The stiff leg syndrome

P Brown, J C Rothwell, C D Marsden

Abstract

Four patients had a chronic progressive disorder beginning in middle age and involving stiffness and painful spasms of the lower limbs. Spasms were spontaneous, reflex, and induced by voluntary movement. Patients had rigidity and abnormal postures of one or both legs. There was no truncal rigidity or exaggerated lumbar lordosis. Despite the presence of symptoms for up to 16 years, symptoms and signs of brainstem, pyramidal, and sensory dysfunction were absent. Sphincter disturbance developed after many years in one patient. Extensive investigation, including imaging of the whole neuroaxis, failed to disclose a cause. Anti-GAD antibodies were absent. Baclofen and diazepam led to some reduction in the painful spasms, but patients remained disabled by the condition.

There were four core electrophysiological features. (1) Continuous motor unit activity was present at rest in at least one limb muscle. (2) Spasms tended to involve the repetitive grouped discharges of motor units. (3) Cutaneous reflexes were abnormal. (4) There was little or no electrophysiological evidence of long tract disturbance.

The patients form a characteristic syndrome, separate from the stiff man syndrome, and distinguishable from encephalomyelitis with rigidity. It is suggested that the condition is due to a chronic spinal interneurinosis.

(J Neurol Neurosurg Psychiatry 1997;62:31–37)

Keywords: stiffness; spasms; spinal interneurinosis

The combination of chronic axial rigidity, reflex, and action induced spasms and continuous motor unit activity at rest (CMUA) is well recognised in the stiff man syndrome. Occasionally, the same features may be confined to one or both legs, when corticobasal degeneration, focal lesions of the spinal cord, and encephalomalitis must be excluded. In these instances there are associated symptoms and signs of cerebral, extrapyramidal, brainstem, or long tract involvement. Here we report four patients with a chronic progressive disorder characterised by painful involuntary spasms, stiffness, and CMUA confined to the legs, with no evidence of cerebral, brainstem, extrapyramidal, pyramidal, or sensory dysfunction. We suggest that the stiffness and spasms in these patients is due to an indolent interneurinosis of the spinal cord.

Methods

Investigations were performed with the approval of the local ethics committee and with the consent of each patient. Surface EMG recordings were made using bipolar silver/silver chloride electrodes placed 2 to 4 cm apart longitudinally over the muscle bellies. The minimum number of muscles recorded were right and left lumbar paraspinus muscles, quadriceps, hamstrings, tibialis anterior, and the gastrocnemius-soleus complex. Biceps, sternocleidomastoid, and thoracic paraspinals were also recorded in patients 1, 2, and 3. Muscle spasms were elicited by various stimuli, and were recorded by triggering the computer at the time of delivery of the stimulus. The stimuli consisted of electrical stimulation of peripheral nerves (rectangular pulses of 200 μs duration, taps to the body with a tendon hammer equipped with a microswitch, auditory tone bursts (1000 Hz, 50 ms duration, and 100 dB) presented binaurally through earphones, or magnetic stimulation of the motor cortex using a 9 cm diameter round coil powered by Novametrix Magstim 200. The duration of the silent period in the tibialis anterior was measured with magnetic shocks 30% above resting motor threshold. Cutaneous (sometimes referred to as exteroceptive) reflexes were elicited by a train of four nerve shocks separated by 3 ms and repeated about every 90 s, except in patient 1 in whom single shocks were used. Shocks were delivered to the tibial nerve at the ankle of the worst affected leg. EMG signals were bandpass filtered at 1000 Hz with a time constant of 30 ms. The sampling rate was 2000 Hz per channel. Reflex latencies were measured by the visual inspection of single trials on a computer display.

Patients

The clinical histories and abnormal findings of the four patients are summarised below. There was no relevant medical or family history, except in patient 3. Symptoms and signs suggestive of brainstem or sensory dysfunction were absent, and only patient 2 developed sphincter disturbance. There was no hyperlordosis of the lumbar spine or abdominal rigid-
ity. Pyramidal signs were absent. The following tests were normal or unremarkable: basic blood screens, creatine phosphokinase, B12, copper, caeruloplasmin, treponemal and HTLV1 serology, short synacthen test, nerve conduction studies, and visually evoked responses (VERs), and MRI or CT of the head. The table summarises the results of autoimmune antibody screens and CSF analysis. Serum anti-GAD antibodies were negative (anti-GAD antibodies were measured by immunoprecipitation of a radiolabelled recombinant human GAD65 antigen). Imaging of the chest, abdomen, and pelvis showed no evidence of a primary tumour. Spinal cord MRI (all patients) and myelography (patient 2) were normal. Diazepam (up to 30 mg daily) and baclofen (up to 90 mg daily) alone or in combination partially alleviated stiffness and spasms in patients 1, 3, and 4.

