Stiff-man syndrome associated with nocturnal myoclonus and epilepsy

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SUMMARY A case of stiff-man syndrome associated with primary generalised epilepsy is reported. In addition, nocturnal polygraphic recording revealed a nocturnal myoclonus. Detailed examination of the central nervous system did not show specific changes. There is no direct proof as to a spinal or supraspinal origin of the stiff-man syndrome. The absence of specific anatomical lesions may indicate a functional rather than a structural disturbance in its physiopathogenesis.

Stiff-man syndrome is characterised by progressive fluctuating muscular rigidity which increases in spasms related to sensory and emotional stimuli. Neurophysiological study has demonstrated the presence of involuntary muscular contraction of agonists and antagonists without signs of primary or secondary muscular lesions. The pathogenesis is still obscure (Moersch and Woltman, 1956; Berti Ceroni et al., 1967; Gordon et al., 1967; Sigwald and Guilleminault, 1971).

A detailed anatomopathological examination of the central nervous system was reported by Trethowan et al. (1960), while in another case (Moersch and Woltman, 1956) only the brain was examined. Other postmortem examinations disclosed no abnormality (Asher, 1958; Cohen, 1966). However, in Asher's case the part of the central nervous system studied was not specified, while in Cohen's case the spinal cord was not examined. In no case were structural alterations different from those associated with aging discovered.

We report here a comprehensive study of a case which also involved generalised epilepsy and nocturnal myoclonus.

Case report

At the age of 52 years this retired man began to feel muscle rigidity in the legs which increased to the point of disturbing his gait markedly. Rigidity intensified spontaneously at times, becoming painful. At 58 years of age, he began to suffer from chronic bronchitis and emphysema which worsened progressively. At age 61 years, grand mal seizures began, and they recurrent one month, mainly during sleep or while watching television.

Neurological examination at the age of 62 years showed marked rigidity of the muscles of the lower half of the trunk and legs which were fixed in extension and adduction. From time to time, either spontaneously or in relation to emotional or tactile stimuli, the spasms became stronger and painful. The patient had some difficulty in sitting still or standing up because the trunk and thighs constituted a single “block.” His gait was disturbed by the rigidity, and he was able to move only by taking small steps while his legs crossed in scissors-like fashion. The plantar responses were irregularly in extension; the patellar reflexes were exaggerated. No further neurological abnormalities were noted.

After admission to hospital, the patient experienced two more convulsive seizures, one of which was set off by intermittent light stimulation during a routine electroencephalogram (EEG). Painful rigidity remained localised to the lower part of the body for about 30 days, but then extended to the arms and the upper part of the trunk and the neck. The facial and oropharyngeal muscles were the only ones not involved. After 40 days, the...
respiratory insufficiency worsened to such a point as to necessitate admission to a pulmonary intensive care unit where the patient subsequently died.

LABORATORY ANALYSES
The following routine laboratory examinations were normal: urinalysis, blood Wasserman reaction, level of blood urea nitrogen, fasting blood sugar, blood count, and haematocrit, erythrocyte sedimentation rate, serum potassium, serum sodium, total and partial serum protein, serum creatine kinase, lactate dehydrogenase, aldolase, and tests for circulating rheumatoid factor.

ELECTROPHYSIOLOGY
Electromyography (EMG)
The EMG showed a spontaneous activity composed of motor unit potentials of normal morphology and amplitude, simultaneously involving agonists and antagonists “at rest.” Gentle stimulation of the skin over the muscles explored markedly accentuated such activity (Fig. 1).

A full recruitment pattern during maximum effort was observed. However, it provoked diffusion of the contraction to the ipsilateral and contralateral muscles.

No signs of denervation were found; motor nerve conduction velocity of the left ulnar nerve was normal (64 m/s) as was that of the right peroneal nerve (54 m/s).

Passive shortening of the muscle and, to a lesser extent, stretching, provoked an increase in spontaneous tonic contraction.

The silent period of the right tibialis anterior, obtained by electrical stimulation of the peroneal nerve at the head of the fibula, was normal (105 ms).

The H reflex and its recovery cycle were normal. With vibration (100 Hz) of the Achilles tendon, the H reflex showed variable behaviour; increases of 100% were recorded as well as inhibitions of 50%. At the end of the vibration the H reflex demonstrated an inhibition which persisted for several minutes. Polysynaptic flexion and extension reflexes (Hugon, 1967; Delwaide, 1971) were normal. Non-nociceptive reflexes described by the same authors behaved abnormally, lacking habituation phenomena and exhibiting co-contraction—that is, these reflexes were abnormally present also in the antagonist.

