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Review Article

The early diagnosis and treatments in multiple sclerosis

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Multiple sclerosis (MS) is a chronic inflammatory demyelinating disorder of the central nervous system that leads to neurological disability. The diagnosis of MS relies on the MRI criteria, which can demonstrate dissemination in space and time. Exclusion of other demyelinating mimics is essential because there are no specific biomarker for MS and MRI criteria are still have imperfect. There is incremental improvements in MS treatment option that have contributed to the delay of disease progression. The early initiation of DMT may ameliorate the neurological disability. In this review, we discusses the new diagnostic MS criteria and summarize the evidences supporting the early treatment in the course of MS.

Key Words: Diagnosis, Multiple sclerosis

Multiple sclerosis (MS) is a chronic inflammatory disease occurring in the brain and spinal cord, and which manifests as various neurological symptoms. MS mainly occurs at a young age when individuals are socially active and the physical disabilities create a socioeconomic and individual burden.[1] Because there are no characteristic clinical symptoms or tests with high diagnostic specificity, the diagnosis of MS is based on excluding MS-like diseases, and finding imaging evidence of time and spatially diffuse lesions in the central nervous system. Over the last decades, disease modifying treatment (DMT) has been applied at the onset of MS based on several studies, and it is known that starting DMT early slows down the disease progression and prevents the disability. The first step for rapid treatment is correct diagnosis, and this review looks at MS diagnostic criteria newly published in 2016 and highlights the importance of differential diagnosis and early treatment.

There is no single test to confirm an MS diagnosis. For this reason, researchers have changed and applied various diagnostic criteria for MS over the past two decades based on new evidence and expert recommendations. MS diagnosis, including clinical approaches, should exclude other explanatory diseases and the demyelinated lesion of the central nervous system should be identified in many places (dissemination in space; DIS) and several times (dissemination in time; DIT). Although the diagnosis is based on clinical evidence, magnetic resonance imaging

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Table 1. CIS clinical features and likelihood of signaling an MS diagnosis[4]

CIS features typically seen in MS	Less common CIS features which may be seen in MS	Atypical CIS features not expected in MS
Optic nerve		
Unilateral optic neuritis	Bilateral simultaneous optic neuritis	Progressive optic neuropathy
Pain on eye movement	No pain	Severe, continuous orbital pain
Partial and mainly central visual blurring	No light perception	Persistent complete loss of vision
Normal disc or mild disc swelling	Moderate to severe disc swellingwithno hemorrhages	Neuroretinitis (optic disc swelling with macular star)
	Uveitis (mild, posterior)	Uveitis (severe, anterior)
Brain stem/cerebellum		
Bilateral internuclear ophthalmoplegia	Unilateral internuclear ophthalmoplegia, facial palsy, facial myokymia	Complete external ophthalmoplegia; verticalgaze palsies
Ataxia and multidirectional nystagmus	Deafness	Vascular territory syndrome, e.g., lateramedullary
Sixth nerve palsy	One-and-a-half syndrome	Third nerve palsy
Facial numbness	Trigeminal neuralgia	Progressive trigeminal sensory neuropathy
	Paroxysmal tonic spasms	Focal dystonia, torticollis
Spinal cord		
Partial myelopathy	Complete transverse myelitis	Anterior spinal artery territory lesion (sparing posterior columns only)
Lhermitte's symptom	Radiculopathy, areflexia	Cauda equina syndrome
Deafferented hand	Segmental loss of pain andtemperature sensation	Sharp sensory level to all modalities andlocalized spinal pain
Numbness	Partial Brown-Sequard syndrome (sparing posterior columns)	Complete Brown-Sequard syndrome
Urinary urgency, incontinence, erectile dysfunction	Faecal incontinence	Acute urinary retention
Progressive spastic paraplegia (asymmetrical)	Progressive spastic paraplegia (symmetrical)	Progressive sensory ataxia (posterior columns)
Cerebral hemispheres		
Mild subcortical cognitive impairment	Epilepsy	Encephalopathy (obtundation, confusion, drowsiness)
Hemiparesis	Hemianopia	Cortical blindness

(MRI) should support the clinical diagnosis. With the development of MRI and the application of new diagnostic criteria, accurate diagnosis of early stage MS has recently become possible. Nevertheless, correct consideration of clinical information is critical for excluding MS-like diseases that may cause white matter degeneration.

