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Clinical short communication

# Serial brain MRI changes related to autoimmune pathophysiology in Hashimoto encephalopathy with anti-NAE antibodies: A case-series study

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ABSTRACT

*Purpose:* Hashimoto encephalopathy (HE) is an autoimmune-mediated encephalopathy associated with anti-thyroid antibodies. We previously discovered serum autoantibodies against the $NH_2$-terminal of α-enolase (NAE), which serve as a specific diagnostic biomarker for HE and may be involved in the autoimmune pathophysiology of HE, including vasculitis. Although the common findings of brain magnetic resonance imaging (MRI) in HE have been recognized as normal or non-specific white matter lesions, serial MRI changes have been less well studied. The aim of this study was to clarify detailed and longitudinal MRI changes in HE associated with anti-NAE antibodies.

*Methods:* We investigated serial brain MR images in 12 Japanese patients with HE who had serum anti-NAE antibodies.

*Results:* Brain MRI showed diffuse white matter abnormalities and/or multiple small subcortical lesions in 10 patients. These lesions were apparently non-specific; however, in 7 of these patients we observed expanding and diminishing white matter lesions, emerging subcortical high-intensity spots on diffusion-weighted images, or reversible limbic lesions, which worsened at relapse and improved after recovery following immunotherapies.

*Conclusion:* MRI lesions that fluctuate according to the disease condition were frequently observed in HE patients with anti-NAE antibodies, which suggests that these fluctuation may be associated with the autoimmune pathophysiology of HE.

## 1. Introduction

Hashimoto encephalopathy (HE), also known as steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT), is characterized by various neuropsychiatric symptoms, the presence of serum anti-thyroid antibodies, and responsiveness to immunotherapies [1–3]. Although the pathological mechanisms underlying HE remain to be completely elucidated, some studies of biopsied or postmortem brains demonstrated brain vasculitis or lymphocyte infiltration in many cerebral small vessels in patients with HE [4,5]. These pathological findings suggest that the underlying pathophysiology of HE consists of reversible cerebral inflammation and vasculitis mediated by autoimmune mechanisms.

Because of the wide spectrum of its clinical features, including disturbed consciousness, psychiatric symptoms, tremor, myoclonus, ataxia, and stroke-like episodes, HE is often underdiagnosed or misdiagnosed. To resolve the diagnostic problem, we previously discovered autoantibodies against the $NH_2$-terminal of α-enolase (NAE) in the serum of patients with HE using proteomic analyses [6]. The antibodies demonstrated high specificity for HE [7], indicating the feasibility of using the antibodies for diagnosis of HE.

In addition to the highly diverse clinical manifestations, HE has

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**Table 1**
Clinical features in patients with Hashimoto encephalopathy associated with anti-$NH_2$ terminal of α-enolase autoantibodies.

| Patient | Age/sex | Past history | Onset | Clinical subtype | Neuropsychiatric symptoms | | | | Response to immunotherapy | Relapse |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Disturbed consciousness | Cognitive impairment | Psychiatric symptoms | Other | | |
| 1 | 78/F | DM, CRF | Acute | AE | + | + | + | − | + | − |
| 2 | 76/M | DM, HT | Acute | AE | + | − | + | − | + | − |
| 3 | 78/F | HT, HL | Acute | AE | + | + | + | Tremor | + | + |
| 4 | 83/F | Af | Acute | AE | + | − | − | Seizures | + | − |
| 5 | 71/F | HT, HL | Acute | AE | + | + | + | Seizures | + | + |
| 6 | 62/M | DM | Acute | AE | + | + | − | − | + | + |
| 7 | 79/M | HT | Acute | AE | + | + | + | − | + | + |
| 8 | 79/F | Af, colon C | Acute | AE | + | + | + | Chorea | + | − |
| 9 | 32/F | − | Acute | LE | + | + | − | Seizures | + | + |
| 10 | 69/F | − | Subacute | LE | + | + | + | Seizures | + | + |
| 11 | 41/F | − | Chronic | Ataxia | − | − | − | Ataxia | + | + |
| 12 | 55/M | − | Chronic | Ataxia | − | − | − | Ataxia | + | + |

