Acute myelopathies
Clinical, laboratory and outcome profiles in 79 cases

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Summary
The main aetiologies of acute myelopathy (AM) are: multiple sclerosis, systemic disease (SD), spinal cord infarct (SCI), parainfectious myelopathy (PIM) and delayed radiation myelopathy (DRM). Although a large amount of data have been published for each individual aetiology, comparison studies are scarce. The aim of this study was to assess the various aetiological and outcome profiles of AM. We studied 79 cases: 34 (43%) in multiple sclerosis; 13 (16.5%) in SD; 11 (14%) in SCI; five (6%) in PIM; and three (4%) in DRM. Myelopathies were of unknown origin in 13 (16.5%) patients. We evaluated clinical, spinal cord and brain MRI, CSF and evoked potentials data at admission, MRI outcome at 6 months and clinical outcome at 12 months. A statistical comparison of clinical, laboratory and outcome data was only performed between multiple sclerosis, SD and SCI patients due to the small number of cases in the other groups. A motor deficit was more frequent in SD and SCI than in multiple sclerosis where initial symptoms were predominantly sensory ($P < 0.001$). Spinal cord MRI showed lateral or posterior lesions of less than two vertebral levels in multiple sclerosis, in contrast to SD and SCI, where lesions involved more vertebral levels and were centromedullar ($P < 0.001$). Brain MRI was most frequently abnormal in multiple sclerosis (68%), but was also abnormal in 31% of SD patients ($P < 0.05$). Oligoclonal bands in CSF were more frequent in multiple sclerosis than in SD ($P < 0.001$) and were never found in SCI. Clinical outcome at 12 months was good in 88% of multiple sclerosis cases, and poor or fair in 91% of SCI and 77% of SD. Aetiologies of AM may be differentiated on the basis of clinical, spinal cord and brain MRI, CSF and outcome data, and allow a probable diagnosis to be made in previously undetermined cases. These findings may have therapeutic implications for cases with a questionable diagnosis.

Keywords: acute myelopathy; multiple sclerosis; spinal cord infarct; systemic disease; MRI.

Abbreviations: Ab = antibodies; AM = acute myelopathy; APTM = acute partial tranverse myelopathy; ATM = acute transverse myelopathy; DRM = delayed radiation myelopathy; PIM = parainfectious myelopathy; SCI = spinal cord infarct; SD = systemic disease

Introduction
Acute myelopathy (AM) is defined as an acute or subacute spinal cord dysfunction secondary to various causes, including parainfectious myelopathy (PIM), multiple sclerosis, systemic disease (SD) such as Sjögren’s syndrome or systemic lupus erythematosus, delayed radiation myelopathy (DRM) and spinal cord infarct (SCI) (Jeffery et al., 1993). However, in some cases the cause of AM remains unknown (Martí-Fabregas et al., 1989). Extensive data have been published on each of these diseases (Pallis et al., 1961; Alexander et al., 1981; Christensen et al., 1990; Dalecky et al., 1997; Misra et al., 1998; Breteau et al., 2000), but studies comparing clinical and laboratory profiles of AM are scarce (Jeffery et al., 1993; Bakshi et al., 1998; Scott et al., 1998). Furthermore, the treatment and follow-up of AM patients have rarely been studied. The aim of this study was to compare the clinical, MRI and laboratory profiles of patients suffering from AM and their outcome.

Methods
Patients
Between 1994 and 1999, we retrospectively studied 79 consecutive cases of AM diagnosed as acute transverse
myelopathies (ATM) according to the clinical features defined by Berman and colleagues (Berman et al., 1981) or acute partial transverse myelopathies (APTM) according to the clinical features defined by Ford and colleagues (Ford et al., 1992).

Inclusion criteria were: (i) acute or subacute motor or sensory symptoms with or without sphincter dysfunction; (ii) spinal segmental level of sensory disturbance with a well defined upper limit; (iii) occurrence of symptoms over no more than a 3-week period, sustained at least 48 h; (iv) no evidence or no radiological evidence of spinal compression; and (v) no known history of neurological disease or symptoms.