1. Clinical Symptoms

Clinical symptoms are manifested as symptoms impacting movement, sensory, visual and autonomic nervous systems. Additionally, most relapsing-remitting MS (RRMS) patients experience central nervous system symptoms such as optic neuritis, incomplete transverse neuritis and acute brain stem syndrome that lasts for more than 24 hours. At this time, the central nervous system symptoms that are experienced first are called

clinically isolated syndrome (CIS).[2] After CIS, many patients experience symptoms of the central nervous system again, and when the second episode occurs, MS can be diagnosed as clinically definite multiple sclerosis (CDMS). About 85% or more of CIS cases will develop into MS that satisfies both DIS and DIT together.[2,3] The clinical features of CIS suggesting MS are summarized in (Table 1).[4]

2. 2016 MAGNIMS Diagnostic Criteria

The diagnostic criteria were determined by McDonald in 2001 and were revised in 2005 and again in 2010. New diagnostic criteria were suggested in 2016 as "The magnetic resonance imaging in multiple sclerosis (MAGNIMS)" (Table 2).[5-8] Diagnosis of MS is possible when DIS and DIT are simultaneously satisfied in CIS patients by applying these diagnostic criteria.

According to the 2016 MAGNIMS diagnostic criteria, among 5 lesions including ≥ 3 periventricle lesions, juxtacortical lesions, posterior fossa lesions, spinal cord lesions, and optic nerve lesions (Fig. 1A-E) if 2 or more lesions are invaded, it satisfies the DIS.[8] DIT is satisfied if a contrast-enhanced lesion and non-contrast-enhanced lesion are present at the same time or a new T2 lesion or contrast-enhanced lesion is observed in the MRI regardless of the follow-up period. In the

