Review - CME

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Update on the treatment of myositis

Siamak Moghadam-Kia[1], Chester V Oddis[1] & Rohit Aggarwal*,[1]

[1]Division of Rheumatology & Clinical Immunology, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

*Author for correspondence:
Tel.: +1 412 648 1897
Fax: +1 412 383 8864
aggarwalr@upmc.edu

Despite a paucity of controlled clinical trials, glucocorticoids remain the mainstay of initial treatment for inflammatory myopathies. Glucocorticoid-sparing agents, either methotrexate or azathioprine, are often begun concomitantly with glucocorticoid therapy. In patients failing to respond, other immunosuppressive or immunomodulatory agents such as mycophenolate mofetil, cyclosporine, tacrolimus, and intravenous immunoglobulin are used alone or in various combinations. In a large clinical trial of rituximab in adult and juvenile myositis, the primary outcome was not met, but most patients met trial criteria of improvement and rituximab use was associated with a significant glucocorticoid-sparing effect. The future therapeutic options for myositis will depend on well-designed clinical trials using validated outcomes and improvements in classification schemes based on serologic and histopathologic factors.

Keywords: dermatomyositis • idiopathic inflammatory myopathy • myositis • polymyositis • treatment

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LEARNING OBJECTIVES

Upon completion of this activity, participants will be able to:

- Describe current treatment of myositis with glucocorticoids, based on a review
- Discuss current treatment of myositis with methotrexate or azathioprine
- Discuss current treatment of myositis with other glucocorticoid-sparing immunosuppressive agents

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Background

The idiopathic inflammatory myopathies (IIMs) are a group of heterogeneous, systemic rheumatic diseases that include adult polymyositis (PM), adult dermatomyositis (DM), juvenile myositis (juvenile DM and juvenile PM), myositis associated with other connective tissue disease or cancer, and inclusion body myositis (IBM). The treatment of IIM has been challenging because of the rarity of these disorders, their heterogeneous clinical phenotypes, and the small number of randomized, double-blind clinical trials [1–4] that have been completed.

There is growing interest in evaluating novel therapies in myositis, including newer biologics that target various pathways implicated in the pathogenesis of disease. New classification schemes based on serologic and histopathologic features may also assist in the choice of therapies, as well as the design of clinical trials and the enrollment guidelines [5,6]. The past several years has heralded the introduction of consensus and data-driven outcome measures in myositis. In particular, two international groups, the International Myositis Assessment and Clinical Studies Group (IMACS) and the Pediatric Rheumatology International Trials Organization (PRINTO), have defined and validated consensus core set measures to assess myositis disease activity and damage in adult and pediatric populations [7–9]. Such measures will assist in studying both standard and novel therapies in a more rigorous fashion along with the current international initiative to develop both data- and consensus-driven response criteria in myositis. In this review, we will update the immunomodulatory and immunosuppressive approach to treating myositis including the use of more novel therapies for PM and DM.

Glucocorticoid therapy

Despite the lack of placebo-controlled trials, glucocorticoids are considered the mainstay of initial treatment of IIM as they normalize serum muscle enzymes and improve or preserve muscle strength [10]. Therapy is generally initiated with prednisone at a dose of 1 mg/kg per day, often in divided doses and generally not exceeding 80 mg daily. After 4–6 weeks of high-dose therapy, prednisone is slowly tapered to the minimum effective dose using the general guideline of tapering the existing dose by 20–25% monthly. The total duration of therapy with prednisone is generally 9–12 months and when the daily prednisone dose reaches 5–10 mg/day, the tapering is frequently held. Although some patients with milder disease can be treated with glucocorticoid monotherapy, most patients will require the addition of another immunosuppressive drug due to refractory disease, disease flares or to minimize glucocorticoid side effects.

Patients who are severely ill (marked weakness, severe dysphagia, or rapidly progressive interstitial lung disease) should be given pulse intravenous methylprednisolone (1000 mg daily for 3 consecutive days) followed by the high-dose oral glucocorticoid regimen noted above [11] in combination with a second-line immunosuppressive drug.

Over 50% of patients with myositis will not have complete response to glucocorticoid monotherapy [5]. Moreover, among those who do respond to glucocorticoids alone, most patients will not regain normal muscle strength and/or would flare up when glucocorticoids are tapered [10]. A failure to initial response or any worsening on glucocorticoids should prompt a reassessment for confirmation of the diagnosis, as well as consideration of steroid myopathy or an unrecognized

malignancy. Thus, a repeat muscle biopsy may be helpful. It is noteworthy that improved muscle strength is a more clinically reliable indicator of treatment response than a drop or normalization of serum muscle enzymes. After the aforementioned possibilities have been considered, the addition of a steroid-sparing agent should follow, if one has not already been started.