Cases of AM were then classified into six subgroups. (i) SD: according to the American Rheumatism Association criteria for systemic lupus erythematosus (Tan et al., 1982), the European criteria of Vitali and colleagues (Vitali et al., 1996) for Sjögren’s syndrome and the Sapporo criteria for antiphospholipid syndrome (Lockshin et al., 2000). (ii) Multiple sclerosis: according to Poser’s criteria for clinically or laboratory definite multiple sclerosis (Poser et al., 1983). Clinically definite multiple sclerosis was diagnosed when a second relapse occurred during the follow-up. Laboratory definite multiple sclerosis was diagnosed when oligoclonal bands were found in CSF of patients with only one relapse. The mean time of follow-up was 21 months (range 12–42 months) in this subgroup. (iii) PIM: this diagnosis was made only if serological proof of a recent infection or reinfection was obtained (serum and CSF). (iv) DRM: the criteria for definite multiple sclerosis was based on an acute deficit, spinal cord imaging corresponding to vascular territories and a lack of an alternative diagnosis after an extensive work-up. (v) Myelopathy of unknown aetiology: this diagnosis was for patients not fulfilling the criteria for any of the other categories. We included, in this subgroup, patients with an initial clinical feature compatible with multiple sclerosis, but without second relapse after the follow-up or oligoclonal bands in CSF.

Clinical findings
We recorded demographic characteristics (age, sex) and clinical features (ATM or APTM) and symptoms (motor, sensory or sphincter dysfunction) at admission, treatment and outcome. For each AM subgroup we analysed the treatment and the outcome. Clinical outcome was evaluated at 1 year and patients were classified into three subgroups, corresponding to good, fair or poor prognosis, according to the Lipton and Teasdall scale (Lipton and Teasdall, 1973). Good prognosis was assigned to patients with normal walking with no, or only mild, neurological examination abnormalities or mild sphincter dysfunction. Fair prognosis was assigned to patients who had the need for unilateral or bilateral help for walking more than 100 m and persistence of mild sensory or sphincter dysfunction. Poor prognosis was assigned to patients with inability to walk 100 m even with help and severe sensory or sphincter dysfunction.

MRI findings
Spinal cord MRI analyses
At admission, all patients underwent a spinal cord MRI with a 1.0 tesla (eight cases) or a 1.5 tesla (71 cases) MRI (Siemens, Erlangen, Germany). Cervical, dorsal and lumbar levels of the spinal cord were evaluated. In the sagittal plane, T1-weighted sequences with and without DTPA–gadolinium and T2-weighted sequences were performed. T2-weighted sequences were also performed in the axial plane. We evaluated the number of lesions, their extent (number of vertebral levels), their localization in the sagittal plane (cervical, dorsal or lumbar) and in the axial plane (anterior, posterior, lateral or central) and the presence of contrast enhancement. Spinal cord MRI was repeated 3–6 months after onset (mean 5 months) in 73 cases.

Brain MRI
All patients underwent brain MRI during the first week after onset. We evaluated MRI according to the criteria of Paty and colleagues for the diagnosis of multiple sclerosis (Paty et al., 1988).

Laboratory findings
We performed serum analysis including routine laboratory tests, antinuclear antibodies (Ab), antinative DNA Ab, precipitation Ab against Ro and La, antiprothrombinase Ab, anticardioliopin Ab, angioconvertase enzyme, serum complement and cryoglobulinaemia. We performed the following viral serologies: Lyme; HIV; cytomegalovirus; hepatitis A, B and C; herpes simplex virus; herpes human virus 6; varicella-zostervirus; enterovirus; coxsackievirus A and B; adenovirus and Epstein–Barr virus. We considered as positive viral serology the occurrence of IgM, and/or an increase of four or more IgG levels on two successive tests. A CSF analysis was performed in all patients with cell count, protein level and electrophoresis (oligoclonal bands) and viral serologsies when positive in the serum.

Other examinations
We performed visual evoked potentials, somatosensory evoked potentials and brain auditory evoked potentials in 65, 59 and 53 patients, respectively. A complete routine ophthalmological examination was performed in 67 patients with a Schirmer test. A salivary gland biopsy was performed in 45 patients. Salivary scintigraphy was performed when Sjögren’s syndrome was clinically or serologically suspected. A chest X-ray was performed in all patients in order to
Table 1 Clinical characteristics at admission in acute myelopathy subgroups

