Pure Relapsing Short Myelitis
Part of the Multiple Sclerosis Spectrum or New Entity?

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Abstract

Background and Objectives
Pure relapsing short myelitis with clinical and paraclinical features suggesting multiple sclerosis (MS) has been described recently. Here, we evaluated the existence of this potential new form of MS by retrospectively searching for similar cases in the databases of the French tertiary MS centers.

Methods
Patients were included based on the present criteria: at least 2 short (< 3 vertebral segments) myelitis episodes; minimum follow-up of 3 years; no MS-like brain lesion during all the follow-up; tested negative for both anti-myelin oligodendrocyte glycoprotein and anti-aquaporin 4 antibodies in serum; presence of oligoclonal bands in CSF; and comprehensive workup to exclude alternative diagnoses.

Results
Eighteen patients fulfilled all criteria. The sex ratio (females/males) was 5/1; the median (range) age at first relapse was 35.5 (25–54) years, the disease duration was 80.5 (50–308) months, and the annualized relapse rate was 0.36 (0.1–0.5). The median (range) number of relapses per patient was 2 (2–5), and the median (range) Expanded Disability Status Scale score at last follow-up was 1 (0–7.5). In CSF, the median (range) protein level was 0.34 g/L (0.18–0.77), and the median (range) number of mononuclear cells was 3 (0–28). Spinal cord MRI demonstrated a median (range) number of 2 (1–5) lesions per examination and 3 [1–7] on the last examination. Fifty-five percent of lesions involved the cervical levels. Secondary progressive evolution occurred in 3 of 18 (17%) patients.

Discussion
Pure spinal MS could be a rare entity in the MS disease spectrum. However, the existence of a distinct entity in the inflammatory CNS disorders cannot be excluded.
Glossary

anti-AQP4 = anti–aquaporin 4; anti-MOG = anti–myelin oligodendrocyte glycoprotein; ARR = annualized relapse rate; DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; MS = multiple sclerosis; NOMADMUS = Neuromyelitis Optica Study Group in France; OCB = oligoclonal band.

Cases of pure relapsing short myelitis with clinical and paraclinical features suggesting multiple sclerosis (MS) have been reported recently.1 Better description of this potential new form of MS is of particular importance because nowadays these patients do not fulfill international diagnostic criteria of MS2 and could be consequently excluded from effective therapeutic strategies. Here, we evaluated the existence of this potential new form of MS by retrospectively searching for similar cases in the databases of the French centers involved in neuromyelitis optica and associated neurologic disorders (NOMADMUS) network.

Methods

Protocol and Participants
To be included, patients had to fulfill the following criteria: age >18 years at inclusion; evidence of at least 2 short (<3 vertebral segments) myelitis episodes; minimum follow-up of 3 years; no typical MS-like brain lesion during all the follow-up; no clinical history or visual evoked potential or eye examination suggesting prior optic neuritis; no history of clinical episode suggesting brain lesion; tested negative for both anti–myelin oligodendrocyte glycoprotein (anti-MOG) and anti–aquaporin 4 (anti-AQP4) antibodies in serum; presence of oligoclonal bands (OCBs) in CSF; and comprehensive workup to exclude alternative diagnoses of myelitis, namely, infections, vascular diseases, and subacute combined degeneration of spinal cord and autoimmune diseases.3–5 Particularly, other inflammatory causes of myelitis, including sarcoidosis, Behcet disease, paraneoplastic disorders, and connective tissue diseases, were excluded by using biological and imaging explorations. Anonymized centralized (Marseille) reinterpretation of brain MRIs by expert neurologists (consensus required among B.A., J.P., A.M., A.R., and C.B.) was performed to exclude all patients with any typical MS-like brain lesion.6

Standard Protocol Approvals, Registrations, and Patient Consent
The authors obtained ethical approval of national ethical authority (NOMADMUS cohort, CNIL decision DR-2014-558) to conduct the present study. Each participant gave free and informed written consent for anonymized use of clinical, MRI, and biological data for research purposes.

Data Availability
All data analyzed during this study will be shared anonymized by reasonable request of a qualified investigator to the corresponding author.

Results
Among 62 patients first screened in the French tertiary MS centers, 18 fulfilled all inclusion criteria (Figure 1).

