2-036

GAD65 and Glycine Receptor-Associated Neurologic Autoimmunity and Stiff-Person Syndrome within the University of Utah Health Care System

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Objective

Describe epidemiological characteristics, antibody status, and treatment outcomes of stiff person syndrome patients within University of Utah Health.

Background

Stiff person syndrome (SPS) is an autoimmune disease that classically causes co-activation of agonist and antagonist muscle groups leading to severe muscle rigidity and spasms.[1] GAD65 is the most common associated neuronal autoantibody; patients may also have associated glycine receptor (GlyR) or amphiphysin autoantibodies.[2]

The incidence of SPS is estimated at 1 to 2 per million people.[3] Average age of onset is 40 years and females are more commonly affected.[4,5]

Diazepam and baclofen are the primary symptomatic treatments. Intravenous immune globulin (IVIg) is often an effective immunotherapy.[5] Large randomized, controlled trials and treatment guidelines for immunotherapy are lacking.

Methods

Retrospective review of patients within the University of Utah Healthcare system from 7/1/2010 to 11/7/2018, meeting criteria 1 and 2, or 2 and 3, and cross-referenced for internal consistency:

1. Positive GAD65 (>100 IU/mL) or amphiphysin serum or cerebrospinal fluid testing at Associated Regional and University Pathologists, Inc. (ARUP Laboratories), or positive GlyR testing (performed on a research-basis) at Mayo Medical Laboratories.
2. At least one visit with a University of Utah clinician in the Department of Neurology.
3. At least one ICD code for stiff person syndrome (333.91 or G25.82), encephalomyelitis (323.9 or G04.90); or ICD code for GAD65 seropositivity (R76.0).

Patient charts were reviewed and further epidemiological and treatment data was collected on patients who had clinical symptoms consistent with SPS or variants along with associated seropositivity or additional clinical data supporting a SPS diagnosis.