F = female; M = male; DM = diabetes mellitus; CRF = chronic renal failure; AE = acute encephalopathy; HT = hypertension; HL = hyperlipidemia; Af = atrial fibrillation; colon C = colon cancer; LE = limbic encephalitis; Ataxia = cerebellar ataxia.

been reported to exhibit various findings in brain magnetic resonance imaging (MRI). Several case-series studies showed that normal findings or non-specific changes in white matter were observed in majority of patients with HE [8–10], whereas other studies revealed low frequencies of mesial temporal involvement or cerebellar atrophy [11–17]. However, anti-NAE antibodies were not examined in most of these reports. Furthermore, a few case reports showed longitudinal changes in MRIs of patients with HE [11,13,18,19].

In this study, we investigated serial brain MRI findings in multiple cases of HE with anti-NAE antibodies, a specific biomarker for HE, to clarify detailed and longitudinal MRI changes in HE associated with anti-NAE antibodies. Because anti-NAE antibodies are assumed to be related to the pathophysiology of HE (i.e., autoimmune-mediated inflammation with vasculitis) [20,21], we further consider the relationship between serial MRI changes and the autoimmune pathophysiology of HE in this paper.

## 2. Material and methods

We investigated brain MR images obtained prior to treatment in 12 Japanese patients with HE who had serum anti-NAE antibodies at University of Fukui Hospital between 2005 and 2013 as a case-series study. The patients consisted of 4 men and 8 women, with a median age of 74 years (range: 32–83). Brain MRI was performed using a 1.5 or 3.0-Tesla unit (SIGNA Excite HD; GE Medical Systems, Milwaukee, WI).

Eleven of the 12 patients also underwent brain MRI after treatment. No follow-up MRI was performed in the remaining one patient (Patient 2) because of normal findings observed on the first MRI. All patients underwent T1-, T2-, and diffusion-weighted imaging (DWI), fluid-attenuated inversion recovery (FLAIR) imaging, and MR angiography as part of routine MRI evaluation. In addition, one patient (Patient 10) underwent arterial spin labeling (ASL) perfusion imaging serially. Three patients (Patients 6, 8, and 10) underwent T2*-weighted imaging during follow-up studies.

The detection of anti-NAE antibodies in the sera was performed using immunoblotting analysis with recombinant NAE protein expressed in cultured human cells (HEK293) in our laboratory, as previously described [6,7]. HE was diagnosed according to both the conventional criteria [1], consisting of presence of neuropsychiatric symptoms, elevated serum anti-thyroid antibodies (antibodies to thyroglobulin and/or thyroid peroxidase), and responsiveness to immunotherapies, and positive for anti-NAE antibodies. To exclude other diseases, we investigated serological markers specific to collagen diseases, such as antinuclear, anti-DNA, anti-Sm, anti-RNP, anti-SS-A, anti-SS-B, and anti-neutrophil cytoplasmic antibodies. Additionally, we screened for tumors on the basis of the presence of serum tumor markers and findings of chest and abdominal CT. Two patients who presented with limbic encephalitis (LE) (Patients 9 and 10) were further examined for antibodies against the *N*-methyl-D-aspartate receptor (NMDAR), leucine-rich glioma-inactivated protein 1 (LGI1), contactin-associated protein-like 2 (Caspr2), γ-aminobutyric acid receptor-B ($GABA_BR$), and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) using a cell-based assay kit (Autoimmune Encephalitis Mosaic 1, EUROIMMUN, Germany) to exclude LE associated with these antibodies. The clinical findings of the 11 patients have been partially reported separately (Patients 1–6, 8–12) [7,12,15,17,22,23], whereas brain MRI findings were not specifically analyzed in these prior reports.

The ethics committees of the University of Fukui and Fukui Prefectural University approved this research, and written permission was obtained from each subject.

