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Anti-Ma2 Antibody-Associated Paraneoplastic Cerebellar Degeneration Mimicking the Cerebellar Ataxic Subtype of Hashimoto's Encephalopathy: A Case Report

Masato Okitsu | Shintaro Nojiri | Tomoya Kawazoe | Akihito Hao | Kazushi Takahashi

Department of Neurology, Tokyo Toritsu Shinkei Byoin, Fuchu, Tokyo, Japan

Correspondence: Masato Okitsu (masato_okitsu@tmhp.jp)

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ABSTRACT

Autoimmune cerebellar ataxia (ACA) is an immune-mediated cerebellar disorder arising from various underlying conditions. Because ACA is potentially treatable, identifying associated neuronal antibodies is important for diagnosis. We report the case of a 55-year-old woman with subacute progressive ataxia who presented with dysarthria and impaired handwriting and gait. Her scale for the assessment and rating of ataxia (SARA) score was 20.5, with particularly high subscores for gait and stance. She had a history of Hashimoto's thyroiditis. Laboratory testing showed markedly elevated antithyroid antibody levels with normal thyroid function, initially suggesting the cerebellar ataxic subtype of Hashimoto's encephalopathy (HE). Cerebral blood flow single-photon emission computed tomography revealed cerebellar hypoperfusion, which was most prominent in the superior cerebellar vermis. Intravenous methylprednisolone (1000 mg/day for 3 days) was administered; however, her response was poor. Further evaluation revealed positivity for anti-Ma2 antibodies, leading to a diagnosis of anti-Ma2-associated ACA. Subsequent intravenous immunoglobulin therapy improved the clinical symptoms and imaging findings, and the follow-up SARA score decreased to 10. Comprehensive imaging revealed no underlying malignancy. This case is unique not only because both rare diseases were key considerations in the differential diagnosis, but also because it is instructive in two respects: the construct of HE remains insufficiently specific and should not preclude consideration of alternative immune-mediated etiologies, and patients positive for anti-Ma2 antibody require sustained oncological surveillance, even in the absence of malignancy at presentation.

1 | Introduction

Autoimmune cerebellar ataxia (ACA) is a representative form of acquired ataxia and an important potentially treatable cause of sporadic cerebellar syndromes mediated by immune mechanisms [1]. Differential diagnoses of ACA include paraneoplastic cerebellar degeneration (PCD), primary autoimmune cerebellar ataxia, antiglutamate decarboxylase-associated cerebellar ataxia, opsoclonus–myoclonus syndrome, Miller Fisher syndrome, and ACA associated with autoimmune encephalitis [2]. Some forms of ACA are potentially treatable with early and accurate diagnosis [1, 3, 4]. PCD, a manifestation of the paraneoplastic neurological syndrome (PNS), usually exhibits subacute limb and trunk ataxia. Several onconeural antibodies are associated with this condition [4]. Ma-2 antibody-associated pure cerebellar ataxia is occasionally observed. Among all PNS cases caused by Ma-2 antibodies, the frequency of exhibiting pure cerebellar ataxia is approximately 5% [5].

Hashimoto's encephalopathy (HE) is an autoimmune disease characterized by favorable steroid responsiveness [6]. Among its diverse clinical presentations, including seizures and

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psychiatric symptoms, a subtype is characterized by cerebellar ataxia [7].

To the best of our knowledge, no previous report has described paraneoplastic PNS initially mimicking HE. Although one previous reported the case of HE preceding lymphomatosis cerebri, direct association between HE and PNS remains unestablished [8]. Distinguishing anti-Ma2-associated PNS, especially the rare isolated cerebellar form, is challenging in the presence of thyroid autoimmunity. Furthermore, functional imaging findings in such cases are limited.

Herein, we report the case of a 55-year-old woman with anti-Ma2-associated cerebellar ataxia mimicking HE who responded to immunotherapy.

