Idiopathic acute myelopathy

M. H. SILBER

Summary
The clinical spectrum of acute intrinsic spinal cord disease remains uncertain because of varying criteria used in different studies. The characteristics of 17 patients with idiopathic acute myelopathy drawn from a larger group of 34 with acute intrinsic myelopathies of varying aetiology are reported. Results, which differ from previous studies, include the finding of a high proportion of patients with evidence of predominantly unilateral cord disease (47%). A higher percentage of patients (24%) than previously reported later developed multiple sclerosis, possibly related to broader inclusion criteria. A rise in protein concentration of the cerebrospinal fluid on repeat lumbar puncture was observed in patients with spinal shock on presentation, and a poor outcome was most clearly associated with these cases.

Acute intrinsic spinal cord disease is an important category of rapidly progressive weakness of the legs. Sometimes a specific cause can be determined but often the condition remains idiopathic. Varying arbitrary inclusion criteria in different studies make the clinical spectrum of the condition difficult to delineate, and the contribution of different causative factors is uncertain.

In order to investigate these aspects a retrospective study of 34 patients with acute intrinsic spinal cord disease presenting to Groote Schuur Hospital over a 7.5-year period was undertaken. Specific causes were determined for 17 patients and certain of these have been reported elsewhere. The clinical and laboratory characteristics of the 17 patients for whom no specific cause could be determined are now reported.

Patients and methods
The Groote Schuur Hospital computerised record system was used to identify all patients with acute or subacute spinal cord disease admitted between January 1977 and June 1984. Patients fulfilling all the following criteria were included in the study:

(i) definite clinical evidence of a myelopathy as shown by either upper motor neuron-type weakness of the legs with increased tone and brisk tendon reflexes, or flaccid areflexic paraplegia in association with a definite truncal sensory level;
(ii) progression of the disease to maximum disability in less than 8 weeks;
(iii) either a normal myelogram or a myelogram showing cord swelling for more than 10 segments or, in the absence of a myelogram, complete clinical recovery; 
(iv) an absence of direct trauma or the use of physical agents such as radiotherapy; and
(v) no previous neurological illness.

Thirty-four patients fulfilled these criteria. Table I classifies the 17 patients with idiopathic acute myelopathy drawn from a larger group of 34 with acute intrinsic myelopathies of varying aetiology. This report describes the 17 patients for whom no specific infectious or other cause could be determined.

Results
There were 8 male and 9 female patients; 6 were white, 10 were of mixed ethnic origin and 1 was black. The mean age at onset was 36 years (range 16 - 62 years).

Onset and course
Four patients (24%) had preceding acute illnesses suggestive of infection (3 upper respiratory illnesses, 1 fever and 1 arthralgia). One patient complained of a preceding minor back strain and 1 had undergone hysterectomy 6 weeks previously. Eleven patients (54%) had no antecedent events. There was no seasonal preponderance.

The initial symptom in 7 patients was pain (41%) (3 with backache and 4 with thoracic radicular pain), in 6 it was sensory disturbance (35%), in 1 leg weakness (6%), and in 1 sphincter disturbance (6%). In 2 patients (12%) motor and sensory symptoms started simultaneously. In 10 patients (59%) the disease followed a smoothly progressive course to maximum disability; in 6 patients (35%) it followed a stuttering course with the illness stabilising before a new symptom developed; and in 1 patient (6%) the disease followed a hyperacute course with maximal disability in less than 1 hour. The median time from onset to maximum disability was 10 days (range < 1 hour - 6 weeks).