## 3. Results

### 3.1. Clinical findings

The clinical features of the patients are shown in Table 1. The median follow-up period was 4.8 years (range: 4 months–13 years). Anti-NAE antibodies as well as anti-thyroid antibodies were detected in the sera of all patients. Patient 10 who showed limbic symptoms tested positive for anti-LGI1 antibodies in addition to anti-NAE antibodies. Three patients had a history of Hashimoto thyroiditis, which had been adequately treated by supplementation of thyroid hormone. Among the 12 patients, 10 (83%) patients showed acute onset with a time from symptom onset to admission of less than 2 weeks or subacute onset with a time of over 2 weeks to 8 weeks. All patients presented with some neurological symptoms: Patients 1–8 presented primarily with disturbed consciousness and psychiatric symptoms, Patients 9 and 10 exhibited some limbic symptoms and limbic lesions in brain MRI, and Patients 11 and 12 presented primarily with cerebellar ataxia. Thus, the patients were classified into 3 clinical subtypes according to the principal features: “acute encephalopathy,” “LE,” and “cerebellar ataxia.” All 12 patients were treated with immunotherapies. Eight (67%) patients relapsed during the follow-up period in association with tapering corticosteroids.

### 3.2. MRI findings

Brain MRI was performed in all 12 patients before treatment (Table 2). Only one patient (Patient 2) showed normal results.

Diffuse high-intensity signals in cerebral deep white matter on FLAIR images were noted in 5 patients (Patients 1, 4, 5, 7, and 8; Fig. 1,

**Table 2**
Brain MRI findings in patients with Hashimoto encephalopathy associated with anti-$NH_2$ terminal of α-enolase autoantibodies.

| Patient | Clinical subtype | Brain MRI before treatment | | | |
|---|---|---|---|---|---|
| | | Diffuse white matter | High-intensity spots on DWIs | Small subcortical | Other |
| 1 | AE | + | − | + | − |
| 2 | AE | − | − | − | − |
| 3 | AE | − | − | + | − |
| 4 | AE | + | +[a] | + | − |
| 5 | AE | +[a] | − | + | − |
| 6 | AE | − | +[a] | + | − |
| 7 | AE | + | +[a] | + | − |
| 8 | AE | +[a] | +[a] | + | − |
| 9 | LE | − | +[a] | + | Limbic lesion[a] |
| 10 | LE | − | − | + | Limbic lesion[a] |
| 11 | Ataxia | − | − | + | − |
| 12 | Ataxia | − | − | − | Cerebellar atrophy |

AE = acute encephalopathy; LE = limbic encephalitis; Ataxia = cerebellar ataxia.
[a] The lesions changed during the course of disease.

Supplemental Fig. 1). All 5 patients who showed diffuse white matter lesions presented with cognitive impairment or psychiatric symptoms. Notably, these white matter lesions varied during the disease course in Patients 5 and 8. A representative case (Patient 5; 71-year-old woman) developed disturbed consciousness and seizures acutely and showed mild periventricular lesions in brain MRI at admission (Fig. 1A). She was treated with intravenous methylprednisolone pulse (IVMP), followed by an oral prednisolone taper, which improved her status. The follow-up MRI showed minor change at 1.8 years after first admission (Fig. 1B). She relapsed with fever and disturbed consciousness 2.5 years later. Remarkably, white matter lesions diffusely expanded on FLAIR images during relapse (Fig. 1C). She was treated with IVMP again and her state of consciousness improved. The white matter lesions were slightly improved after therapy (Fig. 1D).

Five patients showed transiently high-intensity spots in subcortical white matter on DWIs at admission and/or recurrence (Patients 4, 6, 7, 8, and 9; Fig. 2, Supplemental Fig. 2). A representative case (Patient 7; 79-year-old man) presented with disturbed consciousness, agitation, and cognitive impairment. Brain MRI showed a high-intensity spot on DWIs (Fig. 2A) with low-intensity on apparent diffusion coefficient (ADC) maps (Fig. 2B) in the right frontal white matter at admission. As his symptoms improved after treatment with oral prednisolone, the DWI high-intensity lesion disappeared 2 months later (Fig. 2C). Four months later, during recurrence with disorientation, cognitive impairment, abrupt behavior, and agitation, new DWI high-intensity spots appeared in different regions, such as the right frontal white matter (Fig. 2D). After recovery following therapies with IVMP, these DWI high-intensity spots also disappeared.

