MRI of the spinal cord in neuromyelitis optica and recurrent longitudinal extensive myelitis

IRM de la moelle épinière dans la neuromyélite optique et la myélite longitudinale extensive récidivante

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Spinal cord; MRI; Devic syndrome; Neuromyelitis optica; Longitudinal extensive myelitis

Summary
Background and purpose. — Neuromyelitis optica (NMO) is a severe inflammatory and necrotizing disease that clinically affects the optic nerves and spinal cord in a relapsing course. We assessed the baseline and follow-up MRI characteristics of cord attacks in NMO and recurrent longitudinal extensive myelitis (RLEM).

Methods. — We retrospectively reviewed MRI data of 20 Afro-Caribbean patients diagnosed with either NMO or RLEM. MRI data from 51 cord or mixed attacks were evaluated, and 65 follow-up MRI studies were available for 30 baseline acute examinations.

Results. — The cervical cord was involved in 63% of cases. Four attacks were limited to the brainstem. MRI of the spinal cord revealed longitudinal extensive signal abnormalities extending over three vertebral segments, associated with cord swelling in 67% of the 51 relapses. Gadolinium enhancement was observed, preferentially surrounding edema, in 69% of attacks. In the axial plane, signal abnormalities typically involved central areas of the cord. Cavitation was observed in 16% of attacks. Cord attacks recurred in the same or contiguous areas in 67% of cases. Follow-up MRI revealed a gradual decrease in cord swelling and T2 signal hyperintensity, with fragmentation of signal abnormalities in some cases. Cord atrophy was evident in 57% of the follow-up MRI.

Conclusion. — Given the poor prognosis of NMO and RLEM, radiologists need to be aware of the MRI pattern to prevent further attacks with the use of aggressive treatment.

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Introduction

Neuromyelitis optica (NMO), or Devic’s disease, is a severe inflammatory and necrotizing disease that clinically affects the optic nerves and spinal cord in a relapsing course. Although NMO has a worldwide distribution, it frequently strikes nonwhite populations. It has been recently suggested that NMO is distinct from multiple sclerosis (MS) following the identification of a highly specific biomarker called NMO-IgG [1], which targets aquaporin-4, a water channel protein mainly expressed in astrocytic foot processes at the blood-brain barrier [2,3]. NMO-IgG status has helped to define an NMO spectrum of disorders, including the Asian optic spinal form of MS, recurrent longitudinal extensive transverse myelitis (RLEM), recurrent optic neuritis and extensive myelitis or optic neuritis associated with autoimmune diseases [4].

Spinal cord and brain MRI have important diagnostic utility. Spinal cord MRI with signal abnormalities extending over greater or equal to three vertebral segments and brain MRI not meeting diagnostic criteria for MS are supportive criteria proposed by the Mayo Clinic in 1999 for the diagnosis of NMO [5]. However, studies focusing on the neuroradiological aspects of NMO are scarce. In addition, the evolution of MRI lesions has rarely been studied. The aim of this study is to familiarize radiologists with the baseline and follow-up MRI characteristics of NMO and RLEM.

Methods

We reviewed the MRI data of consecutive patients diagnosed with NMO or RLEM since 1998 at the hospital of Fort-de-France (Martinique, French West Indies). The Martinique population is mostly Afro-Caribbean (>90%), with some interbreeding with the Caucasian population. The crude prevalence of NMO in Martinique was evaluated as 2.3/10,000 population as of 31 December 1999 [6]. Patients were included if they had undergone a spinal cord MRI either during two different cord attacks or at the acute phase and follow-up of a cord attack. The diagnosis of NMO required fulfillment of the diagnostic criteria proposed by Wingerchuk et al. in 1999 [5]. Patients presenting with RLEM (but no visual impairment) were also included.

MRI examinations were performed on a Philips Intera 1T machine (Philips Medical Systems, Eindhoven, The Netherlands). Cervical, dorsal and lumbar levels of the spinal cord were analyzed. In sagittal planes, T2-weighted sequences (TR/TE: 3500/120; thickness: 3.0/0.3 mm), and T1-weighted sequences with (T1TSE; TR/TE/Flip: 558/14/65; thickness: 5 mm) and without (T1FFE; TR/TE/Flip: 167/2.2/80; thickness: 5 mm) DTPA—gadolinium enhancement were obtained from all patients. Baseline MRI were performed within 4 weeks of symptom onset. To analyze the temporal profile of MRI data, follow-up MRI were divided in three categories: early MRI (4—8 weeks after cord attack); middle MRI (2—9 months after cord attack); and late MRI (>9 months after cord attack). All examinations were retrospectively evaluated by one blinded neuroradiologist. Lesions were characterized on the basis of signal intensity, morphology, number and location relative to adjacent vertebral bodies. Lesions extending for three or more vertebral segments in length were considered longitudinally extensive lesions (LEL), while lesions of less than three vertebral segments were regarded as short lesions (SL). Cord swelling and atrophy were evaluated visually. The location of enhancing lesions was recorded from post-contrast T1-weighted sequences. The location and pattern of areas of T2 hyperintensity were evaluated on axial planes when available.

