Published in final edited form as:

Semin Arthritis Rheum. 2014 June ; 43(6): 792–796. doi:10.1016/j.semarthrit.2013.12.005.

The Co-Existence of Myasthenia Gravis in Patients with Myositis: A Case Series

Julie J. Paik, MD, MHS, Andrea M. Corse, MD, and Andrew L. Mammen, MD, PhD

Departments of Neurology (A.L.M. and A.M.C.) and Medicine (A.L.M. and J.P.) Johns Hopkins University School of Medicine in Baltimore, MD

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%). 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).

© 2013 Elsevier Inc. All rights reserved.

Address correspondence to: Andrew L Mammen, MD, PhD, Johns Hopkins Bayview Medical Center, Johns Hopkins Myositis Center, Mason F. Lord Building Center Tower, Suite 4100, Baltimore, MD 21224. amammen@jhmi.edu. Phone: 410-550-6962. Fax: 410-550-3542.

Disclosures of conflict of interest: None.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

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 (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), are 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 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 of 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, Maryland, between 1991 and 2012.

Ascertainment of inflammatory myopathies and myasthenia gravis

We identified and reviewed medical records of 6 patients who met both Bohan and Peter's 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 ~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 60mg 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 two 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 ~65% of AChR positive MG patients, ~35% of MuSK positive patients, and ~25% of seronegative patients(25).

Patient #3

This 54 year-old male developed proximal muscle weakness with mild dysphagia over nine 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 80mg 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.

Patient #4

This 38 year-old female with limited scleroderma and anti-Pm-Scl autoantibodies developed proximal weakness over 9 months and was eventually unable to walk up a flight of stairs. She complained of prominent fatigue and double vision at the end of each day. She also developed heliotrope rash and Gottron's sign. Her serum CK was 723 IU/L and EMG showed an irritable myopathy. She had an inflammatory muscle biopsy. Based on her diagnosis of DM, she was treated with prednisone 60mg daily for several months, but this was associated with worsening weakness. At the time of our evaluation she had 4/5 power in arm abductors and hip flexors with prominent neck flexor weakness. Moreover, she complained of prominent fatigue at the end of the day and double vision which did not improve with steroids. Although anti-AChR and anti-MuSK antibodies were negative, she had a decrement on RNS testing. With pyridostigmine therapy, she experienced near complete resolution of her proximal weakness and double vision. A chest CT revealed thymic hyperplasia and she is considering thymectomy.

Patient # 5

A 61 year-old male with history of ulcerative colitis presented with three months of progressive proximal muscle weakness and fluctuating dysarthria that improved with rest. He did not have double vision, ptosis, or dysphagia. On physical exam, he had grade 4/5 strength in proximal arm and leg muscle groups. No rashes suggestive of DM were observed. EMG showed a non-irritable myopathy and there was a marked decrement on RNS testing. Laboratory testing revealed high titer anti-AChR antibodies, a normal serum CK (158 U/L), and a negative myositis autoantibody panel. His muscle biopsy was notable for both endomysial inflammation and perifascicular atrophy. Following several months treatment with pyridostigmine, prednisone, and IVIG he had a marked improvement in his muscle strength with no weakness on exam.

Patient #6

This 24 year-old female with history of ulcerative colitis s/p colectomy presented with 6 weeks of proximal arm and leg weakness. She was unable to walk up a flight of stairs without assistance. On exam, she had 4/5 arm abduction strength and no rashes. Lab testing revealed a CK of 1200, and EMG showed an irritable myopathy. Her muscle biopsy showed an inflammatory myopathy. She was given IVIG with improvement in her weakness and normalization of her CK. However, six weeks after therapy, she developed recurrent proximal arm weakness (MRC grade 3/5) with significant difficulty washing her hair. She also noticed difficulty chewing foods. Following a repeat IVIG infusion, she had persistent proximal arm weakness, easy fatigability with chewing, and neck weakness. Although her legs remained strong, she developed intermittent ptosis and mild dysarthria after conversation and laughing. Further evaluation revealed marked decrements on RNS testing and high titer anti-AChR antibodies. She was placed on pyridostigmine with dramatic improvement in her proximal muscle strength and less fatigability with chewing.

