Linear Pontine Trigeminal Root Lesions in Multiple Sclerosis

Clinical and Magnetic Resonance Imaging Studies in 5 Cases

Ichiro Nakashima, MD; Kazuo Fujihara, MD; Teiko Kimpara, MD; Naoshi Okita, MD; Sadao Takase, MD; Yasuto Itoyama, MD

Background: Magnetic resonance imaging (MRI) is useful for demonstrating demyelinating lesions in patients with multiple sclerosis (MS). Magnetic resonance imaging studies show that MS lesions are generally not uniform in shape, size, or distribution. Linearly shaped lesions at the trigeminal root entry zone have been occasionally reported in single cases of MS, but, to our knowledge, the frequency and the clinical features of such patients have not been comprehensively characterized.

Objective: To describe the frequency and the clinical and laboratory features of patients with MS who had linearly shaped lesions at the trigeminal root as seen on MRI.

Design and Setting: A retrospective review of medical records and MRI films of Japanese patients with MS admitted to a university hospital and its affiliated hospital in Sendai, Japan.

Patients and Methods: Brain MRI films of 74 consecutive Japanese patients with MS (51 females and 23 males) were studied retrospectively and the clinical and laboratory features of the patients with linearly shaped lesions at the trigeminal root were also investigated retrospectively.

Results: Five patients (6.8%) were shown to have T1-weighted–hypointense, T2-weighted–hyperintense, non-enhanced linear lesions in the pons on MRI, and these were uniformly localized in the intramedullary portion of the trigeminal root. All of these patients had clinically definite MS and had various types of facial sensory disturbances, such as neuralgia (1 patient), hypesthesia (2 patients), or paresthesia (3 patients). No other clinical or laboratory feature was characteristic in these 5 patients.

Conclusions: Linear pontine trigeminal root lesions were common in our patients with MS. They were associated with various facial sensory symptoms. Since similar lesions are formed in animal models of herpes simplex virus infection, further study is needed to clarify whether these MS lesions are virally induced.

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Multiple sclerosis (MS) lesions can be detected on magnetic resonance imaging (MRI) as patchy plaques, which are generally not uniform in shape, size, or distribution. Multiple sclerosis can involve any part of the white matter of the central nervous system and the extent of these lesions is unrelated to the neuroanatomical structure with the exception of some predominant localization of lesions in periventricular areas. Several articles have described trigeminal neuralgia in patients with MS that is associated with pontine MRI lesions along the trigeminal nerve root.1,2 In this study, we examine the frequency and clinical features of similar trigeminal lesions within our patients with MS, and discuss potential pathogenetic mechanisms that may account for these peculiar lesions.

Report of Cases

Case 1

A 26-year-old man developed a gait disturbance and numbness of the left side of the face and right half of the body when he was 22 years old. On physical examination, he had nystagmus, left-sided facial sensory loss, dysphagia, right hemiparesis and hemiparesthesia, deep sensory disturbance, and truncal ataxia. After the remission, weakness of the left arm and leg, and severe numbness of the right half of the body recurred. He had nystagmus, diplopia, dysphagia, left hemiparesis, right hemiparesthesia, and truncal ataxia and...
**PATIENTS AND METHODS**

**PATIENTS**

We retrospectively reviewed the brain MRI and medical records of 74 consecutive MS cases (51 females and 23 males) from January 1, 1988, through December 31, 1998. We identified 5 MS cases (6.8%) in which unique, linearly shaped lesions lying in the pontine trigeminal root were confirmed on MRI. Clinical, laboratory, and MRI findings of these 5 patients were analyzed in this study.

**MAGNETIC RESONANCE IMAGING**

In each case, all of the available MRI films, which had been taken since the onset of the illness, were examined. Two neurologists including one of us (I.N.) and a blinded neuroradiologist evaluated each scan. Any T2-weighted–hyperintense areas in the brainstem and cerebellum, which appeared on each T2-weighted image with a moderately long repetition time of 2000 to 3000 milliseconds and an echo time of 60 to 100 milliseconds, were considered abnormal.

was diagnosed as having clinically definite MS. His brain was scanned using a 0.1-T MRI scanner at the time of recurrence. A linear lesion was detected in the left side of the pons (Figure, A). The cerebrospinal fluid (CSF) study revealed a normal cell count and protein level. There were 2 definite oligoclonal IgG bands (OBs) in the CSF.

