



Twists and Triggers: Multimodal Pain Control in Stiff Person Syndrome and Ehlers-Danlos with Chronic Testicular Pain

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Introduction

- **Stiff Person Syndrome (SPS)** is a rare autoimmune disorder characterized by **muscle rigidity, painful spasms, and heightened CNS excitability**, often associated with **anti-GAD antibodies** [1,2,6,7].
- **Ehlers-Danlos Syndrome (EDS)** involves **connective tissue fragility, joint hypermobility, and chronic musculoskeletal pain**, resulting from abnormal collagen synthesis.
- The coexistence of **SPS and EDS** creates a **unique pain phenotype**—a combination of **neuromuscular rigidity and connective tissue instability** that complicates diagnosis and management.
- **Conventional SPS therapies** such as **benzodiazepines, baclofen, and IVIG** can improve stiffness and function but may not adequately control chronic pain or emotional distress [1–7].
- **IVIG** has demonstrated benefit in reducing muscle spasms and improving quality of life in SPS patients [1,4,7].
- **Ketamine infusions**, acting via **NMDA receptor antagonism**, have shown efficacy in **refractory neuropathic and central sensitization-related pain** [8–10].
- Psychological comorbidities—**anxiety, depression, and psychosocial stressors**—can further amplify pain perception, emphasizing the **need for biopsychosocial integration** in treatment.
- This case highlights the **synergistic benefit** of combining **immunotherapy (IVIG), ketamine infusions, and cognitive behavioral therapy (CBT)** for **refractory pain** in a patient with both **SPS and EDS**.

Materials and Methods

- As this is a Case Report devoid of patient identifiers, no IRB approval was required per UMMC policy.
- Informed consent was obtained from the patient for this presentation.

Case Report

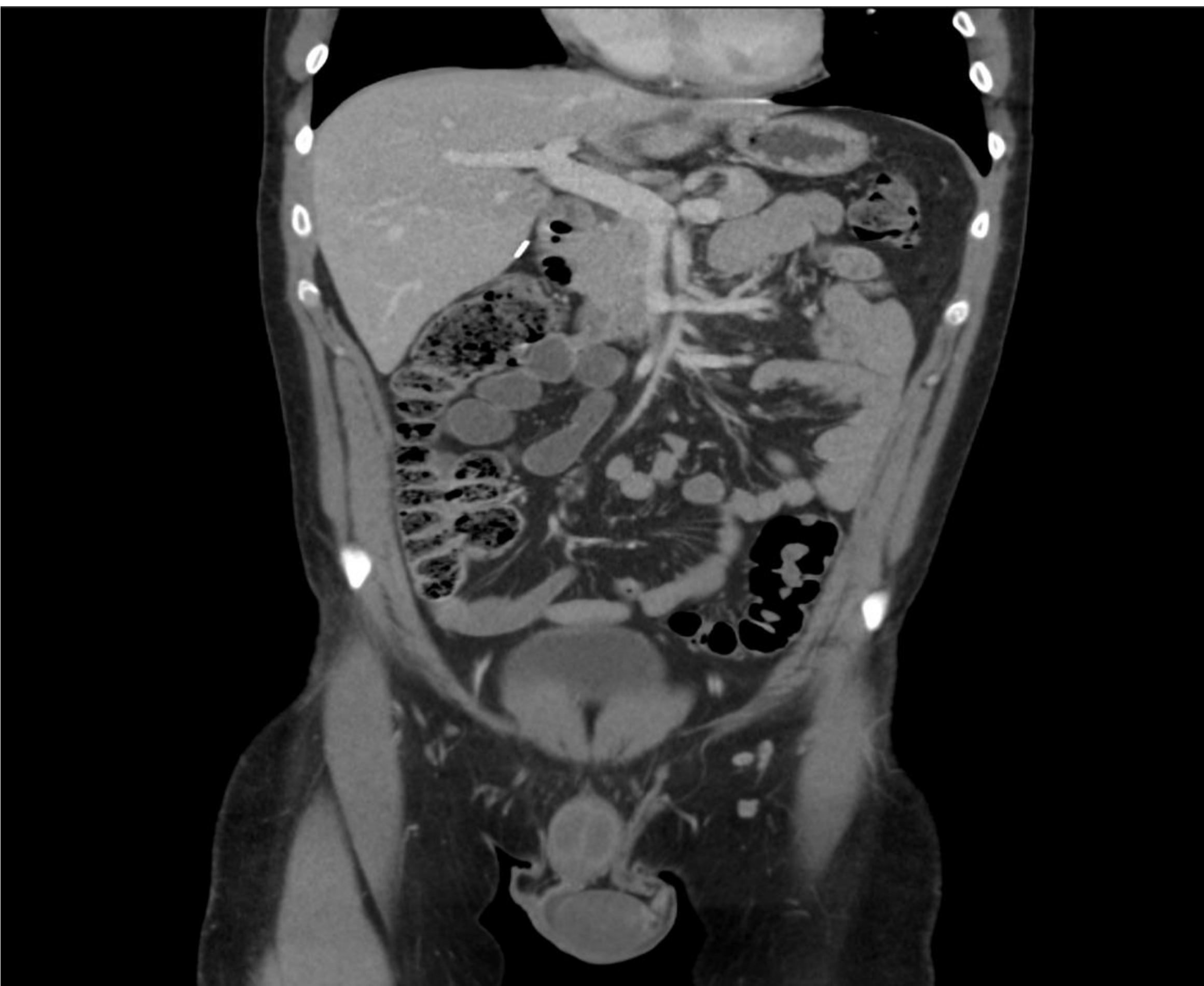
- A **34-year-old male** with a history of **Stiff Person Syndrome (SPS)** confirmed by **anti-GAD antibodies and EMG**, and **Ehlers-Danlos Syndrome (EDS)** diagnosed by clinical features.
- Presented to **Interventional Pain Management** clinic (May 2020) for **chronic testicular pain persisting after orchiectomy**.
- Prior interventions included:

