Paroxysmal symptoms in multiple sclerosis

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SYNOPSIS The clinical features of paroxysmal symptoms occurring in 26 patients with multiple sclerosis are reviewed. The findings are considered to provide further support for the concept of lateral spread of axonal excitation within demyelinated plaques.

The familiar symptoms of multiple sclerosis (MS) are those due either to impaired axonal conduction, temporary or permanent, or to the release of exaggerated reflex activity. Apparently in a different category, not easily attributable to either cause, are brief paroxysmal symptoms. Epilepsy occasionally occurs in MS (Matthews, 1962) and trigeminal neuralgia is well documented but neither presents any distinctive features. In contrast, tonic seizures (Matthews, 1958), paroxysmal dysarthria (Andermann et al., 1959), and certain sensory symptoms (Espir et al., 1966) are highly characteristic of MS, being seldom identifiable in other conditions. I propose to review, from personal experience, the range of paroxysmal phenomena encountered and their significance.

METHODS

Detailed notes were available of 26 patients seen personally between 1956 and 1974 and regarded as having paroxysmal symptoms of MS other than epilepsy or trigeminal neuralgia. The criterion adopted was that of repeated stereotyped symptoms of no more than two minutes' duration, thus excluding many patients with episodic symptoms of less clearly defined character, in particular recurrent pain. The patients were seen in three different centres and no attempt can be made to estimate the incidence of these symptoms in patients with MS. Although three patients are known to have died in hospital after prolonged detailed observation, no necropsy confirmation of the diagnosis could be obtained. Many of the patients were seen before estimation of protein fractions in the cerebrospinal fluid was possible and the diagnosis was established on clinical grounds. Direct observation of motor phenomena was not always possible and reliance sometimes had to be placed on the patient's description.

Four types of paroxysmal symptom that might occur in isolation or in various combinations were identified; tonic seizures, dysarthria, sensory symptoms, and segmental loss of use of the limbs.

TONIC SEIZURES As originally described (Matthews, 1958) tonic seizures were brief, frequent, usually intensely painful episodes in which the limbs on one side adopted the tetanic posture, often precipitated by movement or sensory stimulation and remitting completely in a few weeks. In the present series 15 patients, including five previously published (Matthews, 1958; 1962), had seizures recognizably of this type but the original description must be modified in the light of these observations.

In 11 patients the diagnosis of MS was 'definite' and in one 'probable' (McAlpine et al., 1972) either at the time of the seizures or subsequently. In three patients the diagnosis of MS might well not have been considered in the absence of recognizable paroxysmal symptoms and must remain in doubt at the time of reporting. The seizures were the first symptoms in two patients.

The seizures were unilateral in all patients, the arm being invariably affected while in six the lower limb was not involved in spasm. In nine patients the hand adopted the tetanic posture, being observed to do so in six, but in two the fist was clenched and in two further patients the fingers were extended at the metacarpophalangeal joints, producing a claw hand. In two patients the posture of the hand could not be ascertained. The arm was usually flexed at the elbow.

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and wrist and adducted at the shoulder, but in one patient the arm was extended and in another strongly abducted. When involved, the lower limb was extended at hip and knee and the foot was plantar-flexed. Involvement of the facial muscles was probable in four patients but the face was often contorted by pain, rendering interpretation difficult. The resemblance to the tetanic posture, while often striking, was, therefore, less consistent than at first reported.

The seizures were extremely painful in seven patients, the pain having the same distribution as the spasm. It seemed unlikely that the pain was entirely due to the intense muscular contraction as in two patients pain was experienced before the spasm was fully developed, while eight patients, in whom contraction was not obviously less severe, had no pain. Paraesthesiae in the affected limbs were not commented on apart from one patient who experienced a tickling sensation. Thirteen patients observed precipitation of the seizures by movement or sensory stimulation, the two often being indistinguishable. Putting the foot to the ground on standing up or turning over in bed onto the affected side were the actions most frequently noted but there were also spontaneous complaints of seizures induced by typing, carrying shopping, or tying shoelaces. Overbreathing for a brief period was observed to trigger the seizures in three of the seven patients in whom this was attempted.