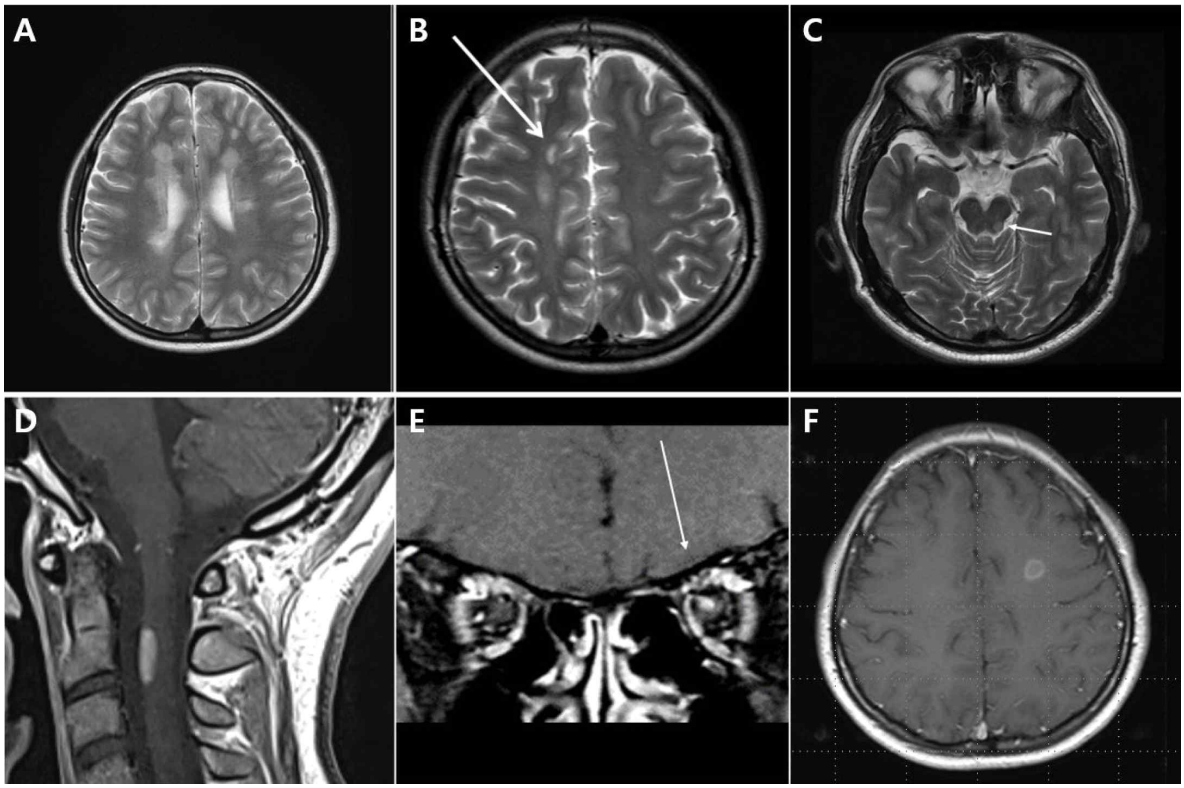

Fig. 1. Example of lesion for multiple sclerosis MRI Criteria of dissemination in space (A) periventricular lesions; (B) juxtacortical lesions; (C) infratentorial lesions; (D) spinal cord lesion; (E) optic nerve lesion. Gadolinium-enhancing lesion in T1 gadolinium weighted image; (F) are visible in the patient with MS.

Table 2. 2010 McDonald criteria and 2016 MAGNIMS Diagnosis criteria[8]

	2010 McDonald criteria	2016 MAGNIMS criteria
Dissemination in space	≥2 of 4 characteristic location ≥1 periventricular lesion ≥1 juxtacortical lesion ≥1 asymptomatic brainstem lesion ≥1 asymptomatic spinal cord lesion	≥2 of 5 characteristic location ≥3 periventricular lesion ≥1 cortical/juxtacortical lesion ≥1 brainstem lesion ≥1 spinal cord lesion ≥1 optic nerve lesion *If a patient has a brainstem or spinal cord syndrome, or optic neuritis, the symptomatic lesion (or lesions) are not excluded from the criteria and contribute to the lesion count. †This combined terminology indicates the involvement of the white matter next to the cortex, the involvement of the cortex, or both, thereby expanding the term juxtacortical lesion.
Dissemination in time	- Simultaneous presence of asymptomatic Gd-enhancing and non-enhancing lesion at any time - A new T2 and/or Gd-enhancing lesion on follow-up MRI irrespective of timing of baseline scan	- Simultaneous presence of asymptomatic Gd-enhancing and non-enhancing lesion at any time - A new T2 and/or Gd-enhancing lesion on follow-up MRI irrespective of timing of baseline scan - Clinical symptoms should be associated with radiologically isolated syndrome

2010 McDonald diagnostic criteria, brain stem or spinal cord lesions that caused symptoms were excluded,[7] but the 2016 MAGNIMS diagnostic criteria reflects the lesions regardless of symptoms.[8] Spinal nerve MRI is recommended for DIS evaluation purposes but it has limitations for DIT identification.[9,10] Abnormal findings of optical coherence tomography and visual evoked potential are recognized to support optic nerve lesions as well as clinical symptoms and MRI findings.[8] These changes in the diagnostic criteria are believed to increase the sensitivity and thus promote early diagnosis.

With the development of imaging technology and the increased accessibility of MRI, there are cases in which a lesion suggestive of MS is found in a person who does not have typical MS clinical symptoms or signs. Such a case is named as radiologically isolated syndrome (RIS).[11] However, even RIS that satisfies the DIS should not be diagnosed as MS based on MRI. However, MS can be diagnosed if at least one episode that is appropriate for demyelinated central nervous system symptom has been confirmed.[8]

3. MRI Findings of MS

There is no specific MS lesion, but lesions of early MS patients are mainly identified around the cerebral ventricle, and are observed as either a oval-shaped lesion with high-intensity signal on T2-weighted MRI or a "Dawson Finger" lesion arranged perpendicular to the lateral cerebral ventricle (Fig. 1-A).[12]

An increase of the contrast enhancement related to damage of the cerebral vascular barrier in the form of a complete or incomplete ring enhancement may be seen in the border of MS lesions (Fig. 1F). However, these findings can also be observed in brain abscess, brain tumors and sarcoidosis, and therefore requires caution in diagnosis. In MS, spinal lesions are localized in the axial region of the MRI not invading the whole, and 90% of the lesions have a short length of less than 2 spinal segments (Fig. 1D).[13]

