

Case Reports

Prominent Bilateral Hand Tremor in Hashimoto's Encephalopathy: A Video Demonstration

Kanterpersad Ramcharan^{1*}, Nadeem Hosein¹, Joel David Teelucksingh², Fidel Rampersad^{3,4} & Surujal Teelucksingh⁴

¹ Neurology Unit, San Fernando Teaching Hospital, University of the West Indies, San Fernando, Trinidad and Tobago, ² Endocrinology Unit, San Fernando Teaching Hospital, University of the West Indies, San Fernando, Trinidad and Tobago, ³ Interventional Radiology, University of the West Indies, St Augustine, Trinidad and Tobago, ⁴ Department of Clinical Medical Sciences, University of the West Indies, St Augustine, Trinidad and Tobago

Abstract

Background: Hashimoto's encephalopathy often presents with neuropsychiatric manifestations including seizures and movement disorders.

Case Report: We describe a patient who presented with bilateral hand tremor and mild cognitive defects that fulfilled the criteria for a diagnosis of Hashimoto's encephalopathy. There was a rapid response to glucocorticoid therapy with relapse following treatment withdrawal.

Discussion: Recently published clinical criteria for the diagnosis of Hashimoto's encephalopathy include seizures, myoclonus, hallucinations, or stroke-like episodes but do not include tremor. Our case had mild cognitive dysfunction and a coarse tremor as the predominant clinical features, which probably represent mild disease.

Keywords: Tremor, movement disorders, Hashimoto's encephalopathy, steroid-responsive encephalopathy associated with autoimmune thyroiditis

Citation: Ramcharan K, Hosein N, Teelucksingh JD, et al. Prominent bilateral hand tremor in Hashimoto's encephalopathy: A video demonstration. Tremor Other Hyperkinet Mov. 2016; 6. doi: 10.7916/D8PV6KJB

*To whom correspondence should be addressed. E-mail: kramcharan79@yahoo.com

Editor: Elan D. Louis, Yale University, USA

Received: July 30, 2016 **Accepted:** September 6, 2016 **Published:** October 12, 2016

Copyright: © 2016 Ramcharan et al. This is an open-access article distributed under the terms of the Creative Commons Attribution–Noncommercial–No Derivatives License, which permits the user to copy, distribute, and transmit the work provided that the original authors and source are credited; that no commercial use is made of the work; and that the work is not altered or transformed.

Funding: None.

Financial Disclosures: We have nothing to declare.

Conflict of Interest: None.

Ethics Statement: Patients that appear on video have provided written informed consent; authorization for the videotaping and for publication of the videotape was provided.

Introduction

Autoimmune encephalitis resulting from many recently discovered antibodies can induce an array of rare illnesses, many of which can cause movement disorders. One such illness, Hashimoto's encephalopathy (HE, also called steroid-responsive encephalopathy associated with autoimmune thyroiditis [SREAT]) is increasingly recognized as a cause of neuropsychiatric morbidity. Recently proposed consensus criteria for HE diagnosis are a major step forward in helping clinicians identify cases of autoimmune encephalitis caused by antibodies to neuronal surface antigens and synaptic proteins and promptly initiate treatment while awaiting research laboratory confirmation.¹ Coarse tremors and myoclonus are often seen in this illness.^{2–5} Higher titers of serum thyroperoxidase antibodies are also correlated with more favorable outcomes.⁶ The illness is characterized by its responsiveness to steroid treatment. We report a case illustrating prominent coarse hand tremors with cognitive impairment but only moderate thyroid

antibody elevation. We discuss challenges in the diagnosis and treatment due to the evolving status of this disorder.

Case Report

A 34-year-old previously healthy female developed progressively worsening, predominantly postural bilateral hand tremor over 3 months (Video 1A). Difficulty concentrating, memory lapses, slowed mentation, apathy, myalgia, and weight loss of 7 kg developed over the 3-month period causing frequent absenteeism from work. A history of catamenial exacerbations of symptoms was negative. The family history was unremarkable.