Clinical Features
The sex ratio (females/males) was 5/1; the median (range) age at first relapse was 35.5 (25–54) years, the disease duration was 80.5 (50–308) months, and the annualized relapse rate (ARR) 0.36 (0.1–0.5) (Table 1). The median (range) number of relapses per patient was 2 (2–5), and the median (range) Expanded Disability Status Scale (EDSS) score during relapse and at last follow-up was 2.5 (0.5–5.5) and 1 (0–7.5), respectively. Among the 50 relapse cases, 24 (48%) showed pure sensitive signs (paresthesia, numbness, or proprioceptive ataxia); 11 (22%) sensitive and motor signs (arm or lower limb weakness); 7 (14%) sensitive, motor, and sphincter signs; 4 (8%) pure motor signs; 2 (4%) motor and sphincter signs; 1 (2%) sensitive and sphincter signs; and 1 (2%) pure sphincter signs. Of the 50 relapse cases, 30 (60%) involved the 4 limbs and 20 (40%) the lower limbs only.

Laboratory Findings
No patient presented atypical CSF findings for MS. In CSF, the median (range) protein level was 0.34 (0.18–0.77) g/L, and the median (range) number of mononuclear cells was 3 (0–28). Nine of 18 patients were tested at least twice for anti-MOG and anti-AQP4 antibodies, 5 of 9 were tested twice, 3 of 9 three times, and 1 of 9 four times.

Brain and Spinal Cord MRI
No typical MS-like brain lesion was detected in any patient despite repeat examination (median [range] number of brain MRI examinations per patient 4 [2–9]) (Figure 2). Importantly, 3D fluid-attenuated inversion recovery imaging was available for 15 of 18 patients. A median of 5 (2–6) spinal cord MRI examinations were performed per patient. All spinal cord MRI examinations included sagittal T2/STIR sequences. At least 1 series of axial sequences was available for 8 of 18 patients. Spinal cord MRI demonstrated a median (range) number of 2 (1–5) lesions per examination and a median (range) number of 3 (1–7) lesions on the last examination. The median (range) sagittal extension of the spinal cord lesions was 1 (0.5–2) vertebral segments. Among all spinal cord lesions (n = 67) depicted, 37 (55%) and 30 (45%) involved the cervical and thoracolumbar levels, respectively. Gadolinium injection was performed in 45 examinations, and 21 of 46 (45%) lesions showed gadolinium enhancement. Overall, 18 lesions in 9 patients were explored on the axial plane, and 12 (67%) showed partial myelitis (Figure 3).
Treatment and Progress

In all, 30 of 50 (60%) relapse cases were treated with high-dose IV corticosteroids. The median (range) EDSS score during relapse and after recovery was 2.5 (0.5–5.5) and 1 (0–4.5), respectively.

Disease-modifying therapy (DMT) was used in 12 of 18 (67%) patients (Table 2). In these patients, the median (range) follow-up before and after DMT onset was 55.5 (3–191) and 40 (4–248) months, respectively. The median (range) ARR before and after DMT onset was 0.5 (0.1–1) and 0 (0–0.5), respectively, after excluding patients with a follow-up <6 months before or after DMT onset. Seven of 11 (63%) patients were free from relapse after DMT onset. The median EDSS (range) score at DMT onset and at last follow-up was 2 (0–6) and 2.5 (0–7.5), respectively.

Secondary progressive evolution occurred in 3 of 18 (17%) patients. The median (range) follow-up of these patients was 242 (236–308) vs 64 (36–296) months for other patients. The median (range) EDSS score of these patients was 7 (6–7.5) vs 1.5 (0–4.5) for other patients.

Discussion

The present study including the French centers involved in the NOMADMUS network reports 18 cases of pure relapsing short myelitis. According to the retrospective design of the study, the number of cases is probably underestimated, which prevents any conclusion about the prevalence of pure relapsing short myelitis. In addition, some cases were probably not reported because they never experienced a second relapse in that treatment onset occurred just after the first myelitis. However, this therapeutic attitude is highly unusual in France, which limits the number of potential underreported cases.

Because all patients included in the present study had to have OCBs in the CSF, we paid careful attention to searching and excluding all known causes of inflammatory myelitis. Moreover, we also excluded vitamin B12 deficiency in terms of its frequency. However, if a search for other rare metabolic causes of myelopathy such as copper deficiency was not available in the medical chart, patients were not excluded because radiologic and CSF findings did not suggest metabolic disorders.