Glucocorticoid-sparing drugs

Most rheumatologists begin a steroid-sparing agent concomitant with or shortly after glucocorticoid therapy is initiated, particularly in patients with moderate-to-severe disease. This is often steroid-sparing serving to reduce the dose and duration of glucocorticoid therapy and the related side effects. Regardless of the choice of initial therapy, early treatment mitigates muscle damage [10]. The first-line conventional immunosuppressive agent choice is usually methotrexate or azathioprine. Patients failing to respond to this combination should be considered for more aggressive immunosuppressive or immunomodulatory therapy including mycophenolate mofetil (MMF), tacrolimus or cyclosporine, rituximab, intravenous immunoglobulin (IVIG), or cyclophosphamide.

Methotrexate & azathioprine

Methotrexate is a folate antimetabolite that irreversibly inhibits dihydrofolate reductase resulting in inhibition of DNA synthesis and repair. It can be given orally or subcutaneously with dose escalation up to 25 mg/week if necessary. There are no placebo-controlled prospective studies of methotrexate in PM or DM. However, a randomized, open-label, assessor-blind, international multicenter trial is ongoing in Europe to investigate the efficacy and safety of combined methotrexate/glucocorticoid treatment with glucocorticoid treatment alone [12]. Several retrospective studies have confirmed the efficacy of methotrexate in PM and DM patients including those who initially failed glucocorticoid therapy alone [10,13]. In an uncontrolled cohort of 55 glucocorticoid-refractory patients with IIM, treatment with methotrexate was associated with partial response in 31 patients, and a complete response in nine patients [10]. Toxicity monitoring should assess bone marrow suppression along with liver enzyme abnormalities and renal dysfunction.

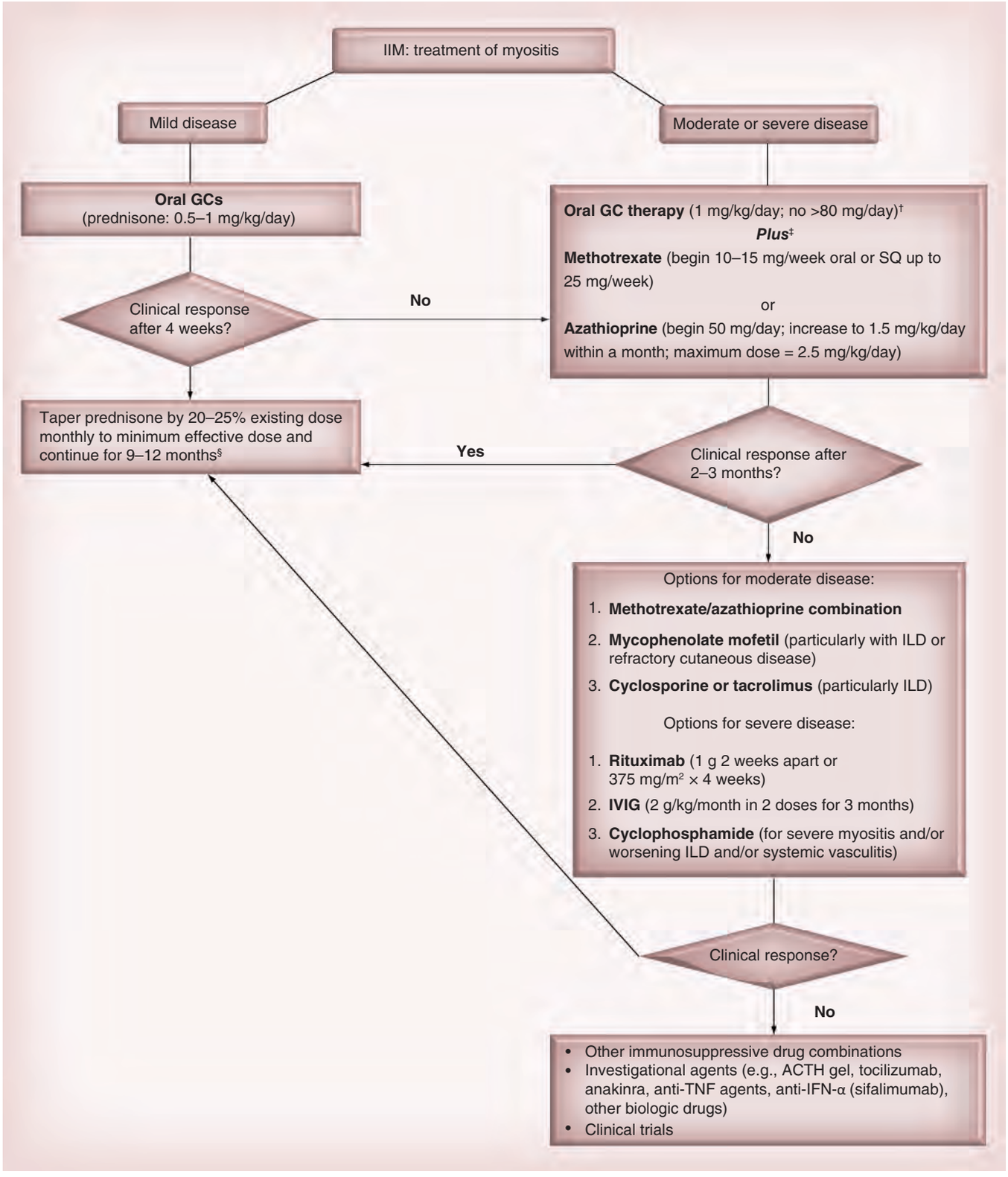
Azathioprine is a derivative of mercaptopurine that inhibits purine metabolism. In a randomized trial of 16 patients with PM, one group was treated with prednisone plus azathioprine and the other with prednisone alone. Although, there was no difference in muscle strength or creatine kinase (CK) between the two groups after 3 months of follow-up [2], the patients treated with combination therapy had better functional status and required less prednisone for maintenance 3 years later [14]. Controlled comparisons with methotrexate have shown that azathioprine has similar efficacy to methotrexate [10,15]. In a recent study, survival was higher between 5 and 10 years of follow-up in patients initially treated with methotrexate compared with those receiving azathioprine, but this was not confirmed in multivariable modeling for the full follow-up period [16]. By contrast, another survival analysis of patients with PM and DM, showed that azathioprine use was associated with better survival [17]. Although methotrexate is usually our first nonsteroid immunosuppressive agent, azathioprine is often preferred in patients with liver disease or those unwilling to abstain from alcohol, or in patients with myositis and interstitial lung disease (ILD). There is no evidence that methotrexate leads to more pulmonary toxicity in patients with myositis-related ILD, but the rare complication of methotrexate-related pulmonary toxicity in a myositis patient may present a diagnostic challenge. It is noteworthy that a response to azathioprine may take as long as 4–6 months [18,19].

