

Stimulus-sensitive spinal myoclonus

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SUMMARY Two cases of spinal myoclonus are described; in both patients myoclonus was responsive to stimuli and absent during sleep. The first patient was considered to have viral neuronitis and the condition resolved spontaneously. The second patient had spinal cord ischaemia; there was electrophysiological evidence of abnormal alpha motor neurone activity and histological study of the spinal cord revealed a severe reduction in small and intermediate neurones. This supports the theory that spinal myoclonus may result from abnormal activity of alpha motor neurones released from control by spinal internuncial neurones.

Halliday has contrasted clinically and electrophysiologically two types of myoclonus: "the irregular, variable, stimulus-sensitive jerking typical of myoclonic epilepsy and the rhythmic, invariable, insensitive myoclonus typical of local lesions of the cord or brainstem".¹ In spinal myoclonus synchronous jerking is seen in muscles innervated by affected adjacent spinal cord segments. The frequency can vary from 2 to 600 contractions per minute.² Numerous causes have been described including tumour,^{3,4} trauma,⁵ spinal anaesthesia,⁶ degenerative processes involving the alpha motor neurone⁷ and spinal inflammation.^{8,9} In view of the rarity of the condition two further cases are described, including the pathological findings in one.

CASE 1

A 40-year-old Indian housewife presented with a two week history of jerking of the lower limbs. This was associated with burning discomfort in her feet and urinary retention which required catheterisation prior to her admission to hospital. She denied recent infection, backache, weakness or numbness in the legs or perineum. On examination, she had rapid, rhythmic, involuntary jerks of the glutei and all muscle groups of both lower limbs. These jerks were intensified by voluntary effort and were absent during sleep. There was no reaction to auditory "startle". Tone, power and tendon reflexes in the lower limbs were normal and the plantar responses were flexor. No sensory abnormality could be found. She was afebrile and examination was otherwise normal. Three days after admission, the patient's urinary catheter was removed and she was able to void spontaneously. The

myoclonic jerks resolved completely, without any specific treatment, over the next few days. Three months later examination revealed no abnormality.

Investigations

Full blood examination and biochemistry including urea and electrolytes, calcium, liver and thyroid function tests, immunoglobulin profile and creatinine phosphokinase were normal. Plain radiographs of the chest and whole spine were normal. CSF examination on the day of admission revealed 30 mononuclear white cells/mm³ with a normal protein of 28 mg%. The IgG level was elevated (21.4% of total protein). CSF protein electrophoresis was consistent with transudation of serum proteins. Complement fixation tests on two occasions did not reveal any rise of mumps, measles, influenza or herpes virus antibody titres. Serological tests for syphilis were negative. Electromyography was performed 3 days after admission. A concentric needle electrode in the right rectus femoris muscle was used and recording showed repetitive discharges of groups of motor units at a rate of 6-7/s. No evidence of denervation was found. Motor and sensory nerve conduction studies were normal in the right arm and leg. The right H reflex was unobtainable, that on the left normal, latency 27 ms. Somatosensory evoked responses on stimulation of both median and posterior tibial nerves were of normal amplitude and latency. The EEG, visual and auditory evoked potentials were normal.

CASE 2

A 75-year-old retired upholsterer developed involuntary jerking of the lower limbs eight days before admission. Jerking started suddenly in the right leg, throwing him to the ground and spread to the left leg a few hours later. He had no sensory symptoms and sphincter function was normal. Seven years earlier an abdominal aortic aneurysm had been repaired. He had a long history of chronic bronchitis with recurrent exacerbations. On examination, he had a right Horner's syndrome but the cranial nerves

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and upper limbs were normal. Frequent shocklike jerks occurred synchronously in both legs, more severe on the right, predominantly affecting the hip and knee extensors and plantar flexors. Increased tone in the lower limbs with features of spasticity and plastic rigidity was evident between the spasms. Assessment of voluntary power was difficult because of the frequent jerks but it was mildly reduced in a pyramidal distribution. The knee and ankle reflexes were increased but the plantar responses were flexor. There was no sensory abnormality. Myoclonic jerks were increased in frequency and amplitude by a variety of stimuli including conversation, mental arithmetic and sudden loud noises. Tapping the patellar tendon on either side produced several myoclonic jerks in both legs, persisting for longer on the right side irrespective of which leg was tapped. Tapping the biceps brachii tendon also enhanced the myoclonus in the lower limbs. Attempts to elicit the plantar reflex resulted in prolonged contraction of all muscle groups on both sides and increased myoclonic jerking on the right. The myoclonus was temporarily abolished by intravenous injection of 10 mg of diazepam. Subsequent therapy with clonazepam 1.5 mg daily largely controlled the jerks and re-ambulation was commenced. The patient's subsequent clinical course was marked by recurrent chest infections. Following his discharge home, he again developed severe pneumonitis and died in another hospital, three months after the first admission.