Her Mini Mental Status Examination (MMSE) score was 30, and the patient declined to see a neuropsychologist or psychiatrist for further cognitive testing. There was a prominent, asymmetric, rhythmic, involuntary tremor of both hands only; it predominantly involved the fingers and was worse in the right hand. It was minimally present at rest (resting tremor) and during activities (kinetic tremor)



Video 1. Segment 1A. Subject at presentation. Hands held outstretched showing a postural hand tremor more prominent in the right hand. **Segment 1B. Subject after relapse.** Postural hand tremor relapse following steroid withdrawal. **Segment 1C. Subject after steroid re-introduction.** Significant tremor reduction on steroid treatment.

and was most prominent on outstretching the hands (postural tremor) as shown in Video 1A. It was also present on the finger to nose test (intention tremor). The tremor had high frequency and moderate amplitude (Video 1A). There was neither entrainment nor change on distraction to support a diagnosis of psychogenic tremor. Features of parkinsonism or dystonia were not present. The rest of the physical exam was normal apart from the presence of mild, diffuse thyroid enlargement.

Blood investigations revealed a normal full blood count, liver function, renal function, collagen vascular screen, and serum copper and serum ceruloplasmin levels. The erythrocyte sedimentation rate was 25 mm/hour. Serum thyroxine, tri-iodothyronine, and thyroid-stimulating hormone were repeatedly within normal ranges. Ultrasonography revealed the presence of mild diffuse thyroid enlargement with solid and cystic components, and fine-needle biopsy revealed characteristics consistent with thyroiditis. Magnetic resonance imaging (MRI) of the brain including T2 fluid-attenuated inversion recovery sequences and diffusion studies, magnetic resonance angiography of the brain, MRI of the spinal cord, and electroencephalogram were normal. Computed axial tomography of the chest, abdomen, and pelvis showed no evidence of malignancy.

The patient’s antithyroid antibodies were only moderately elevated (Table 1). Antibodies to glutamic acid decarboxylase, N-methyl-D-aspartate receptor, and voltage-gated calcium and potassium channels were also all normal (Table 1). Serum autoantibody measurement against the N-terminal of α -enolase and neurophysiologic tremor studies were unavailable. Consent for lumbar puncture was not obtained.

Probable HE was diagnosed, and prednisolone at a dosage of 10 mg orally three times daily was started. After 3 months of treatment, the patient’s tremors had diminished significantly and her subjective cognitive dysfunction was almost completely resolved, but the

Table 1. Serum Antibody Panel

Antibody	Level	Reference Range
Anti thyroglobulin antibody	98.2	0–40 IU/ML
Antithyroid receptor antibody	6.6	>2 IU/L, positive
Antithyroperoxidase	32	0-35 IU/mL
Fixed NMDAR antibody	Negative	Negative
Anti-VGCC antibody	Negative	0–45 pmol/L
Anti-VGKC antibody	6	0–69 pmol/L
Anti-GAD antibody	Negative	Negative

Abbreviations: GAD, Glutamic Acid Decarboxylase; NMDAR, N-methyl-D-aspartate Receptor; VGCC, Voltage-gated Calcium Channel; VGKC, Voltage-gated Potassium Channel.

prednisolone dosage was gradually reduced to 5 mg daily because of weight gain. Unfortunately, there was relapse of tremor (Video 1B) and subjective cognitive symptoms, but re-introduction of prednisolone 60 mg daily led to tremor disappearance within 48 h (Video 1C). Cognitive symptoms again improved over the next few weeks. As a steroid-sparing measure, azathioprine 50 mg orally daily was started with low-dose prednisolone; this regimen controlled the patient’s symptoms and allowed her to return to work. After 8 weeks, her liver enzymes were elevated, and azathioprine had to be withdrawn. Liver enzyme levels subsequently returned to normal in 6 weeks. Despite this, after 8 months of follow-up the patient remains minimally symptomatic, fully functional, and has resumed a normal lifestyle on oral prednisolone 5 mg daily.

Discussion

Recent expert consensus criteria on autoimmune encephalitis suggest that a diagnosis of HE can be made when all six of the following criteria have been met: 1) encephalopathy with seizures, myoclonus, hallucinations, or stroke-like episodes; 2) subclinical or mild overt thyroid disease (usually hypothyroidism); 3) brain MRI normal or with nonspecific abnormalities; 4) presence of serum thyroid (thyroid peroxidase, thyroglobulin) antibodies; 5) absence of well-characterized neuronal antibodies in serum and cerebrospinal fluid (CSF); and 6) reasonable exclusion of alternative causes.¹ However, it was noted that there was no disease-specific cut-off value for these antibodies; antithyroid antibodies are detected in 13% of healthy individuals.^{1,7}

This case fulfils most of the above criteria (apart from CSF analysis) and highlights bilateral coarse hand tremor as a feature at presentation, which was previously described.⁴ Cognitive dysfunction in this case was subtle and not readily objectively detected at the bedside (perfect MMSE score of 30). The mild symptoms, moderate elevation

of antithyroid antibodies, and absence of neuroimaging and electroencephalographic abnormalities suggest that our patient probably has a mild form of the disease. The observation of catamenial worsening of tremor and myoclonus in HE has also been previously noted, and both have been replicated by intravenous administration of thyrotropin-releasing hormone.⁵ Catamenial symptom exacerbation was not noted in this case.