DISCUSSION

Although rare, MG can be associated with myositis. In our literature review, we identified 20 cases of myositis-MG reported since 1976 (Table 1) (3–19). In the only prior report including more than one myositis-MG overlap case, Vasilescu and colleagues described four patients with clinical signs of DM, confirmed by muscle biopsy, who also had MG based on typical electrophysiological findings (4). However, these patients were described in 1978, before the availability of testing for anti-AChR or -MUSK antibodies. There have been several case reports of patients with concomitant PM and MG in association with thymoma (10, 19). There are also two reported cases of concomitant DM or PM with MG presenting with respiratory decompensation (14, 17). More recently, a case of DM-MG overlap with respiratory compromise in the context of invasive ductal breast carcinoma was described (18). Here, we report the largest case series, including 6 patients with DM or PM and MG. Their clinical, laboratory, and electrophysiologic features are summarized in Tables 2, 3, and 4. This easily overlooked group of patients requires a different approach to treatment than patients diagnosed with myositis alone. Consequently, clinicians should be aware of features which may suggest the co-existence of MG in patients with PM or DM.

Diplopia and ptosis are classic features of MG that are virtually never encountered in patients with myositis alone. In this case series, 3/6 (50%) subjects had one of these features and antibody and/or electrophysiologic testing confirmed the diagnosis of MG. In patients with myopathy and ophthalmoparesis or ptosis, potentially life threatening causes of these findings should first be considered; most of these can be excluded by performing a brain MRI. In those with a normal brain MRI and in whom MG has been excluded as a possible diagnosis, a diagnosis of mitochondrial myopathy should be considered. Similarly, in myopathic patients with ptosis (and/or dysphagia), a diagnosis of oculopharyngeal or myotonic muscular dystrophy should be entertained. Finally, ptosis and/or diplopia may be unrelated to the underlying myopathy and result from another disorder such as a third cranial nerve palsy, Horner's syndrome, cavernous sinus disease, multiple sclerosis, or thyroid eye disease; again, most of these are excluded by MRI imaging of the head and neck.

While many myositis patients complain of severe fatigue, true muscle fatigability is not characteristic of myositis. In contrast, fatigability with fluctuating weakness is a hallmark of MG. Mechanistically, fatigability occurs because repeated action potentials produced by sustained effort cause a partial depletion of presynaptic acetylcholine (ACh)-containing vesicles. Therefore, less ACh is released with each subsequent action potential. Under normal circumstances, an adequate number of AChRs are available to bind the ACh and trigger a muscle action potential without fail. However, in patients with MG, the number of available AChRs is reduced and delayed or failed synaptic transmission at the NMJ may occur; this is the pathophysiologic basis of the decrement seen on RNS and the jitter and blocking seen on SFEMG.

In the current series of myositis-MG overlap patients, 5/6 (83%) complained of fatigable weakness. When evaluating weak patients, the clinician should directly inquire about symptoms of fatigability. For example, does the patient have dysphonia that worsens with prolonged speaking and improves with periods of rest (as seen in Cases #2 and #5)? Does the patient experience ptosis or double vision after reading or at the end of the day (as seen in Cases #3 and #4)? Is the patient initially able to raise their head off the bed, but unable to do this on subsequent attempts? Evidence of fatigability should also be ascertained during the physical exam. For example, can the patient maintain up-gaze for three minutes without developing ptosis? Is the patient with good deltoid strength on confrontation testing able to maintain arms abducted at 90 degrees for three minutes? When either the history or physical exam suggests the possibility of fatigable weakness, the clinician should consider serologic and/or electrophysiologic testing for MG.

