Acute transverse myelitis
A localized form of postinfectious encephalomyelitis

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Summary
We analysed the clinical, imaging, electrophysiological, laboratory findings, course and prognostic factors in 31 patients with acute transverse myelitis (20 men and 11 women; mean age, 30 years; range, 18–51 years). All patients were assessed for maximal clinical deficit ‘deficit score’; pattern-shift visual, auditory and somatosensory evoked potentials were measured, CSF was examined, and neuroimaging of the spinal cord and brain (MRI or CT myelography) was carried out. The myelitis was preceded by febrile illness in 25 (81%) of the patients. The site of the lesion was cervical in 11 (36%), upper thoracic in two (6%), lower thoracic in 16 (52%). MRI of the spinal cord was abnormal in 10 out of the 20 patients examined (50%); in the remaining 11 patients, only CT was carried out and it was normal in all of them. Somatosensory evoked potentials were abnormal in 19 (61%), while pattern-shift visual and brainstem auditory evoked potentials were normal in all patients. CSF was abnormal in 94% of patients with pleocytosis, increased protein or both. Eighteen patients (58%) had good outcome. All patients had monophasic pattern-shift visual, auditory and somatosensory evoked potentials were measured, CSF was examined, and illness. Three variables have emerged as being associated with significant worsening of the outcome: (i) abnormal somatosensory evoked potentials; (ii) abnormal imaging and (iii) high ‘deficit score’ at onset. Acute transverse myelitis affects a complete segment of the spinal cord, is monophasic and represents a localized form of postinfectious acute encephalomyelitis.

Keywords: multiple sclerosis; optic neuritis; cerebrospinal fluid; MRI; somatosensory evoked potentials

Abbreviations: BAEP = brainstem auditory evoked potential; PSVEP = pattern shift visual evoked potential; SEP = somatosensory evoked potential

Introduction
Acute transverse myelitis is an intramedullary spinal disorder; it usually involves the spinothalamic tracts, pyramidal tracts, posterior columns and anterior funiculi at one or more adjacent levels (Berman et al., 1981; Jeffery et al., 1993). In Western countries, it may be the presenting feature of multiple sclerosis or it may manifest during the course of this disease (Jeffery et al., 1993). Non-compressive causes are paraneoplastic (Nakagawa et al., 1991), anterior spinal artery embolism (Walsh et al., 1992) or thrombosis (Nagashima et al., 1991; Kume et al., 1992), and vasculitis in autoimmune diseases such as systemic lupus erythematosus (Lavalle et al., 1990; Barile and Tanaka, 1991), and scleroderma (Arizaro et al., 1989; Litman, 1989). Other causes are infections such as herpes zoster (Baethge et al., 1989; Heller et al., 1990), psittacosis (Williams and Sunderland, 1989), HIV (Barakos et al., 1990; Dodson, 1990), Echo-25 virus (Yamada et al., 1990), Epstein–Barr virus (Junker et al., 1991), mycoplasma pneumoniae (Mills and Schoolfield, 1992), rubella (Hess and Bamborschke, 1993), mumps (Nussinovitch et al., 1992), brucellosis (Al Deeb et al., 1988; Al Deeb et al., 1989) and schistosomiasis (Boyce, 1990). It may follow vaccination against cholera, typhoid and poliomyelitis (D’Costa et al., 1990), and has been reported with intramuscular penicillin injections (Runge and Roder, 1989), heroin abuse (Pascual Calvet et al., 1989), sulphasalazine chemotherapy (Olenginski et al., 1991), B-cell lymphoma (Iwashishi et al., 1992), myelomonocytic leukemia (Shiozaki et al., 1990), idiopathic hypereosinophilic syndrome (Tsai et al., 1993), and following general anaesthesia (Gutowski and Davies, 1993) or acupuncture (Sato et al., 1991).

