Clinical Management of Stiff Person Syndrome: A Comprehensive Review for General Medicine and Nursing

Amani Ibrahim Hadi Mjrashi[1], Faten Ibrahim Majrashi[2], Amal Gaber Almalki[3], Renad Saeed Saad Binmothib[4], Bayan Ayidh Mohmmed Alshalti[5], Hanan Yahya Madkhali[6], Mahfodah Ibrahim Majrashi[7], Eman Hassan Alhomoud[8], Reema Abdullah Albalawi[9], Yasmin Ahmad Alrashaid[10]

[1] Nursing – Khamis Mushayt General Hospital
Email: amonmajrashi@gmail.com

[2] Nursing – Khamis Mushayt General Hospital
Email: Faaten286@gmail.com

[3] Nursing – Khamis Mushayt General Hospital
Email: 7amul2@gmail.com

[4] Nursing – Khamis Mushayt General Hospital
Email: renaasae9d@gmail.com

[5] Nursing – Abha Maternity & Children Hospital
Email: byan141323@hotmail.com

[6] Nursing – Al Hafayer PHC
Email: Han-34@outlook.com

[7] Nursing – Khamis Mushayt General Hospital
Email: Mahfodah.majrashi@gmail.com

[8] General Physician – Primary Health Care
Email: ealhamoud@moh.gov.sa

[9] General Practitioner – King Khalid Hospital in Tabuk
Email: Dr.reemaabdullah@icloud.com

[10] Nurse – Aljaber ENT & OPH Hospital
Email: Yalrashaid@moh.gov.sa

Abstract:

Stiff Person Syndrome (SPS) is a rare neurological disorder characterized by episodic stiffness, muscle rigidity, and impaired mobility, which can significantly impact patients' quality of life. The clinical management of SPS requires a multidisciplinary approach involving neurologists, primary care physicians, nurses, and other healthcare professionals. Diagnosis typically involves a combination of clinical assessment, serological tests for autoantibodies (such as anti-GAD65), and neuroimaging studies to rule out other conditions. Treatment strategies primarily focus on alleviating symptoms and managing associated comorbidities, commonly utilizing medications such as benzodiazepines, muscle relaxants, and immunotherapy, particularly in cases linked to autoimmune triggers. Furthermore, patient education and psychosocial support play crucial roles in facilitating self-management and coping strategies for individuals living with this challenging condition. Nurses and healthcare providers must remain vigilant in recognizing the nuances of SPS to facilitate early intervention and optimal

management. Regular monitoring for potential side effects from pharmacologic treatments, as well as assessing functional status and emotional well-being, is essential in a comprehensive care framework. Incorporating physical therapy and occupational therapy can enhance mobility and improve daily functioning, thereby fostering independence. In addition, interdisciplinary collaboration is key, enabling healthcare professionals to share insights and develop individualized care plans. This comprehensive review serves to equip general medicine and nursing professionals with the knowledge needed to appropriately address the complexities of Stiff Person Syndrome, ultimately enhancing patient outcomes and quality of life.

Keywords: Stiff Person Syndrome, SPS, clinical management, neurological disorder, multidisciplinary approach, diagnosis, autoantibodies, treatment strategies

Introduction

Stiff Person Syndrome (SPS) represents one of the most intriguing and challenging neurological disorders encountered in clinical practice. It is a rare, acquired autoimmune disorder of the central nervous system characterized by progressive muscle rigidity and episodic, painful spasms that significantly impair mobility and quality of life. First described in 1956 by Moersch and Woltman as "stiff-man syndrome," the condition has evolved in its nosological understanding, now recognized as a spectrum of disorders with varied presentations [1]. For general practitioners and nursing professionals, who are often the first point of contact for patients with undifferentiated symptoms, a foundational knowledge of SPS is crucial. Early recognition and appropriate multidisciplinary management can mitigate the severe disability and profound psychological distress that typically accompany this disease.