2 | Case Presentation

A 55-year-old woman gradually experienced dizziness and writing disturbance 2 months before admission to our hospital. One month later, she developed gait disturbance and dysarthria. Her symptoms worsened over time and she visited our outpatient clinic. Her medical history included Hashimoto's thyroiditis, which was controlled with levothyroxine (100 mg/day). She had a smoking history of 15 cigarettes per day since the age of 20.

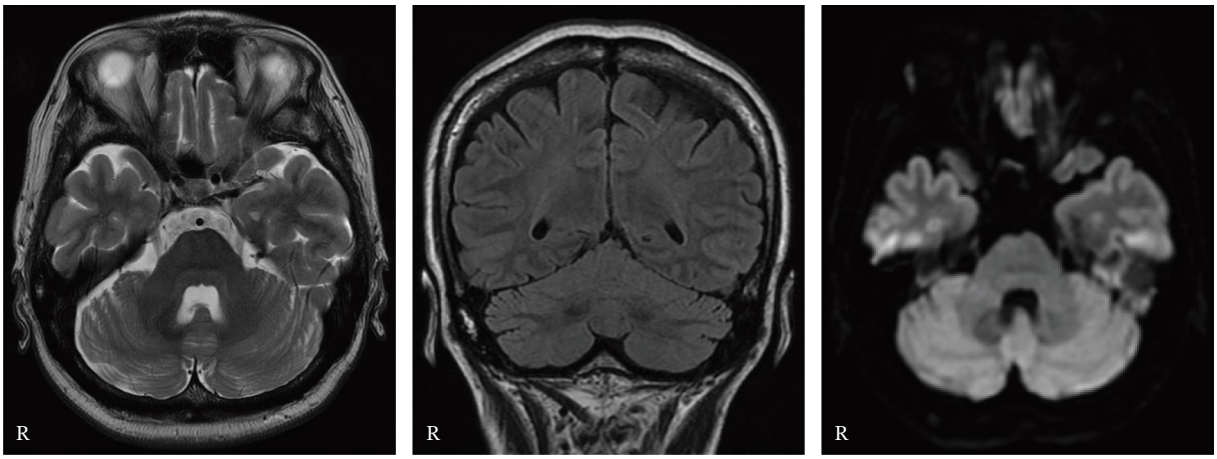
On admission, the patient was awake and alert. General physical examination revealed no abnormal findings related to thyroid disease such as exophthalmos, goiter, or edema. Neurological examination revealed slurred speech, dysmetria, and mild hypotonia in all limbs. She exhibited a wide-based gait with instability and could not walk more than a few steps without assistance. The patient showed a total scale for the assessment and rating of ataxia (SARA) score of 20.5 [9] (Table 1).

Laboratory assessments revealed marked elevation in antithyroglobulin (Tg) and antithyroid peroxidase (TPO) antibodies, surpassing the upper limits of 4000 and 600 IU/mL, respectively (normal: < 28 and < 16 IU/mL). Thyroid function was within normal limits; free T3 was 2.56 pg/mL (normal: 2.14–4.09 IU/mL), free T4 was 1.50 ng/dL (normal: 0.88–1.50 ng/dL), and thyroid-stimulating hormone was 1.058 μIU/mL (normal: 0.610–4.230 μIU/mL). Cerebrospinal fluid, evaluated on postadmission Day 2, showed pleocytosis at 10/μL (normal: 0–5/μL) with nine lymphocytes/μL and normal protein levels at 24.0 mg/dL (normal: 10–40 mg/dL). Oligoclonal bands were negative, and brain magnetic resonance imaging (MRI) on postadmission Day 3 revealed no abnormal findings (Figure 1). I-123-iodoamphetamine cerebral blood flow single-photon emission computed tomography (SPECT) on postadmission Day 8 revealed diffuse hypoperfusion in the bilateral cerebellum (Figure 2A,B).