Autoimmune encephalitis has been associated with various antibodies to neural and synaptic proteins, and in our case assays of were negative apart from antithyroid antibodies, thus ruling out other known possible causes for the patient's symptoms (Table 1).

A limitation of this study was the unavailability of neurophysiologic studies of this tremor as previously summarized by Hess and Pullman.⁸ Serial neuropsychological testing could have been used to assess subtle cognitive dysfunction in this case,^{9,10} but the patient declined to see a psychiatrist or psychologist.

Video demonstration of movement disorders in HE/SREAT is uncommon, and the purpose of this report is to draw attention to this entity in patients presenting with hand tremor and neuropsychiatric symptoms. New-onset hand tremor is a common clinical presentation to neurologists, and HE/STREA T should be considered in the differential diagnosis.¹¹ It is becoming increasingly clear that patients with autoimmune encephalitis fare better when treated earlier with glucocorticoid and immunosuppressive, and this may also hold true for HE/SREAT.¹

Acknowledgments

We thank the patient for consenting to allow her medical data to be published. We thank Dr. S.R. Irani, Dr. Patrick Waters, the Oxford Immunology labs (Department of Immunology, Oxford University Hospitals), NHS Foundation Trust, and the Churchill Hospital, for assistance with some of the neuroimmunological tests. Dr. S. Karim helped prepare the video.

References

1. Graus F, Titulaer MJ, Balu R, et al. A clinical approach to diagnosis of autoimmune encephalitis. *Lancet Neurol* 2016;15:391–404. doi: 10.1016/S1474-4422(15)00401-9.
2. Payer J, Petrovic T, Lisy L, Langer P. Hashimoto encephalopathy: a rare intricate syndrome. *Int J Endocrinol Metab* 2012;10:506–514. doi: 10.5812/ijem.4174.
3. Montagna G, Imperiali M, Agazzi P, et al. Hashimoto's encephalopathy: A rare proteiform disorder. *Autoimmun Rev* 2016;15:466–476. doi: 10.1016/j.autrev.2016.01.014.
4. Gücüyener K, Serdaroglu A, Bideci A, Yazman Y, Soysal AS, Cinaz P. Tremor and myoclonus heralding Hashimoto's encephalopathy. *J Pediatr Endocrinol Metab* 2000;13:1137–1141. doi: 10.1515/JPEM.2000.13.8.1137.
5. Ishii K, Hayashi A, Tamaoka A, Usuki S, Mizusawa H, Shoji S. Case report: thyrotropin-releasing hormone-induced myoclonus and tremor in a patient with Hashimoto's encephalopathy. *Am J Med Sci* 1995;310:202–205. doi: 10.1097/00000441-199511000-00005.
6. Litmeier S, Prüss H, Witsch E, Witsch J. Initial serum thyroid peroxidase antibodies and long-term outcomes in SREAT. *Acta Neurol Scand* 2016 Jan 12. [Epub ahead of print]. doi: 10.1111/ane.12556.
7. Hollowell JG, Staehling NW, Flanders WD, et al. Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *J Clin Endocrinol Metab* 2002;87:489–499. doi: 10.1210/jcem.87.2.8182.
8. Hess CW, Pullman SL. Tremor: clinical phenomenology and assessment techniques. *Tremor Other Hyperkinet Mov* 2012;2. doi: 10.7916/D8WM1C41.
9. Mazzù I, Mosti S, Caltagirone C, Carlesimo GA. Hashimoto's encephalopathy: neuropsychological findings. *Neurol Sci* 2012;33:653–656. doi: 10.1007/s10072-011-0813-z.
10. Wang J, Zhang J, Xu L, Shi Y, Wu X, Guo Q. Cognitive impairments in Hashimoto's encephalopathy: a case-control study. *PLoS One* 2013;8:e55758. doi: 10.1371/journal.pone.0055758.
11. Deuschl G, Bain P, Brin M. Consensus statement of the Movement Disorder Society on Tremor. Ad Hoc Scientific Committee. *Mov Disord* 1998; 13 Suppl 3:2–23. doi: 10.1002/mds.870131303.