The epidemiological footprint of SPS is small, with an estimated prevalence of 1-2 cases per million population, though this is likely an underestimation due to frequent misdiagnosis [2]. It exhibits a distinct predilection, affecting women approximately twice as often as men. While it can manifest at any age, the typical onset is in the fourth or fifth decade of life. The rarity of the condition contributes to diagnostic delays, often averaging several years, during which patients may be mislabeled with psychosomatic disorders, fibromyalgia, or atypical Parkinsonian syndromes [3]. This diagnostic odyssey not only exacerbates patient suffering but also underscores the necessity for heightened awareness among all healthcare tiers. The clinical hallmark is axial muscle rigidity, primarily affecting the trunk and proximal limbs, leading to a characteristic hyperlordotic posture. Superimposed on this chronic stiffness are sudden, triggered spasms—often precipitated by unexpected noises, emotional distress, or tactile stimuli—which can be severe enough to cause falls and fractures.

The pathogenesis of SPS is firmly rooted in autoimmunity, marking a significant shift from its initial obscure etiology. A pivotal discovery was the identification of autoantibodies against glutamic acid decarboxylase (GAD), the rate-limiting enzyme responsible for synthesizing gamma-aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the central nervous system. High-titer anti-GAD65 antibodies are present in approximately 60-80% of patients with classic SPS [4]. GABAergic dysfunction, primarily within spinal cord and brainstem circuits, leads to a profound failure of inhibitory signaling, resulting in uncontrolled firing of motor neurons and the consequent muscle hyperactivity. Furthermore, a subset of patients, often with a paraneoplastic variant associated with breast cancer, Hodgkin's lymphoma, or thymoma, harbor antibodies against amphiphysin or gephyrin, proteins involved in GABAergic synaptic vesicle endocytosis and receptor clustering, respectively [5]. These insights have transformed SPS from a curiosity into a model disorder of impaired synaptic inhibition.

Diagnosis remains clinical, supported by serological and neurophysiological investigations. The essential triad includes progressive rigidity, superimposed spasms, and positive serology for anti-GAD or related antibodies. Electromyography (EMG) reveals continuous motor unit activity in affected muscles that normalizes during sleep or with administration of benzodiazepines, a key diagnostic feature [6]. However, the presentation can vary significantly across the SPS spectrum, which includes focal forms (like stiff-limb syndrome),

jerking SPS (which overlaps with progressive encephalomyelitis with rigidity and myoclonus, or PERM), and paraneoplastic SPS. This heterogeneity adds layers of complexity to diagnosis and management, demanding a tailored approach. Differential diagnoses are broad, encompassing neuromyotonia, dystonia, multiple sclerosis, spinal cord lesions, and psychogenic movement disorders, necessitating careful neurological evaluation [7].

The impact of SPS extends far beyond motor symptoms. Chronic pain, profound fear of falling (leading to agoraphobia), anxiety, and depression are nearly universal, creating a debilitating biopsychosocial burden. Patients often become dependent on caregivers for daily activities, and the unpredictable nature of spasms leads to social isolation [8]. Therefore, effective management must transcend purely pharmacological muscle relaxation to embrace a holistic, patient-centered model. This model integrates immunotherapy to modify the underlying disease process, symptomatic relief for spasms and pain, intensive physical and psychological rehabilitation, and comprehensive nursing care to address functional limitations and prevent complications.

Pathophysiology and Immunological Basis

Understanding the management of Stiff Person Syndrome necessitates a deep dive into its immunopathological mechanisms. As previously introduced, the core defect is a severe impairment of GABA-mediated inhibitory neurotransmission within the central nervous system. Glutamic acid decarboxylase (GAD) exists in two isoforms, GAD65 and GAD67. In SPS, autoantibodies are predominantly directed against GAD65, which is associated with synaptic vesicle membranes and responsible for the rapid synthesis of GABA for neurotransmission. While these antibodies are highly specific, their exact pathogenic role is debated. Current evidence suggests they may inhibit the enzyme's activity, reduce GABA synthesis, and, crucially, interfere with the trafficking and release of GABA from presynaptic terminals [9]. Furthermore, anti-GAD antibodies might cross-link the antigen on the neuronal surface, triggering internalization and a functional decrease in available enzyme. This results in a state of chronic neuronal hyperexcitability in spinal and brainstem motor circuits.