A randomized, crossover study showed that a combination of oral methotrexate and azathioprine might be beneficial for patients with resistant myositis, including those who previously had inadequate treatment responses to either methotrexate and azathioprine alone [20]. This approach of combination therapy is anecdotally supported by many myositis investigators.

Azathioprine is administered orally starting at 50 mg/day and increased by 50 mg increments every 1–2 weeks to 1.5 mg/kg/day. If there is inadequate response after 2–3 months, the dose can be increased to 2.5 mg/kg/day. Imuran toxicity includes gastrointestinal symptoms, myelosuppression, transaminitis, flu-like reactions with fever, and pancreatitis. Monitoring parameters should address myelotoxicity and renal and hepatic side effects. Thiopurine methyltransferase testing is recommended by the US FDA prior to treatment with azathioprine.

Mycophenolate mofetil

MMF a prodrug of mycophenolic acid, inhibits T- and B-lymphocyte proliferation via reversible inhibition of inosine monophosphate dehydrogenase. Several small case series have suggested efficacy for MMF in treating refractory PM and DM [21–24]. In an open study in seven patients with PM and DM, IVIG as add-on treatment with MMF was effective in refractory myositis [25]. Uncontrolled studies and case series have suggested that this agent may be efficacious in refractory cutaneous DM [26,27]. MMF has gained popularity in treating myositis-associated ILD as two small case series reported promising results in connective tissue



disease-related ILD (CTD-ILD) [28,29]. In another case series of four patients with DM-associated ILD receiving prednisone, the addition of MMF normalized the pulmonary function tests with resolution of dyspnea in three patients after 1 year follow-up, along with improvement in the diffusing capacity in the other patient on follow-up [30]. The largest cohort of CTD-ILD demonstrating the effectiveness of MMF also

Figure 1. Treatment of idiopathic inflammatory myopathies (see facing page). Glucocorticoids are considered the mainstay of initial treatment. Either methotrexate or azathioprine, are often begun concomitantly with glucocorticoid therapy. In patients failing to respond, other immunosuppressive, or immunomodulatory agents are used alone or in various combinations.
†For the initial treatment of severe disease (marked weakness, dysphagia, or rapidly progressive ILD), consider pulse intravenous methylprednisolone (1000 mg daily for 3 consecutive days) before oral or intravenous GC therapy.
‡For patients on combination of high-dose GC plus another immunosuppressive agent, add prophylaxis against *Pneumocystis jirovecii* (e.g., trimethoprim–sulfamethoxazole double-strength [160/800 mg] three-times weekly).
§Duration of therapy with GC-sparing agents may be extended to 1–2 years based on clinical response.
ACTH: Adrenocorticotropic hormone; GC: Glucocorticoid; ILD: Interstitial lung disease; IIM: Idiopathic inflammatory myopathy; IVIG: Intravenous immunoglobulin; SQ: Subcutaneous.

suggested efficacy of this immunosuppressive agent in myositis-associated ILD [31]. In this report, 125 patients with CTD-ILD (32 with PM or DM) received MMF for a median of 897 days showing significant improvements in forced vital capacity at 52, 104, and 156 weeks and carbon monoxide diffusing capacity at 52 and 104 weeks after starting therapy.