Symptoms and signs
All 17 patients showed a disturbance of pain and temperature sensation with a spinal cord segmental sensory level below which pain sensation was impaired. This upper level ranged between the 3rd and 10th thoracic dermatomes in all but 3 patients. Position sense in the legs was disturbed in 9 patients and sensation was mildly impaired in the hands in 2 patients, despite a clear thoracic sensory level. Twelve patients (71%) developed increased leg tone and brisk deep tendon reflexes at the onset of the illness, whereas 5 patients (29%) initially developed a flaccid paraplegia with areflexia. Arm weakness developed in 5 patients. Urinary sphincter disturbance

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TABLE I. CLASSIFICATION OF PATIENTS ACCORDING TO AETIOLOGY

<table>
<thead>
<tr>
<th>Classification</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic myelopathy</td>
<td>17</td>
</tr>
<tr>
<td>Meningovascular syphilis of the spinal cord</td>
<td>7</td>
</tr>
<tr>
<td>Myelopathy associated with pulmonary</td>
<td>3</td>
</tr>
<tr>
<td>tuberculosis in the absence of CNS</td>
<td></td>
</tr>
<tr>
<td>tuberculosis</td>
<td>4</td>
</tr>
<tr>
<td>Myelopathy associated with other specific</td>
<td>2</td>
</tr>
<tr>
<td>infections (Epstein-Barr virus and mycoplasma)</td>
<td></td>
</tr>
<tr>
<td>Systemic lupus erythematosus-related</td>
<td>3</td>
</tr>
<tr>
<td>myelopathy</td>
<td></td>
</tr>
<tr>
<td>Spinal cord infarction (ruptured aortic</td>
<td>1</td>
</tr>
<tr>
<td>aneurysm)</td>
<td></td>
</tr>
</tbody>
</table>

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Neurology Unit, Department of Medicine, University of Cape Town and Groote Schuur Hospital, Cape Town

M. H. SILBER, M.B. CH.B., F.C.P. (S.A.), M.MED. (NEUROL.)

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occurred in all 13 patients (76%) and 9 also had anal sphincter dysfunction. Pain occurred at some stage in 10 patients (59%) — 5 with backache alone, 3 with thoracic radicular pain and 2 with both. Fever was noted in 6 patients (35%), 2 of whom had secondary infections (1 urinary and 1 pulmonary).

Eight patients (47%) showed at some stage of the illness evidence of predominantly unilateral cord involvement. In five patients the features were those of a typical Brown-Séquard syndrome with either unilateral or grossly asymmetrical motor signs and spinothalamic sensory loss confined to the contralateral side. In 2 patients the illness started as a Brown-Séquard syndrome and progressed to a complete transverse myelopathy. In 1 patient spinothalamic sensory loss was present in one leg and posterior column loss in the other leg although the motor signs were bilaterally symmetrical.

Brainstem dysfunction occurred in 2 patients at the same time as the myelopathy. A definite thoracic sensory level was present in both patients, 1 of whom developed bilateral facial paresis and 1 nystagmus, bilateral facial, pharyngeal and tongue weakness and bilateral ptosis.

Laboratory findings

Full myelograms were normal in 15 patients. Myelograms were not performed in 2 patients but both made a complete recovery without specific treatment.

Cerebrospinal fluid (CSF) was examined in all patients and was normal in 7. The CSF protein concentration was raised in 5 patients (range 0.5 - 3.0 g/l), CSF pleocytosis was present in 10 patients (range 7 - 305 cells/mm³, all but 1 under 50 cells). In all 10, lymphocytes predominated. CSF glucose concentration was normal in all patients. CSF culture revealed no growth in any patient. Repeat lumbar punctures were performed on 6 patients. In 3 patients, all of whom presented with flaccid areflexic paraplegia, the CSF protein concentration rose (0.9 g/l 2 weeks after onset to 1.4 g/l 10 days later; 0.6 g/l 3 weeks after onset to 4.0 g/l 14 days later and 0.2 g/l 11 days after onset to 3.0 g/l 8 weeks later). This contrasted with 3 patients, all presenting with hyperreflexia and hypertonia, in whom the CSF protein concentration either remained normal or fell. The CSF cell count fell in 1 patient, remained unchanged in 2 and rose slightly in 3. There was no relationship between these changes and the changes in CSF protein concentration.

