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Case Report

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Management of stiff-person syndrome

Abstract

Background: Stiff-Person Syndrome (SPS) is a rare autoimmune neurological disorder. Historically estimated at 1–2 per million, more recent population-based data suggest the prevalence may be higher (up to ~2 per 100,000 in one U.S. health-system study). Characterized by progressive axial rigidity, painful stimulus-triggered spasms, and continuous motor unit activity on electromyography, SPS remains critically under-recognized. Diagnostic delays are common and contribute to preventable morbidity, including falls, fractures, and loss of independence.

Case presentation: We report the case of a 63-year-old gentleman who presented with progressive axial stiffness over several months, beginning in his trunk and spreading to his proximal limbs. He experienced excruciating spasms triggered by minimal tactile stimuli and emotional stress. Examination revealed profound axial rigidity with a hyperlordotic gait. Electromyography demonstrated the pathognomonic pattern of continuous motor unit activity with co-contraction of agonist and antagonist muscles. Serum testing confirmed high-titer anti-glutamic acid decarboxylase 65 (GAD65) antibodies (>10,000 IU/mL). Key mimics including tetanus, parkinsonism, and neuromyotonia were systematically excluded.

Management and outcome: The patient was managed through two simultaneous therapeutic pathways: symptom control (diazepam, baclofen, gabapentin, and environmental modification) and immune modulation. Because corticosteroids can destabilize glycemic control in a population with a high prevalence of type 1 diabetes, immunotherapy was planned with intravenous immunoglobulin (IVIG) as the preferred agent, with corticosteroids used cautiously and with glucose monitoring. The patient demonstrated steady, significant improvement in rigidity and spasm frequency, with enhanced functional mobility at discharge.

Discussion: This case underscores several critical clinical principles: (1) the diagnosis of SPS is primarily clinical—the phenotype combined with EMG findings constitutes the definitive diagnostic tool; (2) prompt recognition and initiation of treatment, including benzodiazepines, baclofen, and immunotherapy, can dramatically improve prognosis; and (3) multidisciplinary coordination between neurology, rehabilitation medicine, and critical care is essential for optimal outcomes.

Conclusion: SPS is rare but highly recognizable when clinicians maintain a high index of suspicion. Early diagnosis, confirmed by EMG, and timely immune-targeted therapy are the keys to improving prognosis and restoring independence in this chronic, complex disorder.

Keywords: Stiff-Person Syndrome, anti-GAD65 antibodies, continuous motor unit activity, intravenous immunoglobulin, neuro-rehabilitation, autoimmune neurology

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Introduction

Stiff-Person Syndrome (SPS) is a rare autoimmune neurological disorder first described by Moersch and Woltman in 1956 as "progressive fluctuating muscular rigidity and spasm." It shows a female predominance (roughly 2:1). The prevalence has traditionally been cited as approximately 1–2 per million; however, more recent epidemiologic studies report divergent and generally higher estimates, including approximately 2.1 per 100,000 in a U.S. population-based study (Crane et al., Neurology, 2024) and lower figures in a Japanese nationwide survey, reflecting ongoing uncertainty and likely under-recognition.[1,2]

The pathophysiology of SPS centers on the loss of GABAergic inhibitory tone within the central nervous system, predominantly affecting the spinal cord. Without this essential inhibitory input, alpha motor neurons fire continuously, producing the syndrome's cardinal features: severe axial rigidity, co-contraction of agonist and antagonist muscles, and violent, stimulus-triggered spasms.[3] This physiological failure accounts for the characteristic "statue-like" gait and hyperlordotic posture observed in affected patients.

Approximately 80–90% of patients with classic SPS harbor high-titer antibodies against glutamic acid decarboxylase 65 (GAD65), the rate-limiting enzyme for gamma-aminobutyric acid (GABA) synthesis.[4] However, the diagnosis remains primarily clinical, supported by characteristic electromyography (EMG) findings and serological testing. Additional antibody phenotypes provide important prognostic and diagnostic information, which includes amphiphysin (associated with paraneoplastic origin) and glycine receptor (associated with the progressive encephalomyelitis with rigidity and myoclonus [PERM] phenotype).[5]

The therapeutic approach to SPS is twofold: symptomatic management aimed at enhancing GABAergic tone and immune modulation to address the underlying autoimmune process. Benzodiazepines and baclofen represent the cornerstone of symptomatic therapy, while intravenous immunoglobulin (IVIG) has the strongest evidence for disease modification, supported by a single Class I randomized, placebo-controlled crossover trial (Dalakas et al., New England Journal of Medicine, 2001).[6]

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We present a case of classic SPS in a 63-year-old male, illustrating the diagnostic approach, therapeutic strategies, and the importance of multidisciplinary care in achieving meaningful functional improvement.