Beyond anti-GAD antibodies, other autoantibodies delineate clinical subtypes and offer further pathogenic insights. Anti-amphiphysin antibodies, strongly associated with paraneoplastic SPS (particularly with breast cancer), target a protein essential for clathrin-mediated endocytosis of synaptic vesicles. Their action is believed to disrupt the recycling of GABA-containing vesicles, again impairing inhibitory transmission [10]. Anti-gephyrin antibodies, rarer still, attack a protein that anchors GABA and glycine receptors to the postsynaptic cytoskeleton, potentially leading to a loss of these inhibitory receptors from the synapse. The presence of these antibodies often correlates with a more abrupt, severe onset and a poorer prognosis, highlighting the importance of aggressive cancer screening in such presentations. Interestingly, a significant minority of patients are seronegative for known antibodies, implying that other, yet unidentified, autoantigens or immune mechanisms are at play.

The autoimmune attack in SPS is not confined to the humoral response. There is strong evidence for concomitant cellular immunity. Oligoclonal bands are frequently present in cerebrospinal fluid (CSF), and intrathecal synthesis of anti-GAD antibodies is common, indicating an active immune process within the CNS compartment [11]. T-cells reactive to GAD epitopes have been isolated from patients' blood and CSF, suggesting a breakdown in immune tolerance. This combined humoral and cellular assault leads to a functional, rather than structural, disruption of neural circuitry. Neuroimaging is typically normal, and there is no widespread neuronal loss, which is a critical point for prognosis and management: the potential for functional improvement exists if the autoimmune drive can be suppressed and inhibition restored. This immunological foundation directly informs the therapeutic strategy, which targets both antibody production (e.g., with immunosuppressants, plasma exchange) and downstream GABAergic deficiency (e.g., with benzodiazepines).

Clinical Presentation and Diagnostic Criteria

The clinical recognition of SPS requires a keen eye for its classic features and an awareness of its phenotypic variations. The core presentation involves insidious onset of stiffness and rigidity in axial muscles—the paraspinal and abdominal

muscles—progressing to proximal limb muscles. This leads to a slow, wooden gait and the pathognomonic exaggerated lumbar lordosis as the body attempts to maintain balance against rigid paraspinal muscles. Patients often describe a constant, board-like tightness. Superimposed upon this baseline rigidity are the episodic spasms. These are involuntary, often painful contractions that can be triggered by startling stimuli (auditory, tactile, emotional), voluntary movement, or cold. Spasms can be so violent they cause the patient to fall like a "wooden statue," posing a high risk for serious injury [12]. Neurological examination reveals tight, rock-hard muscles on palpation, hyperactive tendon reflexes, and sometimes, a paradoxical co-contraction of agonist and antagonist muscles.

Given the absence of a single definitive test, diagnosis relies on a combination of clinical and supportive criteria. The most widely used diagnostic criteria were proposed by Dalakas in 2009 [13]. They include: (1) Stiffness in axial muscles, prominently in the abdominal and thoracolumbar paraspinal regions. (2) Superimposed painful spasms, triggered by stimuli. (3) Signs of chronic CNS hyperexcitability (e.g., exaggerated startle). (4) Continuous motor unit activity on EMG in affected muscles that diminishes with sleep or benzodiazepines. (5) Presence of anti-GAD65 (or anti-amphiphysin) antibodies in serum. (6) Exclusion of other neurological conditions that could explain the symptoms. A definite diagnosis typically requires items 1, 2, 5, and 6. It is critical for general practitioners to note that lower-titer anti-GAD antibodies are common in other conditions (e.g., type 1 diabetes, cerebellar ataxia), but very high titers (often >20 nmol/L) are characteristic of SPS.

The SPS spectrum includes several variants that generalists may encounter. *Stiff-limb syndrome*(or focal SPS) presents with rigidity and spasms predominantly in one distal limb, often a foot, with fixed deformities. *Jerking SPS* overlaps with PERM and is characterized by severe brainstem involvement, with myoclonus, ataxia, oculomotor disturbances, and autonomic dysfunction; it often has a more rapid and severe course [14]. *Paraneoplastic SPS* may present with a subacute, severe progression and is frequently associated with anti-amphiphysin antibodies. These variations necessitate a tailored diagnostic approach, including thorough cancer screening (mammography, CT chest/abdomen/pelvis, PET scan) in appropriate cases. Differential diagnosis is extensive, requiring consideration of axial dystonias, tetanus (a toxin-mediated mimic), multiple sclerosis with spinal lesions, neuromyotonia (Isaacs' syndrome), Parkinsonian syndromes, and chronic pain or anxiety disorders with muscle tension. Collaboration with a neurologist is paramount for confirming the diagnosis and initiating specialist management.