In addition to proximal muscle weakness, characteristic manifestations of both myositis and MG include bulbar symptoms such as dysphagia and dysarthria. While the prevalence of such symptoms is less than 40% in myositis patients (26), about two-thirds of MG patients have bulbar symptoms (21). Among our myositis-MG overlap patients, 5/6 (83%) had prominent bulbar symptoms, two of which required placement of a gastrostomy tube. In our experience, bulbar symptoms are out of proportion to proximal weakness in myositis-MG overlap patients compared to most patients with myositis alone (who usually only develop dysphagia in the context of severe proximal limb weakness). In such cases, the clinician must first consider the possibility of a life-threatening cause of bulbar weakness. Head and

neck MRI can exclude intrinsic or extrinsic lesions affecting the brainstem as well as obstructive or malignant lesions of the nasal and oropharynx. Lower motor neuron disease can be excluded based on the EMG and NCS. Once these causes of bulbar weakness have been excluded, we recommend screening tests for MG. In MG-negative myositis patients with prominent bulbar weakness out of proportion to limb weakness or that fail to respond as expected to treatment, other explanations for severe bulbar symptoms should be re-considered. Importantly, a diagnosis of inclusion body myositis should always be considered in patients with dysphagia and a suspected diagnosis of PM, especially when the motor dysfunction does not improve dramatically with initiation of immunosuppressive therapy.

Several other findings of interest were noted in the patients described in this series. First, 4/6 (67%) myositis-MG overlap patients had an *additional* overlap with one or more autoimmune disorders, including thyroid disease, ulcerative colitis, Sjogren's, scleroderma, and autoimmune hepatitis. Second, only 2/6 (33%) of the patients described here had a myositis-specific (i.e., anti-p155/140) or myositis-associated (i.e., anti-PM-Scl) antibody; one of these antibodies is found in ~75% of patients with myositis alone. Third, while 4/6 of our subjects were positive for anti-AChR antibodies, no patient described here or in the literature has myositis-MG overlap associated with anti-MuSK antibodies, which are found in ~15% of patients with MG. Fourth, although distal extremity weakness is occasionally observed in patients with MG (27), none of our myositis-MG overlap patients had distal weakness; this makes it difficult to ascertain whether limb weakness was due primarily to myositis, MG, or both. Finally, whereas several of the previously described myositis-MG overlap patients had a malignancy, none of the 6 described here had cancer.

We propose that an evaluation for MG should be performed in patients with typical features of myositis and symptoms of ptosis, diplopia, dysarthria, dysphagia, and/or fatigable weakness. The laboratory investigation should begin with anti-AChR testing. Although not reported in patients with myositis-MG overlap, the anti-MuSK antibody is reported to have a sensitivity of 38–70% in patients who have MG but are AChR seronegative (28, 29). As in myositis, different autoantibodies are associated with distinct phenotypes in MG patients. For example, compared to patients with anti-AChR antibodies, anti-MuSK positive patients typically have an earlier age of onset, more frequent bulbar involvement, and may be unresponsive to or intolerant of acetylcholinesterase inhibitors (30).

Electrophysiologic confirmation of myasthenia gravis is also indicated in patients suspected to have MG. Nerve conduction studies should include RNS, which is considered positive if the decrement in the compound muscle action potential amplitude after 6–10 stimulations at 2–3 Hertz is larger than 10% compared to baseline. In those who have negative or equivocal RNS, SFEMG may be used to test for a defect in neuromuscular transmission. In one study of 120 patients with myasthenia gravis, the diagnostic sensitivity of anti-AChR antibody testing, RNS, and SFEMG was evaluated. SFEMG was the most sensitive test (92%), followed by RNS (77%) and anti-AChR antibody testing (73%) (31). In all cases, at least one test was abnormal.

The management of MG includes symptomatic treatment with anticholinesterase agents such as pyridostigmine. Although not all MG patients respond to this medication, in our case

series, 5/6 (83%) patients had improvement with pyridostigmine. As in myositis, steroids and immunomodulators such as azathioprine, mycophenolate, and/or IVIG are commonly used in the management of patients with MG. However, in contrast to starting steroids at a high dose with subsequent tapering, in MG steroids should be started at a low dose and gradually titrated up. The rationale for this cautious approach is that initiation of therapy with high dose steroids can exacerbate weakness in MG, as reported by 2/6 (33%) patients in the current case series. In cases where disease severity requires initiation of high dose steroids, this should be done in a hospital setting and concurrent administration of IVIG could be considered.

Thymus pathology has been known to be associated with MG; thymic hyperplasia is reported in nearly 80% of MG patients undergoing thymectomy (32). It has also been reported that myasthenic symptoms may be attenuated with thymectomy, especially in patients with thymoma (33). Thus imaging of the mediastinum either by CT or MRI is an important aspect of the evaluation of a patient with myositis-MG. Although surgical resection of a thymoma is routinely recommended, the role of thymectomy in myositis-MG overlap patients with thymic hyperplasia has not been studied.

