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Paroxysmal cold-induced unilateral leg stiffness as the initial manifestation of suspected stiff person syndrome: a case report

Richard A. Rison

richardrison@gmail.com

University of Southern California

Anne M. Arikian

UCLA Health

Said R. Beydoun

University of Southern California

Case Report

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Additional Declarations: Competing interest reported. AMA is the patient described in this case report and a coauthor. She provided written informed consent for publication and understands that her authorship publicly identifies her as the patient. AMA is also married to RAR. RAR is the Editor-in-Chief of the Journal of Medical Case Reports. To ensure complete editorial independence, RAR will not be involved in editor assignment, reviewer selection, peer review, or the editorial decision concerning this manuscript. We respectfully request that the submission be assigned to an independent editor and handled outside RAR's editorial oversight. SRB declares no competing interests.

Abstract

Background

Stiff person syndrome is a rare autoimmune neurologic disorder characterized by rigidity and stimulus-sensitive spasms. Focal presentations may be diagnostically challenging, particularly when early imaging and electrodiagnostic studies are unrevealing.

Case presentation

We report the case of a 44-year-old Armenian-Hungarian woman who developed an approximately 7-week history of episodic left leg stiffness provoked by walking and external stimuli. A cold breeze reproducibly precipitated abrupt stiffening with transient inability to advance the leg. The episodes became more frequent and prolonged, causing gait instability, falls, and cane dependence. Brain and lumbosacral magnetic resonance imaging and early nerve conduction and electromyographic studies were unrevealing. Serum glutamic acid decarboxylase 65 antibody was 23,898 U/mL (reference < 0.5 U/mL; Esoterix, Inc.), supporting a clinically suspected focal stiff person spectrum disorder without electrophysiological confirmation. Intravenous immunoglobulin was administered at 2 g/kg over 2 days monthly for 3 months, followed by 1 g/kg monthly for 6 months. Treatment was followed by less stiffness, improved gait, fewer falls, and improvement in cold-triggered episodes; these outcomes were assessed qualitatively.

Conclusions

Paroxysmal cold-triggered unilateral leg stiffness may prompt consideration of a focal stiff person spectrum disorder. A normal routine electromyogram does not exclude the diagnosis, but the absence of electrophysiological confirmation requires cautious interpretation of the clinical and antibody findings and careful assessment of alternative diagnoses.

Background

Stiff person syndrome (SPS) is an uncommon autoimmune neurologic disorder marked by progressive rigidity and painful or disabling spasms triggered by movement, touch, startle, or emotional stress. Impaired inhibitory neurotransmission within central motor pathways is central to current disease models [1].

The stiff person spectrum is clinically heterogeneous. In addition to classic SPS with axial and proximal limb involvement, partial phenotypes may remain confined to one limb and are often termed stiff limb syndrome [1–3]. High-titer antibodies against glutamic acid decarboxylase 65 (GAD65) support an autoimmune SPS phenotype when interpreted in the appropriate clinical context [1, 4]. Diagnostic delay

and misdiagnosis are common, particularly when symptoms are focal, asymmetric, or otherwise atypical [2, 3, 5].

We report the case of an adult with paroxysmal unilateral leg stiffness reproducibly triggered by cold exposure, a markedly elevated serum GAD65 antibody concentration, and clinical improvement following intravenous immunoglobulin (IVIG), supporting a suspected focal stiff person spectrum disorder.

Case presentation

Clinical course and examination

A 44-year-old Armenian-Hungarian woman presented with an approximately 7-week history of episodic stiffness involving the left thigh and leg. Symptoms were most prominent during ambulation and were exacerbated by sudden external stimuli. She described a characteristic episode in which exposure to a cold breeze while standing caused abrupt stiffening of the left leg and transient inability to advance the limb.

Over several weeks, the episodes became more frequent and prolonged. Gait instability progressed, she began using a cane, and she sustained multiple falls. Symptoms remained confined to the left lower extremity without axial, upper-extremity, or contralateral leg involvement. She described episodes of left leg spasms and sudden movements when startled while watching a movie or receiving a message, and when awakened at night by her husband's pager. She denied pain, numbness, paresthesias, or subjective weakness. Magnesium supplementation and quinine-containing tonic water provided only minimal, transient benefit. A trial of physical therapy did not result in any lasting benefit.