A group of patients remains in whom no causative factor can be identified. This group is usually described in the
Table 1  Deficit scoring system

<table>
<thead>
<tr>
<th>Function tested</th>
<th>Absent</th>
<th>Diminished</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Each limb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior column sensation</td>
<td>0</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>Spinothalamic sensation</td>
<td>0</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>Power*</td>
<td>0</td>
<td>0.5–1.5</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All limbs normal</td>
<td>0</td>
<td>–</td>
<td>16</td>
</tr>
<tr>
<td>Sphincter control</td>
<td>0</td>
<td>–</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>0</td>
<td>–</td>
<td>20</td>
</tr>
</tbody>
</table>

*Equivalent MRC (Medical Research Council) scores:
1.5 = MRC 4; 1 = MRC 3; 0.75 = MRC 2; 0.5 = MRC 1; 0 = MRC 0.

literature as ‘idiopathic’, but may also be referred to as acute noncompressive spinal cord syndrome, myelopathy, myeloradiculopathy, myelomalacia, or paraplegia or quadriplegia of unknown aetiology.

In this report we analyse the clinical, neurophysiological, laboratory characteristics, course and prognostic factors in a series of patients with acute transverse myelitis of the idiopathic type.

Methods
All patients admitted to the neurology department during the period 1986–1992 were enrolled if they developed acute illness of <4-weeks duration, with rostrally well-defined spinal, motor and sensory deficit and with or without sphincteric impairment. We excluded from the study cases with spinal compressive lesions, those in whom a cause could be established, and ultimately those who developed neuromyelitis optica (Al Deeb et al., 1993) or multiple sclerosis during the follow-up period. All patients were seen by one of us on admission and the maximal clinical deficit was scored according to the scale presented in Table 1. The score ranged between 0 (maximal deficit) and 20 (normal). All subjects had complement fixation or haemagglutination inhibition assays for antibodies against herpes simplex, mumps, measles, mycoplasma and toxoplasma performed in blood and CSF samples on admission. Three weeks later, the following tests were performed: blood count, differential and blood film, erythrocyte sedimentation rates, liver function tests, glucose, creatinine and electrolytes, antinuclear factors, D-anti DNA, cardiolipin, antiphospholipids, lupus anticoagulants and fungal antigens, blood cultures for tuberculosis bacilli and Brucella, and serology for HIV, syphilis, and Brucella. CSF examination included estimation of cell numbers, protein, glucose and oligoclonal bands.

Evoked potentials measured included pattern shift visual (PSVEPs), brainstem auditory (BAEPs), and somatosensory (SEPs) for both median and posterior tibial nerves bilaterally. Between 1986 and 1988, the imaging methods used were CT with contrast for the brain and CT myelography for appropriate spinal segment(s) (11 patients); from 1989 onwards T1-weighted MRI with and without contrast and T2-weighted MRI of both brain and spinal cord were employed for imaging (20 patients). The site of the lesion was determined by the clinical examination alone if the spinal image (CT or MRI) was normal, and by the image abnormality if it was abnormal. The lesions were classified as cervical, upper thoracic T1–T3, lower thoracic T4–T12, and conus L1–S5. For prognosis and outcome analysis, cervical and upper thoracic lesions were considered as upper cord and those at lower thoracic and conus as lower cord lesions.

Supportive therapy was given from 1986 to 1988 (11 patients), and i.v. methylprednisolone, 1 g daily for 5 days, to all patients from 1989 onward (20 patients).

Follow-up was at 3-monthly intervals for a minimum of 2 years, and then at yearly intervals afterwards. Minimum follow-up period was for 2 years and maximum was for 9 years. A final deficit score was documented by the same investigator at the end of 2 years follow-up. Subsequent follow-up was to determine relapse. The outcome score was determined according to the scale presented in Table 2. For prognostic factors, those with scores 0–2 were considered as good outcome (Group 1), whereas those with scores of 3–5 were considered as bad outcome (Group 2).

Statistical evaluation
Outcome was scored as a dichotomized variable, with ‘0’ representing a good outcome (Group 1) and ‘1’ a poor outcome (Group 2). As possible predictors, we considered the quantitative variables such as age (years), clinical score, and CSF cell count and protein levels, and ordinal parameters such as sex (male or female), preceding febrile illness (yes or no), treatment with steroids (yes or no), SEP (normal, abnormal) and the imaging findings, formed by combining the results of CT and MRI. The predictive power of the variables mentioned was assessed with logistic regression analysis which is similar to multiple regression, except for the dichotomous instead of continuous dependent variable. The dependent variable in this case is the outcome (good or poor). Logistic regression was performed after preselection.
of a subset of variables, by searching for those variables which significantly affected the outcome; the tests applied consisted of the t test (age, clinical deficit score, protein level), the Mann–Whitney test (CSF cell count) or the χ² test (sex, site of lesion, preceding febrile illness, steroid therapy, SEP results, radiological findings), depending on the nature of the distribution of the variable. Variables differing significantly between the two outcome groups were then combined in a logistic regression model, and were also analysed one at a time.

