Case Report

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대한영상의학회지

Hashimoto's Encephalopathy with Unusual MRI Findings Mimicking Meningoencephalitis: A Case Report and Literature Review

수막뇌염을 모방한 드문 뇌 자기공명영상 소견을 보인 하시모토 뇌병증: 증례 보고 및 문헌고찰

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Hashimoto's encephalopathy (HE) is a rare autoimmune disease characterized by a high serum concentration of antithyroid antibodies without evidence of cerebral disease. Magnetic resonance imaging (MRI) findings in HE patients are nonspecific, although diffuse or focal white matter changes have been reported in several cases. We present a rare case involving a 79-year-old woman with elevated antithyroid antibody levels and abnormal imaging findings similar to meningoencephalitis. Serial MRI initially showed multiple T2 hyperintense lesions with diffuse leptomeningeal enhancement that disappeared after steroid therapy.

Index terms Hashimoto's Encephalitis; Autoantibodies; Meningoencephalitis; Magnetic Resonance Imaging

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INTRODUCTION

Hashimoto's encephalopathy (HE) is an extremely rare acute or subacute encephalopathy associated with Hashimoto's thyroiditis (1), and is characterized by a high antithyroid antibody titer. The etiology of HE is unclear, but it is thought to be an immune-mediated disease (2). Clinical manifestations of HE include various neuropsychological symptoms and altered cognitive functions. In the absence of other possible etiologies

of encephalopathy, HE patients have nonspecific electroencephalography (EEG) and magnetic resonance imaging (MRI) findings. (3) Several cases have been reported to show variable T2 and fluid-attenuated inversion recovery (FLAIR) hyperintense lesions in white matter. (3, 4) Here we report on a case of HE initially diagnosed as meningoencephalitis of undetermined origin based on MRI findings, discuss imaging results, and review the literature.