PATIENT 1
This 35 year old woman had a five year history of progressive stiffness and spasms of the legs. She first noticed an ache in the right foot and this was followed a few months later by intermittent and painful spasms of the right calf and thigh. She began tripping due to spasms involving tonic extension of the right knee and plantar flexion of the right foot lasting several seconds. She continued to deteriorate and her right leg became permanently stiff and she developed involuntary jerks of the toes of the right foot. Painful spasms spread to the left leg in the fourth year of her illness. On examination there was abnormal posturing of the right foot, with persistent plantar flexion at the ankle. She was able to take a few steps with the assistance of a stick and one person. Her gait was punctuated by spasms of either leg. These involved knee extension, ankle plantar flexion, and inversion of the foot. There was rigidity of the right leg.

PATIENT 2
This 60 year old man had a 16 year history of painful stiffness of the left leg. This spread after two years to his right leg, and he developed painful spasms involving dorsi flexion and inversion of his left foot. During the spasms he could stand but not walk. The stiffness in his legs slowly progressed, but he remained ambulant. Ten years after onset of his illness he developed erectile impotence, and over the next year noted moderate urinary urgency and frequency. Fifteen years after the onset his handwriting deteriorated due to a jerky tremor of his hands.

On examination he walked independently, but with both feet inverted and slightly plantar flexed. His toes were clawed. There was a mild postural and action tremor of the arms. Both legs were rigid, more so distally and on the left. Power was normal except at the ankles, where active and passive movements were severely limited. The left ankle jerk was absent. Examination of the feet under general anaesthetic disclosed a virtually fixed left foot and ankle. Plantar and dorsi flexion were limited at the right ankle, but inversion and eversion of the foot were preserved. An aerobic exercise test was normal, but muscle biopsies of the left quadriceps and left triceps were abnormal, with scattered ragged red fibres and cytochrome oxidase negative fibres. The quadriceps also showed randomly scattered atrophic fibres, some of which had been reduced to clumps of pyknotic nuclei.

PATIENT 3
This 35 year old woman gave a 20 month history of stiffness and painful involuntary spasms in the left leg. She experienced considerable difficulty in walking within weeks of onset of the illness. Three months later she noticed stiffness of the left arm and involuntary spasms of the left hand, which improved over the course of several weeks. Six months after the onset of symptoms in the left leg she developed painful spasms of the right leg. Over the subsequent months the severity of spasms gradually increased in both legs. She had a history of thyrotoxicosis. On examination she was unable to walk but could transfer unaided. The posture of the left leg was abnormal, with sustained plantar flexion at the ankle. Both legs were rigid. Power was normal but voluntary movement of the legs often precipitated a spasm.

PATIENT 4
This 52 year old man had a two and a half year history of stiffness and spasms of the legs. At first he experienced a dull ache in the right foot. Six months later he developed spontaneous and action induced painful spasms of the right leg, in which the leg would abduct at the hip and flex at the knee. Fourteen months after the onset of his illness he noticed pain and stiffness of both legs, and two months later he developed painful spasms of the left leg. These slowly increased in severity and began to lead to falls. During this time he experienced some spontaneous improvement in the spasms and stiffness of the right leg. On examination he could only walk with assistance. He held his right leg stiffly and made small steps. The toes of the right foot were clawed and tone was increased in this leg. Voluntary movement of the left leg often precipitated a spasm.

ELECTROPHYSIOLOGY
Muscle activity at rest
CMUA was recorded with surface electrodes in one leg in all patients (table), and was confirmed by needle EMG. The EMG also demonstrated polyphasic and large motor units and a reduced interference pattern in many muscles of both lower limbs in patients 2 and 4. In addition, fibrillation potentials and positive sharp waves were recorded in left vastus lateralis, left lumbar paraspinal muscles, and both tibialis anterior in patient 4. There was no evidence of myotonia or neuromyotonia.