Acknowledgements

Supported by: Transverse Myelitis Association and Barbara Gural Steinmetz Family

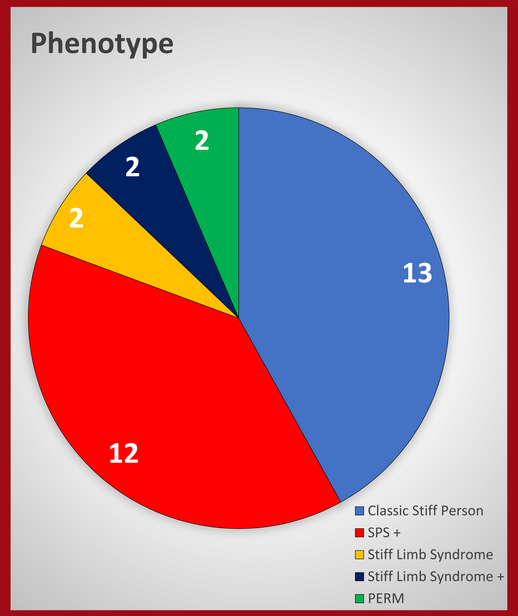
Results

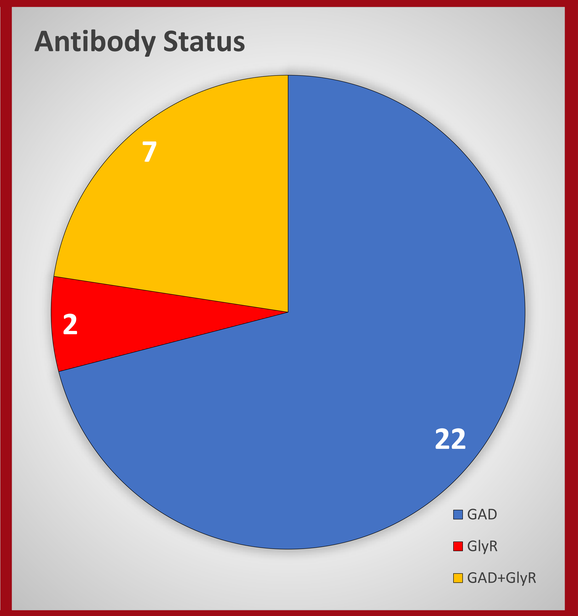
Epidemiological Data

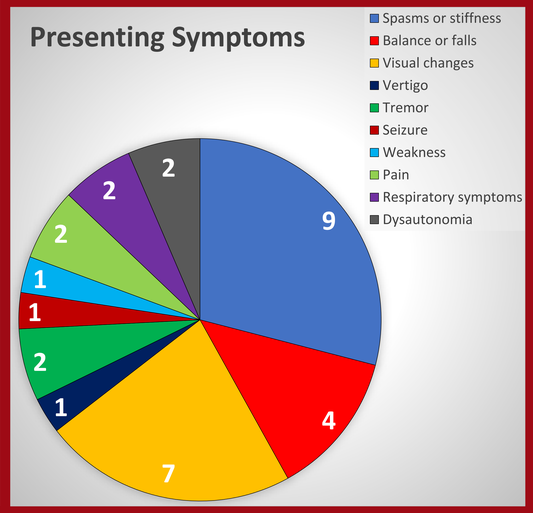
Total # of SPS patients	**31**
Male	7
Female	24
Alive	28
Deceased	3
Caucasian	30
Other (Sudanese)	1
Mean reported age of diagnosis	47 *(15-72)*
Mean age at diagnosis	52 *(26-76)*
Other associated antibodies	**n = 18**
ANA	6
TPO and/or thyroglobulin	11
Intrinsic factor or gastric parietal	4
Other	2
Visual symptoms	**n = 16**
Positive visual phenomenon	2
Visual acuity changes or scotoma	2
Diplopia, nystagmus, or abnormal eye movement	12
Associated Autoimmunity	20
Associated Malignancy	4

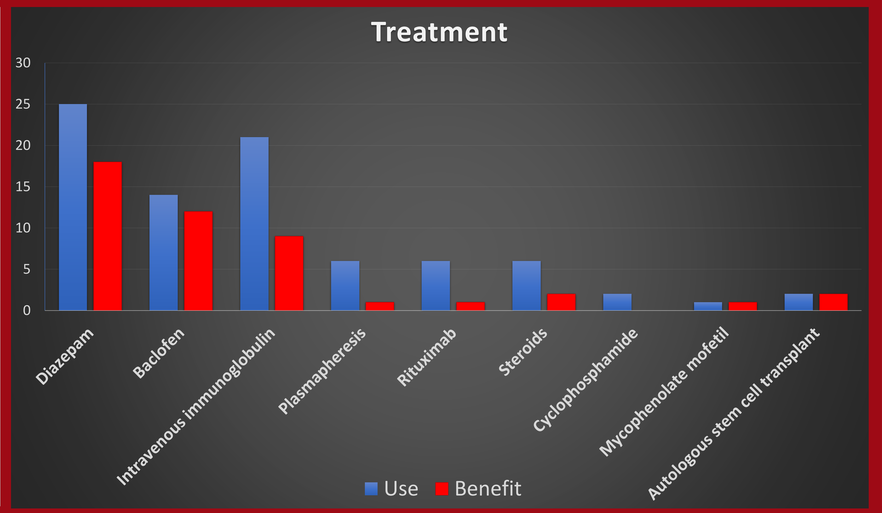
Evaluation

CSF	
Assessed	19
Elevated WBC or protein (WBC >5, Protein >45)	4
Oligoclonal bands checked	13
Positive (unique)	8
Matched	2
EMG	
Performed	10
Consistent with SPS	0
MRI	
Performed	28
Abnormal	0
EEG	
Performed	16
Abnormal	6









Discussion and Conclusions

We identified 31 patients with SPS within the University of Utah healthcare system. Patients were predominantly female (78%) with the most common phenotype being classic SPS or SPS with concomitant cerebellar symptoms or epilepsy.

Our cohort had co-existing autoimmune disease (63%) and malignancy (13%).

GAD65 was the most common associated antibody; GlyR antibody testing should be considered in patients with SPS phenotype with negative or low GAD65 titers.

Diazepam and baclofen was effective in a majority of patients. IVIg was the most commonly utilized immunotherapy (used in 69% of patients) with benefit demonstrated in 41% of patients who received this treatment. Other immunotherapies demonstrated more limited benefit.

Limitations: Due to the electronic search method that was utilized, an accurate incidence could not be calculated. Treatment outcomes need more objective measures. The 2 patients who underwent bone marrow transplant were too early in their course to present additional data.

References

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