Utilization of Dantrolene in Stiff-Person Syndrome: A Case Report

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ABSTRACT

Setting: University hospital-based acute rehabilitation.

Patient: 75-year-old woman with Stiff-Person Syndrome (SPS) with a recent fall and Colles fracture.

Case Description: Four months prior to admission, the patient was diagnosed with SPS, negative for anti-GAD antibodies. Diagnosis was based on a 3-year history of progressive rigidity leading to frequent falls and fractures. Anxiety and fear of falling limited her mobility, and she sustained a pressure ulcer during acute hospitalization. On admission, history was remarkable for unstable gait and muscle cramps exacerbated when startled or excited. Examination was remarkable for rigidity in her axial and limb muscles. She presented at the maximal assist level for transfers and toileting and moderate assist level for grooming and ambulation using a platform walker (right arm in cast). She was unable to tolerate titration of diazepam due to sedation, or baclofen due to hypotension. During acute rehabilitation, rigidity was treated with titration of dantrolene (from 25 to 50 mg four times daily) in addition to maximal tolerated doses of diazepam (1 mg qAM/2 mg qPM) and baclofen (20 mg TID). The addition of dantrolene reduced rigidity and improved range of motion, both subjectively by patient and objectively by exam. Functional gains started with dose decrease and resumed with dose increase. She had pronounced gains in grooming to the supervision level, modest gains in transfers and toileting to the moderate assist level, but remained at the moderate assist level for ambulation. Progress was limited due to a change in weight bearing status of her right arm. Anxiety and depression were improved with buspirole, paroxetine, and psychological counseling.

Discussion: SPS results in significant activity of daily life and ambulatory dysfunction as exemplified by her pressure ulcer and multiple falls. Although GABA agonists are the preferred treatment for SPS, the adverse effects of high doses can increase the risk of falls. Dantrolene reduced muscle rigidity and improved function without sedative or hypotensive effects.

Conclusion: Dantrolene is a useful additional treatment for SPS rigidity.

CASE REPORT

HISTORY

-75-year-old woman, history of anxiety and a right Colles fracture after a fall, treated non-surgically.
- Presently less anxious and ambulatory dysfunction, rigidity, and frequent falls over 3 years.
- Often becomes stiff when startled or scared, had anxiety related to fear of falling.

Diagnosis: SPS, anti-GAD negative. Stiff-Person Syndrome (SPS) 4 months before rehab admission.

PHYSICAL EXAMINATION

-Admitted to acute rehabilitation at the maximal assistance level for transfers and toileting, and moderate assistance level for grooming and ambulation with a platform walker.
- Exam at admission: intact strength without focal neurologic deficit with the exception of notable axial and limb rigidity. Modified Ashworth Score of 3 in all limbs.

PHARMACOLOGIC

- Prior to admission, she demonstrated clinical improvement of rigidity with diazepam, but only tolerated 1mg qAM and 2mg qPM; higher doses caused sedation.
- Addition of Baclofen caused sedation and hypotension, which limited dosing to 20mg TID.
- Addition of Dantrolene, started to 50mg QID, reduced rigidity and increased function.
- A dose-dependent relationship to function was noted: when the dose was reduced to 25mg QID to reduce risk of hepatotoxicity, function declined as rigidity increased, and this change was reversed when the dose was increased again.

THERAPIES

Physical Therapy
- Strength training, balance, endurance, range of motion exercises.
- Personalized therapy activities of daily living, compensatory skills, range of motion exercises.

Rehabilitation Psychology
- Education and counseling focused on facilitating adaptation to the medical and psychosocial impacts of SPS, including management of anxiety and depression.

RESULTS

- She progressed to supervision for grooming, moderate assistance for transfers and toileting, and minimal assistance for ambulation.
- Anxiety and depression were improved with psychological counseling, buspirone, and paroxetine.
- Improvement of Modified Ashworth Score from 3 to 1-2 in all limbs with dantrolene.

Figure 1: Gordon Clinical Diagnostic Criteria for Stiff-Person Syndrome

1. Prodrome of episodic aching stiffness of axial muscles
2. Progression to include stiffness of proximal limbs
3. Painful spasms elicited by triggers
4. Increased lumbar lordosis
5. Normal sensation, motor function and intellect
6. Response to benzodiazepines


Figure 2: Pathogenic Mechanisms in Stiff-Person Syndrome

Discussion

Diagnosis

- SPS is a rare, progressive disorder characterized by rigidity, caused by deficient GABA utilization, that can severely limit quality of life.
- GABA agonists, but central side effects (sedation, hypotension) limit dosing, especially in the elderly who have a high falls risk.
- Dantrolene is not an effective agent for treatment of spasticity and rigidity, but may be used as an adjunct to GABAergic treatments.

Pharmacologic

- Benzodiazepines are GABA-ergic drugs and are considered the first-line treatment; large doses (up to 200mg/day) are often needed with limitation of sedation.
- Antiepileptics such as valproic acid (GABA agonist), tiagabine (blocks GABA reuptake), and gabapentin (similar structure to GABA), valproate (augments GABA transmission), and tiagabine (blocks GABA reuptake).

Conclusion

- SPS is a potentially life-threatening condition that requires prompt diagnosis and management.
- Early intervention with appropriate treatments can improve functional outcomes and reduce the risk of falls.
- Further research is needed to better understand the pathophysiology of SPS and identify effective treatment options.