CONCLUSION

In summary, this is the largest case series of patients with myositis-MG overlap. Our findings suggest that the presence of ptosis, diplopia, bulbar symptoms, and/or fatigable weakness should prompt a screen for co-existing MG in patients who have myositis. Recognition that a patient has myositis-MG overlap should allow for proper management of both conditions. This may include a trial of pyridostigmine, starting steroids at a low dose when possible, and screening for thymic pathology.

Acknowledgments

This work was supported by NIH grant K08-AR-054783 (A.M.) and a T32 grant AR048522 (J.J.P.).

References

1. Furst DE, Amato AA, Iorga SR, Gajria K, Fernandes AW. Epidemiology of adult idiopathic inflammatory myopathies in a U.S. managed care plan. *Muscle Nerve*. 2012; 45:676–83. [PubMed: 22499094]
2. Greenberg SA, Amato AA. Inflammatory myopathy associated with mixed connective tissue disease and scleroderma renal crisis. *Muscle Nerve*. 2001; 24:1562–6. [PubMed: 11745962]
3. De Reuck J, Thiery E, De Coster W, Van Der Eecken H. Myasthenic syndrome in polymyositis. *Eur Neurol*. 1976; 14:275–84. [PubMed: 954774]
4. Vasilescu C, Bucur G, Petrovici A, Florescu A. Myasthenia in patients with dermatomyositis: Clinical, electrophysiological and ultrastructural studies. *J Neurol Sci*. 1978; 38:129–44. [PubMed: 213537]
5. Davis CJ, Gallai V. Myasthenia progressing to polymyositis with respiratory failure. *Acta Neurol (Napoli)*. 1979; 1:365–70. [PubMed: 517210]
6. Hassel B, Gilhus NE, Aarli JA, Skogen OR. Fulminant myasthenia gravis and polymyositis after thymectomy for thymoma. *Acta Neurol Scand*. 1992; 85:63–5. [PubMed: 1546537]
7. Kobayashi T, Asakawa H, Komoike Y, Nakano Y, Tamaki Y, Monden M. A patient with graves' disease, myasthenia gravis, and polymyositis. *Thyroid*. 1997; 7:631–2. [PubMed: 9292954]