Spasms
Spasms of the legs occurred spontaneously and during attempted voluntary movement of
The stiff leg syndrome

Summary of serological, CSF, and electrophysiological findings

<table>
<thead>
<tr>
<th>Patient</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age and sex</td>
<td>35 F</td>
<td>60 M</td>
<td>35 F</td>
<td>52 M</td>
</tr>
<tr>
<td>Duration of illness</td>
<td>5 years</td>
<td>16 years</td>
<td>20 months</td>
<td>2.5 years</td>
</tr>
<tr>
<td>Positive serum antibodies*</td>
<td>Antinuclear antibodies</td>
<td>Gastric parietal cell</td>
<td>Gastric parietal cell</td>
<td>Rheumatoid factor</td>
</tr>
<tr>
<td>CSF</td>
<td>Normal except for monoclonal IgG in CSF and serum</td>
<td>Normal except for oligoclonal IgG in CSF and serum</td>
<td>CMUA left quadriceps</td>
<td>Normal except for protein of 1.2 g/l</td>
</tr>
<tr>
<td>Electrophysiological abnormalities</td>
<td>Cocontracting, segmented spasms</td>
<td>Cocontracting, segmented spasms</td>
<td>Cocontracting, segmented spasms</td>
<td>Cocontracting, segmented spasms</td>
</tr>
<tr>
<td>Lumbar paraspinals</td>
<td>Abnormal cutaneomuscular reflexes</td>
<td>Abnormal cutaneomuscular reflexes</td>
<td>Abnormal cutaneomuscular reflexes</td>
<td>Abnormal cutaneomuscular reflexes</td>
</tr>
<tr>
<td>R tibialis anterior</td>
<td>Normal</td>
<td>CMUA left quadriceps</td>
<td>Denervation L 2, 5, S1</td>
<td>Both legs and paraspinal muscles</td>
</tr>
</tbody>
</table>

*Anti-GAD antibodies negative.

The legs in all four patients. In addition, reflex spasms of the lower limbs could be elicited by electrical shocks to the posterior tibial nerve at the ankle (four patients), and by sounds, taps, or by transcutaneous magnetic shocks to the motor cortex (two patients). Muscle activity in the spasms lasted from one second to five minutes in the calf. The relative and absolute latencies to onset of EMG activity showed considerable variability in the spasms. For example, in the spontaneous spasms recorded in patient 1 EMG activity in the right tibialis anterior had a latency ranging from 6 ms to 14 ms relative to the right quadriceps.

The spasms consisted of cocontracting activity in antagonist muscle pairs and were characterised by a tendency for the normal interference pattern to be replaced by segmented EMG activity in at least some muscles during the spasms. Figure 1 is an example of segmentation of EMG activity during a voluntary action induced spasm of the right leg in patient 3. Four seconds after the onset of movement EMG consists of a series of large amplitude short duration EMG bursts, suggesting the relatively synchronous discharge of many motor units.

Cutaneomuscular reflexes

Cutaneomuscular reflexes at the ankle were of abnormally low threshold or abnormally wide-spread. Stimuli of only 1-5 to three times sensory threshold gave consistent short latency (< 80 ms) responses in the ipsilateral tibialis anterior in all patients. In patient 2 this activity spread to the opposite leg. The short latency response was followed in each patient by a longer latency component, usually beginning about 100 to 120 ms after the stimulus, and lasting for up to 500 ms. During this phase activity spread to the opposite leg, the trunk, and, in patient 1, the upper limbs. Shocks of similar intensity delivered at rest in normal subjects never spread to other limbs. The threshold of the second component was investigated in patients 2 and 3, and found to be identical to that of the first component in the tibialis anterior.

Figure 2 shows the cutaneomuscular reflex in patient 2. Both components were recorded bilaterally after unilateral stimulation, although the early component was bigger in the ipsilateral leg. In patient 1 the first component of the response to shocks to the ankle was of remarkably short and fixed latency (fig 3).
Figure 2 Cutaneomuscular reflex to a train of four shocks (at three times sensory threshold) delivered to the right (A) or left (B) tibial nerve at the ankle in patient 2. Each section is an average of six rectified trials. Stimulus artifact is present at delivery of the shocks (arrowed). The cutaneomuscular reflex consists of two basic components, beginning at about 50 ms (first vertical line) and 112 ms (second vertical line). Both components are recorded bilaterally after unilateral stimulation.