CASE REPORT

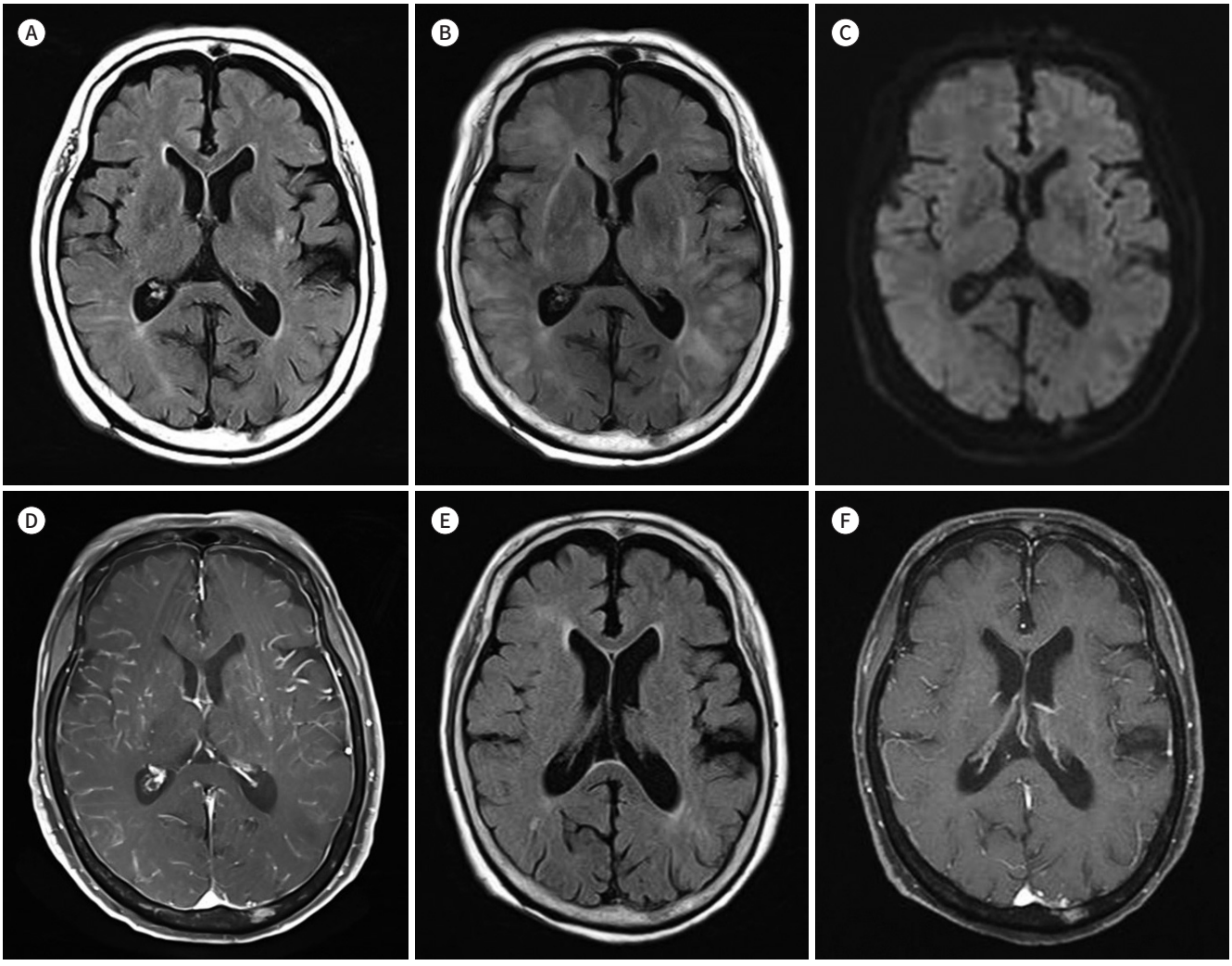
In July 2018, a 79-year-old woman patient visited the emergency room of a local hospital with complaints of disorientation and a confused mental state. MRI without gadolinium performed at that time revealed scattered increased T2 signal in bilateral cerebral white matter (Fig. 1A). She was diagnosed with hypoglycemia and her symptoms subsequently improved after instituting supportive care. A week later she developed an alteration of consciousness manifesting as decreased responsiveness and an inability to recognize family members. In addition, there was also weakness of the right upper extremity, which recovered within hours. The next day she was admitted to our hospital for a confused mental condition. She was unable to speak and had a clouded sensorium. At presentation, the patient complained of generalized weakness and fatigue. Medical history taking revealed hypertension, diabetes mellitus. And her medical history included hypothyroidism following partial thyroidectomy for a benign nodule and she was taking levothyroxine. At time of admission, her vital signs and laboratory test results were normal and she had no sensory or motor deficits. Serum thyroid function testing confirmed an euthyroid state with normal thyroid-stimulating hormone, T3, and FT4 levels. However, serum antithyroid peroxidase antibody (anti-TPO) (> 20000 U/mL; normal < 60 IU/mL) and antithyroglobulin antibody (anti-TG) (1365 U/mL; normal < 60 IU/mL) were greatly elevated. Serologic screening for infectious, toxic, metabolic etiologies and tumor screening tests were negative. Markers of autoimmune disease were also negative, including antinuclear anti-DNA, anti SSA/SSB, anti-neutrophil cytoplasmic and myeloperoxidase antineutrophil cytoplasmic antibodies. EEG showed generalized slowing of background rhythm indicative of severe diffuse cerebral dysfunction. Ultrasound of thyroid showed a diffuse, irregular change with heterogeneous echogenicity. MRI FLAIR images revealed diffuse hyperintensities in periventricular white matter of cerebral hemispheres bilaterally with extension to the subcortical region, but no corresponding diffusion restriction was observed on diffusion weighted image (DWI) images (Fig. 1B, C). Axial contrast enhanced T1 weighted images showed diffuse enhancement along meningeal surfaces without definite parenchymal enhancement (Fig. 1D). Based on considerations of clinical and imaging findings, she was diagnosed as probable meningoencephalitis. However, cerebrospinal fluid (CSF) examination results revealed protein elevation (105.3 mg/dL), but a normal CSF cell count, glucose level, and microbiology findings. A diagnosis of HE was suspected because of the extensive negative work-up and strong positivity for antithyroid antibodies. The patient was treated with pulsed intravenous methylprednisolone 1 g daily for 5 days, followed by oral prednisolone 60 mg/day for additional 5 days, while gradually decreasing the dosage. And after treatment for 10 days, her cognition markedly improved. Follow-up MR images obtained 11 days after steroid discontinuation, revealed extents of multiple FLAIR hyperintense