Electroencephalographic (EEG) and polygraphic findings
Routine EEG tracings showed only rare, sometimes sharp, bilateral theta waves. Intermittent photic stimulation during a routine EEG provoked a generalised tonic-clonic seizure.

A nocturnal polygraphic recording showed important alterations in the quantity and composition of sleep. During nine hours of recording the patient slept for only 88 minutes. Brief periods of sleep alternated with prolonged reawakenings during which the muscle spasms reappeared. Sleep was divided as follows: phase 1 (56%); phase 2 (31%); phase 3 (4%); phase 4 (0%); phase REM (9%). During light sleep (phases 1–2) myoclonic jerks involving the agonists and antagonists of the legs appeared. They were repeated every 15–20 seconds, and continued for a few minutes. The myoclonic jerks were accompanied by signs of

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Fig. 1  EMG recording from (a) right rectus femoris and (b) biceps femoris muscles. At rest a continuous, irregular, asynchronous activity occurs in both muscles, more marked on the rectus femoris. With gentle stimulation of the thigh skin (arrow), the contraction increases markedly and becomes painful.
EEG arousal. However, if they did not awaken the patient fully, they were not followed by reappearance of the muscle spasms (Fig. 2).

PHARMACOLOGICAL STUDY

Intravenous administration of 10 mg of baclofen (Lioresal) with simultaneous EMG control, caused the muscle contraction to disappear after 15 minutes and was associated with mild somnolence. Baclofen administered orally in a dose of 100 mg/day produced only a mild and transitory reduction of muscle spasms. Intravenous administration of 1 mg of clonazepam (Rivotril) and 10 mg of diazepam (Valium) caused spasms to disappear after two minutes. Diazepam provoked somnolence which the patient was able to overcome, but clonazepam caused him to fall asleep within a few minutes. These two benzodiazepines were not used regularly because of the existing respiratory insufficiency. Carbamazepine (Tegretol, 800 mg/day/per os) and sodium dipropylacetate (Depakin, 1000 mg/day/per os) were employed separately but had no effect on the spasms. However, there were no more convulsive attacks after their administration.

NEUROPATHOLOGY

There was slight thickening of the meninges covering the cerebral hemispheres, but it did not conceal a clear convolutional atrophy. On coronal sections the cerebral hemispheres showed a well-demarcated cortical ribbon of normal width. The ventricular system was not appreciably dilated and the basal ganglia, cerebellum, brainstem, and spinal cord appeared normal. Representative blocks of the various structures of the central and peripheral nervous systems were sampled. Frozen and/or paraffin-embedded sections were processed and stained according to the Nissl, Speilmeyer, Bodian, HE, PAS, Sudan, and Holzer methods.

Microscopic examination of the cortical grey matter did not show any appreciable change in neuronal density, nor were gliosis or senile plaques of the neurofibrillary tangles present. Several nerve cells, mainly in the third and fifth layers, contained abundant lipofuscin granules. Pigment granules were found in the nerve cells of the thalamus which was otherwise normal. No significant changes were found in the striatum, the globus pallidus, or the Luys body. The lateral portion of the substantia nigra showed some neuronal loss associated with the presence of melanin pigment granules in the neurone soma. The red nucleus of the midbrain segment was normal. No changes were seen in the pons. The bulbar olives showed a mild fibrillary gliosis, and the olivary neurones contained abundant lipofuscin granules. Scattered loss of Purkinje cells was observed in the cerebellum. Axonal changes, demyelination, gliosis, and Sudan positive fats were not found in the fibre tracts of the spinal cord. Motoneurones of the lateral nuclei of the central horn at C5–6 cord segments seemed slightly decreased, but there was no associated reactive glia or fibrillary gliosis. Peripheral nerves and dorsal ganglia did not show any appreciable changes.

Discussion

This report describes a patient with the typical clinical picture of the stiff-man syndrome with characteristic evolution and electrophysiological data. The painful spasms began in the legs and
reached the trunk within 10 years, then spread very rapidly to the arms and neck, avoiding only the facial and oropharyngeal muscles (Moersch and Woltman, 1956; Berti Ceroni et al., 1967; Gordon et al., 1967; Sigwald and Guilleminault, 1971).