Several features of these cases argue for the existence of a pure spinal form of MS. First, the characteristics of myelitis highly suggest relapsing MS: no clinical presentation suggested transverse myelitis, clinical presentations mostly suggested an involvement of the posterior part of the spinal cord, spinal cord MRI demonstrating most partial and posterior myelitis in the axial plane. Second, all patients showed typical CSF findings for MS. Third, in all patients receiving MS DMTs, disease activity decreased. Fourth, 17% of patients showed secondary progression—an evolution highly suggestive of MS—several years after disease onset. Finally, we were not able to provide a better explanation than MS in all patients despite extensive explorations. In that way, we recommend

Figure 1 Flowchart of the Patients Included

Excluded (n = 11): 
• Clinical history, visual evoked potential, or eye examination suggestive of prior optic neuritis (11)

Excluded (n = 11): 
• Disease duration <3 years (11)

Excluded (n = 2): 
• Longitudinal extension of at least one spinal cord lesion of >3 vertebral levels (2)

Excluded (n = 8): 
• Unknown MOG and AQP4 antibody status (3) 
• Absence of oligoclonal bands in the CSF (5)

Anonymized centralized (Marseille) interpretation of brain MRI to exclude patients with any brain demyelinating lesion 
(n = 30)

Excluded (n = 12): 
• At least one demyelinating lesion on brain MRI (12)