Ten patients showed multiple small lesions in the subcortical white matter. Although multiple white matter lesions are usually considered non-specific findings related to chronic ischemic changes along with aging, such lesions were observed in 2 relatively younger patients (Patients 9 and 11; 32-year-old woman and 41-year-old woman, respectively) who had no pre-existing diseases, such as hypertension, diabetes mellitus, hyperlipidemia, and collagen diseases. Additionally, the subcortical lesions were located immediately below the cortex, which differed from the distribution of typical lacunar infarcts.

Our previous studies showed clinical subtypes of LE and cerebellar

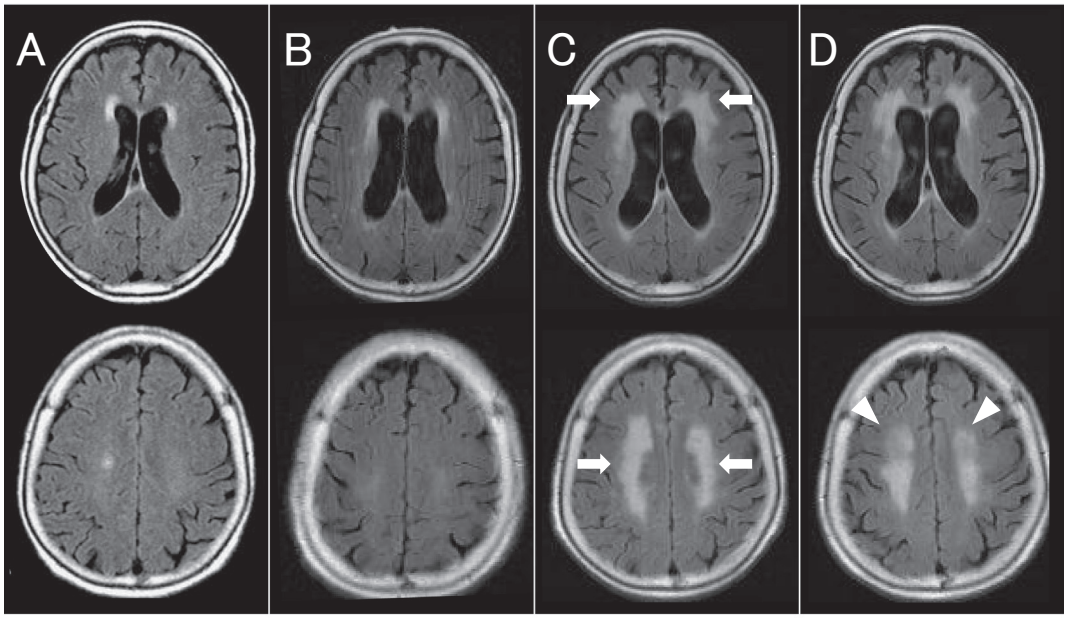


**Fig. 1.** (A) Patient 5 (71-year-old woman) showed mild periventricular lesions and some small lesions in cerebral white matter on FLAIR images at admission. (B) 1.8 years later, serial MRI revealed only mild lateral ventricular dilation. (C) 2.5 years later, she relapsed with disturbed consciousness. Diffuse high-intensity lesions in the deep white matter expanded (arrows). (D) After immunotherapies, the diffuse white matter lesions slightly improved (arrowheads).