Cyclosporine & tacrolimus

Cyclosporine is a calcineurin inhibitor that inhibits production and release of IL-2 and IL-2-induced activation of T lymphocytes. Cyclosporine has been used in refractory myositis to treat the primary disease [32,33], as well as ILD [34–39]. In a randomized open-label controlled trial, administration of cyclosporine or methotrexate added to glucocorticoids was associated with significant improvement in muscle strength, but patients treated with methotrexate showed no better response than cyclosporine [32]. In a retrospective multicenter study in Japan, the combination of cyclosporine and glucocorticoids was associated with a more favorable early and long-term outcome in the majority of patients with myositis-associated ILD than glucocorticoids alone [35]. Another retrospective study of 16 DM patients with acute/subacute interstitial pneumonia showed that an early (within 15 days of diagnosis) combination therapy of cyclosporine and glucocorticoids had improved survival compared with glucocorticoids alone [36]. Similarly, in 14 patients with DM and acute/subacute interstitial pneumonia, combination therapy with glucocorticoids and cyclosporine (4 mg/kg/day) within 12 days from diagnosis resulted in improved pulmonary function tests and high-resolution computed tomography scanning [37]. Importantly, the improvements correlated with time from diagnosis to cyclosporine initiation, as well as cyclosporine levels. Another retrospective study of eight anti-Jo-1-positive PM patients with ILD who were treated with oral cyclosporine showed similar progression of ILD on high-resolution computed tomography compared with those treated with cyclophosphamide [38].

Tacrolimus is a second generation calcineurin inhibitor that binds to FKBP-12, an intracellular protein, resulting in inhibition of T-lymphocyte activation. Tacrolimus has been suggested for patients with inflammatory myopathy, particularly those with coexisting ILD. In one series of eight patients with refractory PM (six anti-Jo-1 and two anti-SRP-positive; five with ILD), tacrolimus was associated with an improvement in muscle strength and CK in all patients and improvement in pulmonary function in three of five patients with ILD [40]. In another report, 13 patients with the antisynthetase-associated ILD (12 with anti-Jo-1 and one with anti-PL-12 antibodies) were treated with tacrolimus for an average of 51 months and showed improvement of muscle strength, CK, and pulmonary functions test parameters [41]. A more recent observational study of sixteen patients with PM and 15 with DM, showed that tacrolimus improved muscle strength and CK 2–4 months after therapy [42]. In three small case series of patients with myositis-associated ILD, tacrolimus appeared to be beneficial in patients resistant to cyclosporine [35,43,44].

Cyclophosphamide

Cyclophosphamide, an alkylating agent may have utility in the inflammatory myopathies but there is a paucity of reports showing efficacy and a pervasive concern of serious adverse events, particularly the development of malignancy [45–47]. Monthly intravenous cyclophosphamide was ineffective in a prospective study of 11 patients with myopathy (two with IBM) [45]. Cyclophosphamide is generally reserved for patients with features of inflammatory myopathy and systemic vasculitis, aggressive ILD, or patients refractory to several other second-line agents.

Rituximab

Rituximab, a B-cell depleting agent, is a monoclonal antibody that targets CD20 antigens on B lymphocytes, activating complement and antibody-dependent B-cell cytotoxicity. In the largest clinical trial of rituximab in IIM, the RIM trial, 195 patients (75 with PM, 72 with DM, and 48 with juvenile DM; all refractory to glucocorticoid therapy or at least one immunosuppressive agent) were randomized to receive two 1 g rituximab infusions either at baseline or 8 weeks later [1]. Although the group treated earlier demonstrated no faster response to therapy than group treated later (thus failing to meet the primary outcome), the definition of

