(1000 mg at days 0 and 14). She continued to experience worsening lower extremity weakness. Eventually, she received 6 plasmapheresis treatments with minimal improvement.

During the entire period of follow-up at our center, she required 20 to 30 mg daily of oral prednisone. Neurological examination prior to the onset of HiCy therapy revealed symmetrically reduced arm abduction (4+/5) and hip flexion strength (2/5) and her CK level was 2920 U/L. Given progressive muscle weakness in the absence of a robust response to any immunosuppression, she was treated with HiCy, 50 mg/kg per day, for 4 consecutive days and supportive care, as previously described. Although she developed neutropenic fever 9 days later, she recovered successfully. She did not require red blood cell or platelet transfusion, and her neutropenia ultimately resolved 2 weeks after HiCy dosing. Muscle strength gradually improved to normal, and her CK level decreased to 537 U/L within 7 months of treatment. A repeated magnetic resonance image was performed 21 months after treatment (Figure, B). Her steroids were tapered off within 2 years of HiCy therapy. At her last visit, she had minimal residual weakness (4+/5 deltoids and hip flexors), which did not affect her activities of daily living. She has remained in clinical remission while not taking any immunosuppressive therapies, including glucocorticoids, with her most recent CK level normal at 100 U/L 6 years after HiCy treatment.

Discussion | HiCy has been successfully used in the treatment of a variety of autoimmune diseases including multiple sclerosis, myasthenia gravis, and chronic inflammatory demyelinating polyneuropathy. The initial response rate to HiCy therapy in refractory severe autoimmune diseases exceeds 90%, but only 20% remain disease-free at 5 years after treatment. In addition, the durability of the response may vary depending on the underlying autoimmune disease. For example, patients with pemphigus and lupus tend to have a less durable response following HiCy therapy than patients with autoimmune hemolytic anemia. Our patient achieved a durable remission after HiCy therapy and remains in remission 6 years after her initial HiCy therapy. This finding suggests that HiCy therapy may be effective and cause more durable remission in refractory idiopathic inflammatory myopathy for which conventional treatments are insufficient.

Arash H. Lahouti, MD
Robert A. Brodsky, MD
Lisa Christopher-Stine, MD, MPH

Author Affiliations: Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, Maryland (Lahouti, Christopher-Stine); Division of Hematology, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland (Brodsky).

Corresponding Author: Lisa Christopher-Stine, MD, MPH, Division of Rheumatology, Johns Hopkins University School of Medicine, 5200 Eastern Ave, MFL Center Tower, Ste 4500, Baltimore, MD 21224 (lchrist4@jhmi.edu).

Conflict of Interest Disclosures: Dr Christopher-Stine reports serving on the advisory board; receiving honoraria from Novartis, Mallinckrodt, Walgreens, and Medimmune; and having membership in the advisory board of Idera. She has intellectual property rights in connection with Inova Diagnostics. No other disclosures were reported.

Funding/Support: This study was supported by the Huayi and Siuling Zhang Discovery Fund.

Role of the Funder/Sponsor: The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.


Wallerian Degeneration of the Superior Cerebellar Peduncle

Wallerian degeneration (WD) occurs after nerve damage in both the peripheral nervous system and central nervous system (CNS). Wallerian degeneration is named after Augustus Volney Waller (1816-1870), a British neurophysiologist who observed distal nerve changes after experimental lesions of the hypoglossal nerve in frogs. The distal part of the axon of the damaged nerve degenerates, a process called orthograde degradation. Histologically, WD is characterized by structural loss of the cytoskeleton, a process that takes roughly 24 hours in the peripheral nervous system and days to weeks in the central nervous system.

Wallerian degeneration of the corticospinal tract is common after ischemia in the primary motor cortex or internal capsule. On imaging, hypointensity on T2 sequences is present in the corticospinal tract during 4 to 12 weeks, after which a permanent T2 hyperintensity is seen. After several months to years, atrophy of the involved tract can be observed. On diffusion-weighted imaging (DWI) sequences, diffusion restriction is found. If present, poor motor outcomes are likely. Wallerian degeneration can occur in every nerve tract.