Patients included in the study 
(n = 18)
| Patient | Age at onset | Comorbidity | Family history | Clinical history | Spinal cord MRI findings | Brain MRI findings |
|---------|--------------|-------------|----------------|------------------|--------------------------|---------------------|
| 1, M    | 35 y         | no          | no             | 2011: first relapse (upper limb paresthesia), EDSS score 1, use of HDST | 2011: C1, C2, and C5-C6 | No typical MS-like brain lesion. Controlled in 2011, 2017, 2019, 2020, and 2021. |
|         |              |             |                | 2012: partial recovery, EDSS score 0.5 |                         |                     |
|         |              |             |                | 2017: second relapse (asymmetric lower limb weakness and numbness), EDSS score 3, use of HDST | 2017: stability |                     |
|         |              |             |                | 2018: poor recovery, EDSS score 3 | 2019: stability |                     |
|         |              |             |                | 2019: third relapse (asymmetric upper limb weakness), EDSS score 3.5, use of CTS | 2021: stability |                     |
|         |              |             |                | 2020: poor recovery, EDSS score 3.5 |                         |                     |
|         |              |             |                | 2021: stability |                         |                     |
| 2, F    | 34 y         | migraine and 4 miscarriages | no             | 1996: first relapse (asymmetric lower limb paresthesia), EDSS score 1 | 1998: C3, C4, C5, C6, T1, and T4 | No typical MS-like brain lesion. Controlled in 1996, 2001, 2008, 2013, 2015, 2017, and 2018. |
|         |              |             |                | 1997: good recovery, EDSS score 0 | 2000: stability |                     |
|         |              |             |                | 1998: second relapse (asymmetric lower limb weakness and numbness), EDSS score 3, good recovery without HDST | 2008: stability |                     |
|         |              |             |                | 1999: third relapse (lower limb weakness), EDSS score 3, good recovery | 2013: +C7 |                     |
|         |              |             |                | 2001: fourth relapse (Lhermitte sign and lower limb weakness), EDSS score 4.5 | 2015: stability |                     |
|         |              |             |                | 2002: poor recovery, EDSS score 4.5 | 2017: atrophy of the entire spinal cord |                     |
|         |              |             |                | 2003-2020: progressive worsening (severe lower limb weakness and sphincter disorder), last EDSS score 7.5 |                         |                     |
| 3, F    | 37 y         | rheumatoid polyarthritis | no             | 1996: first relapse (asymmetric lower and upper limb weakness and sphincter disorder), EDSS score 3 | 2008: C6 | No typical MS-like brain lesion. Controlled in 2008, 2012, 2014, 2017, 2018, and 2020. |
|         |              |             |                | 1997: partial recovery, EDSS score 1 | 2012: stability |                     |
|         |              |             |                | 2002: stability, EDSS score 1 | 2016: +C2-C3 and T3 |                     |
|         |              |             |                | 2007: second relapse (ataxia and asymmetric upper and lower limb weakness), EDSS score 5.5, use of HDST | 2017: stability |                     |
|         |              |             |                | 2008: partial recovery, EDSS score 2 | 2020: +T5-T6 and T10 |                     |
|         |              |             |                | 2013: third relapse (ataxia, asymmetric tetraparesis, and sphincter disorder), EDSS score 3, use of HDST |                         |                     |
|         |              |             |                | 2014: good recovery, EDSS score 2 |                         |                     |
|         |              |             |                | 2016: fourth relapse (asymmetric tetraparesis with numbness and ataxia), EDSS score 5, use of HDST |                         |                     |
|         |              |             |                | 2017: good recovery, EDSS score 2 |                         |                     |
|         |              |             |                | 2017-2021: stability, EDSS score 2 |                         |                     |
| 4, F    | 54 y         | myeloma     | no             | 2002: first relapse (ataxia), EDSS score 1, no recovery | 2017: C3, C5, T2, and L3 | No typical MS-like brain lesion. Controlled in 2017, 2019, and 2020. |
|         |              |             |                | 2007: second relapse (asymmetric lower limb weakness and numbness), EDSS score 3 | 2018, 2019, and 2020: stability |                     |
|         |              |             |                | 2008: no recovery (EDSS score 3) |                         |                     |
|         |              |             |                | 2009-2021: progressive worsening, last EDSS score 6 |                         |                     |
| 5, F    | 44 y         | no          | no             | 2001: first relapse (lower limb paresthesia and asymmetric weakness and saddle hypesthesia), EDSS score 3, use of HDST | 2001: T7-T8 with gadolinium enhancement | No typical MS-like brain lesion. Controlled in 2001, 2003, 2005, 2010, 2011, 2014, and 2016: stability |
|         |              |             |                | 2002: partial recovery, EDSS score 1 | 2018: +C6-C7 |                     |
|         |              |             |                | 2005: second relapse (asymmetric lower limb weakness), EDSS score 3, use of HDST | 2020: +T4-T5 |                     |
|         |              |             |                | 2006: good recovery, EDSS score 1 | 2018: +C2 |                     |
|         |              |             |                | 2008: third relapse (ataxia and lower limb weakness), EDSS score 3, use of HDST | 2020: stability |                     |
|         |              |             |                | 2009: good recovery, EDSS score 1 |                         |                     |
|         |              |             |                | 2011: fourth relapse (ataxia and lower limb weakness and numbness), EDSS score 4, use of HDST |                         |                     |
|         |              |             |                | 2012: partial recovery, EDSS score 2 |                         |                     |
|         |              |             |                | 2014: fifth relapse (ataxia and lower and upper limb weakness and numbness), EDSS score 5.5, use of HDST |                         |                     |
|         |              |             |                | 2015: partial recovery, EDSS score 4 |                         |                     |