The erythrocyte sedimentation rate ranged from 5 mm/1st h to 140 mm/1st h (less than 50 mm in all but 3 patients). Blood leucocyte counts were normal. Tests for serum complement, antinuclear factor and rheumatoid factor were normal, and antibodies against recent Epstein-Barr virus, mycoplasma, herpes zoster and cytomegalovirus infections were absent in all patients. Blood fluorescent treponemal antibody absorption tests were positive in 4 patients but CSF Venereal Disease Research Laboratory tests were negative. Only 1 of these patients showed a CSF pleocytosis and this patient improved clinically without the use of antibiotics. It was not felt that any of these 4 patients had neurosyphilis.

Electromyography (EMG) was performed in 1 patient whose legs remained flaccid and areflexic 2 months after onset — extensive fibrillation potentials were present in many muscles of both legs. Evoked potential studies were not performed.

Management, complications and outcome

Four patients received prednisone, 1 ACTH and 2 acyclovir without any convincing therapeutic responses. The early course was complicated by pneumonia in 1 patient, urinary tract infections in 4, pressure sores in 3 and respiratory failure in 1. Two patients died, 1 from pulmonary emboli 8 weeks after onset of the disease and 1 from suicide 7 months later, at which stage he was still paraplegic with flaccid legs. Two patients were lost to follow-up but the remaining 13 were followed for a mean of 3 years 10 months (range 5 months - 7 years).

Functional outcome was assessed according to the classification of Paine and Byers. Good recovery implied normal gait, minimal if any abnormal neurological signs and either normal micturition or minimal urgency. Fair recovery implied ambulation with a spastic gait, signs of spasticity and abnormal sensation and frequently urgency of micturition. Poor recovery implied lack of ambulation and absence of sphincter control. No patient continued to improve beyond 18 months from onset. Six patients (46%) made a good recovery, 5 a fair recovery (38,5%) and 2 a poor recovery (15,5%). Outcome did not correlate with age, sex, sensory level or previous infection.

Both patients with poor outcomes presented with hypotonic areflexic paraplegia as did a third patient who showed no evidence of recovery at the time of presentation. The latter of these 3 patients showed persistent hypotonia and areflexia for more than 6 months without development of spasticity. Only 1 of 11 patients with fair or good recovery presented in a similar way and this difference is statistically significant (chi-square test with Yates' correction; P < 0,05). The only patient with a hyperacute onset made a poor recovery. Three patients developed clinically definite multiple sclerosis (MS) during the period of follow-up and 1 developed unilateral optic neuropathy 1 month after the onset of the myelopathy, thus falling into the category of neuromyelitis optica. One of these 4 patients had associated facial weakness during the original illness, and 2 of the 4 presented with an asymmetrical myelopathy.

Discussion

The most commonly used term for acute intrinsic spinal cord disease — transverse myelitis — is confusing. The condition is not always inflammatory, often extends rostrocaudally over many segments and does not always affect both sides of the spinal cord equally. The term 'idiopathic acute myelopathy' resolves these difficulties. The selection of 8 weeks as the maximum time of progression of symptoms is arbitrarily based on the criteria of Altrocchi in an attempt to separate acute cord syndromes from the large group of chronic myelopathies. Other series have excluded patients with evidence of disease above the foramen magnum, but in this study patients with simultaneously developing brainstem signs were included as long as the predominant presentation was that of spinal cord disease.

The ages at onset were similar to those described in the adult series of Lipton and Teasdale. The lack of seasonal preponderance was also noted by Altrocchi and Berman et al. while only in the childhood series of Dunne et al. did most cases occur in winter. Nonspecific infections preceded the onset in 25% of the patients in this study compared with 16 - 60% in other series. Backstrain has also been previously noted as a possible antecedent event. The distribution of initial symptoms was similar to that noted by others. It should be emphasised that back pain is a common symptom of intrinsic spinal cord disease, possibly due to stretching of dural structures, and does not necessarily imply an extradural compressive lesion. All patients reached maximum disability in less than 6 weeks but the majority progressed over days to weeks rather than hours.