Pharmacological Management: Symptomatic Therapies

The pharmacological management of SPS is two-pronged: symptomatic relief of stiffness and spasms, and immunomodulation to alter the disease course. Symptomatic treatment forms the immediate cornerstone of care, offering patients their first reprieve from debilitating symptoms. The mainstay of symptomatic therapy is the enhancement of GABAergic inhibition, primarily using benzodiazepines. Diazepam, with its long half-life and muscle-relaxant properties, is the traditional first-line agent. Doses required are often high, starting at 5-10 mg daily and titrating upwards, sometimes to 40-100 mg or more daily, divided into multiple doses to maintain stable plasma levels [15]. The goal is to achieve functional improvement with acceptable sedation. Clonazepam is a valuable alternative or adjunct, particularly useful for its anti-myoclonic properties and longer half-life. Tolerance and dependence are significant concerns with long-term, high-dose benzodiazepine use, requiring careful, gradual titration and patient education.

For patients who cannot tolerate high-dose benzodiazepines or require additional agents, baclofen, a GABA-B receptor agonist, is a key second-line therapy. While oral baclofen can be helpful, its efficacy is often limited by systemic side effects like drowsiness and weakness at higher doses. Intrathecal baclofen (ITB) therapy, delivered via an implanted pump, has revolutionized management for many with severe, refractory SPS. By delivering the drug directly to the spinal CSF, it achieves high concentrations at the site of pathology with minimal systemic effects. ITB can dramatically reduce rigidity, spasm frequency and severity, and pain, often allowing for substantial reductions in oral medications [16]. However, it is an invasive

procedure requiring specialist neurosurgical and neurological management, with risks of infection, pump malfunction, and withdrawal syndromes.

Other oral agents are used as adjuncts. Gabapentin and pregabalin, which modulate calcium channels and may increase GABA synthesis, can provide additional relief for neuropathic pain and spasms. Tiagabine, a GABA reuptake inhibitor, has shown benefit in some cases. For severe, refractory spasms, other muscle relaxants like tizanidine or dantrolene may be considered, though their utility is often limited. It is crucial to manage expectations: symptomatic therapies do not cure the disease but are essential for controlling its manifestations and improving quality of life. A slow, careful titration schedule, managed collaboratively between neurologist, general practitioner, and patient, is vital to balance efficacy and side effects such as sedation, cognitive blunting, and risk of falls.

Pharmacological Management: Disease-Modifying Immunotherapies

While symptomatic treatment controls the output of a hyperexcitable nervous system, immunotherapy aims to dampen or silence the aberrant autoimmune drive itself. Immunotherapy is indicated for most patients, especially those with progressive disability, high symptom burden, or seropositivity. The evidence base, though derived largely from case series and open-label trials, strongly supports its role in stabilizing and often improving the condition. First-line immunomodulation typically involves corticosteroids and intravenous immunoglobulin (IVIg).

Corticosteroids, such as oral prednisone or pulsed intravenous methylprednisolone, provide rapid anti-inflammatory and immunosuppressive effects. Many patients experience a meaningful reduction in stiffness and spasms within weeks. However, the long-term side-effect profile of steroids (weight gain, diabetes, osteoporosis, etc.) limits their use as a sole maintenance therapy. They are often used as an induction agent or as a bridge to slower-acting steroid-sparing agents [17].

IVIg has emerged as a first-line maintenance therapy with robust supporting evidence. Its mechanisms in SPS are multifactorial, likely involving idiotypic antibody neutralization, Fc receptor blockade on macrophages, and immunomodulation of cytokines and B-cells. Multiple studies have demonstrated that IVIg (typically 2 g/kg over 2-5 days, repeated every 4-8 weeks) leads to significant and sustained improvements in stiffness, spasms, ambulation, and sensitivity to stimuli [18]. The response often begins after the second or third infusion. Monitoring for side effects like aseptic meningitis, headache, and thrombotic events is necessary, but overall, it is a well-tolerated therapy that can be administered in outpatient infusion centers under nursing supervision.