<table>
<thead>
<tr>
<th></th>
<th>Age in years (range)</th>
<th>Sex ratio (male : female)</th>
<th>ATM Motor impairment</th>
<th>APTM Motor impairment</th>
<th>Sensory symptoms</th>
<th>Sphincter dysfunctions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple sclerosis (n = 34)</td>
<td>34 (19–54)</td>
<td>11 : 23</td>
<td>2 (6%)</td>
<td>10 (91%)</td>
<td>2 (6%)</td>
<td>8 (23%)</td>
</tr>
<tr>
<td>SCI (n = 11)</td>
<td>67 (50–78)</td>
<td>4 : 7</td>
<td>8 (63%)</td>
<td>3 (27%)</td>
<td>10 (91%)</td>
<td>1 (9%)</td>
</tr>
<tr>
<td>SD (n = 13)</td>
<td>48 (19–70)</td>
<td>1 : 12</td>
<td>10 (77%)</td>
<td>3 (23%)</td>
<td>11 (84%)</td>
<td>2 (16%)</td>
</tr>
<tr>
<td>PIM (n = 5)</td>
<td>29 (20–35)</td>
<td>4 : 1</td>
<td>4 (80%)</td>
<td>1 (20%)</td>
<td>4 (80%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>DRM (n = 3)</td>
<td>58 (33–78)</td>
<td>2 : 1</td>
<td>2 (67%)</td>
<td>1 (33%)</td>
<td>2 (67%)</td>
<td>1 (33%)</td>
</tr>
<tr>
<td>Myelopathy of unknown aetiology (n = 13)</td>
<td>39 (24–68)</td>
<td>4 : 9</td>
<td>4 (31%)</td>
<td>9 (69%)</td>
<td>2 (15%)</td>
<td>7 (54%)</td>
</tr>
</tbody>
</table>

SCI = spinal cord infarct; SD = systemic disease; PIM = post-infectious myelopathy, DRM = delayed radiation myelopathy; ATM = acute transverse myelopathy; APTM = acute partial transverse myelopathy.

**Statistical analysis**

A statistical analysis was performed for only three subgroups of patients (multiple sclerosis, SCI and SD) the number of patients being too low in the other two groups (PIM and DRM). For the oligoclonal band value analysis, we only considered clinically definite multiple sclerosis patients in the multiple sclerosis subgroup as laboratory definite multiple sclerosis diagnosis depends in part on the occurrence of CSF oligoclonal bands. Statistical analysis was based on a chi-square or Fisher’s exact test at a 95% level of significance. All P values lower than 0.05 were regarded as statistically significant.

**Results**

AM was secondary to multiple sclerosis in 34 (43%) patients (16 clinically definite multiple sclerosis and 18 laboratory definite multiple sclerosis), to SD in 13 (16.5%) patients (Sjögren’s syndrome in seven cases, systemic lupus erythematosus in five cases and antiphospholipid syndrome in one case) and to SCI in 11 (14%) patients. PIM was diagnosed in five (6%) patients (Epstein–Barr virus, human herpes virus 6, enterovirus, adenovirus and coxsackie B virus). DRM was diagnosed in three (4%) patients. The aetiology remained unknown in 13 (16.5%) of the 79 patients despite a follow-up of 29.6 months (range 12–42 months) in this subgroup.

**Clinical findings**

The clinical symptoms at admission are shown in Table 1. The sex ratio was not different in the three statistically studied subgroups. Patients were younger in the multiple sclerosis subgroup than in the SCI (P < 0.001) and SD (P < 0.01) subgroups. The age of the patients was not statistically different in the SD and SCI subgroups. ATM was statistically more frequent in the SCI and SD subgroups than in the multiple sclerosis subgroup (P < 0.001). Sensory symptoms were the most frequent presenting symptoms in multiple sclerosis (28 of the 34 patients), whereas motor and sphincter dysfunctions were more frequent in the other groups (P < 0.001). There was no statistical difference between SCI and SD in terms of clinical presentation. SD was previously diagnosed in only six of the 13 patients. In the other seven patients neurological symptoms were the first symptoms. In the multiple sclerosis subgroup, a relapse occurred in 16 patients (47%) after a mean follow-up of 21 months (range 12–42 months), allowing a diagnosis of clinically definite multiple sclerosis. In the other subgroups there was no relapse except in SD, where a relapse occurred in seven patients (54%) (optic neuritis in six patients and cerebellar symptoms in one). The outcome was good in 30 of the 34 multiple sclerosis patients (88%) at 12 months and in all of the PIM patients at 12 months. However, three of the five PIM patients complained of sphincter symptoms at this stage. The outcome was poor or fair in 10 of the 11 SCI patients (91%), in 10 of the 13 SD patients (77%) and in two of the three DRM cases.

