Hashimoto's Encephalopathy: Case Report and Literature Review

Charles F. Guardia^{1*} and James L. Bernat²

¹Section of Sleep Medicine, Dartmouth Hitchcock Medical Center, USA

²Department of Neurology, Dartmouth Hitchcock Medical Center, USA

Received: October 30, 2013; Accepted: January 31, 2014; Published: February 04, 2014

*Corresponding author: Charles F. Guardia, Dartmouth Hitchcock Medical Center, One Medical Center Drive, Lebanon, NH 03756, USA, Tel: 603-650-3630; E-mail: Charles.F.Guardia@hitchcock.org

Keywords: Hashimoto's Encephalopathy; Non-vasculitic autoimmune meningoencephalitis

Introduction

Hashimoto's encephalopathy is a rare disorder that causes relapsing-remitting or progressive confusion, impaired consciousness, seizures, ataxia, psychosis and myoclonus [1]. It is thought to be immune-mediated, though its exact pathophysiology remains speculative. It is also called non-vasculitic autoimmune meningoencephalitis, reflecting evidence of small vessel vasculitis [1-3]. We recently treated a patient with Hashimoto's encephalopathy who responded well to glucocorticoid therapy and cyclophosphamide.

Case Presentation

A 43 year old right-handed man had a generalized tonic-clonic seizure necessitating intubation. Examination revealed spasticity, hyperreflexia, ankle clonus, and T= 38 C. Electrolytes, thyroid function tests, liver function tests, B12, folate, and ammonia were normal. CSF was negative for viral serologies including HSV, enterovirus, and arbovirus. Brain MRI with gadolinium was normal. A diagnosis of encephalitis was entertained. His cortisol level was low and he was discharged on a steroid taper.

He was re-admitted a few weeks later with increasing confusion, headaches and a generalized tonic-clonic seizure. EEG showed generalized slowing. CSF was normal including tests for HSV, EBV, Lyme, Cryptococcus, CMV, and VZV. He was treated with phenytoin, his sensorium cleared and he left against medical advice only to be re-admitted a week later after another seizure. Examination disclosed paranoid psychosis with delusions. Phenytoin was discontinued and Carbamazepine begun. EEG remained diffusely slow. Serum and urine protein electrophoresis, paraneoplastic panel, CT of the chest, abdomen and pelvis, and testicular ultrasound were normal. Brain MRI demonstrated diffusely increased cortical signal in FLAIR sequences bilaterally (Figure 1). Brain MRA was normal. CSF showed a lymphocytic pleocytosis and elevated protein.

Serologies for T. gondii, syphilis (serum and CSF) were

negative. c-ANCA, p-ANCA, MPO, PR3, HIV, urine porphyrins and a heavy metal screen were negative. Thyroid function tests, including thyroid stimulating immunoglobulins, were normal. CSF JC virus PCR was positive and negative on repeat. Pancerebral angiography showed normal appearing cerebral vessels.

He improved after treatment with high dose glucocorticoid therapy and IV-Ig. Thyroid peroxidase antibodies were elevated at 410 IU/mL (normal <34 IU/mL). Thyroid-stimulating antibodies were <1 (normal <1.3) in the setting of a normal quantitative immunoglobulin screen. Thyroid ultrasound showed heterogeneous echogenicity in both lobes. He was treated with high-dose intravenous glucocorticoid therapy followed by a slow taper. Thereafter, he became more alert, conversant and demonstrated marked lessening of myoclonus and ataxia. Brain

Figure 1: MRI Brain. FLAIR Sequence demonstrating increased signal over several cerebral sulci overlying the convexity.

MRI improved. Prednisone was slowly tapered. His psychosis was managed with Quetiapine and Haldol. He remains seizure-free on Levetiracetam and Valproate.

Discussion

Hashimoto's encephalopathy is a controversial disorder with an estimated prevalence of 2.1/100,000 and mean age of onset of 42 years [1]. Patients present, like ours, with acute or subacute confusion, altered sensorium, myoclonus (38%), ataxia, psychosis (30%), diffuse hyperreflexia (85%) and focal or generalized tonic-clonic seizures (67%) [1,4]. The disease can be progressive, manifesting as dementia with cognitive impairment, confusion and hallucinations with rapid progression to coma [1,5].