We initially considered the cerebellar ataxic subtype of HE and conducted methylprednisolone pulse therapy (1000 mg/day for 3 days) on postadmission Day 9. The symptoms did not improve, and the patient became depressed. Within 1 week after therapy, her mental state recovered without any additional medical intervention. As steroid psychosis was suspected, further steroid treatment was discontinued. Because the poor response to steroids was atypical for HE, we further investigated other underlying pathologies. Comprehensive serum onconeural antibody screening, including Yo, Hu, Ri, CV2/CRMP5, Ma2, SOX1, amphiphysin, Zic4, Tr/DNER, GAD65, recoverin, and titin, was performed via immunoblotting (BML Inc., Kawagoe, Japan) and was positive for anti-Ma2 antibodies on postadmission Day 14. Serum testing for the anti-NH2 terminal of alpha-enolase (NAE) antibody yielded negative results. Ultimately, the patient was clinically diagnosed with anti-Ma2-associated ACA. She underwent whole-body computed tomography and fluorodeoxyglucose positron emission tomography; however, no malignant findings were detected. On postadmission Days 16–20, intravenous immunoglobulin (IVIg; 0.4 g/kg/day) was administered. A few days after IVIg therapy, her cerebellar ataxia improved, and the distance she could walk without assistance increased. The follow-up SARA score, which was evaluated on postadmission Day 40, improved to 10 (Table 1). In line with her clinical symptoms, the abnormal SPECT findings improved at follow-up on postadmission Day 25. Improvement in blood flow was evident in the upper region of the

TABLE 1 | Breakdown of scale for the assessment and rating of ataxia (SARA) scores before (upon admission) and after treatment (on postadmission Day 40).

	Before treatment		After treatment	
Gait	6		2	
Stance	4		1	
Sitting	3		2	
Speech disturbance	2		1	
Finger chase	1 (mean)	1 (right) 1 (left)	0.5	1 0
Nose finger test	1	1 1	0.5	1 1
Fast alternating hand movements	1.5	2 1	1	1 1
Heel-shin slide	2	2 2	2	2 2
Total score	20.5		10	



(A) (B) (C)

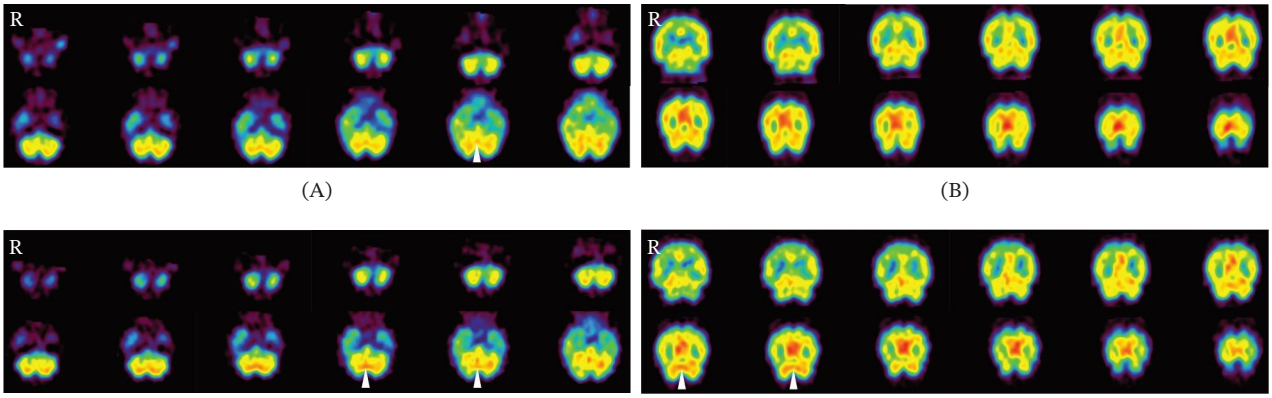
FIGURE 1 | Brain magnetic resonance imaging (MRI) without contrast agent on postadmission Day 2. (A) Horizontal T2-weighted image. (B) Horizontal diffusion-weighted image. (C) Coronal fluid-attenuated inversion recovery image. No abnormal findings such as cerebellar edema or atrophy were observed in any of the images.