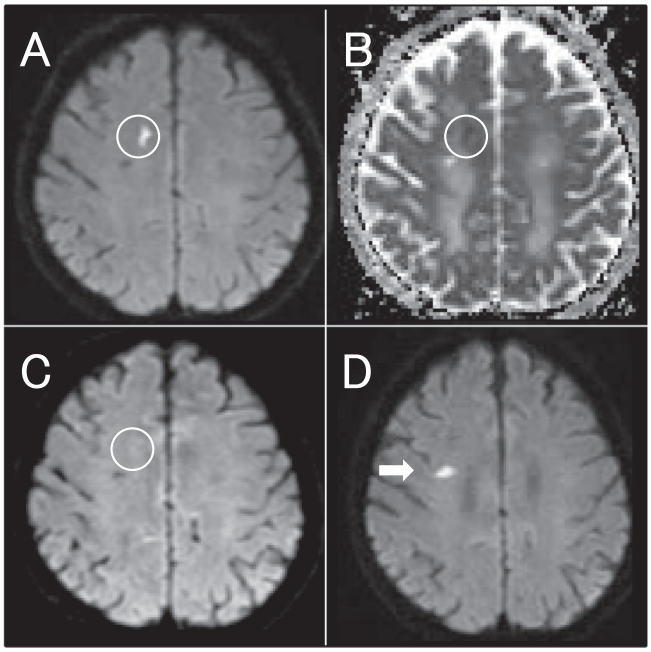


**Fig. 2.** Patient 7 (79-year-old man) showed a high-intensity spot on DWIs (A) with low-intensity on ADC maps (B) in right frontal white matter at admission (circles). (C) 2 months later, the first DWI high-intensity lesion disappeared following treatment (circle). (D) At the time of recurrence, new focal spots appeared in right white matter (arrow) and left frontal white matter on DWIs.

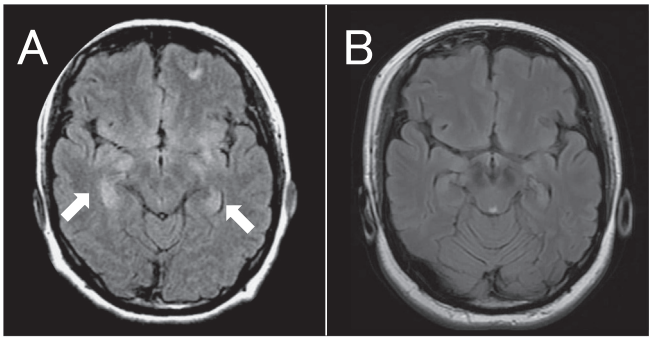


**Fig. 3.** (A) Patient 9 (32-year-old woman) showed abnormal high-intensity signals in the bilateral medial temporal lobes on FLAIR images (arrows). (B) After treatment, these lesions were improved.

ataxia in HE. As we have previously reported, abnormal signals were observed in the unilateral or bilateral medial temporal lobes of 2 patients who presented with limbic symptoms (Patients 9 and 10; Fig. 3A, Supplemental Fig. 3A) [12,23]. These lesions improved after immunotherapies (Fig. 3B, Supplemental Fig. 3C). In addition, Patient 10 showed hyperperfusion in the right hippocampus, as detected by ASL imaging in the incipient phase (Supplemental Fig. 3B) [12]. This hyperperfusion disappeared after immunotherapy (Supplemental Fig. 3D). Patient 12, who presented with pure cerebellar ataxia, showed mild cerebellar atrophy (Supplemental Fig. 3E) [17].

T2*-weighted imaging showed a brain microbleed in the subcortical white matter of the left parietal lobe at the time of recurrence (Patient 10). The remaining 2 patients who underwent T2*-weighted imaging (Patient 6 and 8) showed no microbleeds during the follow-up period.

## 4. Discussion

In this study, we demonstrated detailed and longitudinal changes in brain MRI findings in patients with HE who had anti-NAE antibodies as a serological diagnostic marker of HE. Apparently non-specific white matter abnormalities were mostly observed on the first MRI. Remarkably, serial MRI revealed lesions that varied according to the disease course, such as expanding and diminishing white matter changes, transient DWI high-intensity spots, and reversible limbic lesions in many patients. These lesions newly appeared or expanded at relapse and improved after recovery following immunotherapies, suggesting that the autoimmune pathophysiology of HE is associated with these serial MRI changes.

Recent case-series studies and reviews showed that the most common MRI findings are normal or non-specific abnormalities in HE or SREAT, expressed as diffuse white matter lesions or chronic ischemic changes [3,9,10]. Similarly, the present study showed diffuse white matter abnormalities and/or multiple small subcortical lesions in most (10/12) patients. Some of these white matter lesions may have been aging-related; however, many (7/10) of these patients with apparently non-specific findings exhibited coexisting lesions that changed during the disease course in the present study (Table 2). These serially fluctuating lesions and relatively younger cases without cerebrovascular risks suggest the involvement of cerebral vasculitis in white matter lesions. In addition, all patients who developed seizures (Patients 4, 5, 9, and 10) showed various varying MRI lesions (i.e., expanding and diminishing diffuse white matter lesions, emerging subcortical high-intensity spots on DWI, or reversible limbic lesions) in the present study. These varying lesions are not usually observed in patients with common seizures, which suggests that patients with HE who have seizures tend to show these findings during serial MRI evaluation.