**MRI findings**

The results of spinal cord and brain MRI are summarized in Table 2. The localization of the lesions in the sagittal plane was more frequently cervicodorsal in all the subgroups, except for SCI where infarction of the conus medullaris was the most frequent. However, this difference was not statistically significant. In multiple sclerosis, the lesions were more frequently small (less than two vertebral segments) and lateral or posterior in the axial plane (Fig. 1), than in SCI (P < 0.001) or SD (P < 0.001), where they were more extensive and localized in the centromedullary territory (Figs 2 and 3). Contrast enhancement was found in 21 of the 34 multiple sclerosis patients compared with two of the 11 SCI patients and seven of the 13 SD patients. The difference was only significant between multiple sclerosis and SCI (P < 0.02). Spinal cord swelling was seen in 10 multiple sclerosis patients (30%), two SD patients (15%), two SCI...
Table 2: Spinal cord and brain MRI findings in acute myelopathy subgroups

<table>
<thead>
<tr>
<th>Multiple lesions localization</th>
<th>Multiple lesions enhancement</th>
<th>Cord swelling</th>
<th>Brain MRI (Paty’s criteria)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical Extremity cord</td>
<td>Gadolinium enhancement</td>
<td>Posterior hypersignal</td>
<td>Hypersignal (Paty’s criteria)</td>
</tr>
<tr>
<td>Thoracic</td>
<td></td>
<td>Low (15%)</td>
<td>Percentage 47%</td>
</tr>
<tr>
<td>Lumbar</td>
<td></td>
<td>Low (21%)</td>
<td>Percentage 47%</td>
</tr>
<tr>
<td>MUE</td>
<td></td>
<td>Low (21%)</td>
<td>Percentage 50%</td>
</tr>
<tr>
<td>MUE</td>
<td></td>
<td>Low (21%)</td>
<td>Percentage 32%</td>
</tr>
<tr>
<td>MS</td>
<td></td>
<td>Low (21%)</td>
<td>Percentage 68%</td>
</tr>
<tr>
<td>SCI</td>
<td></td>
<td>Low (21%)</td>
<td>Percentage 82%</td>
</tr>
<tr>
<td>SD</td>
<td></td>
<td>Low (21%)</td>
<td>Percentage 31%</td>
</tr>
<tr>
<td>PIM</td>
<td></td>
<td>Low (21%)</td>
<td>Percentage 0%</td>
</tr>
<tr>
<td>DRM</td>
<td></td>
<td>Low (21%)</td>
<td>Percentage 72%</td>
</tr>
</tbody>
</table>

Paty’s criteria: delayed radiation myelopathy (MTE) = multiple myelopathy of unknown aetiology; limited hypersignal in 1 vertebral level in the central cord; extended hypersignal in >1 vertebral level in the central cord.

patients (18%), four PIM patients (80%) and two DRM patients (66%). This difference was not statistically significant. Brain MRI was more frequently abnormal in the multiple sclerosis group [23 of the 34 patients (68%)] than in the SD subgroup, where we found hypersignals in four patients (31%) ($P < 0.05$).

On the follow-up spinal cord MRI, the lesion had disappeared in 88% of SCI patients, but in only 30% of SD patients and 33% of multiple sclerosis patients ($P < 0.02$). There was no lesion or signal change at follow-up in all of the PIM (Fig. 4) and DRM patients. However, in two of the three patients with DRM the spinal cord was atrophic (Fig. 5).

**Laboratory findings**

SD met the criteria for Sjögren’s syndrome in seven cases, for systemic lupus erythematosus in five cases and for antiphospholipid syndrome in one case. We observed two cases with isolated cryoglobulinaemia and two other cases with antinuclear Ab at a low level in the multiple sclerosis subgroup. None of the patients had increased angiotensin enzyme level. None of the SCI patients had positive antinuclear or anticardiolipin Ab. The five positive serologies in the PIM subgroup were Epstein–Barr virus, coxsackie B, human herpes virus 6, adenovirus and enterovirus. The results of the CSF analysis are summarized in Table 3. The cell count was increased in only two cases of SCI, in 16 of the 34 multiple sclerosis patients and in nine of the 12 SD patients. Furthermore, the cell count was below 30 in all but one of the multiple sclerosis patients and in all the SCI patients, and above 30 in six cases of SD (five of the six cases were Sjögren’s syndrome) ($P < 0.01$). CSF protein levels were similar in each subgroup of myelopathies except for SCI, where proteins were increased (though two patients had diabetes mellitus), and for PIM, where protein level was increased in four of the five cases. CSF oligoclonal bands were found more frequently in multiple sclerosis patients (88%) than in the SD subgroup, where they were present in only two cases ($P < 0.001$). We did not observe oligoclonal bands in the SCI, DRM or PIM subgroups.

