vessel amyloid that was not immunopositive for Aβ, transthyretin, or κ or λ light-chains.[21]

Among sporadic "inflammatory-myopathy" patients, the specific degenerative accumulations of proteins[22-24] occur only in s-IBM, not in PM or DM.[7] Most older patients with lymphocytic myositis have s-IBM. Patients over age 50 years with what can be considered "pure polymyositis " are rare. Infrequently DM begins over age 50 years and is sometimes associated with a remote neoplasm.[7]

s-IBM may be confused with PM and with polyneuropathy or amyotrophic lateral sclerosis. Although no specific clinical features provide absolute diagnosis of s-IBM and ALS, several findings suggest s-IBM, especially early weakness of the finger flexors, weakness of the quadriceps, slow progression, and lack of definite upper motor neuron signs.[25] Clinically visible fasciculations are exceptional in s-IBM. The diagnosis of definite s-IBM is made by muscle biopsy including electromicroscopic study. Recent descriptions of diseases that may minic s-IBM histopathology include a case of Emery-Dreifuss muscular dystrophy and a case with vitamin E deficiency. In addition to light microscopic features such as inflammatory infiltrates and rimmed vacuoles, a further clue to the correct diagnosis is upregulation of major histocompatibility complex (MHC) class I, which has been demonstrated to be a valid test for s-IBM and other inflammatory myopathies.[26,27]

Associated disorders. The occurrence of IBM together with Sjogren's syndrome plus systemic lupus erythematosus, rheumatoid arthritis, scleroderma, macrophagic myofasciitis, thrombocytopenia, granulomatous liver disease, sarcoidosis, DM, and anti-Jo-1 positivity indicates an association with other autoimmune diseases.[5] Dalakas et al found 13 with one or more autoimmune disorders, 43 with elevated titers of one or more autoantibodies (e.g., ANA, rheumatoid factor, anticardiolipin antibody, or an extractable nuclear antibody), and 25 with dysproteinemia or dysproteinuria in 99 patients.[28] Until recently, s-IBM was not thought of as being associated with malignancies. However, a recent population-based study of inflammatory myopathies has challenged that notion by demonstrating an increased risk of malignancies in patients with s-IBM similar to that of PM.[29]

Electrophysiological findings. Electrophysiological findings in s-IBM are similar to those in patients with chronic PM and DM with a few subtle differences.

Sensory Nerve Conduction Studies. Although patients are usually asymptomatic, a mild sensory neuropathy may be evident on clinical examination or nerve conduction studies in approximately 30% of IBM patients.[30] A few of patients have clearly had diabetes mellitus, but a number of patients had no identifiable cause of the abnormality. The sensory nerve action potentials may be diminished in an amplitude in a pattern suggestive of a distal symmetric, preferentially mild sensory peripheral neuropathy. Sural nerve biopsies have revealed mild and nonspecific decreases in myelinated fibers.[31,32] Both the neuropathologic and electrophysiologic findings may be age-related, because s-IBM generally develops in patients over 50 years of age.

Motor Nerve Conduction Studies. As with sensory studies, mild abnormalities of motor nerve

conduction, particularly in the lower limbs, can be observed in some patients with IBM.[31,32] F-waves have been reported to be normal, suggesting that the peripheral nerve slowing is preferentially located distally as opposed to proximally or diffusely. Focal prolongation of the median distal motor latency across the wrist has also been reported, supporting the likelihood of finding a median neuropathy at the wrist in some patients.[33]

Needle Electromyogram. IBM usually displays prominent positive sharp waves and fibrillation potentials.[33] Complex repetitive discharges are also prominent in some patients.[16,33] The majority of patients demonstrate polyphasic MUAPs that are short in duration.[16,31,33,34] A striking feature is the concomitant documentation of long-duration, large-amplitude, polyphasic MUAPs. A few patients have been reported with primary the latter type of MUAPs mixed with normal-appearing ones and few, if any, short-duration MUAPs. Segmental necrosis with regeneration and collateral sprouting, fiber splitting, and fiber hypertrophy lead to the high amplitude potentials when the needle electrode is located in proximity to the remodeled regions of the motor unit. Fiber size variation and motor unit remodeling with expansion of the endplate zone lead to long-duration MUAPs. These findings are all compatible with what is noted in both PM, DM, and s-IBM histologically as well as electrophysiologically. MUAPs with satellite potentials may be observed in s-IBM when a trigger and delay line are used. Recruitment study demonstrate both a reduced (neurogenic) and early (myogenic) recruitment interval in different patients. These apparently disparate findings may simply reflect the chronicity of the disease state with more profound muscle loss appearing more like a motor unit loss (neurogenic) pattern versus less long-standing disease maintaining the random dropout of muscle fibers (myopathic pattern). Because of the frequent mixed myopathic-neurogenic appearance of IBM with conventional qualitative electromyography, quantitative electromyography has been demonstrated to be quite useful.[35] One carefully performed quantitative monopolar needle EMG study on 30 patients with IBM demonstrated three major patterns of MUAP findings, with s-IBM demonstrated three major patterns of MUAP findings, with some type of abnormality noted in all patients.[36] The first pattern demonstrated a combination of significant membrane instability combined with short-duration ($\langle$ 6 ms), small-amplitude ($\langle$ 500 μV) MUAPs in about 56% of patients. The second most common pattern of MUAP findings consisted of membrane instability combined with both short-duration, small-amplitude MUAPs as well as long duration ($\rangle$ 18 ms), large-amplitude ($\rangle$ 5 mV) MUAPs noted in approximately 37% of patients. This combination of abnormalities may be seen in a single patient, even in the same muscle. The least frequently observed pattern of abnormalities was membrane instability and long-duration, large-amplitude MUAPs (7%). Long duration polyphasic MUAPs are correlated with regenerating fibers and are thought to arise slow conduction in regenerating muscle fibers.[37] These MUAPs are probably related to chronicity of the disease, which results in marked fiber heterogeneity and variation in the conduction properties, rather than neurogenic causes.[38]

Macro-Electromyography. In contrast to conventional electromyography, macro-electromyography records the electrical activity from an "entire motor unit". A study of 11 patients with IBM using concentric needle and macro-electromyography demonstrated findings that did not suggest a coexisting neurogenic component.[39] Although conventional needle electromyography revealed a mixture of large-and small-duration polyphasic MUAPs, macro-electromyography demonstrated normal or small amplitudes and areas consistent with a myogenic disorder.

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