Investigations

Full blood examination revealed a mild normochromic, normocytic anaemia (haemoglobin 11.1 g%), with normal white cells and platelet count. The ESR was elevated at 126 mm in the first hour. Blood biochemistry including urea and electrolytes, glucose uric acid, liver and thyroid function tests and B_{12} was normal except for paraprotein studies which revealed a monoclonal IgM lambda band suggestive of Waldenstrom's macroglobulinaemia. Bone marrow biopsy was compatible with this diagnosis. Chest radiographs showed evidence of emphysema and superimposed infection and radiographs of the spine were unremarkable. Cranial CT scan was normal, as was the EEG. Lumbar puncture revealed clear cerebrospinal fluid, with normal manometry, biochemistry and cytology. Electrophysiological studies were first performed on the day after admission. Surface electrodes were placed on the quadriceps, hamstrings, tibialis

anterior and gastrocnemius of both legs and muscle activity was recorded with an EEG machine (fig 1). Semirhythmic bursts of muscle activity generally lasting 0.5-1.0 s occurred in the right leg at 10-30/minute, usually simultaneously in all muscle groups but sometimes confined to the lower leg. Less often similar activity was seen in the left lower limb both independently and simultaneous with right sided bursts. In addition to these large discharges sufficient to move the legs, frequent fasciculations were recorded from both lower limbs especially on the right side. An EEG recorded simultaneously was normal with no discharge corresponding to the jerks. During stage II sleep myoclonus was less frequent but still present. It was absent during deeper sleep. Somatosensory responses of normal amplitude were obtained on stimulating the median and posterior tibial nerves.

Electromyography of muscles of both legs showed fasciculations but no fibrillation or giant units. Motor conduction velocity in the posterior tibial nerve was 36 m/s on each side; normal sensory action potentials were obtained in the median, ulnar and sural nerves. Simultaneous recordings were made from the right and left gastrocnemius muscles during stimulation of each posterior tibial nerve in the popliteal fossa. At a stimulus intensity insufficient to produce a direct (M) response on the stimulated side there was a late response of latency 42-44 ms in both gastrocnemii when stimulating the right posterior tibial nerve, and of 43-45 ms on both sides when stimulating the left side. At the same time widespread myoclonic jerking occurred in both legs. The late response was still seen when the stimulus was increased to produce a direct response (fig 2). Similar findings were obtained 14 days and 28 days later.

Pathology

At examination postmortem there was bilateral bronchopneumonia. The heart showed left ventricular hypertrophy and moderate atheroma of coronary arteries. Atheroma was severe with ulceration in the aorta and moderate in large arteries. The brain was normal to the naked eye and microscopically. The spinal cord was fixed in formalin. On macroscopical examination, the leptomeninges, the nerve roots and the spinal cord were of normal appearance. Transverse sections of the cord were taken at different levels, and paraffin wax embedded sections were stained with haematoxylin and eosin, the Nissl method

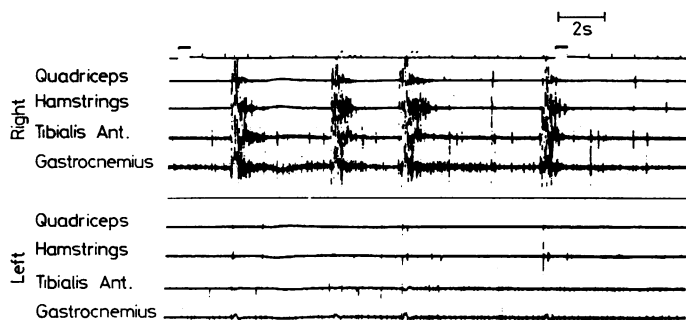


Fig 1 Case 2. Myoclonic jerking of right leg: surface recording of EMG activity in both legs.

and Heidenhain's stain for myelin. Microscopical examination revealed marked atherosclerotic narrowing of the anterior spinal artery and virtual occlusion of a perforating branch at mid-thoracic level (fig 3). Sections from various levels of the spinal cord showed a marked reduction in the total number of neurones in the anterior horns, intermediolateral groups, posterior horns and Clarke's columns especially in the thoracic and lumbosacral segments (see table). The neuronal loss was