Report of a Case | We describe a man in his early 80s who had a deep cerebellar hemorrhage with damage to the dentate and interposite nuclei (Figure 1A). On brain magnetic resonance imaging obtained 5 days after the event (Figure 1B and C), there was a marked hyperintense signal on DWI of the ipsilateral superior cerebellar peduncle (SCP). The apparent diffusion coefficient showed a subtle hypointense signal of the ipsilateral SCP. There were no other hyperintensities on DWI. These changes were due to WD of the dentato-rubral-thalamic (cortical) tract, which is the main output of the dentate nucleus and which travels through the SCP, crosses the midline in the SCP, and runs to the contralateral red nucleus. From the red nucleus, there are projections to the thalamus and to the inferior olivary nucleus (Figure 2).
A new brain magnetic resonance image (3-dimensional T2-weighted imaging; 0.6-mm slice thickness) was performed 4 months after the stroke (Figure 1D-F). On T2-weighted magnetic resonance sequence images, there was a hyperintense signal and atrophy of the ipsilateral SCP, compatible with WD. The contralateral red nucleus was smaller, with some hyperintensity, and the contralateral inferior olivary nucleus was hypertrophic, with marked hyperintensity. These findings confirmed the anatomical brainstem circuit, which is also known as the triangle of Guillain-Mollaret or myoclonic triangle.4 Lesions involving this circuit, such as ischemia involving the central tegmental tract, may cause palatal myoclonus. Palatal myoclonus is typically associated with temporary hypertrophic degeneration of the inferior olivary nucleus. Clinically, our patient experienced nausea and truncal ataxia but palatal myoclonus was not observed.

Discussion | To our knowledge, this is the first report of early WD of the SCP. However, late WD has been described after cerebellar surgery involving the deep nuclei or after hemorrhage in the dentate nucleus.5,6 Several neurodegenerative diseases, such as progressive supranuclear palsy and Friedreich ataxia, are also associated with atrophy of the SCP. Hyperintense lesions on DWI occurring at a distance from the initial cerebral infarction or hemorrhage are not necessarily due to accompanying ischemia but may reflect early WD and may illustrate complex anatomical relationships.

Thomas Decramer, MD
Philippe Demaerel, MD, PhD
Johannes van Loon, MD, PhD
Vincent Thijs, MD, PhD

Author Affiliations: Department of Neurosurgery, University Hospitals Leuven, Leuven, Belgium (Decramer, van Loon); Department of Radiology, University Hospitals Leuven, Leuven, Belgium (Demaerel); KU Leuven-University of Leuven, Department of Neurosciences, Experimental Neurology, Leuven, Belgium (Thijs); VIB-Vesalius Research Center, Leuven, Belgium (Thijs); Department of Neurology, University Hospitals Leuven, Leuven, Belgium (Thijs).
In the study, there were no data about individual family history of neuropathy. In patients who had a familiar predisposition to future neuropathy, neurological symptoms could not be necessarily associated with CD. This element should be considered in the results.

Hadjivassiliou et al demonstrated that a strict gluten-free diet improves neurological symptoms, resulting in stabilization of the neuropathy. We did not find accurate information about the diet of patients with CD in the period between the diagnosis of CD and the onset of neuropathy. The immunomodulatory role of a gluten-free diet is really intriguing in many extraintestinal manifestations of CD and it would be interesting to have precise details about it.

Furthermore, the authors should have considered chemotherapeutic treatments in patients: during the examined period, some of the patients could be exposed to chemotherapy and it could cause iatrogenic neuropathy. Some extraintestinal manifestations of CD and it would be interesting to have precise details about it.

In this context, it is worth noting that the highest risk for future neurological matters was just after diagnosis of CD. Despite the pathogenesis of neuropathies in patients with CD not yet being clear, the need for making a well-structured follow-up program against possible complications of CD, including the neurological manifestations, appears evident.

Too often, patients with CD, especially adults, are neglected after starting the gluten-free diet. The challenge is to realize an effective prevention of all the most feared complications of this frequent enteropathy, only apparently resolved after the start of a gluten-free diet.

Maurizio Mennini, MD
Ilaria Baglivo, MS
Federica Ferrari, MD, PhD

Author Affiliations: Sapienza, University of Rome, Rome, Italy.

Conflict of Interest Disclosures: None reported.

Corresponding Author: Maurizio Mennini, MD, Sapienza–University of Rome, Viale Regina Elena, 324 Rome, Italy (maurizio.mennini@gmail.com).

COMMENT & RESPONSE

Neuropathy and Celiac Disease—When a Gluten-Free Diet Is Not Enough

To the Editor The possible association between celiac disease (CD) and neurologic extraintestinal manifestations has been described in literature since 1966. We read with interest the article by Thawani et al showing the increased risk for neuropathy in patients with biopsy-proved CD. The major strengths of this study were the nationwide population-based design and the high statistical power. Nevertheless, we would like to raise some small constructive criticisms.