Her medical history did not include a neurologic or systemic autoimmune disorder, and there was no family history of neuromuscular or autoimmune disease. She reported an allergy to cephalexin and was not taking prescription medication at presentation.

Neurologic examination showed normal mental status and cranial nerves. Strength was full throughout, without focal atrophy or fasciculations. Tone was mildly increased at the left knee and ankle, with nonsustained left ankle clonus. Reflexes were otherwise symmetric, and sensory examination was normal. The left plantar response was extensor. Her gait was cautious, with difficulty initiating steps and reduced confidence during left-leg weight bearing.

Investigations

Two weeks before the onset of the leg symptoms, she had developed intermittent positional vertigo. Magnetic resonance imaging (MRI) of the brain and internal auditory canals was normal. MRI of the lumbosacral spine showed mild age-related spondylosis without spinal cord or nerve-root compression.

Electrodiagnostic testing was performed approximately 7 weeks after symptom onset. Sensory and motor nerve conduction studies of both lower extremities showed normal amplitudes, conduction velocities, and distal latencies. Peroneal and tibial motor responses, F-wave latencies, and H-reflexes were normal, without temporal dispersion or conduction block. Needle electromyography (EMG) of selected bilateral lower-extremity and lumbosacral paraspinal muscles showed normal insertional activity and voluntary motor-unit recruitment, without spontaneous activity, membrane instability, myotonic discharges, or continuous motor-unit activity at rest.

Routine laboratory evaluation was unrevealing. Because the symptoms were progressive, focal, and stimulus sensitive despite unrevealing brain and lumbosacral imaging and peripheral electrodiagnostic studies, autoimmune testing was obtained. Serum GAD65 antibody, measured by Esoterix, Inc., was 23,898 U/mL (reference < 0.5 U/mL). The markedly elevated result, together with the characteristic clinical phenotype, supported a clinically suspected focal stiff person spectrum disorder; electrophysiological confirmation was lacking.

Treatment and outcome

She received IVIG at a total dose of 2 g/kg administered over 2 days each month for 3 months, followed by 1 g/kg monthly for an additional 6 months. The initial schedule matched the regimen evaluated in the placebo-controlled SPS trial [6]. The subsequent dose was within the reported maintenance range of 1–2 g/kg every 3–6 weeks, adjusted to clinical response in published practice [7]. These data support initial treatment followed by maintenance but do not establish a fixed 6-month maintenance course for this focal presentation.

During treatment, she experienced less stiffness, improved walking, fewer falls, and improvement in cold-triggered episodes. She reported being able to climb over rocks without difficulty, indicating improved mobility compared with her earlier cane-dependent gait. These observations were qualitative. Standardized disability scores, timed walking measurements, numerical fall or spasm counts, and a prespecified remission definition are not available for this report; the outcome is therefore described as clinical improvement.

Discussion and Conclusions

The presentation of our patient was suggestive of a focal SPS phenotype, or stiff limb syndrome, but was not electrophysiologically confirmed. Partial SPS commonly predominates in the lower extremities, but published reports usually describe persistent or progressive limb rigidity and painful spasms, sometimes accompanied by myoclonus or other neurologic features [3, 8–11]. In our patient, the earliest disabling symptom was paroxysmal unilateral leg stiffness reproducibly precipitated by a cold breeze. Cold-related worsening has been described in SPS, including partial forms [5, 12].

To assess the proposed novelty, a targeted web-based literature search was performed on 15 October 2026, including PubMed-indexed records and accessible full-text reports. Searches combined “stiff person,” “stiff man,” or “stiff limb” with “cold,” “cooling,” or “temperature,” and additional terms “unilateral,” “focal,” “paroxysmal,” “initial,” or “onset.” Hyphenated variants were also searched. This was a focused narrative search, not a systematic review. The prior descriptions of cold sensitivity [5, 12] support presenting this case as an illustrative focal, episodic presentation without claiming that this combination is previously unreported.