**CASE 2**

A 35-year-old woman developed right leg weakness when she was 26 years old. Three years later, spastic paraparesis, urinary dysfunction, and left-sided facial pain also developed. The CSF study results were abnormal with an elevated protein level and were positive for OBs. Since that time, the trigeminal neuralgia has frequently recurred. The anti–herpes simplex virus (HSV) antibody titer in the CSF was elevated when she developed intolerable facial pain at the age of 35 years. However, polymerase chain reaction for HSV-DNA showed no abnormalities. Magnetic resonance imaging using a 1.5-T scanner was performed when she developed severe neuralgia. The MRI showed a hyperintensive linear lesion along the left intramedullary trigeminal nerve root on T2-weighted image (Figure, B). There were several other lesions in the cerebral periventricular white matter, the basal ganglia, and the corpus callosum shown on MRI.

**CASE 3**

A 28-year-old man developed bilateral visual disturbance, diplopia, dysarthria, weakness of the whole body, gait disturbance, and urinary retention after the remission of a high fever. At the time of admission to the hospital, he had bilateral visual disturbance, oculomotor palsy, nystagmus, left-sided facial paresthesia, left-sided facial palsy, dysphagia, moderate quadriparesis, and cerebellar ataxia. The results of the CSF study were abnormal with marked pleocytosis and an elevation of the protein level. The results of the OB test were normal. Four years later, he developed mild paresthesia on the left side of the head and was diagnosed as having probable MS. Magnetic resonance imaging at the first episode showed lesions in the medulla oblongata, the left side of the lower pons, the right edge of the upper pons, and the right cerebral peduncle. Four years later when he had paresthesia on the left side of the head, MRI showed a new lesion in the left intramedullary trigeminal nerve root extending from the cerebellopontine angle to its entry zone (Figure, C).

**CASE 4**

A 28-year-old man developed bilateral visual disturbance, diplopia, nystagmus, dysarthria, right hemiparesis, and paresthesia of the whole face and extremities when he was 24 years old. Magnetic resonance imaging (1.5 T) showed multiple lesions in the pons. Most of the lesions were at the belly of the pons and a linear lesion was found along the left trigeminal root (Figure, D). There were no definite lesions in other regions of the brain. The CSF study was normal with no OBs. Two years later, he developed paresthesia and hypesthesia on the right side of the face. Magnetic resonance imaging showed a round plaque lesion at the right trigeminal nerve nucleus of the lower pons.

**CASE 5**

A 15-year-old girl developed paresthesia of the left side of the face and left fingers when she was 14 years old. Magnetic resonance imaging revealed multiple brain lesions including a linear lesion of the intramedullary trigeminal root (Figure, E). Two OBs were seen in the CSF although the CSF cell count and protein level were normal. The symptoms disappeared within a few weeks without any treatment. Six months later, she developed diplopia and her condition was diagnosed as clinically definite MS. Anti–HSV antibody titers and HSV-DNA levels in the CSF were negative when studied at the recurrence.

**RESULTS**

Among the 74 consecutive patients with MS, 5 patients had a linearly shaped MRI lesion in the pons, which corresponded neuroanatomically with the intramedullary trigeminal root. These 5 patients had various kinds of facial sensory manifestations, which are described in the “Report of Cases” section. None of the other patients had asymptomatic linear pontine lesions. Four other patients had rather round and larger plaque lesions near the cerebellopontine angle in the pons, which included the intramedullary trigeminal root and the surrounding regions. These 4 patients tended to have some additional cranial nerve symptoms, such as facial nerve palsies or hearing disturbances, besides facial sensory manifestations.
The clinical features of the 5 patients (2 females and 3 males) with linearly shaped pontine lesions are listed in the Table. The mean age of the 5 patients was 26.4 years and the mean duration of the disease was 4.2 years. Four of them had 2 relapses of MS and the remaining patient (case 2) had more than 5 relapses of MS. All 5 patients had facial sensory disturbances on the same sides as the pontine lesions. These were facial neuralgia (1 patient), facial paresthesia (3 patients), and facial hypesthesia (2 patients). All of the linearly shaped pontine lesions were observed as hyperintense lesions on T2-weighted images and as hypointense lesions on T1-weighted images along the intramedullary trigeminal root (Figure). Gadolinium enhancement was not observed in any of the lesions.

In the CSF study, only 1 (case 3) of these 5 patients had marked pleocytosis and an elevated protein content, while the other 4 had normal CSF cell counts and protein levels. Oligoclonal IgG bands were detected in 3 patients. A patient with trigeminal neuralgia (patient 2) had an elevated anti–HSV antibody titer both in the serum and the CSF during the acute phase of the second bout of MS.