8. Raschilas F, Mouthon L, Andre MH, Azorin J, Couvelard A, Guillevin L. Concomitant polymyositis and myasthenia gravis reveal malignant thymoma. A case report and review of the literature. *Ann Med Interne (Paris)*. 1999; 150:370–3. [PubMed: 10544746]
9. Kornizky Y, Heller I, Isakov A, Shapira I, Topilsky M. Dysphagia with multiple autoimmune disease. *Clin Rheumatol*. 2000; 19:321–3. [PubMed: 10941818]
10. Diaco M, Ancarini F, Montalto M, Verrechia E, Evoli A, Servidei S, et al. Association of myasthenia gravis and antisynthetase syndrome: A case report. *Int J Immunopathol Pharmacol*. 2004; 17:395–9. [PubMed: 15461874]
11. Hausmanowa-Petrusewicz I, Blaszczyk M, Jablonska S. Coexistence of scleromyositis associated with PM-scl antibody and myasthenia. *Neuromuscul Disord*. 1995; 5:145–7. [PubMed: 7767094]
12. Ko KF, Ho T, Chan KW. Autoimmune chronic active hepatitis and polymyositis in a patient with myasthenia gravis and thymoma. *J Neurol Neurosurg Psychiatry*. 1995; 59:558–9. [PubMed: 8530953]
13. Otton SH, Standen GR, Ormerod IE. T cell lymphocytosis associated with polymyositis, myasthenia gravis and thymoma. *Clin Lab Haematol*. 2000; 22:307–8. [PubMed: 11122275]
14. van de Warrenburg BP, Hengstman GJ, Vos PE, Boerman RH, ter Laak HJ, van Engelen BG. Concomitant dermatomyositis and myasthenia gravis presenting with respiratory insufficiency. *Muscle Nerve*. 2002; 25:293–6. [PubMed: 11870702]
15. Shichijo K, Mitsui T, Kunishige M, Kuroda Y, Masuda K, Matsumoto T. Involvement of mitochondria in myasthenia gravis complicated with dermatomyositis and rheumatoid arthritis: A case report. *Acta Neuropathol*. 2005; 109:539–42. [PubMed: 15843907]
16. Avni I, Sharabi Y, Sadeh M, Buchman AS. Eosinophilia, myositis, and myasthenia gravis associated with a thymoma. *Muscle Nerve*. 2006; 34:242–5. [PubMed: 16506154]
17. Yoshidome Y, Morimoto S, Tamura N, Kobayashi S, Tsuda H, Hashimoto H, et al. A case of polymyositis complicated with myasthenic crisis. *Clin Rheumatol*. 2007; 26:1569–70. [PubMed: 17047888]
18. Hill EK, King PH, Hughey LC. Dermatomyositis and concomitant overlap myasthenic syndrome: A rare presentation. *J Am Acad Dermatol*. 2011; 65:e150–2. [PubMed: 22000887]
19. Seton M, Wu CC, Louissaint A Jr. Case records of the massachusetts general hospital. case 26-2013. A 46-year-old woman with muscle pain and swelling. *N Engl J Med*. 2013; 369:764–73. [PubMed: 23964939]
20. McGrogan A, Sneddon S, de Vries CS. The incidence of myasthenia gravis: A systematic literature review. *Neuroepidemiology*. 2010; 34:171–83. [PubMed: 20130418]
21. Silvestri NJ, Wolfe GI. Myasthenia gravis. *Semin Neurol*. 2012; 32:215–26. [PubMed: 23117946]
22. Seybold ME, Drachman DB. Gradually increasing doses of prednisone in myasthenia gravis. reducing the hazards of treatment. *N Engl J Med*. 1974; 290:81–4. [PubMed: 4808454]
23. Bohan A, Peter JB. Polymyositis and dermatomyositis (first of two parts). *N Engl J Med*. 1975; 292:344–7. [PubMed: 1090839]
24. Medical research council. Aids to examination of the peripheral nervous system. 45. London: Her Majesty's Stationary Office; 1976. Memorandum no
25. Nikolic A, Djukic P, Basta I, Hajdukovic L, Stojanovic VR, Stevic Z, et al. The predictive value of the presence of different antibodies and thymus pathology to the clinical outcome in patients with generalized myasthenia gravis. *Clin Neurol Neurosurg*. 2013; 115:432–7. [PubMed: 22770539]
26. Marie I, Menard JF, Hatron PY, Hachulla E, Mouthon L, Tiev K, et al. Intravenous immunoglobulins for steroid-refractory esophageal involvement related to polymyositis and dermatomyositis: A series of 73 patients. *Arthritis Care Res (Hoboken)*. 2010; 62:1748–55. [PubMed: 20722047]
27. Nations SP, Wolfe GI, Amato AA, Jackson CE, Bryan WW, Barohn RJ. Distal myasthenia gravis. *Neurology*. 1999; 52:632–4. [PubMed: 10025802]
28. Chan KH, Lachance DH, Harper CM, Lennon VA. Frequency of seronegativity in adult-acquired generalized myasthenia gravis. *Muscle Nerve*. 2007; 36:651–8. [PubMed: 17654558]
29. Hoch W, McConville J, Helms S, Newsom-Davis J, Melms A, Vincent A. Auto-antibodies to the receptor tyrosine kinase MuSK in patients with myasthenia gravis without acetylcholine receptor antibodies. *Nat Med*. 2001; 7:365–8. [PubMed: 11231638]

30. Pal J, Rozsa C, Komoly S, Illes Z. Clinical and biological heterogeneity of autoimmune myasthenia gravis. *J Neuroimmunol.* 2011; 231:43–54. [PubMed: 21093931]
31. Oh SJ, Kim DE, Kuruoglu R, Bradley RJ, Dwyer D. Diagnostic sensitivity of the laboratory tests in myasthenia gravis. *Muscle Nerve.* 1992; 15:720–4. [PubMed: 1324429]
32. Castleman B. The pathology of the thymus gland in myasthenia gravis. *Ann N Y Acad Sci.* 1966; 135:496–505. [PubMed: 5221360]
33. Blossom GB, Ernstoff RM, Howells GA, Bendick PJ, Glover JL. Thymectomy for myasthenia gravis. *Arch Surg.* 1993; 128:855–62. [PubMed: 8343058]