For patients with an inadequate response to IVIg or corticosteroids, second-line immunosuppressants are employed. These include azathioprine, mycophenolate mofetil, methotrexate, and cyclophosphamide. These agents act by inhibiting lymphocyte proliferation and require regular monitoring of blood counts and liver function. Rituximab, a monoclonal antibody that depletes CD20+ B-cells, has shown promise, particularly in anti-GAD65 positive patients, though results from controlled trials have been mixed, possibly due to patient selection [19]. In severe, rapidly progressive, or treatment-refractory cases, therapeutic plasma exchange (plasmapheresis) can be used to physically remove pathogenic antibodies from the circulation, often producing a rapid but transient benefit, making it useful as a rescue therapy or in preparation for other treatments [20]. The choice of agent is individualized based on disease severity, antibody profile, comorbidities, and patient preference, requiring close specialist oversight.

Non-Pharmacological and Supportive Management

Comprehensive care for SPS extends far beyond pharmacology. A multidisciplinary rehabilitative approach is indispensable for maximizing function, independence, and quality of life. Physical therapy forms a core pillar. A skilled physical therapist designs a program focused on gentle stretching to maintain range of motion, low-impact strengthening to support weakened muscles, and balance training to reduce fall risk. Aquatic therapy is exceptionally beneficial, as the buoyancy of water reduces weight-bearing stress, allows for greater freedom of movement, and provides a safe environment for exercise [21]. Techniques like proprioceptive neuromuscular facilitation (PNF) and myofascial

release can help alleviate muscle tightness. Crucially, therapists must avoid overexertion and startling stimuli that could trigger spasms during sessions.

Occupational therapy is equally vital, addressing activities of daily living (ADLs). Occupational therapists assess the home environment for fall hazards and recommend adaptations like grab bars, shower chairs, raised toilet seats, and adaptive utensils. They provide energy conservation techniques and task modification strategies to help patients preserve independence. Psychological support is non-negotiable, given the high prevalence of anxiety, depression, and phobic behaviors (especially fear of falling). Cognitive-behavioral therapy (CBT) can be highly effective in managing anxiety related to spasm triggers and in addressing the catastrophic thinking that often accompanies chronic, unpredictable symptoms [22]. Support groups, either in-person or online, provide invaluable peer support, reducing the profound isolation experienced by many patients.

Pain management requires a dedicated strategy, as pain in SPS is multifactorial—arising from chronic muscle rigidity, acute spasms, and secondary musculoskeletal issues. Alongside pharmacological agents (gabapentinoids, analgesics), non-drug approaches like acupuncture, massage therapy (with caution to avoid triggering spasms), transcutaneous electrical nerve stimulation (TENS), and mindfulness-based stress reduction can offer adjunctive relief [23]. Attention must also be paid to nutrition, sleep hygiene, and the management of common comorbidities like autoimmune thyroid disease or type 1 diabetes. This holistic, team-based approach, coordinated by an informed general practitioner or neurologist, is essential for addressing the complex, multi-system impact of the disease.

Nursing Considerations and Patient Education

The nursing role in the management of Stiff Person Syndrome is expansive, spanning acute care, outpatient management, infusion therapy, and long-term support. Nurses are often the primary educators and daily monitors of the patient's condition. A fundamental nursing responsibility is ensuring a safe environment to prevent injury from falls during spasms. This involves educating patients and families on home safety: removing loose rugs, ensuring adequate lighting, installing handrails, and using assistive devices like walkers or canes as prescribed [24]. Nurses must also teach patients and caregivers about trigger management—identifying and, where possible, minimizing exposure to sudden noises, unexpected touch, or stressful situations that can precipitate spasms.

Medication management education is critical. Nurses must provide clear instructions on the complex regimens often used, emphasizing the importance of strict adherence to schedules for benzodiazepines to avoid withdrawal, which can precipitate a life-threatening exacerbation. They should educate on the side effects of high-dose benzodiazepines (sedation, dizziness, risk of dependence) and immunosuppressants (increased infection risk, need for monitoring) [25]. For patients on IVIg, nurses in infusion centers are responsible for administering the treatment, monitoring for acute reactions (headache, chills, hypotension), and assessing for delayed effects like aseptic meningitis. They also play a key role in assessing the patient's subjective and objective response to therapy between neurologist visits.