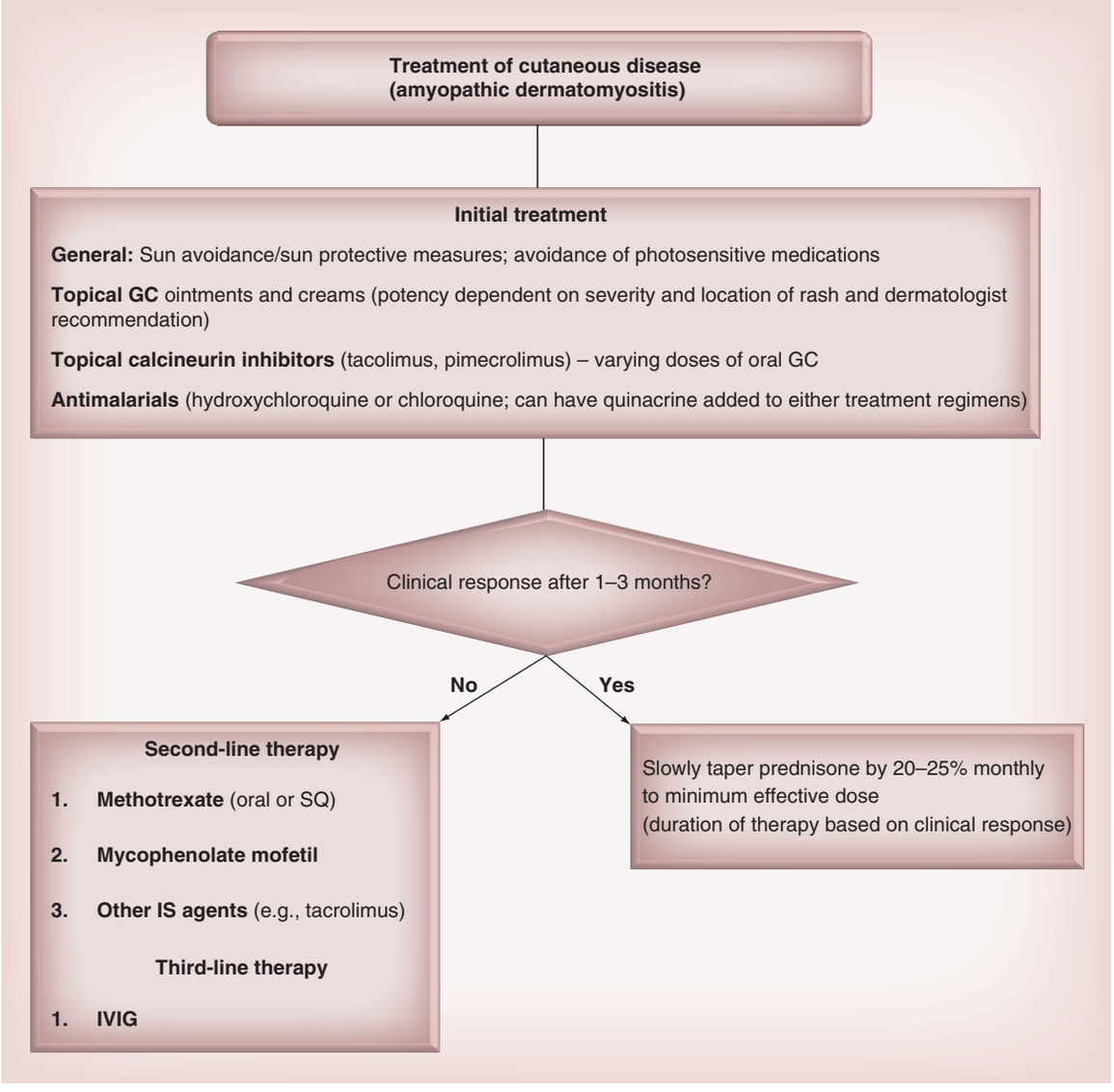


Figure 2. Treatment of amyopathic cutaneous dermatomyositis. Initial treatment include topical GCs, topical calcineurin inhibitors, antimalarials, or varying doses of oral GCs.
GC: Glucocorticoid; IVIG: Intravenous immunoglobulin; IS: Immunosuppressive; SQ: Subcutaneous.

improvement was met by 83% of the patients with a median time to achieving the definition of improvement of 20 weeks. Rituximab also showed a significant steroid-sparing effect and the mean dose of prednisone decreased from 20.8 mg at baseline to 14.4 mg daily at the end of the study. Moreover, patients retreated with rituximab after a disease flare also responded to retreatment. Rituximab was generally well tolerated and most common adverse effects were infections. In an analysis of the RIM study data using a multivariable time-dependent proportional hazards model, the presence of an antisynthetase and anti-Mi-2 autoantibodies, juvenile DM subset, and lower disease damage strongly predicted clinical improvement in this refractory group of myositis patients [48].

Rituximab use in inflammatory myopathies has also been reported in several small case reports and case series [49–56]. In one study, 13 patients with refractory IIM treated with two 1 g rituximab doses 2 weeks apart and followed for a median of 27 months, showed a significant decrease in CK and lactate dehydrogenase, and increase in muscle strength by 22% measured by hand-held dynamometry [49]. In another case series, rituximab therapy was efficacious in six of eight patients with refractory myopathy who tested positive for anti-SRP autoantibodies [50].

In an open-label uncontrolled trial in six patients with DM, rituximab therapy was associated with major clinical improvement in muscle strength and rash [55]. However, in another open-label trial of rituximab

in eight patients with DM, skin disease was not significantly changed from those at baseline and only three patients showed modest improvement in muscle strength [57].

Rituximab is usually administered as two 1 g doses 2 weeks apart. The most common adverse effects include infusion-related reactions, infections, and cytopenias. Some suggest periodic monitoring of peripheral B-cell flow cytometry to monitor return of CD20-positive B cells. All patients should be screened for hepatitis B prior to therapy and high-risk patients require hepatitis C screening.

Intravenous immunoglobulin

IVIG, an immunomodulatory agent, has demonstrated efficacy in a double-blind, placebo-controlled study of 15 patients with refractory DM [3]. In an open study with 35 patients with PM, significant clinical improvement was noted in 70% of the patients, and the efficacy remained stable in 50% of the patients after discontinuation of the IVIG therapy, with a follow-up of approximately 3 years [58].

