STIFF EYES IN STIFF-PERSON SYNDROME

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Two main findings emerged from our study. First, AED users exhibited a higher propensity of switch-back to branded drugs compared to patients treated with other chronic-disease drugs. Secondly, the use of generic lamotrigine was associated with increased physician visits and hospitalizations compared to brand use. We do not attribute these results strictly to seizure activity. As we stated, while these findings may signal reduced clinical effectiveness or increased side effects associated with generic lamotrigine use, this study lacked access to data on whether drugs dispensed were actually taken according to prescribed instructions, or on disease severity.

Dr. Boylan's statement that "anxiety-induced dose escalations contributed to side effects and, in turn, switch-backs" in patients treated with generic lamotrigine could be one of the plausible explanations for the findings.

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STIFF EYES IN STIFF-PERSON SYNDROME

To the Editor: Oskarsson et al.[1] describe a 54-year-old woman with a supranuclear gaze palsy and parkinsonism mimicking progressive supranuclear palsy (PSP). She exhibited some phenomena of stiff-man syndrome (SMS) and was highly seropositive for glutamic acid decarboxylase (GAD65) autoantibody.[2]

Videonystagmography findings—a fatiguing pattern of saccade initiation with repetitive saccades—helped exclude a diagnosis of PSP.[1] Startle-induced spasms typical of SMS and prominent early upgaze palsy also negated this diagnosis. The authors concluded that their observations in this case add a treatable condition to the differential diagnosis of PSP.

The observations that the clinical spectrum of GAD65 autoimmunity is broader than previously recognized and that it also encompasses parkinsonism and PSP-mimics in addition to SMS, cerebellar ataxia, and seizures is not novel. We described 62 patients in whom high GAD 65 antibody levels were detected by indirect immunofluorescence screening on brain tissue in the course of service evaluation for IgG paraneoplastic autoantibodies.[3]

Our findings were confirmed GAD65-specific by radioimmunoprecipitation (median 1,429 nmol/L; range, 69–13,900 nmol/L; normal range, 0.00–0.02 nmol/L). GAD65 autoantibody testing was never requested by the neurologist. Our patients presented with brainstem, extrapyramidal, and spinal cord syndromes.[3] Initially, most were considered to have a neurodegenerative disorder and 10% had a clinical presentation that mimicked PSP or multiple system atrophy.

Brainstem involvement was noted in 18 patients in our series, most of whom had visual symptoms and signs: ophthalmoplegia (13), oscillopsia (4), or nystagmus (13). In addition, we found the following: extrapyramidal signs (10), axial rigidity (8), parkinsonism (4), hyperkinetic dysarthria (1), posture-sensitive dystonia (1), blepharospasm (1), and chorea (1). Stiff-man phenomena (2), cerebellar ataxia (4), and seizures (5)—considered more typical manifestations of GAD65 autoimmunity—were observed in 26%, 63%, and 27% of our patients, respectively.

Also consistent with an underlying autoimmune process were clinical findings atypical for specific neurodegenerative syndromes including multifocality, coexistence of organ-specific autoantibodies or autoimmune disorders, CSF abnormalities (elevated protein in 30%; supernumerary oligoclonal bands in 39%), and immunotherapy responsiveness.[3] Clinical improvement was most frequent with prompt initiation of immunotherapy.

The case described by Oskarsson et al.[1] is an important reminder of the diverse, multifocal, and immunotherapy-responsive syndromes that occur

in association with high serum levels of GAD65 antibody.

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Reply from the Authors: We thank Pittock et al. for their interest in our case report. Their prior large case series encompassed a host of presentations of glutamic acid decarboxylase (GAD65) autoimmunity, including four patients who were suspected of having multisystem atrophy, olivopontocerebellar atrophy, or PSP.[3]

In their case series, they also mention a patient with slow voluntary saccades. Our report described the findings in a similar patient and provided a more detailed description of her eye movements with formal eye movement recordings and a response to treatment.[1]

We strongly agree with Pittock et al. that testing for GAD65 antibodies may be appropriate when a neurodegenerative condition is suspected, especially if there are any atypical features.

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