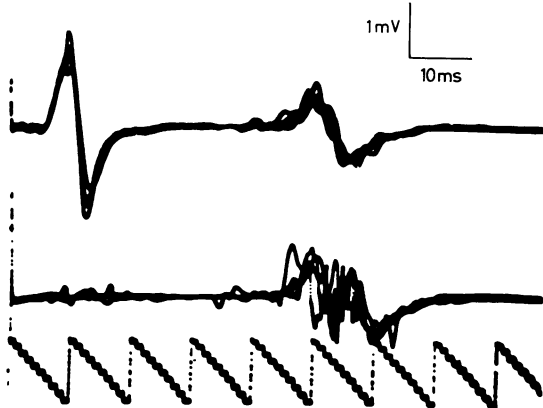


Fig 2 Case 2. Stimulation of right posterior tibial nerve with recording electrodes on right gastrocnemius (upper trace) and left gastrocnemius (lower trace). Direct response on right side and bilateral response at latency 44 ms.

selective; there was a striking reduction in small and medium size ("internuncial") neurones, but relative sparing of large neurones in the anterior horns (fig 4). Surviving neurones showed evidence of ischaemic degeneration, with shrinkage, loss of Nissl substance and cytoplasmic eosinophilia. The white matter was normal apart from slight oedema. There was no evidence of infarction, or of encephalomyelitis and changes of motor neurone disease were not seen.

Table Case 2. Total neuronal counts at three selected levels of the spinal cord. Control figures (in brackets) from a patient of similar age and sex with no spinal neuronal disease

		Right	Left
Cervical 1-2	AH	32 (35)	36 (33)
	IL	12 (17)	16 (15)
	PH	8 (22)	10 (17)
Thoracic 3-4	AH	6 (14)	7 (16)
	IL	3 (16)	9 (14)
	PH	? (12)	? (10)
Lumbar 3-4	Clarke's column	7 (6)	5 (6)
	AH	26 (46)	34 (47)
	IL	4 (3)	3 (5)
	PH	4 (12)	3 (10)

AH = anterior horn; IL = intermediolateral group; PH = posterior horn.

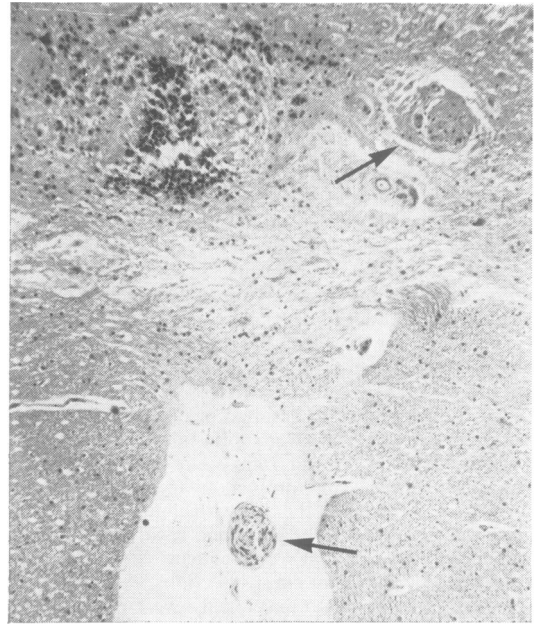


Fig 3 Spinal cord at thoracic 3-4 level. Marked atherosclerotic changes in sulcal branch of anterior spinal artery and almost total occlusion of a perforating branch (arrows). Haematoxylin and eosin $\times 42$.

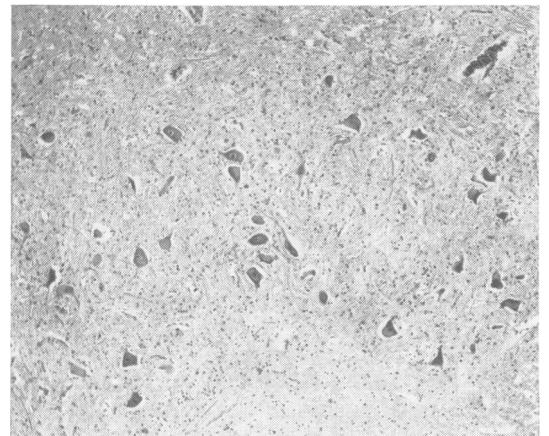


Fig 4 Spinal cord at lumbosacral L5-S1 level. There is conspicuous reduction in number of small and medium sized ("internuncial") neurones with relative sparing of large alpha neurones. The motor neurones show shrinkage, loss of Nissl substance and cytoplasmic eosinophilia. Haematoxylin and eosin $\times 35$.