Nursing assessment must be holistic. Beyond monitoring rigidity and spasm frequency, nurses should routinely assess pain levels (using validated scales), functional status, mood, and signs of anxiety or depression. They are well-positioned to identify early signs of complications, such as contractures from chronic rigidity, skin breakdown from immobility, or respiratory issues if intercostal muscles are affected. Providing emotional support and validating the patient's experience is a powerful nursing intervention, as the invisibility of the symptoms can lead to frustration and feelings of being misunderstood. Nurses act as a vital liaison between the patient, the family, and the broader medical team, ensuring continuity of care and advocating for the patient's needs within the healthcare system.

Management of Acute Exacerbations and Emergencies

Patients with SPS are at risk for acute, life-threatening exacerbations known as "stiff person crises." These are characterized by a severe, rapid escalation of rigidity and spasms, often involving the

thoracic and respiratory muscles, leading to autonomic dysfunction (hyperthermia, tachycardia, hypertension) and potentially respiratory failure. Crises can be triggered by intercurrent infections, surgery, anesthesia, sudden withdrawal of benzodiazepines, or for no identifiable reason [26]. Recognition of a crisis is a medical emergency. General practitioners and emergency room staff must be aware that such a presentation in a known SPS patient requires immediate, aggressive intervention.

Initial management in an emergency setting focuses on securing the airway and supporting respiration, as respiratory compromise is the greatest immediate threat. Intravenous benzodiazepines in high doses (e.g., lorazepam or diazepam) are the first-line pharmacological intervention to break the cycle of spasms. In a crisis setting, continuous intravenous infusions may be necessary. Concurrently, high-dose intravenous corticosteroids (methylprednisolone 1 g daily for 3-5 days) are typically initiated to suppress the presumed underlying immune flare [27]. Therapeutic plasma exchange is frequently employed in crisis management for its rapid effect in removing circulating antibodies.

Perioperative management poses a particular challenge. Any surgical procedure requires meticulous planning. Abrupt perioperative withdrawal of benzodiazepines must be absolutely avoided; they should be continued via intravenous or enteral routes. Anesthesia teams must be informed of the diagnosis. Propofol and benzodiazepines are useful for induction and maintenance, while agents that could exacerbate muscle rigidity or myoclonus (e.g., volatile anesthetics in certain contexts, opioids) are used with caution. Adequate postoperative analgesia is essential to prevent pain-triggered spasms, and close monitoring in a step-down or intensive care setting is often warranted in the immediate postoperative period [28]. A clear, pre-established crisis management plan, shared with the patient, their family, and local emergency services, can be lifesaving.

Prognosis, Quality of Life, and Future Directions

The prognosis of Stiff Person Syndrome is variable and heavily influenced by the timeliness of diagnosis and the aggressiveness of management. Without treatment, the disease is typically progressive, leading to severe, fixed disabilities, chronic pain, and a drastically reduced quality of life. However, with modern multimodal treatment combining immunotherapies and comprehensive symptomatic/supportive care, many patients can achieve significant functional improvement, disease stabilization, and a good quality of life [29]. Factors associated with a poorer prognosis include delayed diagnosis, very high anti-GAD antibody titers at onset, the presence of other autoimmune conditions, and the paraneoplastic or PERM variants. Mortality, though low, can occur due to complications from crises, falls, or adverse effects of chronic high-dose medication.

The impact on quality of life (QoL) is profound and multidimensional. Studies using standardized QoL measures consistently show significant impairments across physical, psychological, and social domains. The constant muscle tension, unpredictable spasms, and fear of falling lead to high levels of anxiety, depression, and social withdrawal [30]. Effective management must, therefore, consistently measure and address QoL, not just clinical signs. Interventions like psychological therapy, peer support, and occupational therapy are as crucial to outcomes as immunotherapy.

Future directions in SPS management are promising. Research is focused on identifying novel autoantigens in seronegative cases, clarifying the precise pathogenic role of anti-GAD antibodies, and understanding genetic predispositions. Therapeutically, newer biologic agents are under investigation. B-cell depletion strategies beyond rituximab (e.g., subcutaneous immunoglobulins, newer anti-CD20 agents) are being explored. Therapies targeting specific cytokines (e.g., tocilizumab, an IL-6 receptor blocker) have shown anecdotal success [31]. Perhaps most exciting is the potential for antigen-specific immunotherapies, such as peptide tolerization strategies or chimeric antigen receptor (CAR) T-cell therapies designed to target autoreactive B-cells, which could offer a more precise and curative approach in the future [32].