Results

Patients

The study group consisted of 20 Afro-Caribbean patients (18 women/two men). Age ranged from 23 to 86 years (mean: 45 years). Their demographic, clinical and biological data are summarized in Table 1. Seventeen patients (16 women/one man) had NMO and the remaining three (two women/one man) had RLEM. Serum samples of all patients were tested for NMO-IgG using an indirect immunofluorescence technique (Neuroimmunology Unit of Lyon, France). NMO-IgG testing was positive in four NMO patients: two had systemic autoimmune disease—namely, systemic lupus erythematosus and Sjögren’s syndrome. From January 1998 to January 2008, a total of 51 spinal cord MRI were performed during the acute phase of a presumed cord or mixed attack. Axial T2-weighted MRI was obtained in 34 cases, and 65 follow-up MRI studies were available for 30 acute baseline scans. Nineteen patients had at least one cord attack with baseline and follow-up MRI, and the remaining patient had undergone MRI evaluation during two cord attacks. Follow-up MRI were performed at the early stage in 11 cases, at the middle stage in 17 cases and at the late stage in 37 cases.

Spinal cord MRI at the acute phase

Forty-seven of the 51 MRI were abnormal. Lesions preferentially involved the cervical cord (Figs. 1 and 2). In 34 of the 51 attacks (67%), confluent lesions extended across three or...
Table 1  Study patients’ demographic, clinical and biological characteristics.

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<th>Patients</th>
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NMO: neuromyelitis; RLEM: recurrent longitudinal extensive myelitis.
Figure 2  Sagittal T2-weighted sequences showing longitudinal extensive myelitis involving the cervical cord (A) and cervicodorsal cord (B).

more vertebral levels (LEL). Cord swelling was associated in each case of LEL. In 13 attacks (25%), lesions extended less than three vertebral levels (SL). In these cases, cord swelling was minimal or absent. Four attacks only involved the brainstem (three in the medulla and one in the mesencephalon). In one patient, the first two attacks only affected the lower medulla; however, the third optic spinal attack correctly pointed to a definitive diagnosis of NMO. Lesions extended to the lower medulla in 18 attacks (35%). In most cases, they were contiguous with upper cervical LEL (Fig. 3).

Increased signal intensity on T2-weighted sequences was seen in all lesions. Decreased signal intensity on T1-weighted sequences was seen in all LEL, but was more variable in the SL. An area of cavitation, defined as well-delineated, fluid-like signal abnormalities, was found in eight attacks (16%) (Fig. 4).

On axial T2-weighted images, four different patterns of high signal intensity were observed (Fig. 5). A holocord abnormal signal intensity sparing the cord periphery was seen in 16 of 34 attacks (47%). This pattern correlated with prominent cord swelling. In seven attacks (20%), we found a central gray matter predominant pattern giving a ‘butterfly’ signal. Bilateral and symmetrical involvement of the spinal posterior columns was seen in another seven attacks (20%). In contrast, peripheral lateral white matter was involved in only four attacks (12%).

Gadolinium enhancement was observed on sagittal and axial T1-weighted images in 35 attacks (69%). There was a wide range of enhancement patterns, with the most common pattern being a diffuse cord enhancement predominantly surrounding areas of maximum high signal intensity and cavitation on T2-weighted images (Fig. 6). Nodular enhancement within areas of T2 hyperintensity was noted in a few cases. In general, contrast enhancement did not correlate with severity of inflammatory response or cord swelling.

Thirteen of the 20 patients had MRI assessments during recurrent attacks in the spinal cord. Eight of these 13 patients presented with relapses in the same cord location. Relapses occurred in the same or contiguous locations (with a minimum of two shared vertebral segments) in 67% of cases.

Follow-up of spinal cord MRI

Follow-up MRI of the spinal cord revealed a gradual decrease of cord swelling and T2 signal hyperintensity, even at the early stages (Fig. 7). Fragmentation of signal abnormalities was frequently seen, especially at the middle stages (Fig. 8). Complete resolution of signal abnormalities was observed on long-term follow-up MRI in only two patients. In contrast, small, persistent, intramedullary T2 signal abnormalities were frequently detected. Development of cord atrophy (Fig. 9) became evident in 17 of the 30 cases (57%).
and occurred in eight cases at the middle stage. Cord atrophy was focal or diffuse, and correlated with the intensity and extent of signal changes at the acute phase. Atrophy was often associated with an ependymal pseudodilatation pattern. Secondary development of cord cavitations was observed at the early stage in only two patients. Cord cavitations previously seen at the acute phase gradually resolved during follow-up in four cases. Persistent cavitations were rarely observed on long-term follow-up.

