Seminars in Arthritis and Rheumatism 43 (2014) 792–796

Contents lists available at ScienceDirect

Seminars in Arthritis and Rheumatism

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

The co-existence of myasthenia gravis in patients with myositis: A case series

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ARTICLE INFO

Keywords:
Myositis
Dermatomyositis
Polymyositis
Myasthenia gravis

ABSTRACT

Objective: Myositis and myasthenia gravis (MG) are both autoimmune disorders presenting with muscle weakness. Rarely, they occur simultaneously in the same patient. Since the management of myasthenia gravis differs from that of myositis, it is important to recognize when patients have both diseases. We reviewed the cases of 6 patients with both myositis and MG to identify clinical features that suggest the possibility of co-existing MG in myositis patients.

Methods: We identified 6 patients with dermatomyositis or polymyositis and MG. We reviewed their medical records to assess their clinical presentations, laboratory findings, and electrophysiological features.

Results: All 6 patients had definite dermatomyositis or polymyositis by the criteria of Bohan and Peter as well as electrophysiologic and/or serologic confirmation of MG. Among overlap patients, 5/6 (83%) had bulbar weakness, 2/6 (33%) had ptosis, and 1/6 (17%) had diplopia. Fatigable weakness was noted by 5/6 (83%) patients. Treatment with pyridostigmine improved symptoms in 5/6 (83%) patients. High-dose steroids were associated with worsening weakness in 2/6 (33%) patients.

Conclusions: Prominent bulbar symptoms, ptosis, diplopia, and fatigable weakness should suggest the possibility of MG in patients with myositis. A suspicion of MG may be confirmed through appropriate electrophysiologic and laboratory testing. In those with myositis–MG overlap, high-dose steroids may exacerbate symptoms and pyridostigmine may play an important therapeutic role.

Introduction

Myositis, including both polymyositis (PM) and dermatomyositis (DM), causes proximal muscle weakness and has an annual incidence rate of ~ 6 per 100,000 person-years [1]. Patients with myositis may also have another autoimmune disease such as systemic lupus erythematosus, Sjogren's syndrome, or systemic sclerosis. Recognizing the presence of overlapping conditions is important and may change management strategies. For example, high-dose steroids are often avoided in patients with myositis–scleroderma overlap because of the risk of renal crisis [2].

Although infrequently described, myasthenia gravis (MG) is another autoimmune disorder that may present as an overlap with myositis [3–19]. In MG, which has an annual incidence rate of ~ 30 per million per year [20], autoantibodies targeting components of the neuromuscular junction (NMJ), such as the acetylcholine receptor (AChR), reduce the number of AChRs, disrupting neuromuscular transmission and causing muscle weakness (reviewed in Ref. [21]). In contrast to patients with myositis, who usually have stable weakness, patients with MG have weakness that worsens with activity and as the day progresses. In the vast majority of MG patients, the ocular muscles are affected first, causing intermittent diplopia and ptosis, symptoms that are not typically observed in myositis. In about two-thirds of patients with ocular MG, the weakness generalizes to cause bulbar symptoms such as dysphagia and dysarthria, which may also be seen in myositis. Patients with generalized MG typically develop proximal limb weakness as is also seen in patients with myositis.

The diagnosis of myasthenia gravis may be made based on fatigable weakness, often in the presence of antibodies recognizing the AChR or muscle-specific kinase (MuSK). Specialized electrophysiologic testing, including repetitive nerve stimulation (RNS) and single-fiber electromyography (SFEMG), is used to support the diagnosis of MG and may confirm the diagnosis in the ~10% of patients who are seronegative.

The acetylcholinesterase inhibitor pyridostigmine facilitates transmission at the NMJ and is the first-line treatment for MG. As in patients with myositis, immunosuppressive therapies are

A.L.M. was supported by NIH Grant K08-AR-054783 and J.J.P. was a clinical fellow supported by T32 Grant AR048522 during the preparation of this article. The study sponsors had no involvement in producing this article.

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0049-0172/$ - see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.semarthrit.2013.12.005

often required to control MG. However, in contrast to myositis, initiation of therapy with high-dose steroids in MG may actually exacerbate muscle weakness. Therefore, most neuromuscular specialists prefer to initiate therapy with low-dose steroids and gradually increase the dose to achieve pharmacologic remission without causing a disease flare [22]. Finally, thymectomy may be considered as a treatment option in MG, particularly in those with a thymoma or thymic hyperplasia. Given that the approach to management may be significantly different in patients with MG versus myositis, it is important to recognize when patients may have an overlap of these two diseases.

Here, we report 6 cases of patients with both myositis and MG, the largest case series of patients with this combination described in the literature.

Patients and methods

Design

This is a retrospective case series review of 6 patients with concomitant dermatomyositis or polymyositis and myasthenia gravis who were evaluated, diagnosed, and treated at the Johns Hopkins Myositis Center (patients 1–5) or Johns Hopkins Outpatient Neurology clinic (patient 6).