Case presentation

Patient information

A 63-year-old male presented to our neuro-rehabilitation service with a several-month history of progressive axial stiffness. The stiffness began in his trunk and progressively spread to his proximal limbs, significantly impairing his mobility and activities of daily living. His spasms were described as excruciating and were triggered by minimal tactile stimuli, sudden auditory stimuli, or emotional stress. There was no history of recent wounds, infections, or significant travel. His past medical history was unremarkable, with no known autoimmune conditions or malignancies.

Clinical findings

On examination, the patient demonstrated profound axial rigidity with a characteristic hyperlordotic posture. The paraspinal and proximal limb muscles exhibited continuous tautness at rest. Startle responses were markedly exaggerated, with violent spasms elicited by unexpected auditory stimuli or gentle handling. Cranial nerve examination was intact. There were no signs of autonomic dysfunction, myoclonus, or brainstem involvement to suggest PERM phenotype. Cognitive function was preserved. There was no evidence of tremor, bradykinesia, or other parkinsonian features.

Diagnostic assessment electromyography

Electromyography (EMG) revealed the pathognomonic pattern of continuous motor unit activity (CMUA) at rest in both paraspinal muscles and proximal limb muscles. Co-contraction of agonist and antagonist muscle groups was evident. Importantly, the CMUA demonstrated partial suppression with diazepam administration—a characteristic physiological feature that both strengthens the diagnosis and provides therapeutic guidance.

Serological Testing

Serum testing returned strongly positive for anti-GAD65 antibodies at high titers (>10,000 IU/mL by ELISA), supporting an autoimmune neurologic etiology. Antibodies against amphiphysin and glycine receptors were negative, reducing concern for paraneoplastic origin or progression to PERM phenotype (Table 1&2).

Table 1 Laboratory Investigations

Investigation	Result	Reference Range
Anti-GAD65 antibodies	>10,000 IU/mL	<5 IU/mL
Amphiphysin antibodies	Negative	Negative
Glycine receptor antibodies	Negative	Negative
Hemoglobin A1c	5.4%	<5.7%
TSH	2.1 mIU/L	0.4–4.0 mIU/L
Vitamin B12	450 pg/mL	200–900 pg/mL
Serum creatinine	0.9 mg/dL	0.6–1.2 mg/dL

Table 2 Differential Diagnosis

Condition	Key Features	Exclusion Criteria in This Case
Tetanus	Recent wound, autonomic storm, trismus, risus sardonicus	No wound history, no autonomic instability, no trismus
Parkinsonism	Rest tremor, bradykinesia, rigidity	No tremor, normal gait initiation, preserved dexterity
Neuromyotonia (Isaacs)	Myokymia, after-discharges on EMG	EMG showed co-contraction without myokymic discharges
Functional/ Psychogenic	Variable findings, distractibility	Consistent exam findings, objective EMG abnormalities
Dystonia	Focal or generalized, pattern-specific	Diffuse axial rigidity, stimulus-triggered spasms
Myelopathy	Sensory level, sphincter dysfunction	No sensory level, no bowel/bladder dysfunction

Therapeutic intervention

Management was organized along two simultaneous paths: symptom control and immune modulation.

Symptom control

Environmental modification: The patient was placed in a quiet, low-stimulus room with gentle handling protocols to minimize startle-triggered spasms. Nursing and therapy staff were educated on the importance of minimizing unexpected auditory and tactile stimuli.

Pharmacologic symptom control

Diazepam initiated at 5 mg thrice daily, titrated to 10 mg thrice daily over one week (GABA-A potentiation)

Baclofen initiated at 10 mg thrice daily, titrated to 20 mg thrice daily (GABA-B agonism)

Gabapentin initiated at 300 mg thrice daily for neuropathic pain and spasm-related discomfort

Patient Education: Emphasis was placed on the critical importance of avoiding abrupt cessation of benzodiazepines and baclofen due to the risk of withdrawal crisis, which can be life-threatening in this population.