Cortical lesions (Fig. 1-B) are classified as leukocortical, intracortical, and subpial lesion pathologically. Approximately 38% of cortical lesions are found in early MS patients,[14] and autopsies reveal the demyelinated lesions in the local cortex in approximately 90% of MS patients. However, it is difficult to find these cortical lesions with conventional clinical MRI protocols. Recently, double inversion recovery, phase-sensitive inversion recovery, and MP-RAGE (magnetization-prepared rapid acquisition with gradient echo sequence) were reported to have high sensitivity for detecting cortical lesions.[8] It is reported that about 30% of CIS patients have cortical lesions when using double inversion recovery images.[15,16]

Recently, with the development of 7T MRI neuroimaging, a central vein sign has been reported in MS patients. Kilsdonk et al. analyzed 1004 cases of brain lesions in 33 MS patients and found a central vessel in around 78% of the lesions.[17] These central vein signs are not observed in ischemic brain white matter degeneration and are likely to be helpful in differential diagnosis.[18]

4. Differential Diagnosis

Infections, neoplasms, congenital diseases, metabolic diseases, vascular diseases and idiopathic inflammatory demyelinated diseases can also meet the MS diagnostic criteria by displaying clinical forms or MRI findings similar to those of MS.[4,19]

Therefore, MS cannot be diagnosed based only on the location of the lesion according to the MRI diagnosis criteria, so efforts should first be concentrated on differential diagnosis. Differential diagnosis is based on clinical observation, blood test results and imaging. In 2008, Miller et al. reported 79 clinical and imaging red flags that should differentiate between MS and non-MS patients.[4] If clinical features such as lung, kidney and bone invading lesions, peripheral neuropathy, myopathy, rash, and arthritis are observed, they are clinical red flags that indicate non-MS diagnoses should be considered (Table 3).

Differential diagnosis of neuromyelitis optica spectrum disorder (NMOSD) or acute disseminated encephalomyelitis (ADEM) is especially important in patients suspected of having idiopathic inflammatory demyelinated disease. Patients with ADEM may not need prophylactic immunotherapy because of their low possibility of recurrence, and it is important to note that if interferon-beta (IFN-b), the primary treatment for MS, is applied to NMOSD, recurrence cannot be effectively prevented.[20] Particularly, since

Table 3. Clinical and MRI major red flags suggestive of alternative diagnosis to multiple sclerosis[4]