Results
Thirty-two patients fulfilled the inclusion criteria, but one was excluded because he developed optic neuromyelitis (Al Deeb et al., 1993). None developed multiple sclerosis. Thirty-one patients were finally evaluated. In all patients, the course was monophasic and no recurrence occurred during the follow-up period.

With respect to the clinical presentation, 11 had quadriplegia, 20 paraplegia, all had sensory deficit with a clear-cut upper delimitation, 24 had urinary retention and four retention-incontinence. Preceding febrile illness was noted in 25 patients: 23 had had upper respiratory tract infection and two had gastroenteritis, occurring 3–10 days before manifestation of the neurological deficit. All titres for viral antibodies were negative. Blood count, blood films and sedimentation rate were normal. Autoimmune screen was negative in all patients.

The brain MRI (20 patients) and CT (11 patients) were all normal. MRI of the spinal cord was abnormal in 10 out of the 20 patients examined. The abnormalities were either: (i) diffuse intramedullary high signal intensity lesions extending over two or more segments, best seen on T₂-weighted images, the T₁-weighted images showing swelling of the cord with scattered enhancing patchy lesions after contrast (Fig. 1), as observed in six patients, or (ii) localized enhancing lesions involving only one segment in four patients (Fig. 2). Spinal CT myelography, done in 11 patients, was abnormal in four. The abnormalities were either swelling of the cord (two patients), or complete block (the remaining two). In both the latter, an intramedullary tumour was suspected, and one of them had laminectomy but no tumour was found. Patients with abnormal CT myelography were considered to have diffuse image abnormality. This makes the overall neuroimaging abnormalities 14, four with localized and 10 with diffuse abnormality. The site of lesion was cervical in 11 upper thoracic in two, lower thoracic in 16 and conus in two.

CSF was normal in two patients, in the others cells, protein or both were high. Cells were raised in 26 (>5 lymphocytes/mm³; normal is <3 lymphocytes/mm³). They were predominantly lymphocytes in all patients, and protein was high in 28 (>0.45 g/l; normal is ≤45 g/l). Oligoclonal bands were absent in all patients.

PSVEPs and BAEPs were normal in all patients, SEPs were abnormal in 19, 11 with quadriplegia and eight with paraplegia. The abnormalities were dramatic; in cervical lesions the median nerve SEP showed the potential at Erb’s point to be preserved, while that at C2 and the contralateral sensory cortex was absent. In patients with thoracic lesions, the potential from the conus was preserved, while subsequent potentials were absent. In conus lesions, all central potentials were absent.

Outcome
As shown in Table 2, 18 patients (58%) had good outcome; they recovered completely or became independent. Thirteen (42%) had a poor outcome and were fully dependent and wheelchair bound; one of them, who was 24-years-old, with 104 kg body-weight, flaccid quadriplegia and a deficit score of 20, died of pulmonary embolism. Post-mortem was not permitted.

Steroid therapy
Twenty patients were treated with i.v. methylprednisolone; 12 (60%) had good outcome and eight (40%) had poor outcome.

Prognostic factors
Three variables emerged as being significant by being associated with bad outcome: (i) a high ‘deficit score’ (P = 0.0004); (ii) abnormal neuroimaging (P = 0.0025); (iii) an abnormal SEP (P = 0.0001). Surprisingly, abnormally high CSF protein was associated with favourable outcome (P = 0.05). Logistic regression analysis of predictors of the outcome resulted in the same percentage (77%) of correct predictions in both ‘deficit score’ and abnormal neuroimaging, while SEP abnormalities had a slightly higher predictive value (81%). When all three variables were combined, a correct classification of 94% was obtained.