Patients

All the patients were evaluated as part of routine clinical care at the outpatient neuromuscular clinic at the Johns Hopkins University Hospital or Johns Hopkins Bayview Medical Center in Baltimore, MD, between 1991 and 2012.

Ascertainment of inflammatory myopathies and myasthenia gravis

We identified and reviewed medical records of 6 patients who met both the Bohan and Peter criteria for PM or DM [23] and had myasthenia gravis. In each case, the diagnosis of MG was confirmed by characteristic electrophysiologic testing, demonstrating impaired transmission at the NMJ: either (a) $>10\%$ decrement on RNS or (b) increased jitter or blocking on SFEMG. Anti-AChR and/or anti-MuSK serologies were obtained for each patient, but a positive result was not required since $\sim$10% of MG patients are recognized to be seronegative.

Assessment of neuromuscular disease

Strength assessment was completed by 1 of 2 physicians (A.L.M. or A.M.C.) through manual muscle testing and graded by the Medical Research Council scale [24]. All patients had a myopathy workup, including electromyography (EMG), laboratory studies (creatine kinase and myositis antibody testing), and muscle biopsy. All patients had evaluation for myasthenia gravis with AChR antibody testing, RNS, and/or SFEMG.

Literature review

PubMed research was carried out: ["myositis" (MeSH Terms) OR "myositis" (All Fields)] AND myasthenia (All Fields) AND Case Reports (ptyp); ["myositis" (MeSH Terms) OR "myositis" (All Fields)] AND myasthenia (All Fields) AND [case (All Fields) AND series(All Fields)]. All case reports available in English were included.

Results

Patient #1

This 75-year-old woman with a history of autoimmune hepatitis, hypothyroidism, and Sjogren's syndrome presented with 4 months of progressive proximal muscle weakness and rash. Her CK was 446 IU/L. She was initially placed on oral prednisone at a dose of 60 mg daily for a presumptive diagnosis of DM. Her weakness markedly worsened upon initiation of high-dose prednisone and she developed severe dysphagia requiring a gastrostomy tube. She denied diplopia. On our evaluation, muscle testing revealed 3/5 power in arm abductors and elbow extensors, 4/5 hip flexor strength, and 5/5 strength in all other muscle groups. Skin exam revealed periorbital edema and diffuse erythema in a shawl distribution consistent with DM. EMG showed a non-irritable myopathy. A left deltoid muscle biopsy demonstrated perivascular inflammation with perifascicular atrophy and necrosis. There was a decrement on RNS testing. High titer anti-AChR antibodies as well as myositis-specific anti-P155/140 antibodies were present. Malignancy screening, including whole-body PET/CT, did not reveal an underlying cancer. She was treated with IVIG and pyridostigmine; within 2 months her strength normalized and her gastrostomy tube was removed.

Patient #2

This 44-year-old male presented with 6 weeks of progressive proximal muscle weakness and severe dysphagia, requiring gastrostomy tube placement. This was accompanied by dysarthria that was markedly exacerbated after prolonged conversations and recovered with rest. Strength exam revealed bilateral deltoid weakness grade of 4/5. Palatal weakness and lower facial weakness were also noted. There was no rash. His serum CK was elevated at 4600 IU/L. EMG showed an irritable myopathy and RNS testing was normal. However, SFEMG revealed findings consistent with neuromuscular transmission defect. Brain MRI with contrast was normal. CT of his chest revealed a thymic mass. Muscle biopsy showed an inflammatory myopathy with prominent perivascular inflammation. Anti-AChR, anti-MuSK, and a myositis autoantibody panel were negative. He was treated with prednisone, IVIG, and pyridostigmine with almost complete resolution of his weakness and dysphagia. A thymectomy was performed and pathological analysis revealed lymphoid follicular hyperplasia. While the presence of lymphoid follicular hyperplasia is not typically used to diagnose MG, this pathologic finding is observed in $\sim$65% of AChR-positive MG patients, $\sim$35% of MuSK-positive patients, and $\sim$25% of seronegative patients [25].

Patient #3

This 54-year-old male developed proximal muscle weakness with mild dysphagia over 9 months. He endorsed fatigability. His serum CK was 854 IU/L and EMG revealed an irritable myopathy. He was presumed to have myositis and subsequently treated with oral prednisone at a dose of 80 mg daily. Initially, he did not notice a significant improvement in his weakness and the prednisone was tapered off over 4 months. On our evaluation, he had 4/5 power in bilateral hip flexors with intact strength in other muscle groups. There was no rash. Muscle biopsy showed an inflammatory myopathy. He had high titer anti-AChR antibodies and SFEMG was consistent with a neuromuscular junction defect. Pyridostigmine monotherapy did not improve his weakness, but he had resolution of his symptoms after prednisone and mycophenolate were initiated. Three years later, he developed intermittent left eye ptosis, most pronounced at the end of the day.