Red flag	Type	Examples of alternative diagnosis
Bone lesions	Clinical	Histiocytosis; Erdheim Chester disease
Lung involvement	Clinical	Sarcoidosis; Lymphomatoid granulomatosis
Multiple cranial neuropathies or polyradiculopathy	Clinical	Chronic meningitis, including sarcoidosis and tuberculosis; Lyme disease
Peripheral neuropathy	Clinical	B12 deficiency; adrenoleukodystrophy; metachromatic leukodystrophy, Lyme disease
Tendon xanthomas	Clinical	Cerebrotendinous xanthomatosis
Cerebral venous sinus thrombosis	MRI	Behçet's disease; vasculitis; chronic meningitis, antiphospholipid or anti-cardiolipin antibody syndromes
Cardiac disease	Clinical	Multiple cerebral infarcts; brain abscesses with endocarditis or right to left cardiac shunting
Myopathy	Clinical	Mitochondrial encephalomyopathy (e.g.,MELAS); Sjögren's syndrome
Cortical infarcts	MRI	Embolic disease; thrombotic thrombocytopenic purpura; vasculitis
Hemorrhages/ microhemorrhages	MRI	Amyloid angiopathy; Moya Moya disease; CADASIL; vasculitis
Meningeal enhancemen	MRI	Chronic meningitis; sarcoidosis; lymphomatosis; CNS vasculitis
Extrapyramidal features	Clinical	Whipple's disease; multisystem atrophy; Wilson's disease
Livedo reticularis	Clinical	Antiphospholipid antibody syndrome; systemic lupus erythematosus; Sneddon's syndrome
Retinopathy	Clinical	Mitochondrial encephalomyopathy; Susac, and other vasculitides (retinal infarction); neuronal ceroid lipofuscinosis
Calcifications on CT scans	MRI	Cysticercosis; toxoplasmosis, mitochondrial disorders
Diabetes insipidus	Clinical	Sarcoidosis; histiocytosis
Increase serum lactate level	Clinical	Mitochondrial disease
Selective involvement of the anterior temporal and inferior frontal lobe	MRI	CADASIL
Hematological manifestations	Clinical	Thrombotic thrombocytopenic purpura; vitamin B12 deficiency; Wilson's disease (hemolytic anemia); copper deficiency
Lacunar infarcts	MRI	Hypertensive ischemic disease; CADASIL; Susac syndrome
Persistent Gd-enhancement and continued enlargement of lesions	MRI	Lymphoma; glioma; vasculitis; sarcoidosis
Mucosal ulcers	Clinical	Behçet's disease
Myorhythmia	Clinical	Whipple's disease
Hypothalamic disturbance	Clinical	Sarcoidosis; neuromyelitis optica; histiocytosis
Recurrent spontaneous abortion or thrombotic events	Clinical	Antiphospholipid antibody syndrome; thrombotic thrombocytopenic purpura; metastatic cancer with hypercoagulable state
Simultaneous enhancement of all lesions	MRI	Vasculitis; lymphoma; sarcoidosis
Rash	Clinical	Systemic lupus erythematosus; T-cell lymphoma; Lyme disease, Fabry disease
T2-hyperintensity in the dentate nuclei	MRI	Cerebrotendinous xanthomatosis
Arthritis, polyarthalgias, myalgias	Clinical	Systemic lupus erythematosus; Lyme disease; fibromyalgia
Amyotrophy	Clinical	Amyotrophic lateral sclerosis; syringomyelia; polyradiculpathy

Headache or meningismus	Clinical	Venous sinus thrombosis; chronic meningitis; lymphoma or glioma, vasculitis, systemic lupus erythematosus
T1-hyperintensity of the pulvinar	MRI	Fabry disease; hepatic encephalopathy; manganese toxicity
Persistently monofocal manifestations	Clinical	Structural lesion (e.g., Chiari malformation); cerebal neoplasm
Large and infiltrating brainstem lesions	MRI	Behçet's disease; pontine glioma
Predominance of lesions at the cortical/subcortical junction	MRI	Embolic infarction; vasculitis; progressive multifocal leukoencephalopathy

CADASIL; cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy,MELAS; mitochondrial myopathy, encephalopathy, lactic acidosis, stroke-like episodes syndrome

there is more NMOSD than MS in the Asian population, it is necessary to check whether aquaporin-4 antibody is detected and if there are any characteristic MRI findings suggesting NMOSD. The 2015 International consensus diagnostic criteria[21] presented characteristic MRI findings suggestive of NMOSD as follows: lesions invading corticospinal tract, prolonged invasion of the optic nerve or invasion of the posterior optic nerve including the optic chiasm, especially, when confirming the invasion of both optic nerves and simultaneous increase of T2 high shading or contrast enhancement in optic chiasm, lesions around the third cerebral ventricle or the thalamus and hypothalamus, medulla oblongata around the fourth cerebral ventricle, large subcortical or deep white matter lesions (tumefative lesion), long lesions of corpus callosum (arch bridge pattern), long contrast-enhanced lesions around the ependyma (pencil-thin lesion), and long myelitis more than 3 spinal segments (longitudinally extensive transverse myelitis).

Mendelian or mitochondrial genetic disorder is also differentiated from MS.[22] There are various diseases that can cause white matter degeneration due to inherent factors, and leukodystrophy which occurs as an adult may appear similar to MS (Table 3). However, there are many cases in which leukodystrophy appears as a bilateral, symmetric white matter lesion in MRI and clinical manifestations are also accompanied by mental symptoms such as cognitive dysfunction and behavioral abnormalities, which can be a lead to the differential diagnosis.