|         |              |             |                | 2016-2021: progressive worsening with persistence of acute deterioration, last EDSS score 6.5 |                         |                     |
| Patient | Age at onset | Comorbidity | Family history | Clinical history | Spinal cord MRI findings | Brain MRI findings* |
| --------|--------------|-------------|----------------|-----------------|--------------------------|-------------------|
| 6, F    | 42 y         | 0           | 0              | 2016: first relapse (4 limb asymmetric paresthesia and Lhermitte sign), EDSS score 2, use of CTS | 2016: C2-C3 with gadolinium enhancement 2017, 2018, and 2019: stability | No typical MS-like brain lesion. Controlled in 2016, 2018, 2019, and 2020. |
|         |              |             |                | 2017: partial recovery, EDSS score 1 |                      |                   |
|         |              |             |                | 2018: second relapse (4 limb hypesthesia), EDSS score 2.5, use of HDST | 2017: C3, T7, T8, and T9 with gadolinium enhancement of all lesions |                   |
|         |              |             |                | 2019: no recovery, EDSS score 2.5 | 2019: stability |                   |
|         |              |             |                | 2021: stability, EDSS score 2.5 | 2020: +C7-T1 and L1 |                   |
| 7, F    | 30 y         | no          | no             | 2017: first relapse (4 limb hypesthesia), EDSS score 1 | 2015: C2-C3 with gadolinium enhancement 2016: stability | No typical MS-like brain lesion. Controlled in 2015, 2016, 2017, and 2020. |
|         |              |             |                | 2018: good recovery, EDSS score 0 | 2017: +T3 |                   |
|         |              |             |                | 2020: second relapse (asymmetric hypesthesia), EDSS score 1, use of HDST | 2020: stability |                   |
|         |              |             |                | 2021: good recovery, EDSS score 0 |                      |                   |
| 8, F    | 25 y         | no          | no             | 2015: first relapse (ataxia, Lhermitte sign, and upper limb weakness and numbness), EDSS score 5, use of HDST | 2016: C5 | No typical MS-like brain lesion. Controlled in 2016, 2017, 2018, 2019, and 2020. |
|         |              |             |                | 2016: good recovery, EDSS score 0 | 2018: +C6 with gadolinium enhancement |                   |
|         |              |             |                | 2017: second relapse (lower limb weakness and numbness), EDSS score 2 | 2020: +T12-L1 |                   |
|         |              |             |                | 2018: spontaneous recovery, EDSS score 0 without HDST 2019-2021: stability, EDSS score 0 | 2021: stability |                   |
| 9, F    | 36 y         | no          | no             | 2016: first relapse (asymmetric upper limb numbness), EDSS score 1, use of HDST | 2016: C5 | No typical MS-like brain lesion. Controlled in 2016, 2017, 2018, 2019, and 2020. |
|         |              |             |                | 2017: good recovery, EDSS score 0 | 2018: +C6 with gadolinium enhancement |                   |
|         |              |             |                | 2018: second relapse (asymmetric lower limb weakness and numbness), EDSS score 3, use of HDST with good recovery, EDSS score 0 | 2020: +T12-L1 |                   |
|         |              |             |                | 2019: third relapse (Brown-Sequard syndrome), EDSS score 2.5, use of HDST with good recovery, EDSS score 0 | 2021: stability |                   |
|         |              |             |                | 2020: fourth relapse (lower limb numbness and paresthesia), EDSS score 2 |                      |                   |
|         |              |             |                | 2021: good recovery, EDSS score 0 |                      |                   |
| 10, F   | 29 y         | T8 to L3 fractures* | no               | 2015: first relapse (ataxia and 4 limb numbness and mild weakness), EDSS score 2.5, use of HDST | 2015: C2-C3 and T9 | No typical MS-like brain lesion. Controlled in 2016, 2017, 2018, 2019, 2020, and 2021. |
|         |              |             | no             | 2016: partial recovery, EDSS score 1.5 | 2016: +T3 |                   |
|         |              |             |                | 2017: second and third relapses (ataxia, 4 limb hypesthesia, and sphincter disorder), EDSS score 4, use of HDST | 2017 and 2018: stability |                   |
|         |              |             |                | 2018: fourth relapse (ataxia, 4 limb numbness and mild weakness), EDSS score 2.5, use of HDST | 2019: gadolinium enhancement within the C3 lesion |                   |
|         |              |             |                | 2019: good recovery, EDSS score 1 | 2020: stability and regression of the gadolinium enhancement |                   |
|         |              |             |                | 2021: stability |                      |                   |
| 11, F   | 26 y         | migraine | no             | 2013: first relapse (hands paresthesia, ataxia), EDSS score 1, spontaneous recovery | 2016: C2-C3, C6-C7, and T8-T9 | No typical MS-like brain lesion. Controlled in 2017, 2019, and 2020. |
|         |              |             |                | 2014: second relapse (upper limb paresthesia), EDSS score 1, spontaneous recovery | 2017: +T10-T11 with gadolinium enhancement |                   |
|         |              |             |                | 2016: third relapse (asymmetric 4 limb numbness), EDSS score 2.5, use of HDST | 2018: +T6 |                   |
|         |              |             |                | 2017: partial recovery, EDSS score 1 | 2020: stability |                   |
|         |              |             |                | 2018: fourth relapse (lower limb paresthesia and ataxia), EDSS score 2.5, use of HDST |                      |                   |
|         |              |             |                | 2019: good recovery, EDSS score 1 | 2021: stability |                   |
| 12, F   | 62 y         | no          | no             | 2015: first relapse (lower limb numbness), EDSS score 0.5 | 2020: C4-C5, C7, T3, and T6 | No typical MS-like brain lesion. Controlled in 2020 and 2021. |
|         |              |             |                | 2016: no recovery but stability, EDSS score 0.5 | 2021: stability |                   |
|         |              |             |                | 2018: second relapse (asymmetric lower limb weakness), EDSS score 2 |                      |                   |
|         |              |             |                | 2019: no recovery, EDSS score 2 | 2021: stability |                   |
|         |              |             |                | 2021: stability |                      |                   |