Seizures were always brief, the longest observed being 90 seconds and the longest estimate by a patient being two minutes, many claiming a duration of 30 seconds or less. In 11 patients the seizures appeared abruptly and persisted for from two days to two months, remitting either spontaneously or in response to treatment, without recurrence when treatment was eventually stopped. In these patients seizures occurred with great frequency, 30 times a day being common, and sometimes every few minutes for many hours. In four patients the pattern was different, with relatively infrequent seizures recurring for from one to over three years.

The physical signs present at the time of onset of the seizures did not indicate any specific pattern of distribution of lesions. In five patients, signs were confined to those of mild or moderate pyramidal tract involvement ipsilateral to the seizures. In two patients abnormal signs were restricted to the optic nerves; three showed evidence of widespread involvement of the spinal cord and brain-stem; one had a severe cervical spinal cord lesion; two had spastic paraparesis with little sensory loss; and two had sensory loss alone.

In five patients tonic seizures were accompanied by other paroxysmal symptoms. Two patients with painless tonic seizures, not involving the face, were dysarthric during the attacks. In one patient tonic seizures involving the left upper limb were invariably preceded by a burning sensation behind the right scapula. In another patient the initial symptom had been brief episodes of loss of use of the left foot, without spasm or change in posture, often precipitated by putting the foot to the ground. After six months these episodes began to be accompanied by painless tonic seizures affecting the left upper limb. In a girl of 16 her second attack of retrobulbar neuritis was accompanied by typical tonic seizures of the left upper limb and simultaneous 'jumping' movements of the right upper limb, unfortunately not witnessed.

Tonic seizures were not accompanied by any disturbance of consciousness and the electroencephalogram recorded both between and during seizures was not disturbed. In one patient, however, there was an unexpected link with epilepsy.

CASE I

Devic's syndrome followed by paroxysmal dysarthria and later by tonic seizures and epilepsy

A man aged 18 years developed a severe illness leading within three days to bilateral blindness from optic neuritis and paraplegia with an upper dorsal motor and sensory level. In the course of a few months both vision and strength partially recovered. Four years later he had an episode of diplopia. A month later he developed attacks of slurred speech during which he felt light headed and unable to control his limbs. These lasted a few seconds only and occurred up to 20 times a day. Attacks could be precipitated by about 20 deep breaths. They were abolished by a small dose of carbamazepine and did not recur when this was stopped six weeks later. Four months later he developed tonic seizures of the right arm which adopted a tetanic posture. These were regularly precipitated by using the hand and were accompanied by dysarthria. While demonstrating that tying his shoelace would cause a seizure the local tonic spasm was immediately succeeded by a generalized convulsion. He was stuporous for four days and subsequently had a right hemiparesis that recovered over the next five months. During this time he had two further major fits but no more tonic seizures. Anticonvulsants had to be withdrawn because of repeated deliberate overdosage but no ill effects resulted.

In addition to the 15 patients with seizures affecting the limbs one patient had a different form of tonic seizure.
CASE 2

Tonic seizures of neck and eye muscles after relapse of MS affecting brain-stem

At the age of 24 years this woman had diplopia and paraesthesiae in the left side of the face and tongue for three weeks and a similar episode a year later with recovery. Two years later, in the course of two weeks, she developed a severe brain-stem syndrome at the height of which she was drowsy, unable to swallow, and had almost complete external ophthalmoplegia, bilateral facial weakness, and weakness of all limbs with bilateral extensor plantar reflexes. A month later, when she was recovering from this relapse and when the ocular palsies had resolved she began to have attacks in which she felt as if her eyes were turning in. Her head would turn slightly to the right and the left eye would adduct (Figure). These attacks lasted about 10 seconds and were extremely distressing, although not painful. For many days they occurred approximately every 10 minutes and could be regularly induced by overbreathing but also by virtually any form of sensory stimulation, rendering nursing care and feeding difficult. Phenobarbitalone and phenytoin did not reduce the number of attacks which gradually lessened and stopped after two months. Carbamazepine was not available. Her improvement continued but she subsequently had repeated relapses and died at the age of 35 years.

