CLINICAL VIGNETTE

A Case of Stiff-Person Syndrome

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Case

A 52-year-old female was diagnosed with GAD65 antibody positive Stiff-person syndrome (SPS) at age 36. She was referred by local neurologist to the University Neuromuscular clinic with progressive stiffness of both lower extremities and mild low back pain, despite baclofen treatment. Her past medical history includes hypothyroidism and hyperlipidemia. Family history was negative for neurologic disorders and she does not smoke.

Neurologic exam noted significantly increased tone in the bilateral lower extremities described as feeling "rigid". Bilateral upper extremities tone and bulk. There was no atrophy. Motor testing revealed 5/5 strength in the bilateral upper and lower extremities, without extraneous muscle movements. Sensory exam was intact to light touch and pinprick throughout. There was very mildly decreased vibratory sensation in bilateral lower extremities at the ankles. Deep tendon reflexes were 3+ at the biceps, brachioradialis, and patellar; 2+ at the triceps and ankles. Gait was slightly widened.

Labs included normal metabolic panel, CRP and CK (172). TSH was slightly elevated at 6.1.

Anti-GAD 65(glutamic acid decarboxylase) was very elevated at 6631, confirmed with repeat testing a month later. Thyroglobulin antibody was borderline elevated at 2.6, with elevated TPO (thyroid peroxidase) of 343. Lactate and pyruvate were normal.

MRI of the brain was notable for a 2- to 3-mm nonspecific focus of white matter signal change in the right frontal lobe. MRI of the cervical, thoracic and lumbar spine showed degenerative changes. EEG was normal and EMG-nerve conduction of the bilateral lower extremities was essentially normal.

Based on her presentation and elevated anti-GAD titer, the patient was started on IVIG. On follow up after 12 weeks, she reports significantly improved stiffness with near normal ambulation. Symptoms were exacerbated by stress and anxiety. She works as a teacher. Diazepam alleviates both her anxiety and stiff-person symptoms. Sixteen years after her diagnosis, she sustained a fall and was not able to resume her teaching job.

Discussion

Stiff-person syndrome is uncommon with incidence of 1 case per million per year. It mainly affects ages 20 to 50 with women affected more than men.[1] The original classic description of SPS include painful spasms, rigidity and hyperlordosis. Since the original description, additional phenotypes are reported. They include partial SPS, with symptoms limited to extremities, often involving only one limb or only the torso; SPS-plus with classic symptoms along with cerebellar and/or brainstem findings, as well as other syndromes.[2] SPS diagnosis is challenging. Several features aid accurate diagnosis: exaggerated startle, stimuli-triggered spasms, unexplained falls, personal autoimmunity; abnormal limb and lumbar spine examination all predict SPS diagnosis.[3] Extreme rigidity can cause falls and spinal deformities. Paroxysms of autonomic dysfunction such as diaphoresis, high fevers, tachypnea, tachycardia, pupillary dilatation and elevated BP may cause sudden death.[4] Deaths from respiratory causes include diaphragmatic spasms, severe respiratory muscle rigidity[5,6] and aspiration from esophageal dysmotility and swallowing problems.[7]

An autoimmune component is thought to be the pathogenesis of SPS. It is associated with type 1 diabetes mellitus, thyroiditis, vitiligo and pernicious anemia. There is association between anti-glutamic acid decarboxylase (GAD) antibodies and SPS.[8,9] These antibodies mainly target GABAergic neurons. The dominant targeted antigen recognized is GABA synthesizing enzyme GAD.[10]

Clinical and paraclinical markers (e.g. high titer anti-GAD 65 antibody) are used for clinical diagnosis. Elevated anti-GAD antibody titers greater than 1000 u/ml are present in 60-80 % of patients.[1] EMG's show excessive muscle activation with acoustic startle or exteroceptive stimulus or presence of continuous paraspinal or agonist/antagonist muscle activity.[3]

Treatment is aimed at relieving symptoms and improving function. Benzodiazepines, baclofen are given initially. With continued symptoms, IVIG and plasma exchange or B cell depletion with rituximab have been used.

The prognosis for SPS varies after functional decline and progressive disability.

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