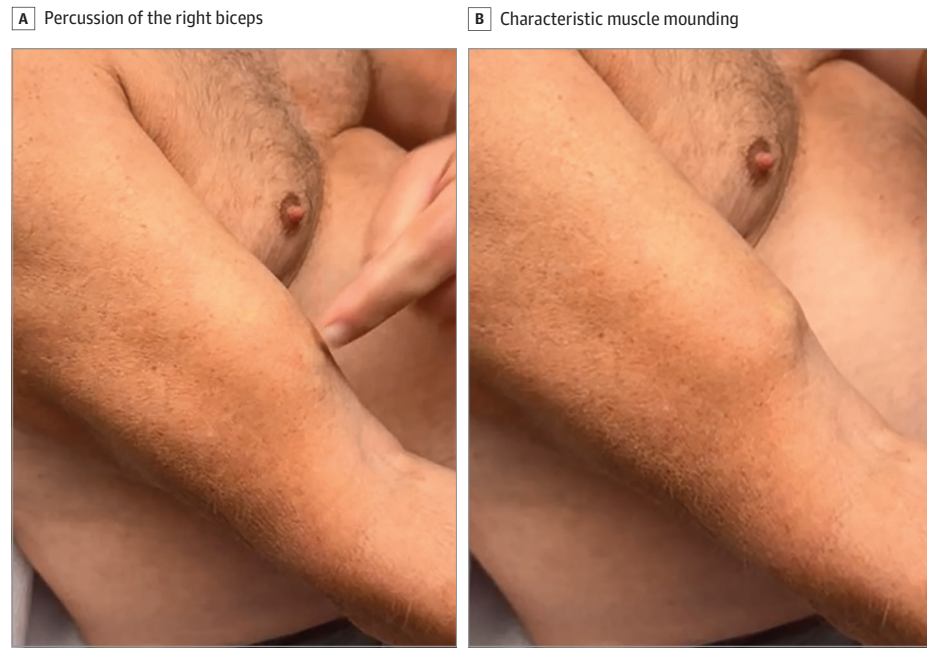


## Images in Neurology

## Complete Remission of Cavin-4 Immunoglobulin G Rippling Muscle Disease After Rituximab Therapy

Tony Zhang, MBChB; William J. Litchy, MD; Divyanshu Dubey, MD

Figure 1. Photographs Showing Muscle Mounding Following Percussion of the Right Biceps



Following percussion of the right biceps (A), characteristic muscle mounding is seen (B).

**Immune-mediated rippling muscle disease** (iRMD) is an uncommon myopathy characterized by visible wavelike muscle contractions (rippling) and percussion- or stretch-induced muscle mounding. Recent work has established circulating cavin-4 immunoglobulin G (IgG) autoantibodies as a disease biomarker in affected adults.<sup>1</sup> However, the optimal immunotherapeutic approach remains undefined, and reported treatment responses have been heterogeneous.

**+**  
Multimedia

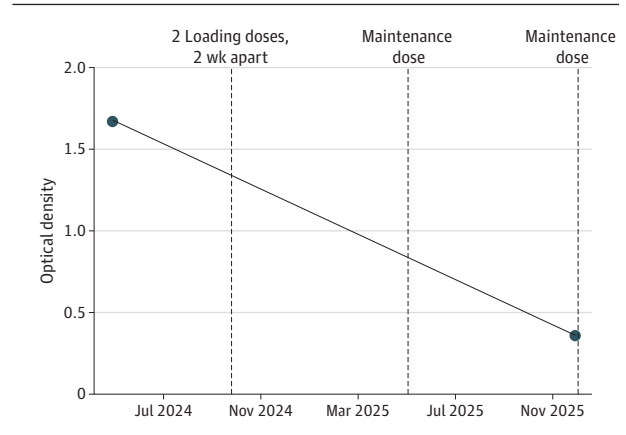
**+**  
CME at [jamacmelookup.com](http://jamacmelookup.com)

remains undefined, and reported treatment responses have been heterogeneous.

A 65-year-old man was evaluated for cavin-4 IgG-positive iRMD, confirmed by enzyme-linked immunosorbent assay (ELISA) and cell-based assay (research-based testing). He had been followed up at our institution for more than a decade for chronic muscle cramps and myalgias. Neurologic examination demonstrated mild proximal weakness and the characteristic phenotype of diffuse, stimulus-induced muscle rippling with percussion-evoked muscle mounding (Figure 1; Video). Electromyography showed features of a mild proximal myopathy without abnormal spontaneous activity.