Antithyroid antibodies – anti-thyroid peroxidase antibody (TPOAb) and or antithyroglobulin antibody (TgAb) – are the hallmark of this disease. There is no clear relationship between the severity of neurologic illness and serum concentration of antibody titers. Interestingly, the serum concentration does not correlate with treatment. Sensitivity ranges from 73-100% for these antithyroid antibodies [1]. Serum auto-antibodies against the anti NH2-terminal of alpha enolase (NAE) have been implicated as a diagnostic marker for Hashimoto's encephalopathy with sensitivity of 90% and specificity of 50%. However, this particular auto-antibody needs to be evaluated further prior in order to elucidate its diagnostic as well as prognostic potential [6].

Patients have thyroid dysfunction. Overt hypothyroidism is seen in 17-20% of patients, 7% are hyperthyroid, and 38-47% are euthyroid [1]. Our patient was euthyroid.

CSF protein elevation is seen in 75% and lymphocytic pleocytosis is present in 10-25% [1]. Our patient demonstrated elevated protein, peaking at 70mg/dL, and lymphocytic pleocytosis. CSF oligoclonal bands have been reported [1] but were absent in our patient. Information regarding sequential CSF analysis in the literature is lacking.

Electroencephalographic abnormalities, when present, are usually nonspecific. Background slowing is observed in 94% of patients. Sharp waves and transient epileptic activity are less commonly seen [1,2,4]. Our patient demonstrated background slowing on several EEGs.

Neuroimaging usually is normal. However, nonspecific T2 sequence abnormalities in the subcortical white matter and focal white matter changes suggestive of demyelination have been described [1,7]. Follow-up imaging is often not obtained, but in some cases the MRI findings regress or resolve [1]. Our patient

demonstrated increased signal on the FLAIR sequence that regressed following glucocorticoid therapy.

Glucocorticoids are the mainstay of therapy in individuals afflicted with Hashimoto's encephalopathy. Systematic investigation into other immunosuppressants in the treatment of this disease is lacking. However, there are reports of anecdotal success with Azathioprine, Methotrexate and Mycophenolate mofetil, and intravenous immunoglobulin either alone, or in combination with Glucocorticoids [1,8]. Cyclophosphamide was chosen in our patient for its effective CNS penetration.

Clinicians should consider Hashimoto's encephalopathy in young patients with unexplained encephalopathy or rapidly progressing dementia. Elevated serum levels of anti-TPOAb and TgAb's coupled with a marked response to corticosteroids is diagnostic. Hashimoto's encephalopathy should be considered in the differential diagnosis of encephalopathies of unknown cause or rapidly-progressing neurodegenerative disorders because it is treatable and often has a favorable prognosis.

References

1. Marshall GA, Doyle JJ (2006) Long-term treatment of Hashimoto's encephalopathy. *J Neuropsychiatry Clin Neurosci* 18(1): 14-20.
2. Rodriguez AJ, Jicha GA, Steeves TD, Benarroch EE, Westmoreland BF (2006) EEG changes in a patient with steroid-responsive encephalopathy associated with anti-bodies to thyroperoxidase (SREAT, Hashimoto's Encephalopathy). *J Clin Neurophysiol* 23(4): 371-373.
3. Fatourehchi V (2005) Hashimoto's encephalopathy: myth or reality? An endocrinologist's perspective. *Best Pract Res Clin Endocrinol Metab* 19(1): 53-66.
4. Ferlazzo E, Raffaele M, Mazzu I, Pisani F (2006) Recurrent status epilepticus as the main feature of Hashimoto's encephalopathy. *Epilepsy Behav* 8(1): 328-330.
5. Spiegel J, Hellwig D, Becker G, Muller M (2004) Progressive dementia caused by Hashimoto's encephalopathy-report of two cases. *Eur J Neurol* 11(10): 711-713.
6. Kishitani T, Matsunaga A, Yoneda M (2013) The biomarker and treatment in Hashimoto's Encephalopathy. *Nihon Rinsho* 71(5): 893-897.
7. Mahad DJ, Staugaitis S, Ruggieri P, Parisi J, Kleinschmidt-Demasters BK, et al. (2005) Steroid-responsive encephalopathy associated with autoimmune thyroiditis and primary CNS demyelination. *J Neurol Sci* 228(1): 3-5.
8. Singh H, Ray S, Agarwal S, Verma RP, Talapatra P, et al. (2013) Spectroscopic correlation and role of azathioprine in long-term remission in patients of Hashimoto encephalopathy. *Ann Indian Acad Neurol* 16(3): 443-446.