medial cerebellum, corresponding to the upper part of the cerebellar vermis (Figure 2C,D). Lesions in the upper cerebellar vermis were particularly associated with truncal ataxia and ataxic gait, consistent with improvement in the SARA score, predominantly in gait and stance. The patient was discharged on postadmission Day 46 with an independent gait. No recurrence of symptoms or development of malignant tumors has been observed.

3 | Discussion

Among various presentations of HE, isolated cerebellar ataxia is less frequently reported [7, 10, 11]. In recent years, HE diagnostic criteria have been proposed [10, 12]. Common core components are the presence of serum thyroid antibodies (TPO and Tg), with TPO levels proposed to be 10 times higher than the upper limit of the normal range, and the absence of neuronal antibodies in serum and CSF. The presence of anti-TPO antibodies should be interpreted with caution because they may reflect a nonspecific autoimmune background rather than being specific to HE [13]. Although anti-NAE antibodies have been reported to be specific for HE, its diagnostic value is currently considered limited [10]. Brain MRI typically shows no abnormalities; however, cerebral blood flow is reduced during the acute phase of HE in SPECT studies [14]. Classically, a favorable response to steroids is also characteristic [6]. As no disease-specific diagnostic biomarker for HE has been established, a broad range of differential diagnoses, including infectious etiologies, stroke, and metabolic encephalopathy, must be excluded [13].

In the present case, the medical history of Hashimoto's thyroiditis and highly elevated thyroid antibodies suggested a cerebellar ataxia subtype of HE. The treatment-responsive cerebellar hypoperfusion findings captured on imaging were consistent with those of HE. However, tests for anti-Ma2 antibodies were positive, and the patient showed poor responsiveness to steroid pulse therapy, although it was a single course; these findings are not characteristic of HE.



(A) (B) (C) (D)

FIGURE 2 | Pre- and post-treatment (I-123)-iodoamphetamine cerebral blood flow single-photon emission computed tomography (SPECT). (A) Horizontal images before treatment and on Day 8 after admission. (B) Coronal images before treatment. (C) Horizontal images after treatment on Day 25 postadmission. (D) Coronal images after treatment. Compared to the image before treatment, the reduction in blood flow improved after treatment, especially in the upper part of the cerebellar vermis (white arrowheads) (B, D).

The anti-Ma2 antibody is frequently detected in lymphoma and testicular cancer [15]. The most common presentation is encephalitis involving the limbic system or brainstem. However, the clinical spectrum is broad and may also include diencephalitis, myelitis, and sensorimotor neuropathy, with symptoms such as short-term memory impairment, disturbed consciousness, seizures, excessive daytime sleepiness, and limb numbness or weakness [15–17]. The course is typically subacute to chronic and often lasts from several weeks to > 6 months. Although rare, Ma2 antibody-associated PCD presenting with cerebellar ataxia has also been reported [15–17].

In an imaging study of PCD cases, regardless of the type of antibody involved, T2-weighted hyperintensity in the cerebellum was occasionally observed during the acute phase [18]. A previously reported case of PCD associated with anti-Ma2 antibody showed no specific changes on brain MRI [17]. Comprehensive data regarding cerebral blood flow in acute-phase PCD are scarce. However, hypometabolism is generally observed using fluorodeoxyglucose positron emission tomography during the chronic phase of the disease [19]. Treatment with steroids and IVIg is typical for anti-Ma2 antibody-associated PNS; a previous case series indicated approximately a 50% improvement rate [18]. Additionally, tumor co-occurrence risk is high in anti-Ma2 cases [15, 20]. While tumor detection occurs before PNS onset in a small number of cases, detection in most cases occurs between 1 month and 19 years later; therefore, regular screening for malignancy is extremely important [18, 20].