**COMMENT**

Magnetic resonance imaging is useful for demonstrating and monitoring demyelinated lesions of the brain and spinal cord in patients with MS. 4,5 Multiple sclerosis lesions are usually not uniform in shape, size, and localization; tend to be round, oval, or irregular in appearance; pinpoint or large; and isolated or disseminated, although they show some predominance of localization near periventricular areas. 4,6 These MRI features of MS lesions are generally recognized. Therefore, such linearly shaped pontine lesions as shown in this study are unique for the shape of the MS lesions and their neuroanatomical localization.

Similarly shaped pontine MRI lesions have been reported in a few cases of MS, especially in those patients with symptoms and signs related to the trigeminal nerve. Gass et al 2 described 2 patients with MS who showed linearly shaped MRI lesions along the trigeminal root from among 6 patients with various diseases who reported trigeminal neuralgia. Meaney et al also described 1 patient with MS who had trigeminal neuralgia and a similar MRI lesion in the intramedullary trigeminal root. Such lesions corresponded only to the pontine trigeminal root, not to other intramedullary cranial nerve roots. 7 It is known that trigeminal neuralgia occurs more commonly in persons with MS than in the general population, 2,8,9 and especially in younger persons with MS who have bilateral trigeminal nerve involvement. 2 In general, idiopathic trigeminal neuralgia is thought to be causally associated with vascular compression on the trigeminal nerve or its root entry zone. 10 However, a different mechanism such as one involving demyelinative changes has to be presumed in MS. Very rare postmortem exami-
nations of the brains of patients with MS who had trigeminal neuralgia have shown demyelinating changes in the pons at the root entry zone.1,11

In this study of 5 patients with MS, we emphasize the uniqueness of the shape and localization of the pontine MS lesions and the relation of such lesions to the trigeminal nerve manifestations. They were linear in shape and neuroanatomically corresponded closely to the intramedullary trigeminal root, which extends from the root entry zone to the fifth nerve nuclei close to the fourth ventricle. Although such pontine trigeminal linear lesions have been observed in some previous reports,12 the pathogenetic mechanisms of the lesion formation have never been discussed. Why does such a demyelinating lesion develop linearly along the course of the intramedullary trigeminal fascicular fibers?

The shape, size, and localization of such demyelinated lesions in these 5 patients with MS has been observed in central nervous system demyelinating lesions of experimental HSV type 1–infected animal models. It is well known that, after an experimental inoculation of HSV type 1 in the cornea of mice or a rabbit, the virus spreads transaxonally to the central nervous system through the first branch of the trigeminal nerve and induces selective central nervous system demyelination in the intramedullary trigeminal root.11-13 The similarities in the localization and shape of these lesions suggest that a common pathogenetic mechanism may be present in both conditions. If so, it will be important to verify whether an infection of HSV plays an active role in developing these unique MS lesions or whether inflammatory responses in MS induce a reactivation of HSV. In 1 of the 5 patients with MS who had a history of recurrent trigeminal neuralgia, we found increased anti–HSV antibody titers in the serum and CSF. The increased anti–HSV antibodies were demonstrated during an episode of recurrent trigeminal neuralgia. However, polymerase chain reaction to HSV-specific DNA was negative in her CSF. Thus, the trigeminal root might have been previously damaged by herpetic infections, and increased anti–HSV antibodies could be the result of nonspecifically activated antigen-specific HSV B cells during an attack of MS and not necessarily a new herpetic recrudescence. It is well known that HSV resides in latent form in the trigeminal ganglia and that HSV-DNA is detected in the trigeminal ganglia in more than half of control subjects,14 and HSV-DNA is also often detected in the brains of persons with MS.15,16 It will be necessary to study the presence of HSV in the pontine trigeminal lesions.17

CONCLUSION

We studied 5 patients with MS who had peculiar MRI lesions at the intramedullary trigeminal root from among 74 consecutive patients, and they had various facial sensory manifestations. The pathogenetic mechanisms of such unique demyelinative lesions in MS may be related to HSV infection.

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Corresponding author and reprints: Ichiro Nakashima, MD, Department of Neurology, Tohoku University School of Medicine, 1-1 Seiryu-machi, Aoba-ku, Sendai 980-8574, Japan, (e-mail: inakashima@neurrol.med.tohoku.ac.jp).

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