Objective: To describe a patient from Southeast Asia with the optic-spinal phenotype of multiple sclerosis who developed syringomyelia and resultant complex regional pain syndrome (formerly named reflex sympathetic dystrophy).

Design: Case report.

Setting: Department of neurology at a tertiary care hospital in the Republic of Singapore.

Patient: A 53-year-old Chinese woman with a history of optic neuritis developed an episode of left hemiparesis leading to a diagnosis of multiple sclerosis. Serial neuroimaging studies revealed an active demyelinating plaque in the cervical area that later progressed into a syrinx. Over a period of 1 year she also developed signs of sympathetic dysfunction including Horner syndrome of the left eye and complex regional pain syndrome in the left hand.

Conclusions: A case of the optic-spinal phenotype of multiple sclerosis that is commonly observed in Southeast Asia is described. This characteristically tissue-destructive form of multiple sclerosis resulted in syringomyelia complicated by a complex regional pain syndrome. Possible pathogenic mechanisms for these associations are discussed.

Arch Neurol. 1999;56:1021-1024

MULTIPLE SCLEROSIS (MS) is a chronic demyelinating disorder with a wide range of clinical manifestations that reflects multifocal areas of central nervous system myelin destruction. Multiple sclerosis is an uncommon disease in Southeast Asia; its typical presentation is as a disorder of optic-spinal dysfunction. Invariably, the spinal form of this illness is manifest as transverse myelitis.1 We present an unusual case of a patient with MS who developed syringomyelia and resultant complex regional pain syndrome (CRPS), formerly known as reflex sympathetic dystrophy.

REPORT OF A CASE

A 56-year-old Chinese woman with an unremarkable medical history presented at age 43 years with right optic neuritis. Later, at age 53 years, she had a second bout of optic neuritis affecting her left eye. Both episodes were treated with pulsed high-dose intravenous methylprednisolone. During her second bout of optic neuritis, she also complained of vague pain in her left hand and forearm that was characterized by cramps and spasms. At that time, results of her neurological examination were remarkable only for left optic neuritis and left arm strength of 4/5. Notably, her reflexes were symmetric. In June 1995, a magnetic resonance imaging (MRI) scan of the brain performed as part of her evaluation showed no evidence of demyelination. Because of persistent complaints of pain and spasms in her left arm, MRI scans of the brain and cervical spine were repeated 2 months later. Bi-parietal lesions that were hyperintense on T2-weighted images and that did not enhance with gadolinium were present; these hyperintensities were suggestive of non-acute demyelinating lesions. The cervical spine showed no evidence of demyelination. A lumbar puncture was unremarkable (white blood cell count, 0.002 × 10⁹/L; glucose, 3.5 mmol/L [63 mg/dL], total protein, 0.3 g/L) and cerebrospinal fluid oligoclonal bands were not detected. In the setting of 2 bouts of optic neuritis, an episode of left hemiparesis, and her neuroimaging findings, the patient was diagnosed as having MS.

Fourteen months later (October 1996), the patient had a recurrent episode of pain in her left hand and forearm.

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and weakness in her left arm and leg. The left hand and forearm pain was again characterized by vague dysesthesias. She also complained of a constant burning pain in the same region, which did not conform to a pattern of dermatomal or peripheral nerve injury. A neurological examination at this time was notable for left optic atrophy, left afferent pupillary defect, and left hemiparesis with diminished left arm (2/5) and left leg (4/5) strength. In addition, left thenar wasting was observed. Her reflexes were present symmetrically with bilateral flexor plantar responses. Although she complained of sensory disturbances in the left arm, no sensory loss or suspended sensory level was apparent on extensive testing. Treatment with high-dose intravenous methylprednisolone resulted in mild improvement in her symptoms. Repeated MRI scans of the brain and cervical spine (October 1996) showed several areas of hyperintensity on T2-weighted images in the deep cerebral white matter that did not enhance with contrast on T1-weighted images. A long segment of increased signal on T2-weighted images was present in the cervical cord extending from the level of C2 to C5 with slight expansion. This cervical cord lesion enhanced after gadolinium administration at its middle and inferior portions. These neuroimaging findings suggested the presence of an active, demyelinating plaque spanning from C2 to C4 (Figure 1). Nerve conduction and electromyographic studies to further assess the left thenar eminence atrophy showed no evidence of neuropathy. Evoked studies were remarkable for prolonged bilateral visual evoked potentials, affecting the left side more than the right. Somatosensory evoked potentials were notable for a conduction abnormality between the left lumbar and left thoracic cord. Brainstem auditory evoked potentials were abnormal on the right side, suggestive of an auditory conduction abnormality in the brainstem.