Continued
| Patient | Age at onset | Comorbidity | Family history | Clinical history | Spinal cord MRI findings | Brain MRI findings |
|---------|--------------|-------------|----------------|-----------------|--------------------------|-------------------|
| 13, F   | 28 y         | migraine    | b: no          | 2016: first relapse (4 limb numbness), EDSS score 2, use of HDST | 2016: C2, C4, C5, and T3 | No typical MS-like brain lesion. Controlled in 2016, 2018, and 2020. |
|         |              |             |                | 2017: good recovery, EDSS score 0 | 2018: +C3 | |
|         |              |             |                | 2018: stability | 2020: +T9-T10 with gadolinium enhancement | |
|         |              |             |                | 2020: second relapse (lower limb numbness), EDSS score 2, use of HDST | 2021: poor recovery, EDSS score 2 | |
| 14, M   | 42 y         | migraine    | b: no          | 2017: first relapse (ataxia, asymmetric numbness, and sphincter disorder), EDSS score 3, use of HDST with partial recovery: EDSS score 1 | 2017: C1, C2, C5-C6, T1, T9, and T12 with gadolinium enhancement of all lesions | No typical MS-like brain lesion. Controlled in 2017, 2018, 2019, and 2020. |
|         |              |             |                | 2017: second relapse (4 limb numbness and weakness), EDSS score 2, use of HDST | 2018: + C3 with gadolinium enhancement | |
|         |              |             |                | 2018: poor recovery, EDSS score 2 | 2019: amelioration | |
|         |              |             |                | 2019-2021: stability, EDSS score 2 | 2020: stability | |
| 15, F   | 34 y         | migraine    | b: no          | 2016: first relapse (sensory deficit), EDSS score 2, use of HDST | Lack of previous MRI | No typical MS-like brain lesion. Controlled in 2016, 2017, 2018, 2019, and 2020. |
|         |              |             |                | 2017: good recovery, EDSS score 0 | 2020: C6, T6, and T7-T8 | |
|         |              |             |                | 2019: second relapse (sensory deficit), EDSS score 2, use of HDST | 2021: stability | |
|         |              |             |                | 2020: complete recovery, EDSS score 0 | 2021: stability, EDSS score 0 | |
| 16, F   | 39 y         | migraine    | b: no          | 2014: first relapse (lower limb numbness), EDSS score 2 | 2015: T11 | No typical MS-like brain lesion. Controlled in 2015, 2017, and 2018. |
|         |              |             |                | 2015: partial recovery, EDSS score 1 | 2016: stability | |
|         |              |             |                | 2017: second relapse (upper limb numbness), EDSS score 2 | 2017: +C3 | |
|         |              |             |                | 2018: partial recovery, EDSS score 1 | 2019: stability | |
|         |              |             |                | 2019-2021: stability, EDSS score 1 | | |
| 17, F   | 33 y         | Raynaud phenomenon | b: no | 2014: first relapse (asymmetric paresthesia), EDSS score 1 with spontaneous full recovery: EDSS score 0 | 2015: C2 with gadolinium enhancement | No typical MS-like brain lesion. Controlled in 2015, 2016, 2017, 2018, 2019, and 2021. |
|         |              |             |                | 2014: second relapse (asymmetric 4 limb numbness), EDSS score 1, full recovery | 2016, 2017, 2018, 2019, and 2021: stability | |
|         |              |             |                | 2015: third relapse (asymmetric 4 limb weakness and numbness and Lhermitte sign), EDSS score 2, use of HDST | 2016: good recovery, EDSS score 0 | |
|         |              |             |                | 2016: good recovery, EDSS score 0 | 2017-2021: stability, EDSS score 0 | |
| 18, M   | 42 y         | no          | b: no          | 2013: first relapse (sphincter disorder), EDSS score unknown | 2015: C2-C3 with gadolinium enhancement | No typical MS-like brain lesion. Controlled in 2015, 2016, and 2019. |
|         |              |             |                | 2015: second relapse (4 limb weakness and numbness), EDSS score 4 | 2016 and 2019: stability | |
|         |              |             |                | 2016: partial recovery, EDSS score 2.5 | | |