Discussion

The presenting clinical feature in both of our patients was myoclonus localised to lumbar and sacral segments of the spinal cord and developing over a period of hours. The clinical findings, normal EEGs and absence of enhancement of somatosensory evoked potentials are typical of segmental myoclonus and there were no features to support a diagnosis of myoclonic epilepsy or essential myoclonus.¹ However, there were important differences between the two cases. In case 1 myoclonic jerks were rapid, rhythmic and symmetrical. The acute onset and self limiting course of the illness and the increased CSF white cell count and IgG are in keeping with an inflammatory disorder, possibly viral and very similar to cases described by Campbell and Garland⁸ and Hopkins and Michael.⁹ In case 2 myoclonus was asymmetrical, relatively irregular and associated with marked plastic rigidity of the legs. The age of the patient, the history of repair of an abdominal aortic aneurysm and the normal CSF strongly suggested an ischaemic myelopathy and the pathological findings confirmed this. Ischaemic myelopathy was postulated in a case described by Frenken *et al* although without pathological confirmation.⁷ Their case was an elderly demented man with ataxia of gait, rhythmic myoclonic jerking in the legs, brisk knee jerks and extensor plantar responses. Electrophysiological studies revealed polyneuropathy in the legs and anterior horn cell dysfunction. As with our case 2 the CSF was normal.

The electrophysiological finding in case 2 of simultaneous responses in both gastrocnemii to tibial nerve stimulation at an intensity insufficient to produce a direct (M) response is similar to that reported by Hopkins and Michael.⁹ The response latency (43 ms) is longer than that of the normal H reflex and indicative of conduction through a pathway confined to the spinal cord but probably involving more than one synapse. Fasciculations and the bilateral response to tibial nerve stimulation imply abnormal alpha motor neurone excitability. The histological finding of a reduction in small and intermediate neurones of the ventral horns suggests hyperexcitability and excessive discharges of surviving alpha motor neurones released from the normal control provided by internuncial neurones. In this context the striking rigidity of the legs in case 2 is of interest. Gelfan and Tarlov induced severe hind limb rigidity in dogs by producing temporary ischaemia of the spinal cord and they found a very marked selective loss of spinal internuncial neurones with relative sparing of larger anterior horn cells.¹⁰ A similar pathological reduction in interneurone numbers has been found in patients with progressive

encephalomyelitis with rigidity, some of whom also had myoclonus.¹¹⁻¹³ Spinal internuncial neurone dysfunction has also been implicated in a case of rigidity of the arms associated with a cervical spinal astrocytoma¹⁴ and in the muscle spasms, rigidity and localised myoclonic jerks of tetanus and strychnine poisoning.¹³

It seems clear from our own case and the work described above that there is a spectrum of clinical manifestations of spinal internuncial neurone dysfunction ranging from segmental myoclonus to extreme muscular rigidity. Presumably the variable clinical features depend on the particular interneurons involved and the relative degree of involvement of alpha motor neurones and internuncial neurones. The jerking of spinal myoclonus is typically but by no means always rhythmic. Inoculation of Newcastle disease virus into the spinal cord of cats produces a rhythmic segmental myoclonus¹⁵ and the experimental work of Dempsher *et al* on the sympathetic ganglion of rats infected with pseudorabies virus suggests that the essential change may be hyperexcitability of presynaptic terminals.¹⁶ Periodicity of discharge may reflect either the underlying trigger process or temporal spacing produced by a period of refractoriness following firing.¹

Myoclonus which is triggered by sensory stimuli has been termed reflex myoclonus and divided into "reticular" and "cortical" types on physiological grounds.^{17,18} In contrast to reflex myoclonus the spinal type is frequently unresponsive to stimuli and unaffected by sleep. However, movement, mental stress, and auditory stimuli affect jerking in some cases and as in our patients it may cease during sleep. Auditory stimuli enhanced myoclonus in cats inoculated with Newcastle Disease virus.¹⁵ Leigh *et al*¹⁹ have recently described a patient with progressive muscular rigidity associated with reflex myoclonus of axial and leg muscles which occurred both spontaneously and in response to muscle stretch of the head and neck and to light touch to the perioral region. As in segmental myoclonus the jerking was rhythmic at times and there was evidence of a focal lesion, in this case an atrophic process affecting the lower brainstem and cerebellum. However, jerks were more widespread than in our cases, of brief duration and time-locked to an EEG evoked response which represented an enlarged sensory evoked potential and preceded the earliest muscle response.