Although a few case reports also showed reversible white matter lesions [18,24,25], DWI high-intensity spots in subcortical regions [11,19], or limbic lesions that improved following immunotherapies [13,14,26] in patients with HE, no case-series studies or reviews regarding these varying findings have been reported involving multiple cases of HE. In addition, in the prior case reports, the diagnosis of HE was made only according to the conventional criteria for HE, the specificity of which is relatively low without testing for anti-NAE antibodies. In contrast, the present study determined accurate diagnoses based on both the conventional criteria and the presence of anti-NAE antibodies as a specific biomarker for HE.

In the present study, all patients investigated had serum anti-NAE antibodies. The α-enolase, which is an antigen of anti-NAE antibodies, has pleiotropic roles in glycolysis as well as the immune response [27,28]. Moreover, α-enolase is expressed abundantly in vascular endothelial cells, which suggests a relationship between anti-NAE antibodies and the pathological findings of cerebral vasculitis in biopsied or postmortem brain tissues of patients with HE [4,5]. Indeed, we demonstrated immunological reaction against α-enolase of cultured human endothelial cells with serum from a patient with HE who had anti-NAE antibodies [20].

As collateral evidence, several studies using SPECT imaging demonstrated global or focal hypoperfusion in HE [29–31]. In particular, we revealed specific regions with decreased cerebral blood flow in patients with HE with anti-NAE antibodies [22]. The hypoperfused lesions were observed in the bilateral anterior cingulate areas and left prefrontal cortex, which were associated with the symptoms. Anti-NAE antibodies were used as a diagnostic biomarker of HE in the current study, but the presence of the antibodies may also be associated with the MRI findings that indicated cerebral vasculitis.

In conclusion, the present study demonstrated detailed and longitudinal MRI changes in Japanese patients with HE who had anti-NAE antibodies. Although apparently non-specific white matter abnormalities were mostly observed, many of these were accompanied by serially fluctuating lesions related to the disease course in the present study. These fluctuating lesions emerged or expanded according to the degree of disease exacerbation and improved after immunotherapies, suggesting that the autoimmune pathophysiology is associated with these serial MRI changes in patients with HE.

## Declaration of Competing Interest

The authors have no conflicts of interest to disclose.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jns.2019.116453.

## References

[1] P.J. Shaw, T.J. Walls, P.K. Newman, P.G. Cleland, N.E. Cartlidge, Hashimoto's encephalopathy: a steroid-responsive disorder associated with high anti-thyroid antibody titers-report of 5 cases, Neurology 41 (1991) 228–233, https://doi.org/10.1212/wnl.41.2_part_1.228.

[2] I. Olmez, H. Moses, S. Sriram, H. Kirshner, A.H. Lagrange, S. Pawate, Diagnostic and therapeutic aspects of Hashimoto's encephalopathy, J. Neurol. Sci. 331 (2013) 67–71, https://doi.org/10.1016/j.jns.2013.05.009.

[3] C. Laurent, J. Capron, B. Quillerou, G. Thomas, S. Alamowitch, O. Fain, et al., Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT): characteristics, treatment and outcome in 251 cases from the literature, Autoimmun. Rev. 15 (2016) 1129–1133, https://doi.org/10.1016/j.autrev.2016.09.008.

[4] K.W. Nolte, A. Unbehaun, H. Sieker, T.M. Kloss, W. Paulus, Hashimoto encephalopathy: a brainstem vasculitis? Neurology 54 (2000) 769–770, https://doi.org/10.1212/wnl.54.3.769 https://n.neurology.org/content/54/3/769.long.

[5] P. Duffey, S. Yee, I.N. Reid, L.R. Bridges, Hashimoto's encephalopathy: postmortem findings after fatal status epilepticus, Neurology 61 (2003) 1124–1126, https://doi.org/10.1212/01.wnl.0000090462.62087.a1 https://n.neurology.org/content/61/8/1124.long.