The EMG studies revealed the typical characteristics of the syndrome: absence of signs of neurogenic lesions, normal motor nerve conduction velocity and silent period, presence of spontaneous activity in agonists and antagonists reinforced by cutaneous stimulation and muscular shortening or stretching, and diffusion of voluntary activity to ipsilateral and contralateral muscles (Mertens and Ricker, 1969; Sigwald and Guilleminault, 1971).

The H reflex is usually decreased markedly during appropriate tendon vibration (De Gail et al., 1966; Hagbarth and Eklund, 1966). In our case, vibration did not evoke a clear-cut and unequivocal decrease of the H reflex, suggesting, among other possibilities, a disorder at presynaptic level (Delwaide, 1974). The lack of habituation and the presence of co-contraction of polysynaptic non-nociceptive reflexes also suggest abnormal functions, even if not specific (Delwaide et al., 1974), of the polysynaptic system.

Administration of physostigmine has produced no effect on the stiff-man syndrome which, therefore, would exclude involvement of Renshaw cells which contain acetylcholine as a synaptic mediator (Schmidt et al., 1975). Nor were there any modifications when glycine was administered, thus excluding the hypothesis of a dysfunction of the inhibitory glycineergic spinal interneurones (Schmidt et al., 1975). L-dopa worsened the rigidity (Guilleminault et al., 1973; Schmidt et al., 1975) while diazepam, clonazepam, and baclofen reduced the spasms (Howard, 1963; Mertens and Ricker, 1968; Guilleminault et al., 1973). On the basis of these pharmacological data, the hypothesis has been formulated that the stiff-man syndrome depends on an imbalance between the cholinergic systems (whose activity is increased by L-dopa and depressed by benzodiazepines) and the GABA system (whose activity is increased by baclofen) (Guilleminault et al., 1973; Schmidt et al., 1975).

The pharmacological study of our patient confirms the published data on the effectiveness of baclofen, clonazepam, and diazepam. However, the ineffectiveness of dipropylacetate, which increases the GABA concentration in the brain (Godin et al., 1969; Simler et al., 1973), suggests some doubts regarding the involvement of the GABA system.

Abnormal movements during sleep have also been reported by other authors who carried out nocturnal polygraphic recordings. Berti Ceroni et al. (1967) observed a particular abundance of non-repetitive myoclonic jerks during REM sleep, localised to the limb predominantly affected by contractions during wakefulness, which seemed to be an intensification of the physiological myoclonic twitches.

Guilleminault et al. (1973) observed "paroxysmal spasms," recurring every 10–45 seconds during phase 1 sleep, every five to eight minutes during phase 2, and disappearing completely during phase 3 and REM sleep. In our patient nocturnal polygraphic recording showed the existence of a typical nocturnal myoclonus (Symonds, 1953) consisting of muscular jerks of the legs occurring every 15–20 seconds during light sleep.

The myoclonus in our case seems similar to the rhythmic spasms described by Guilleminault et al. (1973). Lugaresi et al. (1968) reported on a number of cases of nocturnal myoclonus associated with spinal and supraspinal lesions. Although these data indicate a possible common cause for the stiff-man syndrome and for nocturnal myoclonus, they do not indicate what the cause might be.

It is not unusual to find epilepsy associated with the stiff-man syndrome. Two of Moersch's and Woltman's patients experienced epileptic seizures, one grand mal and the other absences. In Cohen's first case, the patient experienced a grand mal seizure after withdrawal of diazepam. If our case is added to those already described in the literature, it can be calculated that epilepsy is observed in about 10% of patients suffering from the stiff-man syndrome. This percentage is much higher than the prevalence of epilepsy in a general population, and leads us to hypothesise that the association of stiff-man syndrome and epilepsy is not a casual one.

Serial histopathological examination of the nervous system did not reveal any significant changes which might have a possible correlation with the stiff-man syndrome. The few abnormalities observed were absolutely nonspecific. These findings are in keeping with a previous report by Trethowan et al. (1960).

In conclusion, the study of our patient did not reveal the location of the primary dysfunction responsible for stiff-man syndrome which may be at the spinal (interneurones) or supraspinal level (Gordon et al., 1967; Rondot, 1968; Sigwald and Guilleminault, 1971; Cobb, 1974). Our patient's epilepsy does not constitute direct proof that it originates at a supraspinal level, but demonstrates
the existence of disturbances of the neuronal systems at this level. The absence of specific anatomical lesions of the central nervous system indicates that the muscular rigidity and spasms, wherever they originate, are a functional, rather than a structural disturbance.

References


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