Immune modulation

Because IVIG has the strongest (Class I) evidence for disease modification in SPS, it was designated as the preferred immunotherapy. Corticosteroids were considered only as adjunctive/bridging therapy and used with caution, given the high co-occurrence of type 1 diabetes in SPS and the risk of destabilizing glycemic control; when a short corticosteroid course was administered, close glucose monitoring was implemented. A plan was established for outpatient IVIG at 2 g/kg per cycle (divided over 3–5 days), with monthly maintenance based on response.

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Rehabilitation

The physical therapy team implemented a graded mobilization program focusing on maintaining joint range of motion and preventing contractures. Fall prevention strategies and gait training were prioritized, with careful attention to stimulus control during therapy sessions. Occupational therapy addressed activities of daily living and adaptive equipment needs.

Follow-up and outcomes

The patient demonstrated steady, significant improvement in rigidity and spasm frequency over the 14-day hospitalization period. At discharge, the Modified Rankin Scale improved from 4 (moderately severe disability) to 3 (moderate disability). Pain scores decreased from 8/10 to 3/10 on the Visual Analog Scale. Functional mobility improved, with the patient able to ambulate with a walker compared to requiring wheelchair assistance at admission.

At two-month follow-up, the patient continued to show sustained improvement on maintenance diazepam, baclofen, and gabapentin, with outpatient IVIG infusions initiated given the sustained functional deficit and the supporting evidence base. The patient reported improved quality of life and participation in activities of daily living.

Discussion

Diagnostic considerations

SPS remains critically under-recognized. The diagnosis is frequently delayed, often by years, due to the presentation of axial stiffness, altered gait, and startle responses can mimic functional or psychogenic disorders.[7] This case illustrates the essential diagnostic approach: the clinical phenotype, supported by characteristic EMG findings, is definitive. While high-titer anti-GAD65 antibodies provide valuable supporting evidence, they should not be relied upon as the sole diagnostic criterion, as a proportion of clinically confirmed cases may be seronegative.[8]

The EMG hallmark of SPS, continuous motor unit activity at rest with co-contraction of agonist and antagonist muscles, distinguishes it from mimics.[9] The suppression of this activity with benzodiazepines is a diagnostically useful feature that also confirms the therapeutic target (Table 3).

Table 3 Antibody Phenotyping

Antibody	Frequency in SPS	Clinical Significance
Anti-GAD65	80–90%	Most common; classic phenotype; associated with T1DM and thyroid disease
Amphiphysin	5–10%	Paraneoplastic association (breast, lung, thymus); often more rapid course
Glycine receptor	Variable	Associated with PERM phenotype; more severe course
DPPX	Rare	Associated with diarrhea, weight loss, encephalopathy

Pathophysiology

The loss of GABAergic inhibition within the spinal cord creates a state of unchecked alpha motor neuron activity, producing (1) axial rigidity, (2) co-contraction of agonist and antagonist pairs, and (3) exaggerated startle responses. This understanding informs both diagnosis and therapy, with benzodiazepines (GABA-A agonists) and baclofen (GABA-B agonist) serving as rational first-line symptomatic treatments.

While anti-GAD65 antibodies correlate with disease activity in high titers, the intracellular location of GAD65 suggests that T-cell-mediated mechanisms likely contribute substantially to the pathology, which may explain the partial responses observed with B-cell-directed therapies and supports multimodal immunotherapy.[10]

Treatment approach

The treatment of SPS requires a biphasic approach addressing both symptoms and the underlying autoimmune process.

Symptom Management- First-Line Agents:

a) Benzodiazepines (diazepam, clonazepam): GABA-A receptor agonists that enhance inhibitory neurotransmission. Diazepam is preferred for rapid effect, while clonazepam offers steadier dosing.[3]

b) Baclofen: GABA-B receptor agonist that reduces excitatory input to motor neurons.

Adjunctive agents:

a) Gabapentin/Pregabalin: For neuropathic pain and spasm-related discomfort.

b) Tizanidine: Alpha-2 adrenergic agonist with antispasticity effects.

Critical Safety Consideration: These medications must never be stopped abruptly due to the risk of a potentially life-threatening withdrawal crisis characterized by severe spasms, autonomic instability, and rhabdomyolysis.