[6] A. Fujii, M. Yoneda, T. Ito, O. Yamamura, S. Satomi, H. Higa, et al., Autoantibodies against the amino terminal of alpha-enolase are a useful diagnostic marker of Hashimoto's encephalopathy, J. Neuroimmunol. 162 (2005) 130–136, https://doi.org/10.1016/j.jneuroim.2005.02.004.

[7] M. Yoneda, A. Fujii, A. Ito, H. Yokoyama, H. Nakagawa, M. Kuriyama, High prevalence of serum autoantibodies against the amino terminal of alpha-enolase in Hashimoto's encephalopathy, J. Neuroimmunol. 185 (2007) 195–200, https://doi.org/10.1016/j.jneuroim.2007.01.018.

[8] I. Kothbauer-Margreiter, M. Sturzenegger, J. Komor, R. Baumgartner, C.W. Hess, Encephalopathy associated with Hashimoto thyroiditis: diagnosis and treatment, J. Neurol. 243 (1996) 585–593.

[9] F. Graus, M.J. Titulaer, R. Balu, S. Benseler, C.G. Bien, T. Cellucci, et al., A clinical approach to diagnosis of autoimmune encephalitis, Lancet Neurol. 15 (2016) 391–404, https://doi.org/10.1016/S1474-4422(15)00401-9.

[10] V. Menon, K. Subramanian, J.S. Thamizh, Autoimmune encephalitis: pathophysiology and imaging review of an overlooked diagnosis, J. Neurosci. Rural Pract. 8 (2017) 261–267, https://doi.org/10.3174/ajnr.A5086.

[11] N. Chen, W. Qin, C. Wei, X. Wang, K. Li, Time course of Hashimoto's encephalopathy revealed by MRI: report of two cases, J. Neurol. Sci. 300 (2011) 169–172, https://doi.org/10.1016/j.jns.2010.09.019.

[12] M. Ishitobi, M. Yoneda, M. Ikawa, A. Matsunaga, K. Ueno, H. Kimura, Y. Wada, Hashimoto's encephalopathy with hippocampus involvement detected on continuous arterial spin labeling, Psychiatry Clin. Neurosci. 67 (2013) 128–129, https://doi.org/10.1111/pcn.12019.

[13] Y.M. Song, D.W. Seo, G.Y. Chang, MR findings in Hashimoto's encephalopathy, Am. J. Neuroradiol. 25 (2004) 807–808 http://www.ajnr.org/content/25/5/807.long.

[14] D.J. McCabe, T. Burke, S. Connolly, M. Hutchinson, Amnesic syndrome with bilateral mesial temporal lobe involvement in Hashimoto's encephalopathy, Neurology. 54 (2000) 737–739, https://doi.org/10.1212/wnl.54.3.737 https://n.neurology.org/content/54/3/737.long.

[15] H. Nakagawa, M. Yoneda, A. Fujii, K. Kinomoto, M. Kuriyama, Hashimoto's encephalopathy presenting with progressive cerebellar ataxia, J. Neurol. Neurosurg. Psychiatry 78 (2007) 196–197, https://doi.org/10.1136/jnnp.2006.093005.

[16] Y. Tang, C. Chu, M.T. Lin, G. Wei, X. Zhang, Y. Da, H. Huang, J. Jia, Hashimoto's encephalopathy mimicking spinocerebellar ataxia, J. Neurol. 258 (2011) 1705–1707, https://doi.org/10.1007/s00415-011-5976-2.

[17] A. Matsunaga, M. Ikawa, A. Fujii, Y. Nakamoto, M. Kuriyama, M. Yoneda, Hashimoto's encephalopathy as a treatable adult-onset cerebellar ataxia mimicking spinocerebellar degeneration, Eur. Neurol. 69 (2013) 14–20, https://doi.org/10.1159/000342217.

[18] N.I. Bohnen, K.J. Parnell, C.M. Harper, Reversible MRI findings in a patient with Hashimoto's encephalopathy, Neurology. 49 (1997) 246–247, https://doi.org/10.1212/wnl.49.1.246.