DYSPHARIA Ten patients experienced paroxysmal dysarthria including the two already mentioned who had concurrent tonic seizures, one of whom had had a previous series of dysarthric attacks (case 1). Eight were eventually classified as definite cases of MS and two as probable cases, the diagnosis sometimes only being established after prolonged follow-up. For example, the patient who was reported as a possible example of MS occurring with ankylosing spondylitis (Matthews, 1968) later developed characteristic symptoms and signs of the disease (Dr Michael Espir, personal communication). In this patient and in one other the paroxysms were the presenting symptom.

The attacks began suddenly and occurred from one to 50 times a day for a period varying from one week to 12 months. In those in whom the paroxysms remitted spontaneously the frequency declined gradually from the initial high level. The attacks were always brief, varying from an observed five seconds to the longest estimate by a patient of two minutes. Excluding those paroxysms that occurred with tonic spasms, five additional patients had noted precipitating factors. Sudden movement of any part of the body was the usual trigger in four patients and one believed that even changing his train of thought was sufficient. One woman complained of attacks immediately after sexual intercourse. In four of the five patients in whom it was attempted overbreathing for a brief period induced a paroxysm. Despite these precipitating factors in all patients the majority of paroxysms appeared to be spontaneous. Less observant patients would describe the attacks as ‘dizziness’ and their nature could only be determined by detailed questioning.

The speech disturbance was variously described by the patients as slurring, stammering, or loss of control. The six patients whose attacks were observed were reluctant to continue speaking and precise observation was also limited by the brevity of the episodes. The slurred disjointed syllables that could sometimes be recognized certainly suggested dysarthria rather than dysphasia but no detailed analysis was possible. Dysarthria was never the only component of the paroxysms. As noted, in two patients dysarthria was accompanied by tonic seizures. Three patients complained of feeling faint or light headed,
combined with a sensation of generalized loss of control of the limbs, sometimes causing stumbling. One of these patients fell off his bicycle in a number of attacks. Consciousness did not seem to be disturbed, even momentarily.

In six patients the paroxysms began with sensory symptoms in the face, variously described as burning, numbness, or tingling. These sensations were always confined to one side of the face, the left in five patients and the right in one, and in three patients invariably began in a specific restricted site such as the forehead or upper lip. In four patients, apparently simultaneously with the onset of dysarthria, similar sensory symptoms developed in the upper limb, in two ipsilateral and two contralateral to the facial sensations. Again the paraesthesiae were often sharply localized, affecting the identical digits on every occasion. Two patients said that during an attack they were unable to use the arm contralateral to the paraesthesiae but it was not possible to determine, even when witnessing an attack, whether this was due to weakness or ataxia. Most patients found the paroxysms highly distressing.

At the time of development of the paroxysmal dysarthria four patients had widespread signs of MS, including evidence of brain-stem lesions, but in two there were no abnormal signs and in the remaining four only minor signs, not specifically related to the brain stem.

SENSORY SYMPTOMS  One patient had paroxysmal sensory symptoms in isolation.

CASE 3  

Paroxysmal sensory symptoms as first symptom of MS

A man of 45 years of age began to experience a sensation of quivering in the right side of the face, spreading to the right arm, index finger, and thumb. This would last for a few seconds and was not accompanied by any involuntary movement or by dysarthria. The sensation, which was highly unpleasant, was not precipitated by any obvious factor. The frequency gradually increased until after about a year he suddenly began to have attacks ‘every few seconds’ causing such distress that his doctor had to be called out twice in one night and eventually gave an injection of morphia that allowed the patient to fall asleep. The attacks continued many times a day but on treatment with carbamazepine rapidly subsided after a total duration of 15 months and did not return when treatment was stopped some months later.

