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OLGU SUNUMU

İNKLÜZYON CİSİMCİKLİ MİYOZİT: YAŞLILARDA ZOR BİR TANI

Öz

İnküzyon cisimcikli miyozit (İCM) enflamatuar miyopatiler arasında oldukça ender olmakla birlikte, 50 yaş üzeri hastalardaki enflamatuar miyopatilerin en sık sebebidir. Yavaş ilerleyen, sakatlayıcı kas gücü kaybı ve kas biyopsisinde gözlenen inklüzyon cisimcikleri ile karakterizedir.

Hastalığın yavaş ilerleyişi, diğer miyopatilerle histolojik benzerliği ve hekimlerin farkındalıklarının sınırlı olması nedeniyle tanı sıklıkla gecikir ya da yanlışlıkla polimiyozit tanısı konur. Ayrıca yaşlı hastalardaki ko-morbiditeler de tanıyı güçleştirebilir.

Yaşlılardaki ilerleyici kas gücü kaybının irdelenmesinde, İCM tanısı olarak düşünülmelidir. Tanı kriterlerinin iyi bilinmesi ve hastalıktan şüphe düzeyinin yüksek tutulması yanlış tanıdan kaçınmak için esastır. Bu makalede başlangıçtan 5 yıl sonra İCM tanısı konan 63 yaşındaki bir erkek hastayı sunuyor ve literatürü gözden geçiriyoruz.

Anahtar Sözcükler: Miyozit/inklüzyon cisimcigi; Rehabilitasyon; Egzersiz; Yaşlı.



CASE REPORT

INCLUSION BODY MYOSITIS: A DIFFICULT DIAGNOSIS IN ELDERLY PEOPLE

ABSTRACT

Inclusion body myositis (IBM) is the most common inflammatory myopathy in patients older than 50 years, however, it is very rare amongst the inflammatory myopathies. It is characterised by slowly progressive, disabling muscle weakness and inclusion bodies visible on muscle biopsy.

Due to the slow progression of the disease, histologic similarity with other myopathies and limited awareness of physicians, the diagnosis is frequently delayed or it is misdiagnosed as polymyositis. Furthermore, the co-morbidities of older people may render clinical diagnosis difficult.

IBM should be a diagnostic consideration in the evaluation of progressive weakness in older patients. A high index of suspicion along with knowledge of the diagnostic criteria is essential to avoid misdiagnosis. In this article, we report a 63 year old man diagnosed with IBM 5 years after the initial presentation and review the literature.

Key Words: Myositis/Inclusion body; Rehabilitation; Exercise; Elderly.

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INTRODUCTION

The idiopathic inflammatory myopathies (IIMs) are a group of rare disorders that share many similarities. IBM, polymyositis, and dermatomyositis are three distinct categories of inflammatory myopathy. Most recently, a fourth inflammatory myopathy subtype called necrotizing myopathy was described (1). However, these 4 IIMs are pathogenically, histologically and clinically distinct entities.

IBM is the most common acquired, progressive and disabling inflammatory myopathy affecting patients over the age of 50 years (2).

Because of its similarity with other inflammatory myopathies, particular importance should be given to the differential diagnosis of the disease. Polymyositis, dermatomyositis and autoimmune necrotizing myopathy may be associated with cancer or collagen vascular disease. On the other hand, IBM may mimic motor neuron disease. Therefore, distinction of IBM from other forms of IIMs and neuromuscular disorders has great importance.

CASE

A 63 year old male with a 5 year history of slowly progressive, painless weakness and atrophy on the left arm and both lower extremities was admitted to our clinic. Initially, he had difficulty in getting out of chairs and climbing steps. Subsequently, he noticed that his left foot tripped while walking. Gradually he was unable to dorsiflex his left ankle and recurrent falls and steppage gait occurred. His symptoms dramatically progressed over the past 5 years and he also felt weakness in the left upper extremity. Fine motor skills of his left hand and fingers were increasingly affected leading to difficulty in grasping and manipulating small objects. He was independent in basic activities of daily living (ADLs) such as dressing, feeding, and grooming however, he needed assistance for transfers from sitting to standing, climbing stairs, and to get in and out of a car.