- **Iliohypogastric and spermatic cord nerve blocks**
- **Intravenous lidocaine infusions**
- **IVIG therapy** for SPS
- **PRN benzodiazepines and opioids** for symptom control

- Despite multiple treatments, the patient reported **minimal and transient pain relief**, with **progressive decline in functional status**.
- Increasing **anxiety, marital stress, and emotional distress** further exacerbated his pain experience and coping ability.
- A **multidisciplinary treatment plan** was initiated, integrating:
 - Ongoing **IVIG infusions** for immune modulation
 - **Ketamine infusions** targeting refractory neuropathic and central sensitization pain
 - **Cognitive Behavioral Therapy (CBT)** to address psychological and coping factors

- Collaborative management involved **Pain Medicine, Psychiatry, and Psychology** services.
- After **three months of combined therapy**, the patient reported:
 - **Significant improvement in pain intensity and reduction in spasm frequency**
 - **Improved mood, coping skills, and overall functional capacity**
 - **Enhanced quality of life** with greater independence in daily activities

Relevant Images



Discussion

- The coexistence of **Stiff Person Syndrome (SPS)** and **Ehlers-Danlos Syndrome (EDS)** illustrates how **autoimmune, neuromuscular, and connective-tissue disorders can intersect to produce highly complex, refractory pain** [1,2,6,7].
- **Pain in these patients is multifactorial**—involving central sensitization, immune dysregulation, and mechanical instability—necessitating **comprehensive assessment beyond standard nociceptive vs. neuropathic frameworks**.
- **IVIG therapy**, the mainstay of SPS management, remains essential for immune modulation and improvement in muscle rigidity [1,4,7]; however, **its analgesic effect alone is often insufficient**, underscoring the need for adjunctive strategies.
- **Ketamine infusions** provide an additional therapeutic pathway by **targeting NMDA receptor-mediated central sensitization and cortical hyperexcitability**, offering relief in cases of **refractory neuropathic and mixed-mechanism pain** [8–10].
- **Cognitive Behavioral Therapy (CBT)** serves as a critical adjunct for patients whose pain is intensified by emotional distress, anxiety, and maladaptive coping, helping to **stabilize affective states and improve pain tolerance**.
- This case demonstrates that **integrating biologic, pharmacologic, and psychologic treatments** can achieve functional improvement even when conventional pharmacotherapy fails.
- For **pain specialists**, key clinical implications include:
 - Prioritizing **mechanism-specific and multimodal treatment** over dose escalation of single agents.
 - Recognizing **central sensitization** early and addressing it through NMDA antagonism and behavioral therapies.
 - Maintaining **immunologic vigilance** in patients with SPS, as lapses in IVIG or immune control can precipitate clinical relapse [1,2,6,7].
 - Incorporating **mental-health screening and psychological support** as standard components of chronic pain management.
- **Outcome focus should shift** from short-term analgesia to **sustained functional recovery, emotional resilience, and quality-of-life restoration**.
- Future directions include prospective evaluation of **combined IVIG–ketamine–CBT protocols** for patients with overlapping autoimmune and connective-tissue disorders, aiming to optimize pain modulation across physiologic and psychologic domains.

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