In our patient, the markedly elevated GAD65 antibody concentration supported the clinical suspicion of an autoimmune stiff person spectrum disorder in the appropriate clinical setting [1, 4]. Nevertheless, GAD65 antibodies must be interpreted together with the clinical phenotype because they also occur in other autoimmune neurologic and endocrine disorders [1, 4]. Contemporary diagnostic work stresses the combination of characteristic stiffness or spasms, stimulus sensitivity, supportive serology or electrophysiology, and exclusion of more plausible alternatives [1, 2].

Continuous motor-unit activity is a characteristic electrophysiologic feature of SPS, although routine studies may be normal in some clinically diagnosed patients [2, 5, 12]. In our patient, EMG approximately 7 weeks after onset showed no continuous motor-unit activity. The report does not document recordings during a typical episode, simultaneous agonist-antagonist recordings, or testing of acoustic startle or exteroceptive responses. The timing and episodic presentation may have affected detection, but cannot be assumed to explain the negative study. The lack of electrophysiological confirmation limits diagnostic certainty.

The principal differential diagnostic considerations included paramyotonia congenita and other skeletal-muscle channelopathies, neuromyotonia, focal dystonia, structural upper motor neuron disease, and focal motor seizures. The subacute adult onset, stimulus sensitivity, markedly elevated GAD65 antibody, and improvement after immunotherapy favored a suspected focal autoimmune SPS phenotype, but neither antibody positivity nor treatment response is diagnostic in isolation. The left extensor plantar response and ankle clonus warrant particular caution regarding a central structural cause; the reported brain and lumbosacral imaging does not exclude cervical or thoracic cord pathology. The mechanism of the cold trigger remains speculative. Cold-related afferent input may have acted as an unusual sensory stimulus in motor pathways already rendered hyperexcitable by impaired inhibition.

Controlled evidence supports IVIG for GAD65-positive SPS [6], and case literature describes improvement of stiff limb phenotypes with immunotherapy [8–10]. In our patient, clinical improvement occurred during a 9-month IVIG course. The qualitative outcome data support symptomatic and functional benefit, but do not establish remission according to a predefined endpoint or its duration after treatment. The response adds clinical support to the working diagnosis without providing electrophysiological confirmation.

The stiff person spectrum should be considered when adult-onset focal limb stiffness is episodic yet reproducibly stimulus sensitive, including with cold exposure. In patients with supportive serology and a

normal routine EMG, targeted electrophysiological assessment and careful evaluation of alternative diagnoses can help clarify diagnostic certainty. This case illustrates a clinically suspected focal presentation with improvement following IVIG.

Abbreviations

EMG
electromyography
GAD65
glutamic acid decarboxylase 65
IVIG
intravenous immunoglobulin
MRI
magnetic resonance imaging
SPS
stiff person syndrome

Declarations

Ethics approval and consent to participate

Not applicable. This report describes observations made during routine clinical care and did not involve a research intervention.

Consent for publication

AMA, who is the patient described in this case report and a co-author, provided written informed consent for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Competing Interests

AMA is the patient described in this case report and a coauthor. She provided written informed consent for publication and understands that her authorship publicly identifies her as the patient. AMA is also married to RAR.RAR is the Editor-in-Chief of the Journal of Medical Case Reports. To ensure complete editorial independence, RAR will not be involved in editor assignment, reviewer selection, peer review, or the editorial decision concerning this manuscript. We respectfully request that the submission be assigned to an independent editor and handled outside RAR's editorial oversight. SRB declares no competing interests.

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Author Contribution

RAR drafted and edited the manuscript.AMA verified and rewrote some details including the time course and symptoms.SRB examined the patient, provided exam findings, and suggested work up and treatment.All authors reviewed the final manuscript and approve and fully verify the scientific content.

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Artificial intelligence (AI) tools were used to assist with the drafting, language editing, and clarity of this manuscript. The authors critically reviewed, verified, and take full responsibility for the accuracy and integrity of this work.

Availability of data and materials

All data supporting the conclusions of this case report are included in the article. Additional clinical records are not publicly available because of patient privacy but may be available from the corresponding author on reasonable request and subject to applicable privacy requirements.

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