In the right quadriceps the latency (34 ms) was only 14 ms longer than the latency of the tendon jerk after taps to the knee. In normal subjects the difference in latency of the F wave recorded in the abductor hallucis with shocks to the tibial nerve at the knee and ankle is about 9 ms. Adding this to the latency of the knee jerk gives 29 ms, leaving some 5 ms (or less if slower conducting peripheral afferents are employed) for central delay in the short latency response to tibial nerve stimulation. Thus this response must arise in the lower spinal cord.

Response to taps and auditory stimuli
Taps to the knee or ankle also evoked a spasm in the ipsilateral calf in patients 1, 2, and 4. Similarly, unexpected auditory stimuli delivered about once every 10 seconds elicited consistent reflex responses in the lower limb in patients 1 and 2, with a mean latency of 74 ms in the tibialis anterior. By contrast, the response recorded in sternocleidomastoid and biceps habituated within three to five trials.

Cortical SEPs and magnetic stimulation
Cortical SEPs were of normal amplitude and latency, except for a small delay in the P40 on stimulating the left tibial nerve at the ankle in patient 1. The latency of the direct response to transcutaneous stimulation of the motor cortex was normal in tibialis anterior in every patient. The silent period was absent, or replaced by a spasm, in patients 1, 2, and 3. The latency of the spasm ranged from 52 ms to 72 ms in the tibialis anterior. Figure 4 gives examples of the responses in patient 1. Direct responses are of normal latency. Spasms have a similar threshold to the direct response in the same muscle, and begin about 52 ms after shocks of low intensity (see arrows in fig 4A). With higher intensities of stimulation the spasms have a longer latency, but still replace...
Discussions

We have presented four patients with a distinct clinical and electrophysiological picture. Each patient developed chronic and progressive stiffness and painful spasms of the legs beginning in middle age. Spasms induced by voluntary movement maintained the clinical picture, but could also be spontaneous or follow auditory or somesthetic stimulation. There was no truncal rigidity or exaggerated lumbar lordosis. All four patients had rigidity and abnormal postures of one or both legs. Despite the presence of symptoms for up to 16 years, symptoms and signs of brainstem or sensory dysfunction were absent. Sphincter disturbance was only seen late in patient 2.

There were no pyramidal signs and power seemed normal except when interrupted by spasms or hampered by severe rigidity. Baclofen, sometimes in combination with diazepam, led to some reduction in the painful spasms and stiffness, but patients remained disabled by the condition.

Extensive investigation, including imaging of the whole neuroaxis, failed to disclose a cause. In particular, anti-GAD antibodies were absent. All of the patients had been suspected of a psychogenic disorder at some time during their illness. However, electrophysiological studies disclosed clear abnormalities. CMUA was present at rest in at least one leg muscle and there was evidence of denervation in the lower limbs in two patients. Spasms tended to involve an abnormal pattern of muscle activity consisting of the repetitive grouped discharge of motor units. Cutaneous reflexes were abnormal, and there was no significant electrophysiological evidence of long tract disturbance.

Differential Diagnosis

Voluntary action and reflex induced painful spasms were the most striking feature of the illness. Dystonia was an unlikely explanation as dystonic spasms are generally less painful
and are not stimulus sensitive. Neither was spasticity the cause, as there were no upper motor neuron signs and central motor conduction times were normal. CMUA is rarely, if ever, present in dystonia or spasticity, and the spasms in these conditions generally consist of a normal looking interference pattern.

Pathological signs were restricted to the legs. Clinically, a spinal disorder was suspected and this contention was supported by the presence of CMUA in one or both lower limbs in all patients, and evidence of denervation in two patients. The abnormal responses of very short latency and the sphincter disturbance in patients 1 and 2 would be consistent with a spinal disorder. In addition, the prominence of the second component of the cutaneous muscular reflexes was similar to that found in patients with pathology of the spinal cord.4

The combination of stimulus sensitive and action induced jerks and spasms and CMUA of the limbs and trunk is seen in several conditions in which the brunt of pathology is generally considered to be spinal (with the possible exception of the stiff man syndrome). Idiopathic encephalomyelitis with rigidity causes most diagnostic difficulty. It is a complex progressive illness dominated by painful rigidity and spasms.5,6 It can be readily distinguished from the condition described here by the development of brainstem or long tract signs within a year, the presence of inflammatory CSF, and by its catastrophic course. Death occurs within three weeks to 39 months after the onset of symptoms.