The prognosis of spinal myoclonus clearly depends upon the underlying lesion. In our first case spontaneous resolution occurred, consistent with the postulated aetiology of viral neuronitis. In case 2 myoclonus was temporarily abolished by intravenous diazepam and alleviated by oral clonazepam, con-

firming previous reports of the efficacy of benzodiazepines in this condition.²⁰ This group of drugs has previously been shown to be of benefit in cases of rigidity associated with progressive encephalomyelitis and strychnine poisoning.²¹

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References

- ¹ Halliday AM. The neurophysiology of myoclonic jerking—a reappraisal. In: Charlton M, ed. *Myoclonic Seizures*. Amsterdam: Excerpta Medica, 1975: 1-29.
- ² Hoehn MM, Cherington M. Spinal myoclonus. *Neurology (Minneapolis)* 1977;**27**:942-6.
- ³ Garcin R, Rondot P, Guiot G. Rhythmic myoclonus of the right arm as the presenting symptom of a spinal cord glioma. *Brain* 1968;**91**:75-84.
- ⁴ Nohl M, Doose H, Selbeck GG, Jensen HP. Spinal Myoclonus. *Eur Neurol* 1978;**17**:129-35.
- ⁵ Patrikios MJ. Sur un cas d'automatisme moteur particulier des membres supérieurs après traumatisme de la moelle cervicale. *Rev Neurol (Paris)* 1938;**69**: 179-88.
- ⁶ Fox EJ, Villaneuva R, Schutta HS. Myoclonus following spinal anaesthesia. *Neurology (Minneapolis)* 1979;**29**:379-80.
- ⁷ Frenken CWGM, Notermans SLH, Kosten JJ, Horstink MWIM. Myoclonic disorders of spinal origin. *Clin Neurol Neurosurg* 1978;**79**:107-18.
- ⁸ Campbell AMG, Garland H. Subacute myoclonic spinal neuronitis. *J Neurol Neurosurg Psychiatry* 1956;**19**:268-74.
- ⁹ Hopkins AP, Michael WF. Spinal myoclonus. *J Neurol Neurosurg Psychiatry* 1974;**37**:112-15.
- ¹⁰ Gelfan S, Tarlov IM. Altered neurone population in L7 segment of dogs with experimental hind limb rigidity. *Am J Physiol* 1963;**205**:606-16.
- ¹¹ Kasperek S, Zebrowski S. Stiff-man syndrome and encephalomyelitis. *Arch Neurol* 1971;**24**:22-30.
- ¹² Whiteley AM, Swash M, Urich H. Progressive encephalomyelitis with rigidity. *Brain* 1976;**99**:27-42.
- ¹³ Howell DA, Lees AJ, Toghil PJ. Spinal internuncial neurones in progressive encephalomyelitis with rigidity. *J Neurol Neurosurg Psychiatry* 1979;**42**: 773-85.
- ¹⁴ Rushworth G, Lishman WA, Hughes T, Oppenheimer DR. Intense rigidity of the arms due to isolation of motoneurons by a spinal tumour. *J Neurol Neurosurg Psychiatry* 1961;**24**:132-42.
- ¹⁵ Luttrell CN, Bang FB, Luxenberg K. Newcastle disease encephalomyelitis in cats. *Arch Neurol* 1959; **81**:285-91.
- ¹⁶ Dempsher J, Larrabee MG, Bang FB, Bodian D. Physiological changes in sympathetic ganglia infected with pseudorabies virus. *Am J Physiol* 1955;**182**: 203-16.
- ¹⁷ Hallett M, Chadwick D, Adam J, Marsden CD. Reticular reflex myoclonus: a physiological type of human post-hypoxic myoclonus. *J Neurol Neurosurg Psychiatry* 1977;**40**:253-64.
- ¹⁸ Hallett M, Chadwick D, Marsden CD. Cortical reflex myoclonus. *Neurology (Minneapolis)* 1979;**29**:1107-25.
- ¹⁹ Leigh PN, Rothwell JC, Traub M, Marsden CD. A patient with reflex myoclonus and muscle rigidity: "jerking stiff-man syndrome". *J Neurol Neurosurg Psychiatry* 1980;**43**:1125-31.
- ²⁰ Eadie MJ. Electrophysiological observations in a patient with segmental myoclonus. *Proc Aust Assoc Neurol* 1969;**65**-8.
- ²¹ Hardin JA, Criggs RC. Diazepam in a case of strychnine poisoning. *Lancet* 1971;**2**:372-3.