According to the updated diagnostic criteria, our patient scored 7 points on the PNS Care Scale, meeting the requirements for "Probable PNS." The score comprised 3 points for a high-risk neurologic phenotype (rapidly progressive cerebellar syndrome, < 3 months) and 3 points for a high-risk antibody (anti-Ma2). Despite the absence of detectable malignancy at diagnosis, 1 point was added for a follow-up period of < 2 years [20]. To verify our case as anti-Ma2-associated PNS, comprehensive data remain limited, particularly regarding SPECT findings in the acute phase. Therefore, further case accumulation is warranted.

Here, we describe the case of a middle-aged woman who developed subacute ACA associated with anti-Ma2 antibody, mimicking the cerebellar ataxic subtype of HE. This case demonstrates the novelty of an anti-Ma2-associated ACA that mimics the cerebellar ataxic subtype of HE, highlighting a rare but clinically important diagnostic overlap. This further emphasizes the importance of careful differential diagnosis and sustained oncological surveillance in patients who are positive for anti-Ma2 antibody.

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Consent

No written consent has been obtained from the patient as there is no patient identifiable data included in this case report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data supporting the findings of this study are available upon request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1. P. Chunowski, N. Madetko-Alster, and P. Alster, "Homer-3 Antibody in Autoimmune Cerebellar Syndromes: A Potentially Treatable Mimic of MSA-C – A Review," *Frontiers in Immunology* 16 (2025): 1660587, https://doi.org/10.3389/fimmu.2025.1660587.

2. M. Hadjivassiliou, F. Graus, J. J. Honnorat, et al., "Diagnostic Criteria for Primary Autoimmune Cerebellar Ataxia-Guidelines From an International Task Force on Immune-Mediated Cerebellar Ataxias," *Cerebellum* 19, no. 4 (2020): 605–610, https://doi.org/10.1007/s12311-020-01132-8.

3. Y. Cai, Z. Hua, Y. Chen, et al., "Clinical Features of Autoimmune Cerebellar Ataxia Related to Neuronal Antibodies," *Frontiers in Immunology* 16 (2025): 1497695, https://doi.org/10.3389/fimmu.2025.1497695.

4. A. L. Jones, E. P. Flanagan, S. J. Pittock, et al., "Responses to and Outcomes of Treatment of Autoimmune Cerebellar Ataxia in Adults," *JAMA Neurology* 72, no. 11 (2015): 1304–1312, https://doi.org/10.1001/jamaneurol.2015.2378.

5. J. Dalmau, F. Graus, A. Villarejo, et al., "Clinical Analysis of Anti-Ma2-Associated Encephalitis," *Brain* 127, no. 8 (2004): 1831–1844, https://doi.org/10.1093/brain/awh203.

6. C. Laurent, J. Capron, B. Quillerou, et al., "Steroid-Responsive Encephalopathy Associated With Autoimmune Thyroiditis (SREAT): Characteristics, Treatment and Outcome in 251 Cases From the Literature," *Autoimmunity Reviews* 15, no. 12 (2016): 1129–1133, https://doi.org/10.1016/j.autrev.2016.09.008.

7. C. Wei, Y. Shen, W. Zhai, et al., "Hashimoto's Encephalopathy With Cerebellar Ataxia as the Main Symptom: A Case Report and Literature Review," *Frontiers in Neurology* 13 (2022): 970141, https://doi.org/10.3389/fneur.2022.970141.

8. R. Amano, S. Tsukada, S. Kosuge, et al., "Case Report: Paraneoplastic Hashimoto's Encephalopathy Associated With Lymphomatosis Cerebri With Periodic Synchronous Discharges Resembling Creutzfeldt-Jakob Disease," *Frontiers in Neurology* 12 (2021): 701178, https://doi.org/10.3389/fneur.2021.701178.