In one open study, combined treatment with IVIG, prednisone, and cyclosporine was associated with a significantly higher rate of complete remission in patients with refractory or relapsed myositis after 4 years of follow-up than those treated with prednisone and cyclosporine alone [59]. An alternative subcutaneous form of IVIG was used in a small case series of seven patients (four DM and three PM) [60]. It was administered by a programmable pump and the patient's usual IVIG monthly dose was fractioned into equal doses given subcutaneously at weekly intervals. All patients showed significant improvement in CK,

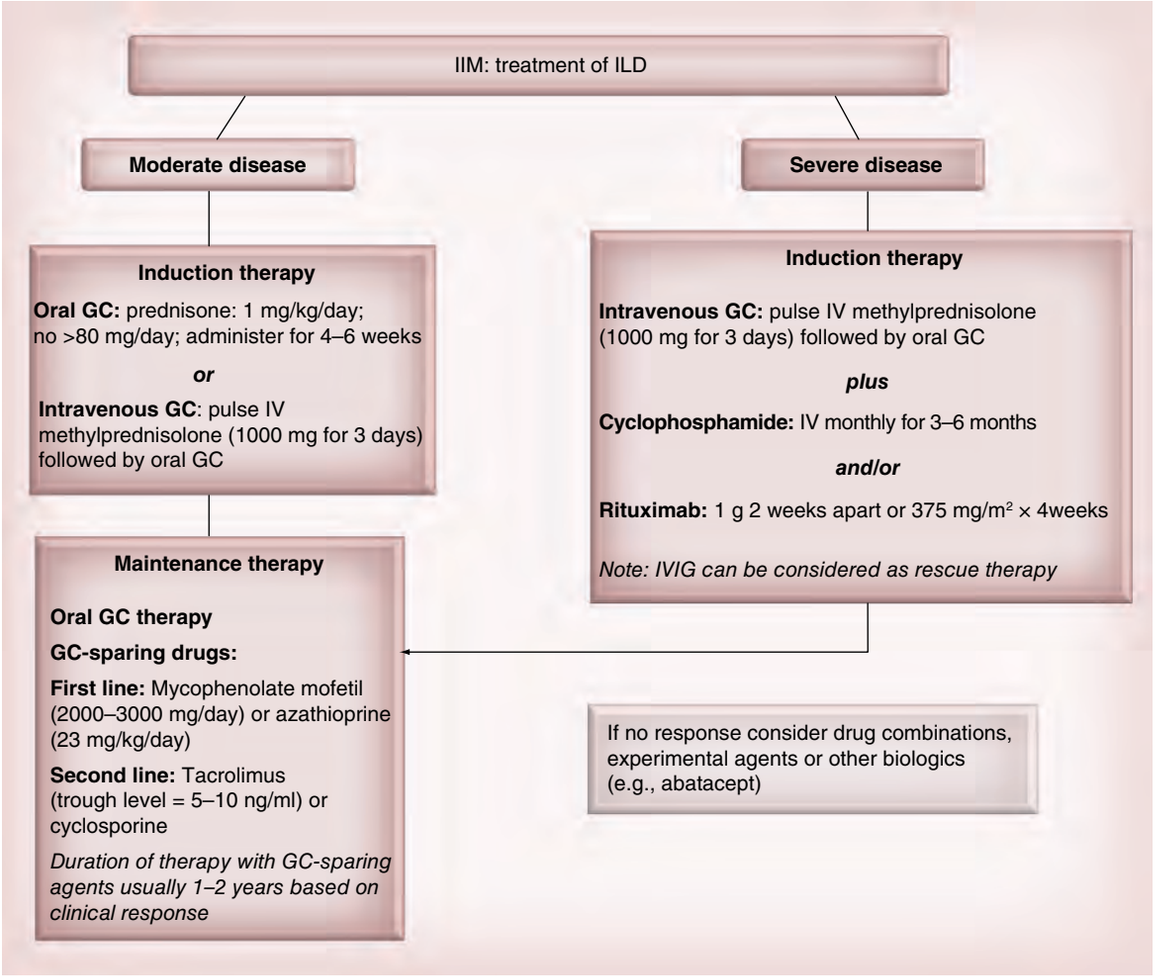


Figure 3. Treatment of interstitial lung disease in the setting of idiopathic inflammatory myopathies. Mycophenolate mofetil or azathioprine are the first-line GC therapy for maintenance therapy. In particular, mycophenolate mofetil has gained popularity in treating myositis-associated interstitial lung disease in the past couple of years.
GC: Glucocorticoid; IIM: Idiopathic inflammatory myopathy; ILD: Interstitial lung disease; IV: Intravenous; IVIG: Intravenous immunoglobulin.

muscle strength, and quality of life and were able to reduce their maintenance prednisone dose. The 2012 American Academy of Neurology guidelines support IVIG use for refractory DM but report insufficient evidence to support or refute its use in PM [61]. IVIG is thought to suppress inflammatory or immune-mediated processes, and is usually administered as infusions of 2 g/kg monthly, but the dose or interval can be changed based on the response to therapy. The majority of adverse events are minor and include headache and mild infusion-related reactions that are rate-related. However anaphylactic reactions, thrombotic, hematologic, neurologic, and renal complications have been reported [62]. The high cost of IVIG may influence decisions on its long-term use, thus limiting its use to refractory cases or those with severe dysphagia. A major advantage of IVIG is that it is safe in the setting of infections and it can be used concomitantly with other immunosuppressive drugs.