Over the next year, the patient complained of pain in her left hand and forearm, which she described as a constant burning. She also observed that the nails and skin of her left hand appeared shinier and less wrinkled than the right hand. At the time of her neurological examination in October 1997, she had developed Horner syndrome in the left eye with ptosis, miosis, and anisocoria. Her left afferent pupillary defect persisted. Her left hemiparesis had improved and her strength remained at 4/5. The thenar eminence and interosseous muscles of her left hand were atrophied. Her reflexes continued to remain brisk and symmetric. The skin of her left hand appeared red, shiny, and unwrinkled. Compared with the right hand, her left hand was intermittently edematous, indurated, hyperhidrotic, mottled, and cool to touch (Figure 2). These findings suggested a CRPS involving the left hand. Laboratory data including complete blood cell count; electrolytes; glucose, calcium, and magnesium levels; liver function tests; and collagen vascular markers were all unremarkable. A repeated MRI scan of the cervical spine showed that on T1-weighted images, after gadolinium administration, no enhancement was noted in or around the hypodense area from C3 to C7 to suggest the presence of an active demyelinating plaque. On T2-weighted images, hyperintensity was present from C2 to C7. No cord swelling was observed. These neuroradiologic findings were consistent with a syrinx formation (Figure 3). The signs and symptoms of sympathetic dysfunction, particularly her CRPS, have been recalcitrant to conventional treatment options of tricyclic antidepressants, anticonvulsants, and physiotherapy. Further treatment considerations include a trial of gabapentin.

**COMMENT**

Our patient’s clinical course is characterized solely by optic nerve and cervical cord involvement. She does not fulfill strict criteria for Devic neuromyelitis optica, which include a severe transverse myelitis and an acute unilateral or bilateral optic neuropathy developing within days or weeks of each other. However, she clearly manifests an optic-spinal phenotype of MS. During the course of her illness, the patient initially developed a demyelinating plaque in the cervical area that over a year progressed to a syrinx. The clinical manifestations of our patient’s cervical syrinx included segmental weakness and atrophy of the left hand and an ipsilateral Horner syndrome. Although the pathogenesis of this syrinx is unclear, we can postulate on its cause. We do know that the gross pathological manifestation of MS is characterized by areas of local demyelination commonly referred to as MS plaques. These plaques are frequently found in areas adjacent to cerebrospinal fluid pathways. The spectrum of pathology observed in MS in-
prognosis of the coexistence of syringes in MS we re-
cause of greater than 7 years. Syrinx-like le-
3 years, and atrophic change was observed in patients with
administration in patients with a disease duration of less than
sions were swollen and enhanced after gadolinium ad-
curred more frequently than other spinal cord lesions. At
lesions has been reported in association with MS. In a se-
remains to be elucidated. A spectrum of spinal cord le-
sociated with Devic neuromyelitis optica are character-
In our patient’s case, she is likely to have
had an active MS plaque in the cervical region demon-
strated on MRI scan by gadolinium enhancement. Later,
the plaque may have undergone degenerative change with
resultant cervical syrinx formation involving areas of the
plaque site and spinal cord rostral to this plaque. The ne-
crotic process may have begun centrally, extending ros-
trally and caudally from the poles of the lesion.⁵ Alternatively,
a syrinx-like lesion may have developed following atrophy of the swollen spinal cord that had undergone de-
myelinating changes.⁶,⁷ The spinal cord lesions typically as-
associated with Devic neuromyelitis optica are character-
ized by demyelination, inflammation, and necrosis.⁸,⁹ Our
patient with the optic-spi nal phenotype of MS is likely to
have undergone tissue destruction and necrosis resulting
in a cervical cord syrinx that has persisted for 3 years.

Since the coexistence of syring formation in MS is un-
common, the neurological prognosis of such coexistence
remains to be elucidated. A spectrum of spinal cord le-
sions has been reported in association with MS. In a se-
ries by Kato et al⁰ of 37 patients with clinically diagnosed
MS with spinal cord lesions, cervical cord lesions oc-
curred more frequently than other spinal cord lesions. At
the thoracic level, higher thoracic lesions occurred more
often than lower level lesions. Characteristically, these
lesions were swollen and enhanced after gadolinium ad-
ministration in patients with a disease duration of less
than 3 years, and atrophic change was observed in patients
with a disease duration of greater than 7 years. Syrinx-like
lesions were found in 4 patients.⁷ To begin to determine
the prognosis of the coexistence of syringes in MS we re-
viewed previous case reports.³,¹⁰-¹⁴ Remarkably, a major-
ity of the cases reported appeared in the Japanese litera-
ture. Since the optic-spi nal form of MS is more common
in Asian countries and the acute demyelinating spinal cord
lesions may have subsequent development of myeloma-
lacia or frank cavitary degeneration, syringes that are the
result of spinal disease may occur more frequently in this
population. Of the 7 case reports, all but 1 were women.