He was taking amlodipine besylate 10 mg/day for hypertension. He had no family history of any neuromuscular disease. Clinical examination showed muscle atrophy and weakness of both quadriceps muscles (3/5 on the MRC scale), right deltoid muscles (4/5), left wrist and long finger flexors (3/5). There was marked side-to-side asymmetry between the legs and ankle strength testing revealed severe loss of dorsiflexion strength on the left side (2/5) (Figure 1, 2). Facial muscles were intact. He had no sensory abnormalities. Deep tendon reflexes were absent at the knees. There was no history of difficulty on swallowing.



Figure 1— Atrophy of both quadriceps muscles.

Relevant laboratory data including complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum magnesium, calcium, phosphate, AST, ALT, LDH, creatinine and vitamin D levels were normal. Antinuclear antibodies, rheumatoid factor, HIV, hepatitis B and hepatitis C markers were negative. Thyroid function tests, Complements C3, C4 and anti-dsDNA antibody titres were at normal levels. The only abnormal result was the creatinine phosphokinase level of 529 u/l (normal:49-397 u/l). Tests for any possible internal malignancy (chest X-ray, tumour mar-



Figure 2— Marked atrophy of left ankle dorsiflexors.

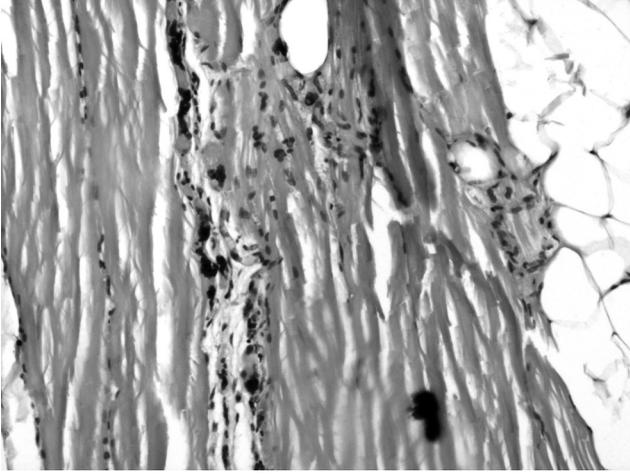


Figure 3— Lymphocytic mononuclear cell infiltration and atrophic fibres.

kers, abdominal ultrasound, LFT, immunoglobulin and protein electrophoresis) proved inconclusive.

An electromyographic study (EMG) showed positive sharp waves, fibrillations, and short duration low amplitude polyphasic motor units of the proximal upper extremity muscles and similar findings in the lower extremity muscles consistent with a myopathy. Nerve conduction studies were normal.

A muscle biopsy was obtained from the left vastus lateralis. In the light microscopic examination, lymphocytic mono-

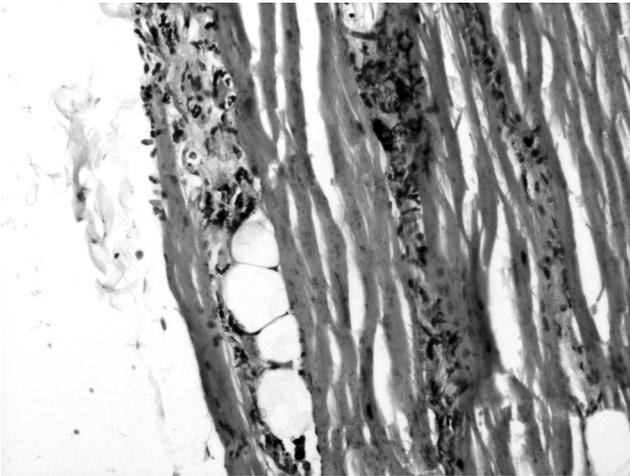


Figure 4— Increased connective tissue and fatty replacement of muscle fibres.

nuclear cell infiltration, groups of atrophic fibres, increased connective tissue and fatty replacement of muscle fibres were observed (Figure 3, 4). Congo red stains were negative for amyloid. Electron microscopic investigation was not performed.

According to the clinical and laboratory findings, the patient was diagnosed as having IBM. A rehabilitation program was implemented comprising mild to moderate strengthening exercises for weak muscles, aerobic water exercises in pool, and endurance and transfer exercises. An ankle-foot orthosis was prescribed for his left leg. Although, no significant changes were observed in physical examination, the muscle strength and functions were improved to some extent following 4 weeks of the rehabilitation program.

DISCUSSION

IBM was first described in 1971, but it is still a poorly understood form of IIM. It is clinically and pathologically distinct from the other inflammatory myopathies.