lesions in whole brain had diminished and resolution of the meningeal enhancement (Fig. 1E, F).

DISCUSSION

"HE" was first described by Brain et al. in 1966 (1), and is a rare disease and with a prevalence of approximately 2.1/100000. HE is more common in women than in men (M/F ratio 5:1) and its prevalence is highest in those aged between 45 and 55 years (5). The clinical features of HE may be classified into two types, that is, a vasculitis type, which is similar to stroke

Fig. 1. Imaging findings in a 79-year-old woman with Hashimoto's encephalopathy.
A. Axial FLAIR magnetic resonance images showing multiple hyperintense lesions in both frontoparietal lobes and the basal ganglia.
B-D. Axial FLAIR images obtained at admission (B) demonstrating extensive high-signal–intensity lesions in the periventricular, deep, and subcortical white matter of the cerebral hemispheres. These lesions did not show diffusion restriction on diffusion-weighted images (C). Diffuse patchy and leptomeningeal enhancement was also observed on contrast-enhanced T1-weighted images (D).
E-F. Follow-up FLAIR images obtained 11 days after completion of steroid therapy (E) showing that the extent of multiple hyperintense lesions had diminished in the whole brain. Post-contrast images (F) showing disappearance of the diffuse meningeal enhancement.
FLAIR = fluid-attenuated inversion recovery



and characterized by hemiparesis, aphasia, ataxia, and mild cognitive dysfunction, and a diffuse type, which follows a progressive course and is accompanied by cognitive disorders, changes in consciousness, and psychological symptoms (3). In our case, patient's clinical features are more consistent with the second form, which is more common. In most HE cases, routine blood tests are normal (4). However, thyroid function test results of HE patients may reveal subclinical hypothyroidism or hypothyroidism, subclinical hyperthyroidism or hyperthyroidism or be normal, though subclinical hypothyroidism is most common (3). Anti-TPO antibodies are positive in most HE patients, and anti-TG antibodies are also present in many cases. Recently, anti-α-enolase antibodies, which are expressed in vascular endothelial cells were suggested to be a potential diagnostic factor of HE. The level of anti-thyroid antibodies does not correlate with the severity of disease (6). The pathogenic role played by anti-thyroid antibodies in HE remains uncertain, but three hypothetical mechanisms have been proposed (2). The first hypothesis concerns cross-reactivity between shared thyroid and brain antigen. The second hypothesis involves perivascular lymphocytic infiltration, which is supported by the presence of anti-α-enolase antibodies in HE and single-photon emission CT findings of focal or generalized hypoperfusion (7). The third hypothesis is that the clinical features of HE are caused by the toxic effects of thyrotropin-releasing hormone (TRH). In almost all cases, EEG is abnormal and usually shows slow waves that are diffuse or restricted to forehead or temporal area. CSF studies usually demonstrate increased protein without pleocytosis (2). To achieve a diagnosis the following five factors are important: 1) acute or subacute encephalopathy; 2) exclusion of other toxic, metabolic, inflammatory, ischemic, and infectious causes; 3) euthyroidism or thyroid hormone changes not explaining symptoms; 4) increased autoimmune thyroid antibodies; and 5) good response to steroid treatment (3). Our case compatible with the diagnostic criteria. MRI is normal in approximately 50% of HE patients, and the most common findings are cerebral atrophy, white matter abnormalities, cortical irregularities, and vasculitic changes. Cerebellar T2 hyperintensities or atrophy are rarely seen (8). Few cases have reported diffuse hyperintesities on DWI and marked resolution of lesions after steroid therapy (7). And focal lesions in HE may simulate cerebral tumor, granuloma, infection, ischemic stroke or degeneration (3, 9). Most MRIs in HE patients reveal two types of imaging findings. The more frequently reported leukoencephalopathy-like type demonstrates diffuse or multiple periventricular hyperintese lesions in the cerebral white matter on DWI and T2 weighted image (10). Several cases have been reported to exhibit variable T2 and FLAIR hyperintense lesions in cortex, subcortex, brain stem, basal ganglia, hippocampus, corpus callosum, and white matter, which may diminish after commencing steroid treatment (3, 4). Limbic encephalitis-like type shows bilateral or unilateral high signal intensity area in the mesial temporal lobes or severe hippocampal swelling (10). As has been previously reported, multiple FLAIR high signal intensity lesions were observed in our case. However, we noted leptomeningeal enhancement, which is unusual. Dural enhancement has been reported in one case and extensive dural enhancement was observed on MRI. Biopsy was performed and histologic findings revealed striking dural thickening (9). However, as far as we know, meningeal enhancement has not been previously reported. HE is difficult to diagnose and initial misdiagnoses were common. The differential diagnosis of HE should consider any condition with various neurologic deficits. The most