Significance and Innovations

- In patients with myositis, prominent bulbar symptoms, diplopia, ptosis, and/or fluctuating weakness suggest the possibility of myasthenia gravis.
- Patients with co-existing myositis and myasthenia gravis require a different therapeutic approach than those with myositis alone.

Table 1

Previously described cases of myositis-MG overlap.

First Author	# cases	Age	Gender	Myositis Type	Treatment
Seton (19)	1	46	F	PM	Steroids and pyridostigmine; surgery for thymoma
Hill (18)	1	67	F	DM	Steroids and IVIG
Yoshidome (17)	1	62	F	PM	Steroids and IVIG
Avni (16)	1	66	M	PM	Steroids and IVIG
Shichijo K (15)	1	57	M	DM	Steroids
Van de Warrenburg (14)	1	28	F	DM	Steroids and Pyridostigmine
Oton (13)	1	71	M	PM	Steroids and azathioprine
Ko (12)	1	25	F	PM	Steroids, pyridostigmine, azathioprine
Hausmanovwa-Petrusewicz (11)	1	58	F	DM	Steroids, pyridostigmine
Diao (10)	1	47	F	PM	Steroids, methotrexate, then cyclosporine PM; For myasthenia gravis: pyridostigmine and surgery for thymoma.
Kornizky (9)	1	69	F	PM	Steroids, methotrexate
Raschilas (8)	1	66	F	PM	Steroids, pyridostigmine
Kobayashi (7)	1	14	F	PM	Amibenonium, thymectomy; steroids
Hassel (6)	1	37	M	PM	Thymectomy, steroids, cyclosporine, plasma exchange
Davis (5)	1	71	F	PM	Pyridostigmine, prostigmine, steroids
Vasilescu (4)	4	18, 24, 42, 46	3 F, 1 M	DM	Steroids and prostigmine
De Reuck (3)	1	23	M	PM	Pyridostigmine and steroids

Table 2

Demographics and myositis subtypes of myositis-MG overlap patients.

Patient #	Age at onset	Sex	Race	B&P Criteria diagnosis	Myositis-antibody	Other autoimmune diseases
1	75	F	C	Definite DM	Anti-P155/140	+
2	44	M	AA	Definite PM	-	-
3	54	M	C	Definite PM	-	-
4	38	F	C	Definite DM	Anti-PM/Scl	+
5	61	M	C	Definite PM*	-	+
6	24	F	C	Definite PM	-	+

C=Caucasian, AA=African-American, B&P= Bohan and Peter.

* The muscle biopsy showed perifascicular atrophy, which is more consistent with DM; however, the patient had no rash.

Table 3

Clinical features suggestive of MG in myositis-MG overlap patients.

Patient	Dysarthria	Dysphagia	Diplopia	Ptosis	Fatigable weakness
1	-	+	-	-	-
2	+	+	-	-	+
3	-	+	-	+	+
4	-	-	+	-	+
5	+	-	-	-	+
6	+	-	-	+	+

Table 4
Laboratory, electrophysiologic, radiographic, and clinical findings of MG in myositis-MG patients.

Patient	AChR Ab	MuSK Ab	SFEMG	RNS	Thymic hyperplasia*	Pyridostigmine response#	Worse with steroids
1	+	Not done	Not done	Abnl	-	+	+
2	-	-	Abnl	Normal	+	+	-
3	+	Not done	Abnl	Not done	-	-	-
4	-	-	Normal	Abnl	+	+	+
5	+	-	Not done	Abnl	-	+	-
6	+	Not done	Not done	Abnl	-	+	-

Ab = antibody, Abnl =abnormal, “-” = negative or symptom not reported, “+” = positive or symptom present

* determined by chest CT scan.

defined as an immediate (within hours of administration) but transient improvement with pyridostigmine.