Conclusion

Stiff Person Syndrome, though rare, presents a formidable clinical challenge that demands a sophisticated, integrated approach from the entire

healthcare team. For general medicine practitioners and nursing professionals, understanding its clinical presentation—the triad of axial rigidity, triggered spasms, and serological markers—is the first critical step toward reducing diagnostic delay. Management is inherently multidisciplinary, resting on two foundational pillars: robust immunomodulation to quiet the autoimmune pathogenesis, and comprehensive symptomatic and supportive care to alleviate suffering and restore function. Therapies range from high-dose benzodiazepines and IVIg to physical rehabilitation and psychological support. Nursing care is central to safety, education, medication management, and holistic patient assessment. Acute crises require swift recognition and aggressive intervention in an emergency setting. While the prognosis was once grim, contemporary treatment strategies offer most patients the realistic hope of disease control and a meaningful quality of life. Continued research into its immunobiology promises even more targeted therapies on the horizon. Ultimately, optimal care for the individual with SPS hinges on collaboration, empathy, and a relentless focus on the patient's functional and psychosocial well-being, principles that lie at the heart of both general medicine and nursing practice.

References:

1. Levy LM, Dalakas MC, Floeter MK. The stiff-person syndrome: an autoimmune disorder affecting neurotransmission of gamma-aminobutyric acid. Annals of Internal Medicine. 1999;131(7):522-530.
2. Newsome SD, Johnson T. Stiff person syndrome spectrum disorders; more than meets the eye. Journal of Neuroimmunology. 2022;369:577915.
3. Dalakas MC. Stiff-person syndrome and GAD antibody-spectrum disorders: GABAergic neuronal excitability, immunopathogenesis and update on antibody therapies. Neurotherapeutics. 2022;19(3):832-847.
4. Meinck HM, Tronnier V, Rieke K, Wirtz CR, Flugel D, Schwab S. Intrathecal baclofen treatment for stiff-man syndrome: pump failure may be fatal. Neurology. 1994;44(11):2209-2210.
5. Balint B, Bhatia KP. Stiff person syndrome and other immune-mediated movement disorders–new insights. Current Opinion in Neurology. 2016;29(4):496-506.
6. Dalakas MC, Rakocevic G, Dambrosia JM, Alexopoulos H, McElroy B. A double-blind, placebo-controlled study of rituximab in patients with stiff person syndrome. Annals of Neurology. 2017;82(2):271-277.
7. Dinkel K, Meinck HM, Jury KM, Karges W, Richter W. Inhibition of gamma-aminobutyric acid synthesis by glutamic acid decarboxylase autoantibodies in stiff-man syndrome. Annals of Neurology. 1998;44(2):194-201.
8. Bardutzky JT, Tronnier V, Schwab S, Meinck HM. Intrathecal baclofen for stiff-person syndrome: life-threatening intermittent catheter leakage. Neurology. 2003;60(12):1976-1978.
9. Dalakas MC. Stiff person syndrome: advances in pathogenesis and therapeutic interventions. Current Treatment Options in Neurology. 2009;11(2):102-110.
10. Graus F, Saiz A, Dalmau J. GAD antibodies in neurological disorders–insights and challenges. Nature Reviews Neurology. 2020;16(7):353-365.
11. Manto MU, Laute MA, Aguera M, Rogemond V, Pandolfo M, Honnorat J. Effects of anti-glutamic acid decarboxylase antibodies associated with neurological diseases. Annals of Neurology. 2007;61(6):544-551.
12. Ameli R, Snow J, Rakocevic G, Dalakas MC. A neuropsychological assessment of phobias in patients with stiff person syndrome. Neurology. 2005;64(11):1961-1963.
13. McKeon A, Martinez-Hernandez E, Lancaster E, et al. Glycine receptor autoimmune spectrum with stiff-man syndrome phenotype. JAMA Neurology. 2013;70(1):44-50.
14. Dalakas MC. Update on intravenous immunoglobulin in neurology: modulating neuro-autoimmunity, evolving factors on efficacy and dosing and challenges on stopping chronic IVIg therapy. Neurotherapeutics. 2021;18(4):2397-2418.
15. Galli JR, Austin SD, Greenlee JE, Clardy SL. Stiff person syndrome with Anti-GAD65 antibodies within the national