frequent misdiagnoses include Creutzfeldt-Jakob disease (CJD), rapidly progressive dementia, vasculitis, limbic encephalitis, and primary psychiatric disease (4, 9). The clinical findings of HE are similar to those seen in CJD, but CJD doesn't respond to the steroid treatment. Vasculitis responds to steroid or immunosuppression therapy, however, the titer of antithyroid antibodies is within the normal range. Limbic encephalitis shows high T2 signal intensity in the medial temporal lobe, and is sensitive to steroid treatment (3). In this case, specific serum antineuronal antibodies found in limbic encephalitis were negative. Response to steroid therapy is usually good in HE patients, and in those irresponsive to steroids, azathioprine, cyclophosphamide or methotrexate, intravenous immunoglobulin, and plasma exchange may be used in combination (6). HE should be considered in the differential diagnosis of acute or subacute unexplained encephalopathy, especially in the presence of autoimmune thyroid disease, and if HE suspected, thyroid antibody testing should be performed. Prompt initiation of steroid therapy is dependent on awareness of the clinical and imaging findings of HE.

Author Contributions

Conceptualization, S.H.B.; investigation, K.H.; supervision, K.H.J.; visualization, K.H.; writing—original draft, S.H.B.; and writing—review & editing, K.H.J.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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수막뇌염을 모방한 드문 뇌 자기공명영상 소견을 보인 하시모토 뇌병증: 증례 보고 및 문헌고찰

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하시모토 뇌병증은 다른 대뇌 질환의 증거가 없이 항갑상선 항체의 높은 혈청 농도를 특징으로 하는 드문 자가 면역 질환이다. 하시모토 뇌병증의 자기공명영상 소견은 비특이적이고, 현재까지 미만성 또는 국소 백질 변화가 보고 된 바 있다. 저자는 증가된 항갑상선 항체와 동반하여 수막뇌염과 유사한 영상 소견을 보인 79세 여성의 하시모토 뇌병증을 경험하여 이에 대해 보고하고자 한다. 환자의 일련의 자기공명영상에서 치료 전 관찰되던 여러 T2-고강도 병변과 미만성의 뇌수막 조영증강은 스테로이드 요법 후 소실되었다.

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