Leber hereditary optic neuropathy (LHON) is an inherited disease caused by mitochondrial genetic mutation, which causes loss of central vision in one or both eyes and causes severe vision loss. It occurs mainly between the ages of 25 to 35 years. RRMS was diagnosed in MS patients by genetic testing and detection of a mitochondrial genetic mutation (LHON-MS, Harding disease), therefore, for MS patients with a family history of LHON or severe visual impairment, the possibility of accompanying LHON disease should be considered.[23]

5. Need for Early Treatment

Axonal damage starts at the beginning of the MS, but does not lead to significant clinical symptoms, initially due to the complementary elements of the central nervous system; but over time, extensive axonal damage causes irreversible clinical symptoms.[24] Encephalatrophy is also observed in clinically isolated syndrome (CIS), the period when the first symptoms of MS occur. According to a study on brain volume in 263 CIS patients, brain volume reduction measured at the first symptom and at 1 or 2 years after the onset of symptoms was greater in patients who were converted from CIS to CDMS than in CIS patients who did not experience recurrence. In addition, the number of newly developed T2 lesions during the first year of the disease after symptoms occurred was found to be related to the brain volume change rate in the second year, indicating that damage to brain parenchyma progresses very rapidly in the early stages of the disease.[25] Decreased cognitive function is also observed in advanced MS as well as in CIS. In a study on CIS patients and RRMS patients, within two years of onset, about 19.6% of patients showed abnormalities in more than four cognitive measures and showed a concentration of disorders, performance abnormalities, and a significant decrease in memory and learning abilities compared to the control group.[26]

T2 lesion load seen in early MRI lesions is related to the long-term prognosis of the patient. Filippi et al. analyzed the initial MRI results in MS patients and the expanded disability status scale (EDSS) of disease severity after 5 years. In early MRI results, 52% of patients with a lesion load of more than 1.23 ㎤ had an EDSS score of 6 or greater and 23% of patients with a lesion load less than 1.23 ㎤ showed an EDSS score of below 6.[27] Based on these studies, the need for therapeutic intervention at the beginning of MS has become apparent.

Large clinical studies (CHAMPS, ETOMS, BENEFIT, Precise, and TOPIC) were conducted in CIS, the first symptomatic stage of MS, and demonstrated that preventing recurrence and delaying the conversion to CDMS could reduce the risk of disease progression.

The CHAMPS study[28] was a 3-year follow-up study of 383 patients with CIS by dividing them into an IFN-b-1a 30 mg (Avonex®) treatment group and placebo group. The incidence of CDMS was significantly lower in the IFN-b-1a group than in the placebo group (P = 0.002). At Month 18, the volume of brain lesions in the treatment group was significantly smaller (P < 0.001), and newly developed T2 lesions and contrast-enhanced lesions were also significantly less than the placebo group (P < 0.001). Conversion from CIS to CDMS was approximately 66% lower in the IFN-b-1a treatment group than in the placebo group. In a 10-year follow-up study,[29] an early treatment group that started treatment within one month after CIS diagnosis showed lower CDMS conversion (hazard ratio = 0.64) and lower annual recurrence rate (P = 0.03) than the delayed treatment group which started treatment after an average

of 30 months from diagnosis.

The ETOMS study[30] was a 2-year follow-up study on 308 patients with CIS by dividing them into an IFN-b-1a 22 mg (Rebif®) treatment group and a placebo group. During the follow-up period of 2 years, the IFN-b-1a treatment group (34%) showed lower CDMS conversion than the placebo group (45%) (P = 0.047). CDMS conversion was significantly prolonged in the IFN-b-1a treatment group (569 days) compared to the placebo group (252 days) (P = 0.034). The annual recurrence rate was also significantly lower in the IFN-b-1a treatment group (0.33) than the placebo group (0.43) (P = 0.045). In MRI, the lesion load was significantly lower in the treatment group, demonstrating the effectiveness of IFN-b-1a treatment using brain imaging as well as clinical effects in early MS patients.

The PreCISe study[31] was a 3-year study comparing 481 CIS patients with more than two T2 lesions greater than 6 mm in size, which divided the patients into a glatiramer acetate 20 mg (Copaxone®) treatment group and a placebo group. CDMS conversion was significantly lower in the glatiramer acetate treatment group (25%) than the placebo group (43%) (P = 0.0001) and the time when CDMS conversion occurred was also significantly prolonged in the glatiramer acetate treatment group (722 days) than the placebo group (336 days) (P = 0.0005). In the last observation, the number of newly developed T2 lesions was significantly less in the glatiramer acetate treatment group (0.7 lesions) compared to the placebo group (1.8 lesions) (P = 0.0001).

