Variant Stiff Person Syndrome or Multiple Sclerosis?

To the Editor: We read with interest a recently published case report by Naik et al[1] wherein the authors describe a man who presented with symptoms of progressive myelopathy with elevated antiglutamic acid decarboxylase (GAD) antibodies, for whom the authors made a diagnosis of variant stiff person syndrome (SPS). The authors indicate that the man also carried a diagnosis of multiple sclerosis (MS), which is quite interesting, as to our knowledge there have been no reports of co-occurrence of MS with SPS. SPS can certainly masquerade as MS and vice versa[2]; hence, we raise some concerns regarding this patient's concurrent diagnoses. SPS indeed presents with varied phenotypes, which have been increasingly recognized over the years, including stiff limb syndrome, cerebellar ataxia, and progressive encephalomyelitis with rigidity and myoclonus (PERM) among others.[3,4]

PERM with antiglycine receptor antibodies in the serum was first described in 2008 in a report[5] of a 54-year-old man who presented with myoclonus, hyperkplexia, rigidity, and autonomic dysfunction. Features of PERM include early brain stem involvement, myoclonus, and prominent autonomic symptoms.[5,6] Brain stem abnormalities most commonly include bulbar symptoms and oculomotor dysfunction.[5,6] There is an association of PERM with both anti-GAD antibodies and antiglycine receptor antibodies.[5,6] Brain and spinal cord imaging is typically normal in individuals with SPS and its variants, including PERM,[5–7] and should have been described in this case report, especially given the individual's prior diagnosis of MS, as MS can present with progressive myelopathy and bulbar symptoms as described in this case. Diagnosis of SPS and its variants is quite difficult—it is a rare condition, and extensive evaluation of alternative diagnoses should be pursued, as misdiagnosis can have significant consequences.[2] Other important features that are helpful in supporting an SPS diagnosis include presence of anti-GAD antibodies in the cerebrospinal fluid, electromyography findings of cocontraction of agonist and antagonist muscles or continuous motor unit activity in affected muscles (commonly paraspinal muscles or legs), and early robust response to GABAergic agonist therapies.[3,7] In addition, it is important to recognize the occurrence of anti-GAD antibodies in both type I and II diabetes mellitus, as anti-GAD is also an antibody against pancreatic antigens.[8] The presence of anti-GAD antibodies has been recognized in the majority of individuals with type I diabetes mellitus, as well as a proportion of patients with type II diabetes mellitus, with prior studies citing prevalence of the antibody reported to be up to 10% of individuals with type II diabetes mellitus.[8] Moreover, these antibodies have been seen in other disorders (such as thyroid disease), and in up to 5% of individuals with other neurologic conditions and 1% of healthy controls.[9] Hence, there is a potential for diagnostic errors when relying too heavily on individual paraclinical test results, especially in neurologic conditions that have overlapping symptoms and signs.

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Dr Naik and colleagues were shown this letter and declined to comment.

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