**Other examinations**

Visual evoked potentials were performed in only two cases of SCI but were normal in both. We found no difference between multiple sclerosis and SD patients for visual evoked potential testing. We found visual evoked potential abnormalities in 15 of the 34 multiple sclerosis patients (41%) and in six of the 13 SD patients (46%). Furthermore, brainstem auditory evoked potentials and sensory evoked potentials were not significantly different in each subgroup of myelopathies. Chest X-ray was normal in all cases. In suspected SCI, cardiac and cervical vessel echography and spinal arteriography were normal. No patients had aortic dissection.
**Myelopathy of unknown origin**

The aetiology of AM remained unknown in 13 patients after a mean follow-up of 29.6 months (range 12–42 months). The characteristics of this subgroup were heterogeneous. When we applied the criteria shown in Table 4 to this subgroup, a possible diagnosis could be proposed in six cases (two multiple sclerosis, two PIM and two SCI). In the seven remaining patients the diagnosis was undetermined.

**Treatment**

All multiple sclerosis patients were treated by intravenous corticosteroids, with good results in 92% of cases. Interferon β1a was proposed to seven patients (21%) who experienced one or two new relapses. Four of the SCI patients were treated by intravenous corticosteroids, with no improvement in motor function. The remaining seven patients were treated by anticoagulation (heparin) and their clinical status remained stable. In all cases, antiplatelet therapy (aspirin, 300 mg per day) was proposed for secondary prevention. All but one of the SD patients were treated by intravenous corticosteroids. Neurological signs improved in three cases with a mild neurological deficit. In the other 10 cases, treatment with intravenous cyclophosphamide was proposed, and was partially effective in eight patients, with an increase of one or two points on the Lipton and Teasdale scale after 1 year. All five PIM patients were treated by intravenous corticosteroids, with a dramatic improvement of neurological symptoms in all cases, mild sphincter disturbances persisting in three cases only. DRM patients were also treated by intravenous corticosteroids but no efficacy was noted and the patients remained stable with severe motor and sphincter symptoms in two cases and predominantly sensory symptoms in the third.

**Discussion**

Our study establishes distinct profiles for the different aetiologies of myelopathy. The criteria suggesting each aetiology of AM are proposed in Table 4.
Fig. 2 Spinal cord MRI. T₂-weighted sequences. Extended hypersignal in a patient with a Sjögren’s syndrome (A) localized in the centromedullary territory (B).
Multiple sclerosis
Multiple sclerosis is the most frequent studied aetiology of AM (Dalecky et al., 1997; Simnad et al., 1997; Scott et al., 1998; Iffenecker et al., 1998). Our results confirm some of the previous data. All but two of our multiple sclerosis patients were APTM, in line with recently published findings (Dalecky et al., 1997; Simnad et al., 1997; Scott et al., 1998). Severe motor deficit and urinary dysfunctions were found in only 6% and 23% of our multiple sclerosis patients, respectively. MRI results were in accordance with previous studies showing that spinal cord lesions in clinically definite multiple sclerosis are frequently small in size and localized in the lateral or posterior regions (Tartaglino et al., 1995). As in previous studies concerning spinal cord in multiple sclerosis, the lesions were more frequently cervical (50%) (Kidd et al., 1993; Tartaglino et al., 1995; Dalecky et al., 1997). Brain MRI met the criteria of Paty in 68% of our multiple sclerosis patients but was also frequently found in SD (31% of cases). To our knowledge, there have been no studies comparing brain MRI in patients with various aetiologies of AM. Nevertheless, previous studies have suggested that brain lesions are probably underestimated in SD (Alexander et al., 1988; Rovaris et al., 2000).