The stiff man syndrome bears the closest similarity to the patients presented here. This chronic disorder also involves stiffness, rigidity, and painful spasms, in association with CMUA and abnormal cutaneous muscular reflexes.6-8 Signs of cerebral brainstem or long tract disturbance are absent, except in the rare variant, the jerking stiff man syndrome.9 However, there are some clear differences between the stiff man syndrome and the group of patients described here. In the stiff man syndrome the core feature is rigidity, spasm, and CMUA of the trunk muscles, with slow progression to involve proximal limb muscles.8 The calf and foot muscles are rarely, if ever, involved.9,10 In our patients this distribution was reversed, and rigidity and CMUA in trunk muscles were absent. Similarly, an exaggerated lumbar lordosis was not seen in our patients. Instead there was an abnormal posturing of one or both feet. Repetitive synchronised discharges during spasms are not a feature of the stiff man syndrome. Finally, about 50% of patients with the stiff man syndrome have oligoclonal bands in the CSF and anti-GAD antibodies in blood and CSF.11 Anti-GAD antibodies were absent in our patients.

Rarely, structural or vascular lesions of the spinal cord may lead to spinal rigidity and spasms, but detailed imaging of the spinal cord failed to show any focal abnormality in our patients. Neither was there any clinical evidence to support a diagnosis of paraneoplastic encephalomyelitis, especially given the long duration of the disorder. Finally, the presenting patients must be distinguished from the syndrome of continuous muscle activity of peripheral nerve origin, often termed Isaacs' syndrome or neuromyotonia.12,13 Although stiffness may be distal, pain is not a prominent feature, reflex spasms are absent, and myokymia and fasciculations are evident clinically and electrophysiologically.

PATHOPHYSIOLOGY

In summary, our four patients have a distinctive clinical and electrophysiological picture, with some evidence to suggest a spinal disorder. It is our hypothesis that disinhibition within the spinal cord determines the prolonged spasms in the limbs to peripheral somaesthetic stimuli, descending voluntary commands, or startle related reticulospinal activity. This disinhibition seems to remain relatively localised to the lumbosacral cord.

One of the striking features in our patients was the relative scarcity of specific symptoms, signs and causation. Physical abnormalities attributable to the long tracts of the spinal cord. This suggests an abnormality of those spinal interneurones essential to the elaboration of responses to supraspinal and segmental inputs.

The major evidence linking the disorder described here to a localised spinal interneuropathology is the similarity to other patients with known focal pathology preferentially involving the grey matter of the spinal cord. Thus intrinsic tumours,4-11 syringomyelia,12 vascular insufficiency,7,13 and paraneoplastic myelitis14 may be associated with CMUA, and reflex and action induced spasms of the trunk and lower limbs. The relatively selective destruction of spinal interneurones in some of these patients has been confirmed histologically.5,14 Effective stimuli need not be restricted to somaesthetic stimulation below the level of the spinal cord pathology. Paradoxically, jerks and spasms of the legs can be precipitated in patients with spinal lesions by startle inducing stimuli, including sounds.13,15

Presumably this represents an excessive response at the segmental level to descending reticulospinal activity. It is known that auditory stimuli facilitate the H reflex at short latency in normal subjects, even in the absence of an obvious startle response.20 The spasms after magnetic stimulation of the motor cortex may be a similarly excessive response at the segmental level to descending pyramidal tract volleys.

AETIOLOGY

The aetiology of the stiff leg syndrome is obscure. The disorder is progressive, but patients 3 and 4 had superimposed relapses followed by partial improvement. This raises the possibility of an inflammatory illness. The presence of autoantibodies in all four patients and a history of thyrotoxicosis in one suggest that this might have an autoimmune basis. Anti-GAD antibodies were negative, and the history was too long for a paraneoplastic phenomenon. There was no evidence of an infective aetiology, and the consistently normal CSF white cell count would be against such a
The stiff leg syndrome

case. Patient 2 had two muscle biopsies with abnormal numbers of ragged red and cytochrome oxidase negative fibres. An aerobic exercise test was normal. Given the unusual nature of the phenotype, evidence of mitochondrial cytopathy in other patients must be awaited before mitochondrial disease can be considered one of the causes of this syndrome.

In conclusion, we have presented four patients with a chronic progressive idiopathic disorder affecting the lower limbs and involving CMUA at rest, and painful muscle spasms particularly on voluntary movement or after somesthetic stimulation. We suggest that this disorder is due to a chronic spinal internu-

We thank Dr S J Ellis, Professor W J McDonald, Professor M Ron, and Dr F Rudge for referring the patients, and Dr J Morgan Hughes for the histopathology in patient 2.