The BENEFIT study[32] was a study comparing 468 CIS patients by dividing them into an IFN-b-1b 250 mg (Betaferon®) treatment group and a placebo group. Two years later, 45% patients in the placebo group were converted into CDMS, however, only 28% of patients in the IFN-b-1b treatment group were converted into CDMS, reducing the risk of CDMS conversion by about 50% when administering IFN-b-1b. Since then, an 11-year extended follow-up study[33] showed that early treatment within 60 days after CIS occurrence reduced the risk of the first recurrence by 34.5% compared to a delayed treatment group (start of treatment after the second clinical recurrence or 2 years after CIS occurrence) and reduced the annual recurrence rate by 19.1%. There was no significant change in EDSS between the early treatment group and the delayed treatment group, but after 11 years the EDSS score remained low and the conversion of SPMS was low in both groups.

The TOPIC study[34] compared 618 patients with CIS for more than 108 weeks by dividing them into two treatment groups administering 7 mg or 14 mg of teriflunomide (Aubagio®) daily and a placebo group. Compared with the placebo group (28%), CDMS conversion in the 14 mg (18%) and 7 mg (19%) teriflunomide treatment groups was significantly reduced (P = 0.0087, P = 0.0271). The risk of recurrence or new MRI lesions was also significantly reduced in the 14 mg treatment group compared to the placebo group (HR 0.651, P = 0.0003).

In addition to large-scale clinical studies of single agents, there was a study demonstrating that factors affecting cumulative impairment are related to the onset of treatment with various DMTs (IFN-b-1a, IFN-b-1b, glatiramer acetate, natalizumab, fingolimod, and rituximab).[35] In 639 MS patients, by applying a regression analysis model for about 8 years, the risk of reaching 4 points of EDSS was investigated by dividing the patients into three DMT treatment groups that started treatment after either 1 year, between 2 and 3 years, or more than 3 years after the first clinical symptoms developed. As the time of treatment was delayed, the risk increased by 7.4% per year, and patients who started treatment 3 years after the first clinical symptoms developed had a relative risk of 2.63 until reaching 4 points of EDSS, compared to patients who started treatment within 1 year after the first symptoms. Therefore, early treatment may be a factor that affects the occurrence of long-term disability.

It has been reported that various anti-inflammatory drugs and DMTs (dimethyl fumarate, fingolimod, alemtuzumab, rituximab, laquinimode, daclizumab, and ocelizumab) reduce the frequency and severity of new demyelinated episodes in RRMS as well as CIS.[36,37] However, when the disease has progressed to secondary progressive MS (SPMS), there is no effective drug. As for the pathological features, the cerebrovascular barrier is compromised and lymphocytes infiltrate into the central nervous system, so that the active inflammatory lesions can be identified at the time of RRMS. On the other hand, once the disease has progressed to SPMS, the effect of DMT or anti-inflammatory drugs is reduced because inflammatory changes in the central nervous system are reduced, and it is compartmentalized within the cerebrovascular barrier.[38] Whether newly introduced drugs can effectively prevent SPMS or not requires more research, but there is no doubt that aggressive treatment is needed at the time of RRMS where therapeutic effects can be expected.

CONCLUSION

In MS, axonal damage and encephalatrophy are initiated prior to progression to CDMS, which is related to the patient's severity of impairment. Many studies have shown that since DMT treatment reduces the frequency and severity of demyelinated episodes in MS patients, it is prudent to start DMT treatment at the early stage of disease, which is the period of the highest inflammatory activity. The most important thing for treatment of patients and their prognosis is to accurately diagnose CIS and MS as early as possible. Therefore, it is necessary to understand various differential diseases, to make an accurate diagnosis by collecting clinical symptoms and MRI findings and to perform frequent follow-ups.

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Peer Reviewer's Commentary

Multiple sclerosis (MS) is a chronic inflammatory disease occurring in the brain and spinal cord. The most important thing for treatment of patients and their prognosis is to accurately diagnose MS as early ad possible. This review summarized the MS diagnostic criteria newly published in 2016.

(Editorial Board)