An important finding not adequately emphasised in previous studies was that 47% of the patients showed evidence of predominantly unilateral cord involvement at some stage of the illness. Some previous studies have deliberately omitted...
such cases thus artificially narrowing the clinical spectrum of the condition. Paine and Byers commented on cases with some degree of lateralisation and Dunne et al. mentioned asymmetrical patterns of weakness.

Dissociated sensory loss with preservation of proprioception was common. This study confirms previous reports, that the commonest site of the upper sensory level was one of the thoracic dermatomes.

A good outcome occurred in 46% of the patients, slightly higher than the 26 - 33% found in three adult or mixed adult-childhood series but less than the 57% and 60% reported in two childhood series. Presentation with spinal shock was significantly more likely to result in a poor prognosis and the 1 patient with hyperacute onset also had a poor outcome. These findings confirm the results of previous studies. When faciodynia and areflexia persist in the legs for several months after onset, then extensive necrosis over many segments is likely and EMG may be useful in demonstrating this.

The CSF protein concentration rose dramatically 3.5 - 8 weeks after onset in 3 patients presenting with spinal shock but either remained normal or fell to normal in 3 other patients who presented with initial hyperreflexia. Although the numbers are small, it is possible that this later rise in CSF protein concentration is indicative of extensive cord necrosis. Ropper and Poskanzer noted without further details that 2 patients with initially normal CSF protein concentrations had elevated concentrations when re-tested within a year.

In previous studies with variable follow-up periods, MS developed in 2 - 13% of patients. Three of the patients in this study developed MS and 1 neuro-myelitis optica. This figure of 24% is of interest in view of the South African white and mixed ethnic populations being at only moderate and low risk respectively for the development of MS. A possible explanation is that 2 of these 4 patients had asymmetrical cord involvement and 1 had associated facial weakness. These patients might have been excluded from certain previous studies, thus reducing the proportion of patients who developed MS. However, 6 other patients with asymmetrical signs and 1 with associated brainstem dysfunction in the present series did not progress to MS.

As regards aetiology, idiopathic acute myelopathy is not a homogeneous group. In a minority of patients the illness is the first manifestation of MS. In the past, a vascular pathogenesis was considered likely for the remainder, and occasional patients have been shown to have unexpected intramedullary vascular malformations. However, it would appear that the majority of these conditions represent a spectrum of immune reactions affecting the spinal cord, many in response to infectious agents. Supporting clinical evidence for this includes the similarity of the disease to acute myelopathy after infection by a specific pathogen and after vaccination. Nonspecific infectious illnesses precede idiopathic myelopathy in 16 - 60% of cases. The marked asymmetry of clinical features found in many patients, especially in this study, is more in favour of an inflammatory or demyelinating pathogenesis. The suggestion that these Brown-Séquard syndromes are due to occlusion of a single central sulcal artery is unlikely to be correct, since the posterior columns are often affected, and considerable overlap exists between the longitudinal territories of supply of the central sulcal arteries. The occasional progression of clinical signs from a Brown-Séquard syndrome to a complete transverse lesion is also unlike the course of vascular cord disease. Preservation of posterior column function seen in some patients is not specific for anterior spinal artery syndromes and probably represents another form of incomplete inflammatory or demyelinating myelopathy. The rare occurrence of simultaneous brainstem disturbances also favours this pathogenesis.

Studies of the pathology of the disease show that most cases have either extensive necrosis of the grey and white matter of the cord or post-inflammantly demyelination with perivenous inflammatory infiltrates. The former appearance is similar to that of the hyperacute necrotising form of experimental allergic encephalomyelitis (EAE), whereas the latter is similar to what is seen in both acute disseminated encephalomyelitis and in most cases of EAE. Thus studies of the pathological aspects also suggest that an immune-mediated mechanism represents the pathogenesis in most cases.

In summary, idiopathic acute myelopathy is an important clinical SM syndrome comprising a large proportion of cases of acute intrinsic spinal cord disease. Prospective studies including investigation for viruses and magnetic resonance imaging are needed to delineate the pathogenesis more fully.

REFERENCES