Comment:
Is 3,4-DAP a new option in treating MuSK MG?

Myasthenia gravis (MG) with antibodies to muscle-specific tyrosine kinase (MuSK) receptors is characterized by prominent weakness of facial and bulbar muscles. MuSK MG often requires aggressive immunosuppression, and inadequate treatment may leave patients with permanent, fixed weakness due to structural changes in the neuromuscular junction. Even with appropriate therapy, only 50% of patients reach minimal manifestations of disease or remission.1

In this case report, Evoli et al.2 describe a 61-year-old woman with MuSK MG since age 13 who responded well to treatment with 3,4-diaminopyridine (3,4-DAP). This is an unexpected finding given her long history of refractory disease and the lack of nonimmunomodulatory therapy. Patients with MuSK MG have substantial cholinergic sensitivity that is believed to accelerate dispersal of acetylcholine receptor clusters at endplates.3 This results in poor response to treatment with acetylcholinesterase inhibitors, leaving no option for short-term, symptomatic relief.1,4 3,4-DAP has long been used in the treatment of Lambert-Eaton myasthenic syndrome. There are no long-term side effects of 3,4-DAP and it is safe when taken as directed.

The findings in the current case are very encouraging. The current treatment armamentarium for MuSK MG is limited, with patients responding best to high doses of corticosteroids, plasmapheresis, and rituximab. These options have a risk of serious adverse effects, and both plasmapheresis and rituximab carry high costs. By contrast, 3-4-DAP is a convenient, orally dosed medication with a low incidence of serious side effects.

Single case reports are not adequate to recommend widespread use of 3,4-DAP in MuSK MG. However, given the rarity of this disorder and the acute need for better therapies, this case should provide the foundation for a prospective, multicenter trial.


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