The primary cause of IBM is unknown. It may be a degenerative muscle disorder, or triggered by a virus or an autoimmune disorder. The roles of oxidative stress, ageing, genetic factors and viruses have also been highlighted.

IBM is the most common myopathy after age 50. Symptom onset before age 60 occurs in 18% to 20% of patients with a frequent delay in diagnosis of five to eight years from IBM symptom onset (3).

The prevalence of IBM varies between different populations and ethnic groups. While, a study from Netherlands (4) has shown a prevalence of 4.9 per million, in another study from Turkey (5), the prevalence was found to be 1 per million. Men are more frequently affected than women with a ratio of 3/1 (6).

IBM is slowly progressive and affects proximal and distal muscles, the weakness and atrophy often being asymmetric. Characteristically, IBM causes a selective pattern of muscle weakness, predominantly involving the forearm flexor and quadriceps femoris muscles early in the disease course. Weakness of the wrist and finger flexors is often disproportionate to that of their extensor counterparts. Hence, loss of finger dexterity and grip strength may be a presenting or prominent symptom. Dysphagia is common in IBM. Some patients develop mild facial weakness, peripheral neuropathy and vasculitis.

A muscle biopsy is required to make a definitive diagnosis of IBM. The biopsy not only confirms the diagnosis but also enables the clinician to rule out other conditions that resemble myositis. Light microscopic features include



lymphocytic mononuclear cell infiltration, muscle fibres with vacuoles containing amyloid, ragged-red fibres and atrophic muscle fibres.

Two types of diagnostic criteria have been described to define IBM: Mendel's diagnostic criteria and the European Neuromuscular Centre Diagnostic Criteria (7,8). According to these criteria, a diagnosis of "definite inclusion body myositis" is made if muscle biopsy shows mononuclear cell infiltrates, vacuoles, and either amyloid deposits or 15–18 nm tubulofilaments by electron microscopy. A diagnosis of "possible sporadic inclusion body myositis" is made if the clinical features are indicative but the muscle biopsy is not diagnostic.

In our case; the clinical presentation was quite typical compared to other idiopathic inflammatory myopathies. As seen in our patient, the selective and asymmetrical weakness and atrophy of the volar forearm muscles, quadriceps, and ankle dorsiflexors are the clinical hallmarks of IBM. Male sex, lower creatine kinase levels, slower rate of progression are also more common in inclusion body myositis. Muscle biopsy specimens demonstrated lymphocytic mononuclear cell inflammation, atrophic fibres in groups, increased connective tissue and fatty replacement of muscle fibres. We couldn't show red-rimmed vacuoles or amyloid deposits. Inability to detect these signs may be related to sampling. Repeated biopsies are essential due to patchy involvement of the muscles. However, in some patients with IBM, rimmed vacuoles and other characteristic histopathological features may be scarce or absent and clinical examination is often the key to diagnosis. The presence of inflammatory findings in conjunction with the clinical features, satisfies the diagnostic criteria of IBM. Repeat muscle biopsy may lead to correct diagnosis.

Patients with inflammatory muscle disease benefit from mild to moderate muscle training and endurance exercises. In the past, patients with myositis were discouraged from exercising owing to a fear of increased muscle inflammation. However, studies in the 1990s reported that exercise might bring about a non-specific benefit.

There certainly is a role for physical therapy, orthotic devices, occupational therapy, a healthy well balanced diet and exercise in IBM. A tailored home exercise program, five days a week for 12 weeks, was found to be safe in seven patients (9). There was no strength deterioration, no change in serum CK, and no increase in muscle inflammation on biopsy. Other investigators recently reported on an aerobic exercise program using a stationary cycle ergometer at 80% of the initial maximum heart rate (for two minutes less than the total time achieved during maximal aerobic test) combined with resistance isometric and isotonic exercises of the upper and lower limbs in a group of seven IBM cases (10). Besides being safe,

they found this exercise routine to improve aerobic capacity and muscle strength.

In our patient the rehabilitation program had a striking positive effect. After 4 weeks of specifically tailored rehabilitation program, our patient's physical functions were improved to some extent without evidence of increased muscle damage. He was able to use his left hand more easily, and he felt that his endurance was increased.

IBM is uncommon in the elderly. The diagnosis is often overlooked or delayed. The present report, besides a review of the literature, clearly documents that IBM can be diagnosed by its clinical appearance. Furthermore, our study supports the role of rehabilitation in patients with IBM.

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