Abbreviations: EDSS = Expanded Disability Status Scale; HDST = high-dose steroid therapy; MS = multiple sclerosis.

* Anonymized centralized (Marseille) interpretation of brain MRI by expert neurologists (B.A., J.P., A.M., A.R., and C.B.) to rule out patients with any typical MS-like brain lesion.

* Family history: first-degree family history.

* Patient 10 had a history of T8-L3 vertebral fractures.
Figure 2 Last Brain and Spinal Cord MRI of the Patients

The patient's number is displayed in each image.
preferentially using DMTs with demonstrated efficacy in MS to treat pure relapsing short myelitis.

Nevertheless, several features may argue for the existence of a possible distinct inflammatory entity. First, the sex ratio was more imbalanced in favor of females as compared with MS. Second, it is unexpected in a pathologic perspective that brain involvement could be totally absent after several years of evolution with MS.

Whatever the nosological classification, the existence of patients with pure relapsing short myelitis argues for systematically adding spinal cord MRI to brain MRI for the imaging surveillance of patients followed after an isolated myelitis episode with OCBs in the CSF. For patients with recurrent myelitis, we recommend performing imaging at least annually as recommended for MS but systematically adding spinal cord imaging to brain imaging. According to the relative low disease activity evidenced in the patients reported here, we do
Table 2 Characteristics and Evolution of Treated Patients (n = 12)

| Patient | M/F | Age at onset | Disease duration at DMT onset (mo) | Type of DMT | Mean follow-up after DMT onset (mo) | ARR* before DMT | ARR* after DMT | EDSS score at DMT onset | EDSS score at last follow-up |
|---------|-----|-------------|-----------------------------------|-------------|-------------------------------------|-----------------|-----------------|------------------------|--------------------------------|
| 1, M    | M   | 35 y        | 108                               | Fingolimod: 01/20– | 18                                 | 0.33            | 0               | 3.5                    | 3.5                            |
| 2, F    | F   | 34 y        | 60                                | Azathioprine: 09/01–01/02 Cyclophosphamide: 01/02–08/02 Mitoxantrone: 2002–2006 Cyclophosphamide: 09/08–2012 Rituximab: 04/16–05/16 Fingolimod: 01/17– | 247               | 0.6              | 0               | 6                    | 7.5                            |
| 4, F    | F   | 54 y        | 191                               | Dimethyl fumarate: 12/17–06/18 Rituximab: 08/18– | 44               | 0.13             | 0               | 6                    | 6                             |
| 5, F    | F   | 44 y        | 72                                | Glatiramer acetate: 2007–2012 Fingolimod: 2012–2016 Rituximab: 03/17– | 175               | 0.33             | 0.21            | 2                    | 7                             |
| 6, F    | F   | 42 y        | 24                                | Teriflunomide: 11/18– | 33               | 1                | 0               | 2.5                   | 2.5                           |
| 10, F   | F   | 29 y        | 40                                | Interferon beta: 02/19–09/19 Dimethyl fumarate: 09/19–08/20 Natalizumab: 08/20– | 30               | 0.33             | 0               | 2.5                   | 4.5                           |
| 11, F   | F   | 26 y        | 60                                | Interferon beta: 01/18– | 43               | 0.6              | 0               | 1                    | 0.5                           |
| 13, F   | F   | 28 y        | 56                                | Azathioprine: 10/20– | 9                | 0.5              | 0               | 2                    | 2                             |
| 14, M   | M   | 42 y        | 3                                 | Mycophenolate mofetil: 10/17– | 45               | NA*             | 0               | 2                    | 2                             |
| 15, F   | F   | 26 y        | 55                                | Mycophenolate mofetil: 05/21– | 3                | 0.5              | NA*            | 0                    | 0                             |
| 16, F   | F   | 34 y        | 44                                | Mycophenolate mofetil: 08/18– | 35               | 0.66             | 0               | 1                    | 1                             |
| 18, M   | M   | 42 y        | 42                                | Interferon beta: 12/16–09/17 Dimethyl fumarate: 09/17– | 55               | 0.66             | 0.5            | 0                    | 0                             |

Abbreviations: ARR: annualized relapse rate; DMT: disease-modifying therapy; EDSS: Expanded Disability Status Scale.

* Patients with a follow-up < 6 months before or after DMT onset were excluded from the analysis.
not recommend exceeding annual imaging in the absence of relapse or therapeutic considerations.

Pure spinal MS could be a rare entity in the MS disease spectrum. However, the existence of a distinct entity in the inflammatory CNS disorders cannot be excluded. Future studies are needed to disentangle these 2 interpretations.

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