Visual evoked potential abnormalities were not discriminant in multiple sclerosis compared with SD. Optic neuritis has previously been reported in SD case studies, but its frequency is still unknown (Alexander et al., 1982; Wise and Agudelo, 1988; Tesar et al., 1992). Our results also confirm the relevance of CSF analysis in AM, especially with regard to oligoclonal bands. The presence of CSF oligoclonal bands in multiple sclerosis has been widely reported, but has not been compared with other aetiologies in a large cohort of AM patients. Oligoclonal bands were present in the CSF of 88% of patients with clinically definite multiple sclerosis, in only two patients with SD and in none of the other aetiological subgroups. This result confirms the high predictive value of oligoclonal bands for developing clinically definite multiple sclerosis after inaugural AM with oligoclonal bands (Miller et al., 1989; Dalecky et al., 1997).
Except for the two cases with ATM, the outcome was good in all multiple sclerosis patients. However, a second relapse occurred in 47% of cases with a mean follow-up of 21 months. This result is in accordance with recently published data showing that the cumulative probability of the development of clinically definite multiple sclerosis during the 2-year following a first neurological event suggestive of multiple sclerosis is 40% (Jacobs et al., 2000).

Systemic disease
AM associated with SD has rarely been reported in the literature (Alexander et al., 1981; Alexander et al., 1982; Mok et al., 1998). The frequency of AM in systemic lupus erythematosus is estimated to be ~3%, but is unknown in Sjögren’s syndrome (Alexander et al., 1981; Alexander et al., 1982; Mok et al., 1998; Rovaris et al., 2000). AM occurs more frequently during the first year of SD, where it may be the first clinical manifestation, as in 46% of our cases (Barile and Lavalle, 1992; Chan and Boey, 1996). Clinical symptoms are frequently ATM with severe motor and sphincter dysfunctions. Spinal cord MRI characteristics have been studied more frequently in systemic lupus erythematosus than in Sjögren’s syndrome. In systemic lupus erythematosus, the lesion is frequently large and centromedullar (Provenzale et al., 1994). Normal spinal cord MRI or mild hypersignal has also been reported, but is less frequent (Chan and Boey, 1996; Mok et al., 1998). In Sjögren’s syndrome, spinal cord MRI has only been studied in case reports (Konttinen et al., 1987; Wright et al., 1999). Our study shows that MRI characteristics are highly similar to systemic lupus erythematosus findings. All but two of our seven patients had a large centromedullar hypersignal, as described in systemic lupus erythematosus. The pathophysiological hypotheses of AM in SD are still a matter for discussion. The most likely hypothesis is a vascular mechanism secondary to ischaemic lesions (Harisdangkul et al., 1995). However, more slowly progressive myelopathy due to demyelination with axonal loss has also been described (Johnson and Richardson, 1968).

CSF analysis was of major interest in our study, allowing SD and SCI to be differentiated from multiple sclerosis (cell
Fig. 5 Spinal cord MRI. Extended hypersignal in T₂-weighted sequences in the cervical cord following laryngeal radiation with a swelling of the cord (A). MRI after 4 months of follow-up shows normal cord signal in T₂-weighted sequences, but an atrophic cord in T₁-weighted sequences (B).

Table 3 Cerebrospinal fluid analysis in acute myelopathy subgroups

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Cell count (cell/mm³)</th>
<th>Patients with cell count &gt;30 cells/mm³</th>
<th>Protein level (g/l) mean (range)</th>
<th>Oligoclonal bands</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinically definite MS (n = 16)</td>
<td>9.7 (1–38)</td>
<td>1 (3%)</td>
<td>0.48 (0.2–0.92)</td>
<td>14 (88%)</td>
</tr>
<tr>
<td>SCI (n = 11)</td>
<td>1.9 (0.1–8)</td>
<td>0 (0%)</td>
<td>0.75 (0.23–3)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>SD (n = 13)</td>
<td>35.4 (1–160)</td>
<td>6 (46%)</td>
<td>0.72 (0.4–1.39)</td>
<td>2 (17%)</td>
</tr>
<tr>
<td>PIM (n = 5)</td>
<td>119.2 (53–320)</td>
<td>5 (100%)</td>
<td>1.17 (0.5–1.97)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>DRM (n = 3)</td>
<td>0.8 (0.1–1.2)</td>
<td>0 (0%)</td>
<td>0.31 (0.2–0.45)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Myelopathy of unknown aetiology</td>
<td>13.2 (1–70)</td>
<td>2 (15%)</td>
<td>0.39 (0.19–1.07)</td>
<td>3 (23%)</td>
</tr>
</tbody>
</table>