Discussion
Acute transverse myelitis is occasionally used as a synonym of noncompressive myelopathy (Berman et al., 1981; Nakagawa et al., 1991; Kume et al., 1992; Jeffery et al., 1993). This may cause confusion because the latter term covers a heterogeneous group. Proper use of the term ‘transverse’ denotes that the entire cross-section area of the spinal cord at the level of at least one segment is involved, including pyramidal tracts, spinthalamic tracts, and posterior columns; this will produce a special disease entity as shown in our patients. Transverse myelitis does not mean that only one segment is affected; our study showed that the lesion extended longitudinally beyond two segments in 10 out of 14 patients (71%). Lesions, such as those which occur in, for example, ischaemic myelitis or multiple sclerosis rarely affect a complete segment of the cord.
Fig. 1 MRI of a 36-year-old man with acute transverse myelitis. Midsagittal MRI. (A) $T_2$-weighted image of the spinal cord showing a high intensity lesion in the upper cervical cord $C_2$ segment. (B) $T_1$-weighted image with contrast (magnevist) showing localized enhancing lesion of the upper cervical cord. (The $T_1$-weighted image without contrast was normal and did not show the lesion.) (C) Transverse section at the upper cervical cord showing the enhancing lesion posteriorly located. (D) $T_1$-weighted image with contrast 6 months later showing normal cord. (The $T_2$-weighted image showed the same lesion as before.)
Acute transverse myelitis is uncommon as the presenting feature of multiple sclerosis and ranges between 1.6 and 6% (Altrocchi, 1963; Lipton and Teasdall, 1973; Berman et al., 1981). None of our patients developed multiple sclerosis during a follow-up of up to 9 years. High incidence of acute transverse myelitis in multiple sclerosis is only seen in patients with acute partial spinal cord syndromes where not all the components of spinal cord are involved (posterior column, lateral column and spinothalamic tracts) or with noncompressive spinal cord syndromes (Miller et al., 1987).

Male predominance was evident in our patients, confirming other reports (Berman et al., 1981; Jeffery et al., 1993). The mean age of onset in our patients was 31 years, which is older than that observed in a series of multiple sclerosis patients examined by the authors’ group in Saudi Arabia (Yaqub and Daif, 1988) but younger than that reported in the studies of Berman et al. (1981) and Jeffery et al. (1993). Previous studies may have included ischaemic myelopathy, which has a later age of onset.

Our prospective study addresses the clinical, neurophysiological and neuroradiological aspect, and the factors affecting outcome. MRI was superior to CT in visualizing the abnormalities. In our study, MRI was abnormal in 50% of the 20 patients examined; the figure reported by Austin et al. (1992) was 39%. In the latter series, contrast was not given, which might explain the lower figures. Contrast-enhanced T₁ reveals scattered lesions, which is of importance in the differentiation from intramedullary tumours. Yamamoto et al. (1992) described lack of lesion enhancement with Gd-DTPA (gadolinium–diethylenetriamine penta-acetic acid) in a 15-year-old girl with acute transverse myelitis. In all our patients, enhancement was consistently noticed during the acute phase. A similar finding was reported by Sanders et al. (1990) in a 20-year-old patient. Localized MRI lesions in our patients were larger than those which occur in multiple sclerosis and similar to those seen in the brain in postinfectious encephalomyelitis (Sanders et al., 1990). MRI assessment is of prognostic as well as diagnostic value (Shen et al. 1992), as our patients with normal MRI had better outcome than those with abnormal MRI, unlike the findings by Austin et al. (1992), and those with localized MRI lesions did better than those with extensive lesions.

**Fig. 2** MRI of a 46-year-old woman with acute transverse myelitis. Midsagittal MRI. (A) T₂-weighted image showing long high intensity lesion extending over many segments. (B) T₁-weighted image with contrast (Gd-DTPA) showing focal enhancing lesion extending over more than two segments and mimicking cord tumour.
Table 3  Clinical features of Groups 1 and 2

