Refractory Myositis: What Can Be Done?

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Little evidence exists to guide the management of treatment-resistant myositis. This brief guide describes the best available options for a challenging and heterogeneous condition.

Source: Rheumatology Network

Treating the idiopathic inflammatory myopathies can be challenging. These rare and heterogeneous diseases do not lend themselves well to the large randomized trials that guide treatment standards. Other than corticosteroids and adrenocorticotropic (ACTH) gel, the FDA has not approved any medications for treatment of myositis. Different immunosuppressants are used with varying success, largely based on expert opinion and case reports.

In our practice, we commence treatment with high-dose prednisone in combination with methotrexate, azathioprine, or mycophenolate mofetil. These agents are usually enough to treat mild, non-refractory disease.

The disease is considered refractory if a patient has not responded after taking an adequate dose of steroids plus one other immunosuppressant for an adequate duration, and after other possible explanations for the poor response—myositis mimics (dystrophies, endocrinopathies, etc.) as well as malignancy—have been ruled out.

The best evidence supports the following alternative treatment strategies for refractory disease (inclusion body myositis excluded):

**Rituximab:** Case series have reported promising results for B-cell depleting therapy in refractory myositis, including SRP associated necrotizing myopathy. The largest randomized trial to date in myositis, the Rituximab in Myositis (RIM trial) enrolled 200 adult and pediatric dermatomyositis or polymyositis patients refractory to steroids and an additional immunosuppressant. Both groups received rituximab, but were randomized into an early and a late group. Although the defined endpoints were not met (there was no significant difference between the groups), 83% of patients met the IMACS (International Myositis Assessment and Clinical Studies Group) definition of improvement. Predictors of improvement with rituximab included the presence of an anti-synthetase antibody, anti-Mi-2, juvenile dermatomyositis and lower physician global damage scores. This intravenous infusion is given as 1g on Day 0 and Day 14. The optimal time to redosing of the medication has not yet been established, but can be guided by symptoms and rising CD19/20 levels.

**Intravenous Immunglobulin:** IVIG is highly effective in refractory myositis, and the therapeutic benefit appears to be effected through many pathways. It acts fairly rapidly to bring about a clinical response, and should be considered in cases of rapid deterioration despite steroids. It is an important agent in the setting of esophageal involvement, for patients with contraindications to immunosuppressants, and for refractory lung disease. There is also data to support its use in statin-associated immune-mediated necrotizing myopathy as well as calcinosis. IVIG is given as a 2g/kg monthly dose, divided over 2-5 days for at least 3-6 months. When response to infusions wanes, a brand switch often achieves good results.

**Cyclosporine/Tacrolimus:** These calcineurin inhibitors are used mainly for concomitant interstitial lung disease such as with anti-synthetase syndrome or MDA5 disease. Improvements or stabilization in lung function have been seen. Tacrolimus has also been used in patients with dermatomyositis and polymyositis refractory to steroids and IVIG, achieving significant improvements in strength and CPK levels. There is data to support its use in skin disease, suggesting that it may be more useful in dermatomyositis than polymyositis.

**ACTH gel:** This is the long-acting formulation of the full-sequence ACTH including pro-opiomelanocortin peptides. Its action appears to involve more than steroidogenesis, with anti-inflammatory and immunomodulatory effects exerted through the melanocortin system. Originally approved by the FDA for treatment of myositis in 1952, its renewed FDA approval in 2010 has brought a resurgence of interest in ACTH gel. However, the clinical data are limited. A small retrospective case series showed clinical improvement in weakness and rash in 3 patients with dermatomyositis and 2 with polymyositis refractory to steroids and multiple other...
immunosuppressants.\[13\] ACTH gel was given as an 80U (1ml) subcutaneous injection once or twice weekly over 12 weeks for short-course treatment of exacerbations.

**Cyclophosphamide:** Due to its side-effect profile as an alkylating agent and concern for later malignancy, this is generally reserved for severe refractory myositis with rapidly progressive lung involvement and cutaneous or gastrointestinal vasculitis. But it remains an important option for severe refractory myositis with life-threatening organ involvement. Although there is no standard regimen for myositis, either oral or monthly IV cyclophosphamide has been used. Remission rates are high among patients who tolerate cyclophosphamide.\[14,15\]

**References:**


13. Nagappa M, Taly AB, Sinha S, et al. *Efficacy and limitation of pulse cyclophosphamide therapy in...


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