MS = multiple sclerosis; SCI = spinal cord infarct; SD = systemic disease; PIM = post-infectious myelopathy, DRM = delayed radiation myelopathy. *Two of these patients had diabetes mellitus. †We included only clinically definite multiple sclerosis as the presence of oligoclonal bands is a criterion for laboratory definite multiple sclerosis.

count higher than 30 cells in SD, oligoclonal bands in multiple sclerosis, normal CSF in SCI). In neurological Sjögren’s syndrome, Alexander and colleagues found oligoclonal bands in CSF of 50% of cases (Alexander et al., 1982), but this study included chronic myelopathies where clinical symptoms, MRI data and CSF findings are clearly different from AM. In AM associated with systemic lupus erythematosus, CSF can be normal or shows pleiocytosis. Oligoclonal bands are possible but remain rare (Barile and Lavalle, 1992; Harisdangkul et al., 1995; Mok et al., 1998).

The clinical outcome was frequently poor in our patients, implying the need for intensive therapy when AM is associated with SD. Initial treatment by intravenous corticosteroids can be recommended, as already suggested...
Table 4 Discriminative criteria for each aetiology of acute myelopathy

<table>
<thead>
<tr>
<th></th>
<th>MS</th>
<th>SCI</th>
<th>SD</th>
<th>PIM</th>
<th>DRM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (&gt;50 years)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Severe motor deficit</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Urinary disturbances</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Favourable outcome</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cell count</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Oligoclonal bands</td>
<td>+</td>
<td>+</td>
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<td>+</td>
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<tr>
<td>Spinal cord MRI</td>
<td>+</td>
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<td>+</td>
</tr>
<tr>
<td>Brain MRI</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Intraspinal myelitis, DRM = delayed radiation myelopathy, + = suggestive of, -- = not suggestive of.

by two authors (Barile and Lavalle, 1992; Harisdangkul et al., 1995), but is probably relevant only in moderate forms of AM associated with SD. In other cases, treatment by immunosuppressive drugs (intravenous cyclophosphamide) seems to be necessary and is probably more effective if administered as early as possible (Barile and Lavalle, 1992; Harisdangkul et al., 1995; Mok et al., 1998). These data were only reported for systemic lupus erythematosus. In our patients, the optimal therapy regimen in severe AM associated with SD appears to be intravenous cyclophosphamide in both systemic lupus erythematosus and Sjögren’s syndrome. Further prospective multicentre studies are required to confirm this result.

Spinal cord infarcts
The diagnosis of AM secondary to SCI is difficult because of the lack of clear diagnostic criteria at the acute stage. Our study shows that SCI occurs more frequently in patients over the age of 50 years. The initial clinical symptoms were ATM in 63% of patients. Severe motor and sphincter dysfunctions were found in all cases. The high frequency of sphincter dysfunction has already been reported (Sandson et al., 1989; Inatomi et al., 1998). Spinal cord MRI showing an isolated centromedullary hypersignal is of major diagnostic value. CSF analysis shows absent or low cell count and no oligoclonal bands. A mild cell increase in the CSF of SCI patients has previously been reported (Cheshire et al., 1996).

There are no clear guidelines for the treatment of SCI. Several studies have suggested that intravenous heparin or steroid treatment could be of interest, but in partial or transitory AM, rather than in severe and persistent SCI (Cheshire et al., 1996). Another study proposed intravenous nimodipine, but there has not been a controlled trial with this drug (Schittek et al., 1992). In our study, neither of the treatments (heparin or corticosteroids) showed a clear efficacy, and outcome was poor or fair in 91% of cases. Previous studies have shown that clinical outcome is not always poor in SCI (Pou-Serradell et al., 1994; Cheshire et al., 1996). However, in the study by Cheshire and colleagues, 20% of patients died and 46% showed minimal or no improvement (Cheshire et al., 1996). In another study, all 10 patients had persistent neurological impairment after 3 years of follow-up (Pelser and van Gijn, 1993). Multicentre studies with clinical, and radiological investigations and treatment of SCI will be required in order to improve our knowledge of this rare aetiology of AM.