[19] C. Grommes, C. Griffin, K.A. Downes, A.J. Lerner, Steroid-responsive encephalopathy associated with autoimmune thyroiditis presenting with diffusion MR imaging changes, Am. J. Neuroradiol. 29 (2008) 1550–1551, https://doi.org/10.3174/ajnr.A1113.

[20] M. Yoneda, A. Matsunaga, M. Ikawa, Hashimoto's encephalopathy, in: S. Kusunoki (Ed.), Neuroimmunological Diseases, Springer, New York, 2016, pp. 235–244.

[21] H. Mitoma, M. Yoneda, F. Saitow, H. Suzuki, A. Matsunaga, M. Ikawa, et al., Presynaptic dysfunction caused by cerebrospinal fluid from a patient with the ataxic form of Hashimoto's encephalopathy, Neurol. Clin. Neurosci. 2 (2014) 104–108, https://doi.org/10.1111/ncn3.105.

[22] T. Muramatsu, M. Ikawa, M. Yoneda, K. Sugimoto, A. Matsunaga, O. Yamamura, et al., Pathophysiological decrease in the regional cerebral blood flow in Hashimoto's encephalopathy: a multiple-case SPECT study, Eur. Neurol. 72 (2014) 13–19, https://doi.org/10.1159/000358220.

[23] T. Kishitani, A. Matsunaga, M. Ikawa, K. Hayashi, O. Yamamura, T. Hamano, et al., Limbic encephalitis associated with anti-$NH_2$-terminal of α-enolase antibodies: a clinical subtype of Hashimoto encephalopathy, Medicine (Baltimore) 96 (2017) e6181, , https://doi.org/10.1097/MD.0000000000006181.

[24] P. Pozo-Rosich, P. Villoslada, A. Canton, R. Simo, A. Rovira, X. Montalban, Reversible white matter alterations in encephalopathy associated with autoimmune thyroid disease, J. Neurol. 249 (2002) 1063–1065, https://doi.org/10.1007/s00415-002-0788-z.

[25] P. Castillo, B. Woodruff, R. Caselli, S. Vernino, C. Lucchinetti, J. Swanson, et al., Steroid-responsive encephalopathy associated with autoimmune thyroiditis, Arch. Neurol. 63 (2006) 197–202, https://doi.org/10.1001/archneur.63.2.197.

[26] Y. Tang, Y. Xing, M.T. Lin, J. Zhang, J. Jia, Hashimoto's encephalopathy cases: Chinese experience, BMC Neurol. 12 (2012) 60, https://doi.org/10.1186/1471-2377-12-60.

[27] B. Terrier, N. Degand, P. Guilpain, A. Servettaz, L. Guillevin, L. Mouthon, Alpha-enolase: a target of antibodies in infectious and autoimmune diseases, Autoimmun. Rev. 6 (2007) 176–182, https://doi.org/10.1016/j.autrev.2006.10.004.

[28] A. Diaz-Ramos, A. Roig-Borrellas, A. Garcia-Melero, R. López-Alemany, Alpha-enolase, a multifunctional protein: its role on pathophysiological situations, J. Biomed. Biotechnol. 2012 (2012) 156795, , https://doi.org/10.1155/2012/156795.

[29] M. Bertoni, M. Falcini, S. Sestini, L. Niccoli, C. Nannini, F. Cantini, Encephalopathy associated with Hashimoto's thyroiditis: an additional case, Eur. J. Int. Med. 14 (2003) 434–437 https://www.ejinme.com/article/S0953-6205(03)00142-0/fulltext.

[30] J. Kalita, U.K. Misra, C. Rathore, P.K. Pradhan, B.K. Das, Hashimoto's encephalopathy: clinical, SPECT and neurophysiological data, QJM. 96 (2003) 455–457, https://doi.org/10.1093/qjmed/hcg075.

[31] C.S. Hsu, Y.C. Wu, M.K. Lu, Y.T. Hsu, T.S. Chiou, C.H. Tsai, et al., 99m Tc ECD and 99m Tc TRODAT-1 SPECT in Hashimoto encephalopathy, Clin. Nucl. Med. 37 (2012) e86–e88, https://doi.org/10.1097/RLU.0b013e31824430fb.