Discussion

In our series of NMO and RLEM cases, conventional MRI during medullary attacks revealed LEL in 67% of cases, SL in 25% cases and normal findings in 8% of cases. T1-weighted hypointensity signals associated with medullary widening and corresponding to reactive edema were present in the majority of attacks. On axial plane sequences, T2 hyperintensity signals involved predominantly the central regions. Contrast retention after gadolinium injection was present in 69% of the medullary attacks in our series. These values should be compared with those observed in the Mayo Clinic series where, in the medullary MRI taken within 8 weeks of a medullary attack, LEL were observed in 88% of 50 cases, and were associated with edema in 50% and contrast retention in 64% of cases [5]. Central medullary cavitation, already described in the literature [7,8], was observed in approximately one out of five attacks, starting as early as at the acute phase. Development toward medullary atrophy was observed over the long-term in 13–22% of cases [5,9].

In our series, the cervical cord was affected in 61% of attacks; in 41% of cases, it only affected the cervical cord while, in 20%, it was in conjunction with the thoracic spine. While the preferential involvement of the cervical and thoracic spine has been suggested in several studies [7,10,11], to the best of our knowledge, the clear predominance of cervical cord involvement has not been evaluated in the literature. In addition, the bulbous is affected in 37% of attacks, most often contiguous with a lesion of the cervical spine, but separately in three cases. This involvement was described in only three out of 28 patients in the Wingerchuk series [5]. In addition, the distribution of the T2 hyperintensity signal on axial sections has only rarely been described. In our series, the hyperintensity signal extended most often almost through the entire marrow section (holocord), sparing only a thin layer of peripheral white matter. Less often, the hyperintensity signal coincided with the central medullary gray matter and affected, among other parts, the anterior horns. This lesion pattern may correspond to the high levels of expression of aquaporine-4 in medullary gray matter [12], but it has also been described in other myelopathies [13] — namely, in medullary infarction involving the anterior spinal artery — thus corroborating the NMO pathophysiology, which suggests the involvement of the walls of the small medullary arteries [7,14]. In the majority of cases, gadolinium enhancement extends to the regions of maximum edema. This pattern suggests that the inflammatory reaction is found predominantly in the areas surrounding either the edema or medullary necrosis.

We have shown that the regression of medullary edema, and of the size and intensity of T2 hyperintensity signals, starts early, probably favored by aggressive treatment of attacks (intravenous corticosteroid therapy and plasmapheresis). The T2 hyperintensity signal can be fragmented at the early phase, but this development occurs preferentially over the medium term. Disappearance of the hyperintensity signal is possible over the long term, but rarely occurs.
More frequently, abnormalities of the consequential signals persist in the form of nonconfluent T2 hyperintensity signals, often small in size and with a nonpredictable pattern on axial sections. Cavitation lesions are formed during the acute phase of attack or, in rare cases, during the second month following an attack. These are gradually resorbed over the course of disease development. Their persistence over the long term after an attack is rare. In our series, the course towards medullary atrophy was frequently seen—involving more than half the attacks. Atrophy was found in half the cases over the medium term and, in the other half, over the long term, and was often associated with an ependymal channel pattern that was “too visible”, and slightly irregular and serpiginous. This pattern could originate from the loss of neurons in the areas surrounding the ependymal channel, and needs to be differentiated from the cavitation observed at the early phases. Follow-up of lesion development has also enabled us to observe that patients presented with a high rate of relapse (67%) at the same medullary location. This suggests that, after an NMO or RLEM attack, inactive inflammatory centers may persist within the marrow and be reactivated by triggers as yet unidentified.

Our study had several limitations related mainly to the retrospective nature of the analysis. It is also important to recall that our series of NMO and RLEM cases include exclusively patients of Afro-Caribbean origin. In addition, it is probable that the disease presents variations depending on geographical location and ethnicity. These variations could lie at the origin of the sensitivity disparities of the NMO-IgG observed in studies. Initially, the sensitivity of NMO-IgG was evaluated at 73% for a series of 102 North American patients with NMO [1], according to Wingerchuk’s criteria. However,
a study of 48 Japanese subjects with an optic spinal form of MS demonstrated a sensitivity of NMO-IgG of 27% [15]. This seropositivity was statistically higher when the LEL affected the thoracic spinal cord and when the hyperintensity signal was in the axial plane of the central medullary gray matter. The NMO-IgG sensitivity in our series is closer to that of the Matsuoka study than that of the Mayo Clinic. In fact, it can be seen that most of our patients presented with lesions extending to the cervical cord level, with a holocord type of lesion pattern in the axial plane. Another limitation of our study is the lack of nonconventional MR imaging sequences. Magnetization transfer, diffusion tensor MRI (DTI) and functional MRI have already proved their value in the analysis of the brain in NMO patients [16,17] and in the diagnosis of NMO [18]. Diffusion sequences and DTI could improve our knowledge of the nature of edema during an acute attack of the spinal cord. DTI could also allow grading of the extent of cord damage in patients with NMO and correlation of diffusion abnormalities with levels of disability [19].

Conclusion

The present study demonstrates the main MRI characteristics in NMO and RLEM patients in cases of cord attack, with analysis of the outcomes of signal abnormalities. Radiologists need to be aware of NMO and RLEM MRI patterns, as they require aggressive treatment to prevent relapses and to improve functional recovery.

References