Soon after the onset of these symptoms he developed progressive difficulty in walking. When examined after the severe exacerbation of his paroxysms he was found to have pallor of the right optic disc, increased tendon reflexes in the left limbs, absent abdominal reflexes, bilateral extensor plantar reflexes, and an ataxic gait.

LOSS OF USE  Two patients with probable MS, one of whom had previously had paroxysmal dysarthria, experienced attacks of a sensation of loss of use of the limbs on one side. These bore many points of resemblance to other paroxysmal symptoms in that they were brief, began suddenly, and occurred with great frequency for two weeks in one patient and for one week in the other, in whom they responded immediately to carbamazepine. It was not possible to determine the precise nature of the loss of use complained of even when an attack was witnessed. There is some resemblance to the motor accompaniment described by two patients with paroxysmal dysarthria but more obviously to the paroxysmal loss of use of the foot described by one patient with upper limb tonic seizures.

TREATMENT  These 26 patients had 28 episodes of paroxysmal symptoms. Of these, 12 stopped spontaneously without the effect of drugs being observed. Conventional anticonvulsants, phenobarbitone, and phenytoin, appeared to arrest the paroxysms in six patients, three with tonic seizures, one with combined tonic seizures and dysarthria and two with paroxysmal dysarthria. The response was sometimes obvious, with complete relief immediately on beginning treatment and temporary relapse on attempted withdrawal of the drug. In four patients, two with tonic seizures, one with dysarthria and one with motor symptoms involving the eyes and head there was no response to these drugs in full dosage. Carbamazepine was immediately effective in the six patients in whom it was used, comprising one patient with sensory symptoms, one with tonic seizures, and four with dysarthria, in one of whom phenobarbitone had proved ineffective. Carbamazepine was not available for use in the other three patients in whom phenobarbitone and phenytoin had failed. The effect of carbamazepine on paroxysmal dysarthria was particularly striking. In one patient who was having up to 50 attacks a day there was complete relief within an hour of the first dose of 100 mg. The maintenance dose required was low, seldom exceeding 300 mg a day in divided dosage.

DISCUSSION  

Paroxysmal symptoms of the type described here must be distinguished from other symp-
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Symptoms of brief duration encountered in MS. Many patients describe unsystematized fluctuation in their symptoms, and more specific entities include Lhermitte's sign, flexor and extensor spasms and, in particular, the transient deterioration in vision or walking induced by heat or exertion. These appear to be related to the demyelinating process but the duration and precipitating factors are distinctive. Many of the brief episodes of weakness described by Zeladowicz (1961) were probably of this nature as were the visual symptoms reported by Franklin and Brickner (1947).

The frequency of paroxysmal symptoms has been variously estimated. Kuroiwa and Araki (1963) reported that 13% of 56 patients with demyelinating disease had tonic seizures and Shibasaki and Kuroiwa (1974) 17% of 64 patients with MS, there apparently being little overlap between these two series from the same centre in Japan. Espir and Millac (1970) reported 13 patients with tonic seizures or paroxysmal dysarthria in approximately 600 patients with MS in addition to nine with trigeminal neuralgia. Identical paroxysmal symptoms undoubtedly occur in patients who appear to have acute disseminated encephalomyelitis rather than classical MS (Ekbom et al., 1968).

The full range of paroxysmal symptoms has almost certainly not been recognized. In many of the examples of tonic seizures reported from Japan (Kuroiwa and Araki, 1963; Shibasaki and Kuroiwa, 1974) the spasm has been widespread, involving both arms or one arm and both legs or even all four limbs. Kreindler et al. (1962) also reported bilateral involvement. The paroxysmal sensation of loss of use of the limbs described by two patients in the present series as an isolated phenomenon was also reported by Castaigne et al. (1970) one of whose patients would be unable to move for 20 seconds, although he did not fall. This brief akinesia is described by patients in different terms from the loss of control complained of by some patients during paroxysmal dysarthria which is probably cerebellar ataxia. Distressing paraesthesiae can occur as an isolated paroxysmal symptom as in the patient reported here (case 3) and in Espir and Millac's (1970) case 4, but less convincingly in their other examples. In personal experience, episodic pain in MS, other than trigeminal neuralgia, has different characteristics, the attacks lasting for much longer and showing little response to therapeutic agents effective in preventing other paroxysmal symptoms, although partial success was claimed by Espir and Millac (1970).