Disease-modifying therapy:

a) Intravenous Immunoglobulin (IVIG): Supported by a single Class I randomized, placebo-controlled crossover trial demonstrating significant improvement in stiffness and sensitivity scores at 2 g/kg per cycle, typically administered monthly (Dalakas et al., *New England Journal of Medicine*, 2001).[6] Long-term observational data suggest sustained benefit in approximately two-thirds of patients on monthly maintenance over multi-year follow-up (Yi and Dalakas, *Neurology Neuroimmunology & Neuroinflammation*, 2022).[11]

b) Corticosteroids: Variable response; may be used as adjunctive/bridging therapy but require caution and glucose monitoring given the high prevalence of type 1 diabetes in SPS.

c) Plasmapheresis: Helpful for acute flares or severe disability.

d) Rituximab: Growing observational evidence; consider in refractory cases or non-GAD phenotypes.[12]

e) Botulinum Toxin: To paraspinal muscles may reduce pain and stiffness in case series.

f) Intrathecal Baclofen: Can help severe, refractory rigidity when oral therapy fails.[13]

Comorbidity screening

SPS is associated with several autoimmune conditions that warrant screening. Pooled data indicate diabetes (type 1/LADA) in approximately 29% and autoimmune thyroid disease in roughly one-quarter of patients (Table 4).

Table 4 SPS is associated with several autoimmune conditions that warrant screening

Comorbidity	Prevalence	Screening
Type 1 Diabetes	30–50%	Fasting glucose, HbA1c
Autoimmune Thyroid Disease	10–35%	TSH, thyroid antibodies
Pernicious Anemia	Variable	Vitamin B12, intrinsic factor antibodies
Vitiligo	Variable	Clinical examination
Celiac Disease	Variable	Tissue transglutaminase antibodies (if symptomatic)

Prognostic considerations

With appropriate treatment, SPS is a chronic but highly modifiable condition. Early recognition and timely immunotherapy lead to meaningful functional gains and improved quality of life.[11] However, certain phenotypes carry a more guarded prognosis:

PERM phenotype: Associated with glycine receptor antibodies, brainstem/autonomic features, and a tougher clinical course.

Paraneoplastic forms: Associated with amphiphysin antibodies and require urgent malignancy work-up (breast, lung, thymus) with implications for overall survival.

Limitations

This case report is subject to the inherent limitations of single-case observations. The patient's response to treatment cannot be generalized, and the decision-making process reflects the individual clinical context. Future studies with larger cohorts are needed to further refine treatment algorithms.

Conclusion

Stiff-Person Syndrome is rare but highly recognizable when clinicians maintain a high index of suspicion. The cardinal features—axial rigidity, hyperlordotic gait, and exaggerated, painful startle responses—should prompt immediate investigation.

Key Messages for clinicians:

1. Diagnose Clinically: The clinical phenotype combined with EMG findings constitutes the definitive diagnostic tool. Do not wait solely for antibody results, which support but do not define the diagnosis.
2. Screen the Autoimmune Neighborhood: Investigate for associated conditions including type 1 diabetes and thyroid disease. Amphiphysin antibodies or a rapid, systemic presentation are red flags for a paraneoplastic work-up.
3. Treat Comprehensively and Sequence Rationally: First-line symptomatic therapy includes benzodiazepines and baclofen, with careful education regarding abrupt-withdrawal risk. When immunotherapy is indicated, IVIG carries the strongest (Class I) evidence and is preferred; corticosteroids should be used cautiously given the risk of destabilizing glycemic control in this diabetes-prone population.

Early recognition, confirmed by EMG, and timely immune-targeted therapy are the keys to improving prognosis and restoring independence. This case demonstrates that a multidisciplinary, proactive approach (coordinating neurology, neuro-rehabilitation, and critical care) can yield meaningful success in managing this challenging condition.

Author contributions

Faheem Jafri: conceptualization, data collection, manuscript drafting, critical revision. Shane Bolina: clinical management, critical revision. Barry Cohen: clinical management, critical revision. Ahmed Shehata: data interpretation, critical revision. Bilal Chaudhry: conceptualization, supervision, critical revision.

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Conflicts of interest

The authors declare no conflicts of interest.

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Patient consent

Written informed consent was obtained from the patient 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.

Ethics approval

This case report was conducted in accordance with institutional ethical guidelines.

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