LETTER TO THE EDITOR

To The Editor

Adolescent Stiff Person Syndrome: Long-Term Symptom Remission on Immunomodulatory Therapy

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A 15-year-old female presented to emergency with a 1½-week-history of progressive difficulty in bending her left knee. She also developed tightness of the musculature and occasional spontaneous "twitching" and visible spasms of the left quadriceps. Her balance and co-ordination had worsened over a similar period of time. She was able to ambulate with her knee rigidly extended, but had fallen once on the stairs. Initially, no symptoms were noted at other joints.

The associated symptoms included an ill-defined numb sensation around both knees in a band distribution, but without loss of sensation or paresthesia. There was no saddle anesthesia, no bowel or bladder symptoms, and no weakness. She was previously well, with no significant past medical or family history, and was on oral birth control.

On examination, the range of motion at the left knee was limited to 5 degrees of flexion. A clear spastic catch was noted at the right knee, with clonus at the right ankle, and mildly reduced range of motion at the left ankle. Left patella reflex was 4+ (clonus). Reflexes were otherwise 2+, and toes were downgoing. Her left leg remained fixed and straight during ambulation. Neurologic and musculoskeletal examinations otherwise unremarkable. Spontaneous contractions were observable in the left quadriceps.

Over the following 2–3 weeks, she developed increasing stiffness in the lower extremities and lower trunk to the extent that both knees could not be flexed. She became unable to ambulate safely due to poor stability and would have sudden jerks evoked by touch or surprise, leading to falls.

Initial investigations included needle electromyography (EMG), revealing spontaneous near continuous motor unit activity in the left quadriceps, which disappeared with voluntary activation. The serum anti-GAD (glutamic acid decarboxylase) 65 antibodies were very high (>25,000 units/mL). A lumbar puncture was considered, but deferred. Magnetic resonance imaging (MRI) of the brain and whole spine was normal. Bloodwork for autoimmune disorders including diabetes was negative. Subsequent whole body positron emission tomography - computed tomography (PET/CT) was negative. Testing for further stiff person spectrum associated antibodies was deferred due to diagnostic anti-GAD 65 antibodies and low index of suspicion of a paraneoplastic process.

Treatment with diazepam and baclofen mildly reduced the frequency of spasms and severity of stiffness, but both knees remained locked, and dosage was limited by sedation. She continued to need a walker to ambulate safely and to have stiffness in all prior locations. Immunotherapy was initiated, initially with intravenous (IV) methylprednisolone (20 mg/kg × 3 days), then intravenous immunoglobulin (IVIG) (2 g/kg over 2 days), and followed by rituximab (500 mg/m^2) 2 weeks later. Consequently, she regained the ability to flex her knees voluntarily.

She improved significantly over the following 3 months, with resolution of subjective symptoms, and resumption of prior function. With maintenance therapies, she subsequently developed a significant drug reaction to her third exposure to rituximab (progressive rashes on face/trunk, fever, and nausea). She declined prednisone (concern over weight gain) and did not tolerate a reduced dexamethasone dose of 12 mg × 3 days every 2 weeks due to migraines. As such, she was maintained on IVIG monotherapy (1 g/kg/day monthly).

At one point, discontinuation of IVIG was attempted at the patient's request due to difficult IV access. However, after 5½ weeks, she re-presented to emergency with recurrence of her prior prodromal symptoms, with a band of abnormal sensation around the knees bilaterally. Of note, her symptoms dissipated within 2 days of a 1.5 g/kg IVIG loading dose (administered over 2 days). IVIG 1 g/kg/day per month was restarted and maintained without further relapses. She is currently asymptomatic with restored function at over 2 years and 3 months of follow-up. She continues to have a residual catch at the knees. Her serum anti-GAD 65 titer remains elevated (>25,000 units/mL). In the interim, mycophenolate was introduced for a few weeks, but discontinued due to the emergence of severe mouth sores.

Stiff person syndrome (SPS) is a rare debilitating autoimmune disorder typically characterized by lumbar and lower extremity stiffness plus superimposed muscle spasms and high anti-GAD antibodies.[1] Childhood SPS with GAD seropositivity is rarely reported, with 11 GAD seropositive cases in total in the literature.[2–6] Three of these demonstrated glycine receptor alpha-1 subunit autoantibodies, though this testing was not readily available.[2]

Our patient has had an essentially complete response to immunotherapy. Her rapid and significant response contrasts with moderate improvements seen in larger studies.[7] Total resolution of symptoms is atypical; it has not been reported in GAD 65 positive pediatric patients to the best of our knowledge. Our patient also presented within weeks of first symptoms, compared to a mean delay of 14 years for patients with pediatric onset (some diagnosed in adulthood).[2] This early treatment may have contributed to her positive response.

In the adult literature, IVIG had positive effects in a small randomized controlled trial.[7] The degree of sensitivity of our patient to IVIG therapy, with recurrence of symptoms on discontinuation of therapy and rapid resolution on resumption of treatment, is noteworthy. Though very subjective, heightened sensitivities and anxiety are recognized as acquired comorbidities in SPS.[1,7] There are four other reports of GAD positive SPS pediatric patients receiving IVIG therapy, three with positive responses, but not complete recovery,[2,5] and one with poor effect.[2]

This is the third report of a rituximab trial in a child with SPS, with a positive response in both prior cases.[4,6]

Our patient presented with primarily asymmetric leg involvement, with less prominent trunk symptoms, which while less typical of classic SPS, it is described.[2,8] One reason for this difference may also be that our patient was diagnosed relatively early, after less than a month of symptoms. In at least some cases, the severe truncal rigidity occurred later in the disease course, as progression after onset in one limb.[4,5,8]

In summary, this case highlights that pediatric SPS can be effectively managed with early immunomodulatory therapy.

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Furthermore, it supports the role of IVIG monotherapy in maintaining remission, particularly if other treatments are not tolerated.

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Disclosures

None.

Statement of Authorship

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