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Childhood Stiff-Person Syndrome Improved with Rituximab

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Abstract

Go to:

Introduction

Stiff-person syndrome (SPS) is manifested by fluctuating rigidity of axial musculature with painful episodic spasms due to simultaneous co-contraction of agonist and antagonist muscles. We present a case report and video illustrating response to treatment with rituximab.

Materials and Methods

Case description and video are provided. A literature search for other reports of treatment with rituximab was performed.

Results

Nine cases in addition to our case were described. Substantial clinical benefit was reported in 7/9 (78%) cases. Four out of 9 (44%) cases displayed persistent anti-glutamic acid decarboxylase (GAD) antibody positivity.

Conclusion

Rituximab is an important treatment strategy in SPS. The persistence of anti-GAD antibody positivity even with clinical remission remains to be elucidated.

Key Words: Rituximab, Stiff-person syndrome, Myoclonus

Introduction

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Stiff-person syndrome (SPS), first described by Moersch and Woltman in 1956 [1], typically presents between the 3rd and 6th decade of life and is manifested by fluctuating rigidity of axial musculature with painful episodic simultaneous co-contraction of agonist and antagonist muscles. Episodes may be triggered by tactile,

emotional, or auditory stimuli. Comorbid anxiety may be present which may raise suspicion of a psychogenic disorder and delay diagnosis [2]. Antibodies against glutamic acid decarboxylase (GAD), gamma-amino butyric acid A receptor-associated protein, and amphiphysin I have been identified in this disorder [2, 3].

Case Report

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The patient is a 12-year-old right-handed Hispanic boy who presented for evaluation of painful axial muscle contractions and exaggerated startle response.

His first symptom, stiffness of the right leg during ambulation, occurred at age 5. At age 7, he had a generalized seizure lasting 5 min with unresponsiveness and jerking movements of all extremities, but without tongue biting, bowel or bladder incontinence. He was controlled on levetiracetam until age 11. At that time, he developed episodes of nightly awakening with a prodrome of anxiety and tachycardia typically followed by up to 20 min of painful hyperlordotic posturing. Occasional episodes lasted for up to 2 h. Frequency of episodes gradually worsened from once to several times a day. Startle response to auditory and tactile stimuli triggered many of the episodes. In order to prevent falls, the patient became wheelchair bound. There is no family history of similar disorder, but there is consanguinity (the patient's paternal grandmother and grandfather are second cousins).

On examination, the patient manifested sustained right ankle clonus, markedly contracted thoracolumbar paraspinal muscles, hyperlordotic posture, and classic 'board-like' abdomen. Tactile or auditory stimulation triggered episodes with right lower extremity sustained myoclonus, diaphoresis, painful exacerbation of the hyperlordosis with thoracolumbar axial and abdominal muscle co-contraction, and rocking movements which were likely a response to the axial contraction.

Magnetic resonance imaging of the brain and video electroencephalography studies were normal. Anti-GAD antibody was positive at 4,405 nmol/l, but there were no detectable anti-amphiphysin antibodies. Muscle biopsy was normal. There was mild improvement with diazepam or clonazepam and monthly intravenous immunoglobulin treatment (IV Ig) [4]. Baclofen and gabapentin did not improve his symptoms. A course of rituximab, a monoclonal antibody which binds to B-lymphocyte CD surface antigens, consisting of two 500 mg/m^2 treatments spaced 14 days apart, markedly reduced the frequency and severity of axial contractions, diminished startle response, and abolished sustained ankle clonus. Most importantly, his gait markedly improved and he is now able to ambulate with minimal assistance, partly because of residual phobia of falling (for online suppl. video, see www.karger.com/doi/10.1159/000339446). Post-treatment anti-GAD antibody levels were not available.

Materials and Methods

A Medline search for 'stiff-person syndrome' and 'rituximab' was performed.

Results

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The initial Medline search yielded 12 articles, of which 8 were relevant case reports [5, 6, 7, 8, 9, 10, 11, 12]. The details are provided in **table 1**. Substantial clinical benefit was reported in 7/9 (78%) cases (1 report described monozygotic twins). In 4/9 (44%) of these cases, anti-GAD antibodies remained positive after treatment.

Table 1

Summary of reported SPS cases treated with rituximab

Discussion

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This childhood case demonstrates the classic features of SPS and the remarkable clinical improvement with rituximab (table 1; online suppl. video). Thus, rituximab should be added to other treatments of SPS such as IV Ig, plasmapheresis, cyclophosphamide, and mycophenolate. Other antispasmodic treatments reported to be effective in patients with SPS include tizanidine, piracetam, phenobarbital, and local botulinum toxin injections [5].

Although a double-blind placebo-controlled trial of rituximab on 2 patients 'did not support a profound benefit' [7], experience with rituximab, based on open-label case reports, has suggested that at least 2 doses of rituximab at 350–375 mg/m²/infusion spaced 1–2 weeks apart [5, 12] or 4 weekly infusions [9] provide clinically meaningful improvement in SPS symptoms. If a relapse occurs, a repeat dose 6–8 months later may be needed [9, 12].

Hence, rituximab should be considered as an effective and less expensive alternative in patients with SPS and other autoimmune movement disorders who fail to obtain adequate response to benzodiazepines and other conventional antispasmodic and immunologic therapies [13].

Disclosure Statement

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Supplementary Material

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Supplemental Video

Click here for additional data file. (11M, mov)

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