The association of tonic seizures with a partial Brown-Séquard syndrome (Matthews, 1958) that was originally suggested could not be confirmed in this larger series. A number of authors have emphasized the importance of spinal cord lesions (Kreindler et al., 1962; Shibasaki and Kuroiwa, 1974) and the association with Lhermitte's sign noted by Kuroiwa and Araki (1963) could be regarded as supporting evidence of spinal cord disease. The simultaneous occurrence of tonic seizures and dysarthria in two patients in the present series could not be accounted for by any disturbance of function resulting from a single spinal cord lesion.

The nature of these paroxysmal symptoms is a matter of some interest. Epilepsy of cortical origin is an unlikely explanation, although closely similar tonic seizures can result from focal lesions of the medial surface of the hemispheres (Kennedy, 1959). The patient in the present series in whom a tonic seizure induced by movement was observed to lead immediately to generalized status epilepticus appears to be unique. The confused literature of tonic fits as a form of subcortical epilepsy was reviewed by Matthews (1958) who concluded that unilateral tonic seizures were not characteristic of fits originating in any subcortical structure. The question of epilepsy of spinal cord origin is largely a matter of definition. Certainly tonic spasms not readily explained as due to reflex activity have been described in spinal cord compression (Nathanson, 1962) but their epileptic nature is problematical.

In some patients with paroxysmal symptoms features are detectable that could not be attributed to neuronal discharge from any single site in the cerebral hemisphere. Ekbom et al. (1968) drew attention to tonic seizures accompanied or preceded by contralateral paraesthesiae of the type associated with lesions of the spinothalamic tract. They postulated lateral spread of excitation between axons in the lateral column of the spinal cord as a cause for this sequence. In the brain-stem a similar possibility is even more strongly suggested by the facial paraesthesiae
followed by crossed brachial paraesthesiae and ipsilateral ataxia that occurred in two patients with paroxysmal dysarthria. Sensory symptoms contralateral to tonic seizures are relatively rare, occurring in only one patient in the present series, but, if this hypothesis is correct, isolated tonic spasm could result from lateral axonal spread in plaques in the corticospinal pathway not involving the spinothalamic tract, or perhaps causing ipsilateral pain or other sensory symptoms from spread into the posterior columns. If this were so, similar motor symptoms might result from involvement of the corticospinal pathway at any level, brain-stem plaques accounting for tonic seizures accompanying dysarthria and a plaque subjacent to the cortex being responsible for the sequence in the patient described here in whom epilepsy immediately followed a tonic seizure.

All authors have noted that paroxysmal symptoms of every type are frequently precipitated by sensory stimulation or movement. Shibasaki and Kuroiwa (1974) were able to identify trigger zones in some patients but in personal experience these seldom approach the specificity found in trigeminal neuralgia. Although in any patient many paroxysms appear to be spontaneous, this effect of the sensory input must be taken into account in any theory of causation. A possible explanation is that afferent impulses reaching an area of demyelination spread laterally to neighbouring afferent and efferent axons within the plaque, resulting in the clinical phenomena of the paroxysm.

The clinical resemblance of tonic seizures to hemitetany of metabolic origin has been noted by all observers and the possible significance of this fact was reviewed by Matthews (1958). This resemblance is sometimes less precise than at first described but the implications may yet be something more than ‘assez superficielles’ (Castaigne et al., 1970). Both tetany and tonic seizures may be precipitated by overbreathing. From clinical evidence overbreathing and other methods of reducing ionic calcium appear to facilitate transmission through plaques of demyelination (Davis et al., 1970; Becker et al., 1974). The precise action of carbamazepine that is so effective in controlling all forms of paroxysmal symptoms has been little investigated at cellular level but an effect on ionic concentra-

REFERENCES


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