The age range of the patients was from 26 to 40 years. Four
cases involved syringes in the cervical cord and 3 were in
the thoracic cord. Unlike the presentation in our case, not
all these cases of spinal cord lesions and subsequent syr-
inx formation were accompanied or preceded by visual
symptoms. These cases suggest that the prognosis of MS
with syrinx formation is variable, even following re-
peated episodes of myelopathy.

Recently, Vernant et al¹⁵ described a syndrome of
recurrent optic neuromyelitis with endocrinopathies in
8 Antillean women. All 8 women had a demyelinating
disease involving only the spinal cord and optic nerves.
In 7 cases, the neurologic examination revealed a band-
like, dissociated sensory loss and in 2 of these cases there
was anterior horn cell involvement or amyotrophy. Cavi-
tation of the cervical cord was noted in 3 and in 1 of the
3, Horner syndrome was observed. All 8 patients had evi-
dence of endocrinopathies resulting in amenorrhea, ga-
lactorrhea, hypothyroidism, hyperphagia, or diabetes in-
sipidus.¹⁶ Our patient is similar to these described patients
in that throughout the course of her illness, clinical mani-
festations have been limited to the optic nerves and spi-
nal cord and neuroimaging studies showed a cavitation
of the spinal cord. However, our patient is postmeno-
pausal and did not demonstrate any evidence of hypo-
thalamic or hypophyseal dysfunction.

Coincident to the development of a syrinx, our pa-
tient also developed signs of sympathetic dysfunction in-
cluding Horner syndrome in the left eye and left-hand
CRPS type 1. In our patient, frequent and periodic neu-
roimaging studies exclude any other cause for the Hor-
ner syndrome apart from the development of a syrinx.
Although the descending sympathetic fibers are largely
or totally uncrossed, their exact course is not clear. Pre-
sumably, fibers from the lateral hypothalamic area run
dorsal to the red nucleus, then descend in the lateral teg-
men tum of the midbrain, pons, and medulla to the in-
termedialateral cell column of the spinal cord.¹⁶ Our hy-
pothesis is that the syrinx involved the fibers to the left
intermedialateral cells disrupting sympathetic flow and
resulting in Horner syndrome of the left eye and left-hand
CRPS. Complex regional pain syndrome is a pain
syndrome that usually develops after an initiating noc-
ious event. Typically, evidence of edema, changes in skin
blood flow, abnormal sudomotor activity in the region of
the pain, and alldynia or hyperalgesia are observed.
The site is usually the distal aspect of an affected extrem-
ity.¹⁷ Of the wide variety of precipitating factors that can
cause injury to peripheral or central neural tissue, syr-
gomyelia is a central nervous system cause of CRPS.¹⁸-²⁰

Autonomic dysfunction likely contributes to the patho-
physiology of CRPS. When a peripheral nerve is injured,
avasodilatory neuropeptides, including substance P, are re-
leased from stimulated cutaneous nerves with cell bodies
in the dorsal root ganglia. Excessive vasodilation and in-
creased vascular permeability result in the affected limb be-
coming edematous and causing the cutaneous nerves to be
further activated. Stimulated cutaneous neurons nor-

Figure 3. Magnetic resonance imaging scan of the cervical spine before (left)
and after (right) gadolinium enhancement done in October 1997, showing a
syrinx from C2 to C7.
CRPS is also likely due to the cervical syrinx formation. She had no preceding peripheral nerve injury and the distribution of the pain is not in a dermatomal or peripheral nerve pattern. We postulate that due to the syrinx formation, the intermediolateral cell column is stimulated rather than inhibited by branches of second-order sensory neurons. The hyperresponsive sympathetic vasoconstrictor motor fibers severely restrict blood flow to the affected area, resulting in cyanosis, mottling, and hypothermia. This somatosympathetic reflex is likely responsible for our patient’s intermittently edematous, mottled, and cold hand.

This case report highlights the peculiar optic-spinal phenotype of MS that is observed in Southeast Asia. The association of syrinx in the setting of MS is rare. However, since degeneration and necrosis of demyelinating lesions characterize the optic-spinal phenotype of MS, an increased risk of syrinx formation is likely to exist. Newer techniques including magnetic resonance cyster-nography may be useful in confirming the diagnosis of syringes.

Accepted for publication February 8, 1999.

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