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Immunological, Physical, and Psychological Interventions in Young-Onset Stiff-Person Syndrome

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Dear Editor,

Young-onset stiff-person syndrome (SPS) is rare, with most patients presenting initially to non-neurology doctors, and the majority not being diagnosed until adulthood.[1]

A 16-year-old female presented with progressively unsteady gait that first appeared at the age of 13 years. At 12 years old she noticed generalized body aches when remaining in one position for too long, and at 14 years old she started experiencing recurrent falls, leading to worsening basophobia. At home, she was extremely anxious about climbing stairs or taking a shower, and she feared crossing roads when outside. She was easily startled by sound and touch sensations, which triggered painful muscle spasms. She had a normal intellect and no relevant family history. She first sought medical help at 15 years old, and was diagnosed with anxiety and depression. After receiving a third opinion, the patient consulted a neurologist.

A physical examination revealed prominent axial stiffness and rigidity (Supplementary Video 1, Section 1 in the online-only Data Supplement). She had a forward-leaning posture with thoracic and cervical hyperlordosis. Her gait was stiff, wide-based, and high-stepping due to stiffness. She had an exaggerated startle response and a positive head-retraction reflex.

Laboratory investigations revealed elevated creatinine kinase (302 U/L; normal, 29−168 U/L) and lactate dehydrogenase (275 U/L; normal, 130−250 U/L). Antinuclear antibodies were positive, and extractable nuclear antigens were negative. Serum anti-glutamic-acid decarboxylase (anti-GAD) antibodies were strongly positive, at >2,000 IU/mL (normal, <10 IU/mL). CSF demonstrated five unique intrathecal oligoclonal bands. Brain MRI was unremarkable, while whole-spine MRI demonstrated premature scoliosis. Serology tests for type 1 diabetes and autoimmune thyroid disease were negative. Surface EMG revealed continuous motor-unit activity of the paraspinal muscles, which increased during spontaneous painful muscle spasms (Supplementary Video 1, Section 2 in the online-only Data Supplement).

Treatment with clonazepam (0.5 mg TDS) and baclofen (10 mg BDS) was inadequate, and so two cycles of IVIG at 0.5 mg/kg were administered over 5 days. Repeat EMG demonstrated a significant reduction in motor-unit activity, and her gait visibly improved (Supplementary Video 1, Section 3 in the online-only Data Supplement). Weekly physical therapy sessions comprising massage and stretching exercises significantly relieved the muscle stiffness, while psychotherapy and cognitive behavioral therapy (CBT) alleviated her anxiety and basophobia. The clinical improvement was sustained at 3 months post-IVIG, and the patient resumed participating in sports at school. Her anti-GAD antibody had decreased to 250 IU/mL. Symptom progression was reviewed at 3-monthly follow-ups.

Young-onset SPS accounts for 5% of SPS cases.[2] The median age at symptom onset is 11 years (range, 1−15 years).[1] The most commonly associated antibody is anti-GAD65, followed by anti-glycine-receptor antibody. Paraneoplastic antiamphiphysin antibody has been reported with a pediatric malignancy.[3] Concurrent autoimmune diseases are common and must be screened for, especially autoimmune thyroid disease and autoimmune diabetes. A family history of auto-

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immune diseases may be present, particularly type 1 diabetes.[4]

Due to its rarity, young-onset SPS can be mistaken for hereditary spastic paraparesis, spastic cerebral palsy, generalized dystonia, or parkinsonism. Bizarre and fluctuating symptoms including task-specific phobia (e.g., when crossing streets), agoraphobia, exacerbation of symptoms with emotional stress, startle, and anxiety, which could be mistaken for psychogenic movement disorder. Furthermore, comorbid psychiatric illnesses are common,[5,6] and misdiagnosis can result in further decline in the mental health of these young patients. Clinicians should therefore consider SPS in children with insidious body stiffness, muscle spasms occurring spontaneously or triggered by innocuous auditory or tactile stimuli, and a rigid wide-based gait, especially if they have normal cognition.

Young-onset SPS cases are described in the supplementary tables reported by Clardy et al.[1] and Yeshokumar et al.[4] Compared with adult-onset SPS, young-onset SPS might be less likely to be associated with malignancy. Psychiatric comorbidities in young-onset SPS may be more difficult to recognize, since the vocabulary of children might not have developed sufficiently for them to express their emotions intelligibly. Almost all young-onset cases require early immunotherapy.[4] Furthermore, a top-down approach (i.e., early use of immunotherapy) may be prudent in young-onset SPS to reduce long-term disability.

Physical therapy is relevant in the management of SPS, although evidence is limited to case studies in adults.[7,8] Psychotherapy probably plays an important role especially in young-onset SPS due to the greater fragility of the mental health of younger sufferers. CBT alleviates anxiety and phobias in adult-onset SPS,[9] but this has not been studied in a pediatric setting. The present case suggests that physical therapy, psychotherapy, and CBT are useful in young-onset SPS.

For patients receiving IVIG, regular infusions may be required when the treatment efficacy starts decreasing. In the long term, most SPS patients progressively become more disabled, especially regarding their gait. Given the longer duration of disability accumulation in young-onset SPS, life expectancy may be more-adversely affected than in adult-onset cases.

Young-onset SPS is rare, but it presents with a unique constellation of signs and symptoms, frequently coupled with an autoimmune background. Physical therapy, psychotherapy, and CBT may be as important as pharmacotherapy in its management. Awareness of this condition will allow earlier diagnosis and treatment, thus maximizing the functional status of affected patients.

Supplementary Video Legend

Video 1. Clinical examination and EMG of the patient with young-onset stiff person syndrome. Section 1: The patient demonstrated difficulty in bed transfers due to axial stiffness and rigidity. Thoracic and cervical hyperlordosis was present, as was a stiff, wide-based, and high-stepping gait. The startle response was exaggerated. Section 2: Paraspinal EMG showed continuous motor-unit activity that increased during painful muscle spasms. Section 3: Post-IVIG, EMG showed reduced motor-unit activity and improved gait.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.3988/jcn.2022.18.4.487.

Ethics Statement

Written informed consent was obtained from the participant in this study.

Availability of Data and Material

Data sharing not applicable to this article as no datasets were generated or analyzed during the study.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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