9. T. Schmitz-Hübsch, S. T. du Montcel, L. Baliko, et al., "Scale for the Assessment and Rating of Ataxia: Development of a New Clinical Scale," *Neurology* 66, no. 11 (2006): 1717–1720, https://doi.org/10.1212/9.wnl.0000219042.60538.92.

10. S. Mattozzi, L. Sabater, D. Escudero, et al., "Hashimoto Encephalopathy in the 21st Century," *Neurology* 94, no. 2 (2020): e217–e224, https://doi.org/10.1212/WNL.0000000000008785.

11. M. Okitsu, K. Sugaya, M. Yoneda, and K. Takahashi, "Hashimoto Encephalopathy Presenting With Acute Psychosis and Inappropriate Secretion of Antidiuretic Hormone: A Rare Case Responding to Steroid Therapy," *American Journal of Case Reports* 24 (2023): e942297, https://doi.org/10.12659/AJCR.942297.

12. F. Graus, M. J. Titulaer, R. Balu, et al., "A Clinical Approach to Diagnosis of Autoimmune Encephalitis," *The Lancet Neurology* 15, no. 4 (2016): 391–404, https://doi.org/10.1016/S1474-4422(15)00401-9.

13. N. Manocchio, V. M. Magro, L. Massaro, A. Sorbino, C. Ljoka, and C. Foti, "Hashimoto's Encephalopathy: Clinical Features, Therapeutic Strategies, and Rehabilitation Approaches," *Biomedicines* 13, no. 3 (2025): 726, https://doi.org/10.3390/biomedicines13030726.

14. T. Muramatsu, M. Ikawa, M. Yoneda, et al., "Pathophysiological Decrease in the Regional Cerebral Blood Flow in Hashimoto's Encephalopathy: A Multiple-Case SPECT Study," *European Neurology* 72, no. 1-2 (2014): 13–19, https://doi.org/10.1159/000358220.

15. S. Binks, C. Uy, J. Honnorat, and S. R. Irani, "Paraneoplastic Neurological Syndromes: A Practical Approach to Diagnosis and Management," *Practical Neurology* 22, no. 1 (2022): 19–31, https://doi.org/10.1136/practneurol-2021-003073.

16. Y. Guo, M. T. Cai, Q. L. Lai, Y. Zheng, C. H. Shen, and Y. X. Zhang, "Anti-Ma2 Antibody-Associated Paraneoplastic Neurological Syndromes: A Pilot Study," *Brain Sciences* 11, no. 12 (2021): 1577, https://doi.org/10.3390/brainsci11121577.

17. R. Inui, K. Saito, Y. Shimomura, D. Yamashita, M. Kawamoto, and T. Ishikawa, "Anti-Ma-Associated Paraneoplastic Cerebellar Degeneration in a Patient With Nodular Lymphocyte-Predominant Hodgkin Lymphoma: A Case Report," *BMC Neurology* 20, no. 1 (2020): 355, https://doi.org/10.1186/s12883-020-01929-4.

18. S. G. Ortega, N. Sola-Valls, D. Escudero, A. Saiz, and F. Graus, "Anti-Ma and Anti-Ma2-Associated Paraneoplastic Neurological Syndromes," *Neurologia* 33, no. 1 (2018): 18–27, https://doi.org/10.1016/j.nrl.2016.05.010.

19. A. A. Madhavan, C. M. Carr, P. P. Morris, et al., "Imaging Review of Paraneoplastic Neurologic Syndromes," *American Journal of Neuroradiology* 41, no. 12 (2020): 2176–2187, https://doi.org/10.3174/ajnr.A6815.

20. F. Graus, A. Vogrig, S. Muñiz-Castrillo, et al., "Updated Diagnostic Criteria for Paraneoplastic Neurologic Syndromes," *Neurology: Neuroimmunology & Neuroinflammation* 8, no. 4 (2021): e1014, https://doi.org/10.1212/NXI.0000000000001014.

Supporting Information

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