Anti-TNF agents

Infliximab and etanercept have been used for the treatment of inflammatory myopathies, but the results have not been encouraging.

A few anecdotal reports suggested that infliximab might be efficacious [63–65]. However, a follow-up report of two patients who initially appeared to respond to infliximab had an exacerbation of their myositis and resuming infliximab was associated with anaphylaxis and the development of anti-dsDNA autoantibodies [66]. In a larger uncontrolled series of eight patients with DM or PM, infliximab therapy led to improved motor strength and fatigue, but only partial improvement in CK elevation [67]. In a more recent pilot study of 13 patients with refractory myositis, infliximab treatment was not effective [68]. An unpublished randomized controlled trial of infliximab also failed to show efficacy [69]. A multicenter open-label controlled trial of infliximab combined with weekly methotrexate in patients with PM or DM was terminated prematurely because of a low inclusion rate and high disease progression [70].

Etanercept has also shown mixed results and its efficacy in myositis is yet to be established. Five patients with DM failed to respond to etanercept, but later improved after methotrexate or azathioprine treatment [71]. By contrast, a randomized double-blind placebo-controlled trial of etanercept for 52 weeks in 16 DM patients showed that etanercept therapy resulted in a significantly longer time to treatment failure and a significantly lower average prednisone dosage [72]. However, anti-TNF utility is limited by recent reports suggesting the potential for inducing autoimmune disease including PM and DM [73–76].

Adrenocorticotropic hormone gel

Adrenocorticotropic hormone (ACTH) gel is a long-acting full-sequence ACTH that includes other proopiomelanocortin peptides and is thought to have anti-inflammatory and immunomodulatory effects mediated via melanocortin receptors [77]. In a recent retrospective review, five patients with refractory myositis (three DM, two PM) received ACTH gel subcutaneous injections of 80 U twice weekly (four patients) or once-weekly (one patient) for 12 weeks. All patients had improvement in manual muscle testing and functional activities, as well as skin involvement [78]. All patients tolerated the ACTH gel treatment well, and no major side effects were reported.

ACTH gel has been an FDA-approved therapy for PM and DM since 1952 and its approval was retained by the FDA in 2010. Given its FDA label, some rheumatologists are considering ACTH gel in refractory patients or those who with glucocorticoid-related side effects. However, clinical efficacy has not been established an open-label clinical trial is underway to evaluate the efficacy and safety of ACTH gel in refractory PM and DM.

Other agents & future therapeutic prospects

Since approval of tocilizumab, an anatagonist of the IL-6 receptor, for rheumatoid arthritis, there has been growing interest in the use of this biologic agent in other rheumatic diseases. IL-6 is overexpressed in the serum and infiltrating mononuclear cells in the muscles of patients with inflammatory myopathy [79–81]. In the first report of tocilizumab treatment in inflammatory myopathy, two patients with refractory PM had improvements in the serum CK and MRI of their thigh muscles [82]. There were no adverse events except for a mild elevation of serum low-density lipoprotein in one patient. Further investigations are required to assess the effectiveness of tocilizumab in PM and DM and a trial is planned to assess the efficacy of this agent in refractory PM and DM.

In a recent report, therapeutic plasma exchange in two patients with DM-ILD appeared to be beneficial [83]. However, evidence supporting the use of plasma exchange in myositis patients is still lacking. A double-blind, placebo-controlled trial of plasmapheresis in chronic refractory PM or DM failed to demonstrate efficacy [8].

Although a single course of alemtuzumab, an anti-T-cell signaling agent, in a patient with refractory PM resulted in rapid improvement in her muscle strength, further studies are warranted to verify its effectiveness in myositis [85].

A recent Phase Ib randomized, double-blinded, controlled, multicenter clinical trial evaluated

sifalimumab, an anti-IFN-α monoclonal antibody, in PM and DM [86]. Sifalimumab treatment was associated with suppression of the IFN signature in blood and muscle tissue which correlated with clinical improvement.

Fingolimod (BAF312) is a sphingosine 1-phosphate receptor modulator that traps T lymphocytes in the lymphoid organs. It was recently approved by the FDA for the treatment of multiple sclerosis. A multicenter double-blind placebo-controlled trial of fingolimod in myositis is underway.