<table>
<thead>
<tr>
<th></th>
<th>Group 1: good outcome</th>
<th>Group 2: bad outcome</th>
<th>P-value</th>
<th>Correct prediction: logistic regression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 18)</td>
<td>(n = 13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male : female</td>
<td>14 : 4</td>
<td>7 : 6</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>31.5 ± 9.65</td>
<td>31.3 ± 13.99</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Range</td>
<td>(21–55)</td>
<td>(18–60)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preceded by febrile illness</td>
<td>14</td>
<td>11</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Deficit score</td>
<td>10.6 ± 2.4</td>
<td>15.4 ± 3.6</td>
<td>0.0004</td>
<td>77%</td>
</tr>
<tr>
<td>Site</td>
<td></td>
<td></td>
<td>0.055</td>
<td></td>
</tr>
<tr>
<td>Upper cord</td>
<td>4</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower cord</td>
<td>14</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal imaging (CT, MRI)</td>
<td>4*</td>
<td>10</td>
<td>0.0025</td>
<td>77%</td>
</tr>
<tr>
<td>Localized extension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extensive (&gt;2 segments)</td>
<td>0</td>
<td>10†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal SEP</td>
<td>6</td>
<td>13</td>
<td>0.0001</td>
<td>81%</td>
</tr>
<tr>
<td>CSF protein g/l</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1.0, SD ± 0.4</td>
<td>0.8 ± 0.3</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>(0.46–1.6)</td>
<td>(0.4–1.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSF cells/mm³</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>35.33</td>
<td>42.69</td>
<td>0.34</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>(2–250)</td>
<td>(2–130)</td>
<td></td>
<td></td>
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<tr>
<td>Prednisolone treatment</td>
<td>12 (67%)</td>
<td>8 (62%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*All had MRI. †Six with MRI and four with CT myelography.

Tippet et al. (1991) reported two cases of relapsing transverse myelitis, one had a prolonged SEP latency while the other had bilateral leminiscal involvement. No reports were available on SEPs in acute transverse myelitis. SEPs are not only of diagnostic value; they are also of prognostic value, as our study showed. The normal PSVEPs and BSAEPs, taken together with the SEP results, indicate localized rather than multifocal lesions. This has also been reported by Ropper et al. (1982).

The CSF was abnormal in 94% of patients, a much higher proportion than in those reported by other investigators (Altrocchi, 1963; Lipton and Teasdall, 1973; Berman et al., 1981; Jeffery et al., 1993), reflecting the prospective nature and strict inclusion criteria of our study. Oligoclonal bands were absent in our patients; this agrees with other reports (Berman et al., 1981; Jeffery et al., 1993). Kaiser and Lucking (1993) recently reported GFAP (glial fibrillary acidic protein) specific oligoclonal IgG bands in CSF patients with acute myelitis. This was not tested in our patients. The number of CSF cells had no effect on the outcome, while high CSF protein was linked to a better outcome. This has never been reported and has to be considered with caution.

We analysed the effect of clinical symptomatology, paraclinical tests (MRI and evoked potential measurements), laboratory results (CSF) and steroid therapy on the outcome (for a summary see Table 3). Severe clinical deficit at presentation and abnormal MRI and SEP were accompanied by poor prognosis. Other factors such as age, sex, preceding febrile illness, and CSF pleocytosis were not linked to the outcome. Patients with lower cord lesions did better than those with upper cord lesions, but this just missed statistical significance (P = 0.055). Intravenous methylprednisolone reportedly improves the outcome in acute transverse myelitis (Dowling et al., 1980; Chang et al., 1992). Our study showed no benefit of steroids on the final outcome, but it was not double-blind placebo-controlled.

Preceding febrile illness was seen in 25 patients (81%). This is much higher than in the previous reports (25–37%) (Berman et al., 1981; Nakagawa et al., 1991; Walsh et al., 1992; Jeffery et al., 1993). This is not surprising as the previous series were retrospective, nonhomogeneous and probably included ischaemic myelopathy. Our data yield an indicator to the causation of acute transverse myelitis. Many clinical, neuroradiological and laboratory similarities exist between acute transverse myelitis and postinfectious encephalomyelitis. We feel convinced that acute transverse myelitis probably represents a localized form of postinfectious encephalomyelitis. The same may well apply to Bickerstaff brainstem encephalitis, and some cases of optic neuritis. Post-mortem material of true acute transverse myelitis histologically showed necrosis of white and grey matter with relative preservation of blood vessels and marked astrocytic gliosis with no evidence of primary demyelination (Berman et al., 1981). Interestingly, one of the patients with paraplegia...
and acute transverse myelitis showed similar lesions in brainstem, basal grey matter and cerebral hemisphere. Chang et al. (1992) reported six cases of postinfectious encephalomyelitis after viral-like illness. One of them had isolated acute transverse myelitis. In our patients, 81% had preceding viral infection which was the only likely cause. Accordingly, instead of acute transverse myelitis, a better terminology would be postinfectious transverse myelitis.

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