Post-infectious myelopathy
In a previous study, PIM was frequently diagnosed, but the diagnostic criteria were based on clinical infection with fever (Jeffery et al., 1993). Serological confirmation of the infection was rarely obtained. As we used more specific criteria, the frequency of PIM was lower in our study. In PIM, clinical symptoms are frequently severe with motor and sphincter
dysfunctions, as observed in our five patients with ascending spinal cord dysfunction (Jeffery et al., 1993; Breteau et al., 2000). MRI abnormalities with a large centromedullar hypersignal on T2-weighted images associated with cord swelling have previously been described in PIM (Jeffery et al., 1993; Gilden et al., 1994). The most frequent localization is cervicodorsal (Jeffery et al., 1993; Caldas et al., 1994; Ku and Lee, 1998; Nakajima et al., 1998). Brain MRI is frequently normal. Nevertheless, brain MRI abnormalities have previously been reported in several studies (Epperson et al., 1988; Tselis and Lisak, 1995). In these cases, white matter changes were very similar to those found in acute demyelinating encephalomyelitis.

CSF abnormalities (pleiocytosis higher than 30 cells, without oligoclonal bands) were suggestive of an infectious phenomenon and were highly discriminative between PIM and multiple sclerosis (Jeffery et al., 1993). Clinical outcome of PIM was good in all five of our patients, with only mild sphincter dysfunctions after a follow-up of at least 1 year. In a few reported cases, outcome was severe, especially in acute necrotizing myelopathy (Wiley et al., 1987). However, this feature remains rare and could be specific to viruses such as herpes simplex virus (Wiley et al., 1987; Jeffery et al., 1993). All of our patients improved after treatment by intravenous corticosteroids, but this could be due to the natural course of the disease. There is no consensus in the literature on treatments may be proposed.

Delayed radiation myelopathy

DRM is a rare cause of AM, suggested only when there is a previous history of radiation. The delay between radiation and AM can extend 10 years (Jones, 1964). DRM may be differentiated from early radiation myelopathy, which occurs 10–16 weeks after the radiotherapy. In the latter case, the symptoms almost invariably resolve spontaneously 2–9 months after onset (Pallis et al., 1961; Jones, 1964; Jellinker and Sturm, 1971). In DRM, spinal cord MRI shows high intensity signal on T2-weighted images with focal swelling of the cord (Wang et al., 1995; Rampling and Symonds, 1998), as in two of our cases. Follow-up spinal cord MRI in our study showed normal signal intensity but severe atrophy. A similar finding has already been reported, confirming the value of serial MRI examination in AM suggestive of DRM (Wang et al., 1995; Koehler et al., 1996). CSF analysis is also of major interest, as it was normal in all of our cases and in nine cases studied by Angibaud and colleagues (Angibaud et al., 1995). The lack of any cell reaction or oligoclonal bands is of diagnostic importance compared with other aetiologies of AM, such as multiple sclerosis, PIM or SD.

No treatment has conclusively been shown to be of value in DRM. Some patients have derived a short-term benefit from steroids (Schultheiss and Stevens, 1992), which may be related to the oedema and inflammation. In our three patients, steroids did not produce a beneficial effect. Although vasoactive drugs are thought to be useful in traumatic myelopathy, this is not the case in DRM (Rampling and Symonds, 1998). Anticoagulation showed stabilization or improvement in two studies (Glantz et al., 1994; Koehler et al., 1996), but no subsequent publications are available to confirm these findings. Hyperbaric oxygen has been investigated and showed improvement of symptoms in six of the nine patients treated (Angibaud et al., 1995). Depending on the severity of the outcome, and in view of the low risk of side-effects of these three therapies, a combination of treatments may be proposed.

Myelopathies of unknown aetiology

In our study, AM remained of unknown aetiology in 13 cases (16.5%). In previous studies the frequency was extremely variable, ranging from 9 to 60% of cases (Miller et al., 1989; Campi et al., 1995). Clinical and MRI studies on myelopathies of unknown origin have shown that long-term follow-up allows a diagnosis to be made in ~50% of cases (Martin-Fabregas et al., 1989). Differences in the length of follow-up may explain the high variability observed in the different studies. Long-term follow-up of our cohort may well allow us to determine the aetiology of some of the remaining cases of myelopathies of unknown origin. Particularly, several cases would probably have been diagnosed as multiple sclerosis but did not experience a relapse during the follow-up.

Finally, a better knowledge of each profile of AM should improve the efficiency of the diagnostic work-up, help to reduce the number of cases of myelopathies of unknown origin and increase the effectiveness of therapeutic strategies. Other studies with a prospective analysis are necessary to confirm the frequency of each aetiology. Furthermore, there is a need for multicentre therapeutic trials in several aetiologies, such as DRM, SCI and SD.

References


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