Other trials using anti-type IFN antibody, eculizumab (which targets C5 and inhibits the cleavage of C5 to C5a and C5b-9), abatacept (that inhibits the costimulation of T lymphocytes) are also planned.

Conclusion

Despite the lack of controlled trials, systemic glucocorticoids are considered the mainstay of initial treatment of the inflammatory myopathies, specifically PM and DM. Glucocorticoid-sparing agents are often started concomitantly with glucocorticoid therapy, particularly in severe cases of patients presenting to tertiary care centers. The first-line conventional immunosuppressive drugs include either methotrexate or azathioprine. In patients who do not respond adequately to glucocorticoids combined with methotrexate or azathioprine, other immunosuppressive or immunomodulatory agents or biologic drugs are sequentially used alone or in various combinations. Some of these agents are more appropriately used when certain manifestations predominate such as tacrolimus or cyclosporine (ILD) and MMF (ILD and refractory cutaneous disease). Various combinations have been studied such as methotrexate and azathioprine but others should be considered as well, such as tacrolimus and MMF in refractory patients. Figures 1–3 present systematic therapeutic approaches to myositis, ILD in the settings of myositis, and cutaneous DM.

Future perspective

More well-designed controlled trials using emerging validated outcome measures, and newer classification schemes based on serologic and histopathologic factors for better characterization of enrolled subjects, are required to develop an evidence-based approach to the treatment of inflammatory myopathies. Further investigations are required to assess the role of novel therapies such as ACTH gel, tocilizumab, and anti-IFN-α (sifalimumab).

Executive summary

Glucocorticoid therapy

- Despite the lack of controlled trials, systemic glucocorticoids are considered the mainstay of initial treatment of idiopathic inflammatory myopathies.

Glucocorticoid-sparing drugs

- Either methotrexate or azathioprine, are often begun concomitantly with glucocorticoid therapy, particularly in patients with moderate-to-severe disease presenting to tertiary care centers.
- In patients failing to initially respond to glucocorticoids combined with methotrexate or azathioprine, other immunosuppressive, immunomodulatory agents or biologic drugs are sequentially used alone or in various combinations.
- Some immunosuppressive agents are more beneficial when certain disease manifestations predominate such as mycophenolate mofetil (interstitial lung disease and refractory cutaneous disease) and tacrolimus or cyclosporine (interstitial lung disease).
- Intravenous immunoglobulin has demonstrated efficacy in dermatomyositis in a double-blind, placebo-controlled study and can be used in moderate-to-severe refractory patients.
- Rituximab use in a large controlled clinical trial in myositis was associated with clinical improvement and a significant glucocorticoid-sparing effect, although the study failed to meet it's primary end point.

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Update on the treatment of myositis

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Activity evaluation: where 1 is strongly disagree and 5 is strongly agree.					
	1	**2**	**3**	**4**	**5**
The activity supported the learning objectives.					
The material was organized clearly for learning to occur.					
The content learned from this activity will impact my practice.					
The activity was presented objectively and free of commercial bias.					

1. Your patient is an 82-year-old man with polymyositis. According to the review by Moghadam-Kia and colleagues, which of the following statements about current treatment of idiopathic inflammatory myopathies (IIMs) with glucocorticoids is **correct**?

- ☐ **A** Systemic glucocorticoids do not affect serum muscle enzymes or muscle strength
- ☐ **B** Considerable evidence from well-designed randomized trials supports the use of glucocorticoids for initial treatment
- ☐ **C** Starting oral dose of prednisone is 1 mg/kg per day, often in divided doses, not more than 80 mg daily, with taper after 4–6 weeks, for a total duration of 9–12 months
- ☐ **D** Intravenous therapy is not indicated

2. According to the review by Moghadam-Kia and colleagues, which of the following statements about current treatment of IIMs with methotrexate or azathioprine is **correct**?

- ☐ **A** Methotrexate or azathioprine is always given as monotherapy
- ☐ **B** Methotrexate is an irreversible inhibitor of dihydrofolate reductase that can be given orally or subcutaneously with dose escalation up to 25 mg/week if needed
- ☐ **C** Use of methotrexate in adult polymyositis or adult dermatomyositis is well supported by evidence from placebo-controlled prospective trials
- ☐ **D** Methotrexate is preferred versus azathioprine in patients with liver disease or interstitial lung disease

3. According to the review by Moghadam-Kia and colleagues, which of the following statements about current treatment of IIMs with other glucocorticoid-sparing immunosuppressive agents would **most** likely be correct?

- ☐ **A** In patients failing to respond to glucocorticoids and methotrexate or azathioprine, mycophenolate mofetil, cyclosporine, tacrolimus, and intravenous immunoglobulin (IVIG) may be used alone or in various combinations
- ☐ **B** No evidence supports the use of rituximab for adult or juvenile myositis
- ☐ **C** Tacrolimus use is most appropriate in patients with refractory cutaneous disease
- ☐ **D** IVIG has not been tested in dermatomyositis