Over the years, the patient received multiple immunomodulatory therapies, including intravenous immunoglobulin (IVIg), high-dose corticosteroids, and plasma exchange. Each resulted in partial and transient symptomatic improvement without sustained disease control. Following a severe clinical relapse in 2024, he

Figure 2. Line Graph Showing Reduction in Cavin-4 Immunoglobulin G (IgG) Titers Following Rituximab Therapy



Cavin-4 IgG levels, measured by cavin-4 IgG enzyme-linked immunosorbent assay (optical density cutoff, 0.686; based on optical density in healthy control individuals), before and after initiation of rituximab therapy. Dashed vertical lines indicate the timing of rituximab administration at 6-month intervals.

received rituximab induction therapy (two 1-g doses administered 2 weeks apart), followed by maintenance infusions every 6 months. Over subsequent months, he reported progressive

improvement in muscle strength and resolution of cramps and myalgias. Fourteen months after rituximab initiation, he was entirely asymptomatic for the first time since symptom onset. Repeat serum testing demonstrated that cavin-4 IgG, previously detected by ELISA,<sup>2</sup> had declined to below the ELISA cutoff, indicating a negative result (Figure 2). The decline in antibody titers after rituximab therapy, despite plasma cells lacking CD20, may potentially reflect depletion of CD20<sup>+</sup> precursors sustaining CD20<sup>-</sup> plasmablasts, with additional effects on antigen presentation and cytokines.<sup>3</sup>

Management of iRMD generally mirrors treatment strategies used for other idiopathic inflammatory myopathies, as disease-specific clinical trials are lacking.<sup>4</sup> Commonly used therapies

include IVIG, corticosteroids, and steroid-sparing immunosuppressive agents such as azathioprine, with treatment tailored to disease severity and individual response.<sup>1,4</sup> In a previously reported cohort of patients with cavin-4 IgG-positive iRMD,<sup>1</sup> complete remission was achieved in 3 of 8 patients with various combinations of prednisone, IVIG, and azathioprine, while the iRMD remained refractory despite immunotherapy in 2 patients.

To our knowledge, this case represents the first report of sustained clinical and serological remission of cavin-4 IgG-associated iRMD following B-cell-depleting therapy with rituximab. This observation is consistent with a potential role of humoral immune mechanisms and suggests that B-cell-targeted therapy may represent a therapeutic option warranting further study.

#### ARTICLE INFORMATION

**Author Affiliations:** Department of Neurology, Mayo Clinic, Rochester, Minnesota (Zhang, Litchy, Dubey); Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, Minnesota (Dubey).

**Corresponding Author:** Divyanshu Dubey, MD, Department of Neurology, Mayo Clinic, 200 First St SW, Rochester, MN 55905 ([dubey.divyanshu@mayo.edu](mailto:dubey.divyanshu@mayo.edu)).

**Published Online:** June 1, 2026.  
doi:10.1001/jamaneurol.2026.1519

**Conflict of Interest Disclosures:** Dr Dubey reported grants from UCB and DOD, consulting fees (paid directly to Mayo Clinic) from UCB, Immunovant, Argenx, Arialys, and Astellas, and serving as codirector of the Neuroimmunology Laboratory at Mayo Clinic (he receives no royalties

from the sale of neuromuscular antibody testing at the Neuroimmunology Laboratory; however, Mayo Clinic Laboratories does receive revenue for conducting such tests) outside the submitted work; in addition, Dr Dubey had patents pending for cavin-4, SYP, LUZP4, GAP43, and GCT-iSIGN and Sem-iSIGN and a patent licensed for KLHL11. No other disclosures were reported.

**Additional Contributions:** We thank the patient for granting permission to publish this information. We also acknowledge Reghann G. LaFrance-Corey, MS (Mayo Clinic), for technical support with cavin-4 IgG testing; she received no compensation.

#### REFERENCES

1. Dubey D, Beecher G, Hammami MB, et al. Identification of caveolae-associated protein 4 autoantibodies as a biomarker of immune-mediated rippling muscle disease in adults. *JAMA*

*Neurol.* 2022;79(8):808-816. doi:10.1001/jamaneurol.2022.1357

2. LaFrance-Corey RG, Kherbek H, Harinesan N, et al. High-throughput immunoassays for cavin-4 IgG: a diagnostic tool for immune-mediated rippling muscle disease. *Ann Clin Transl Neurol.* 2025;12(4):876-880. doi:10.1002/acn3.70012

3. Lanzillotta M, Della-Torre E, Stone JH. Roles of plasmablasts and B cells in IgG4-related disease: implications for therapy and early treatment outcomes. *Curr Top Microbiol Immunol.* 2017;401:85-92.

4. Selva-O'Callaghan A, Pinal-Fernandez I, Trallero-Araguás E, Milisenda JC, Grau-Junyent JM, Mammen AL. Classification and management of adult inflammatory myopathies. *Lancet Neurol.* 2018;17(9):816-828. doi:10.1016/S1474-4422(18)30254-0