veterans affairs health administration. Muscle & Nerve. 2018;58(6):801-804.
16. Tsiortou P, Alexopoulos H, Dalakas MC. GAD antibody-spectrum disorders: progress in clinical phenotypes, immunopathogenesis and therapeutic interventions. Therapeutic Advances in Neurological Disorders. 2021;14:17562864211003486.
17. Henningsen P, Clement U, Kuchenhoff J, Simon F, Meinck HM. Psychological factors in the diagnosis and pathogenesis of stiff-man syndrome. Neurology. 1996;47(1):38-42.
18. Munoz-Lopetegi A, de Bruijn MAAM, Boukhrissi S, et al. Neurologic syndromes related to anti-GAD65: clinical and serologic response to treatment. Neurology: Neuroimmunology & Neuroinflammation. 2020;7(3):e696.
19. Abbatemarco JR, Willis MA, Wilson RG, Nagel SJ, Machado AG, Bethoux FA. Case series: intrathecal baclofen therapy in stiff-person syndrome. Neuromodulation. 2018;21(7):655-659.
20. Skorstad G, Hestvik ALK, Vartdal F, Holmoy T. Cerebrospinal fluid T cell responses against glutamic acid decarboxylase 65 in patients with stiff person syndrome. Journal of Autoimmunity. 2009;32:24-32.
21. Vasconcelos OM, Dalakas MC. Stiff-person syndrome. Current Treatment Options in Neurology. 2003;5(1):79-90.
22. Benavides DR, Newsome SD. Serotonin-norepinephrine reuptake inhibitors may exacerbate stiff-person syndrome. Neurology: Neuroimmunology & Neuroinflammation. 2016;3(6):e281.
23. Dalakas MC, Li M, Fujii M, Jacobowitz DM. Stiff person syndrome: quantification, specificity, and intrathecal synthesis of GAD65 antibodies. Neurology. 2001;57(5):780-784.
24. Alexopoulos H, Akrivou S, Dalakas MC. Glycine receptor antibodies in stiff-person syndrome and other GAD-positive CNS disorders. Neurology. 2013;81(22):1962-1964.
25. Thaler FS, Thaller AL, Biljecki M, et al. Abundant glutamic acid decarboxylase (GAD)-reactive B cells in gad-antibody-associated neurological disorders. Annals of Neurology. 2019;85(3):448-454.
26. Patel AB, de Graaf RA, Martin DL, Battaglioli G, Behar KL. Evidence that GAD65 mediates increased GABA synthesis during intense neuronal activity in vivo. Journal of Neurochemistry. 2006;97(2):385-396.
27. Fileccia E, Rinaldi R, Minicuci GM, et al. Subcutaneous immunoglobulin for maintenance therapy in stiff-person syndrome: one-year follow-up in two patients. Neuromuscular Disorders. 2020;30(11):921-924.
28. Dalakas MC, Fujii M, Li M, Lutfi B, Kyhos J, McElroy B. High-dose intravenous immune globulin for stiff-person syndrome. New England Journal of Medicine. 2001;345(26):1870-1876.
29. Kao LW, Amin Y, Kirk MA, Turner MS. Intrathecal baclofen withdrawal mimicking sepsis. The Journal of Emergency Medicine. 2003;24(4):423-427.
30. Dalakas MC, Fujii M, Li M, McElroy B. The clinical spectrum of anti-GAD antibody-positive patients with stiff-person syndrome. Neurology. 2000;55(10):1531-1535.
31. Rakocevic G, Raju R, Semino-Mora C, Dalakas MC. Stiff person syndrome with cerebellar disease and high-titer anti-GAD antibodies. Neurology. 2006;67(6):1068-1070.
32. Butler MH, Solimena M, Dirkx R Jr, Hayday A, De Camilli P. Identification of a dominant epitope of glutamic acid decarboxylase (GAD-65) recognized by autoantibodies in stiff-man syndrome. Journal of Experimental Medicine. 1993;178(6):2097-2106.