Paroxysmal itching in multiple sclerosis: a report of three cases

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Summary Paroxysmal itching is described in three Japanese women with multiple sclerosis and previously reported cases are discussed. This paroxysmal symptom is rare, but may be the first and only symptom at the onset of multiple sclerosis.

Since Matthews first drew attention to tonic seizures as a paroxysmal symptom in multiple sclerosis (MS), various other kinds of paroxysmal events have been reported.3-7 These transient neurological symptoms are not uncommon during the course of MS, particularly in the early stage of the disease.2 They include paroxysmal dysarthria and ataxia, paraesthesiae and pain in the limbs, trigeminal neuralgia, and painful tonic seizure. Paroxysmal itching in MS is a rare symptom, first recognised by Osterman and Westerberg.8 Osterman later reported another two cases with paroxysmal itching in MS, while Yabuki and Hayabara reported one case in Japan. This case (3) is reviewed in the present report, together with a further two cases.

Case reports

Case 1 In January 1979, a Japanese woman aged 27 years was admitted to Okayama University Hospital with loss of vision on the left, and frequent attacks of itching affecting initially the lateral side of the right lower leg for two months. These were of sudden onset, lasted only a few minutes and ceased rapidly. The attacks occurred at least five times a day and were not relieved by scratching. Two weeks after the first attack, episodes of itching occurred on the lateral side of the left lower leg and continued for a week in this area. Thereafter, paroxysmal itching migrated to involve both knees, both hips and both lateral thighs. The itching was provoked in both legs whenever she had a hot bath. Continuous pain occurred on the medial side of both thighs. At that stage a physician and a dermatologist did not find signs of abnormality. In December 1978, she noted weakness of her left leg, and by January 1979 she also noted numbness of the left leg. Three days prior to admission she lost vision on the left and paroxysmal itching occurred in the T5,6 segmental areas of her chest and back. Examination showed that physical abnormalities were confined to the nervous system. She was blind in the left eye. There were numbness, hyperalgesia, and hypesthesia in both legs, and weakness of the right leg. The deep tendon reflexes were brisk, and both plantar responses were extensor. Lhermitte's sign was negative. Scratching scars were observed in her chest and left thigh (figure). Complete blood count, serological examination and other laboratory examinations were normal. Cerebrospinal fluid (CSF) was clear, with normal pressure, protein of 0.76 g/l and five white blood cells per l µl: CSF gamma globulin was 25.3%, CSF immunoglobulin-G was 0.068 g/l (normal below 0.04 g/l). Treatment with prednisolone was begun. After two months, her vision was moderately improved, but paroxysmal itching still occurred every day and often at night. Carbamazepine 100 mg a day was given and was increased to 700 mg a day at which dose paroxysmal itching markedly decreased in frequency. Unfortunately, an allergic skin reaction developed which made a further treatment impossible. Paroxysmal itching recurred. Phenytoin and phenobarbitone also were given, but without effect and analgesics (aspirin and indomethacin) were also of no value. By August 1979, vision on the left side had completely recovered, but paroxysmal itching had increased in frequency and intensity. About that time, paroxysmal itching occurred in the medial side of both thighs together with continuous pain. In November 1979, vision on the left side was again moderately impaired. In February 1980, vision was normal, but about this time paroxysmal itching...
Case 1

A 44-year-old woman was admitted to Kochi Prefectural Central Hospital on May 1, 1979, with a history of paroxysmal sensory disturbance affecting her right lower leg, which had occurred and disappeared repeatedly for about 20 seconds. She had been treated with carbamazepine in December 1979, which had been stopped due to an increase in serum creatinine. In February 1980, she developed right-sided weakness of both hands and fingers, which lasted about 10 seconds and occurred at the start of movement. Hyperventilation did not provoke paroxysmal itching. She had a history of bronchial asthma. On June 8, at the moment of changing her position in bed, paroxysmal itching first occurred at the back of neck, on the back and on both arms, lasting about 10 to 20 seconds, then disappeared. About that time, her neurological disturbances improved. Paroxysmal itching occurred in both shoulders and both arms (and occasionally in the upper back), sometimes unilateral, sometimes bilateral. The attacks lasted for about 20 seconds and always occurred at the start of movement. Hyperventilation did not provoke paroxysmal itching. She was given carbamazepine 300 mg a day. Paroxysmal itching did not recur thereafter. After three weeks administration, carbamazepine was stopped and paroxysmal itching recurred. Carbamazepine was begun again. In December 1979, it was stopped, and thereafter paroxysmal itching did not recur.

Case 2

In May 1979, a Japanese woman aged 37 was admitted to Kochi Prefectural Central Hospital for sensory disturbance. In the evening, 36 days prior to admission, the patient felt a smarting pain in her lower leg when she stood up. The pain lasted about 10 seconds, but did not impair her ability to walk. For the next four days paroxysmal dysesthesia below her left knee occurred several times a day. Thereafter, her left shoulder felt heavy on awakening, and a smarting pain also occurred throughout her arm, lasting about 10 to 20 seconds. On examination initially vertical nystagmus was noted and no other abnormality was found. After her first visit to hospital, paroxysmal itching began to occur in the face, and she became unstable when walking. On admission, physical abnormalities were confined to the nervous system. Vertical nystagmus on left lateral gaze was present. This was bilateral intention tremor, and the finger-nose test was very clumsily performed, especially on the left. She could not walk because of severe truncal ataxia. The jaw and deep tendon reflexes were bilaterally hyperactive and the right plantar response was extensor. Left C3 segmental hypesthesia and paraesthesia were present and there was hypesthesia and paraesthesia of the left arm, left trunk and left leg. Deep sensation was moderately diminished in both legs. Lhermitte's sign was negative. Scratching scars were present on her face. Complete blood count was normal, as was examination of the CSF. Paroxysmal itching occurred for about 10 days, but then trigeminal neuralgia developed, which was effectively treated by carbamazepine. In November 1976, when she overbreathed during EEG recording, a tonic seizure affecting the right arm and leg occurred, so phenytoin was added to carbamazepine. Subsequently her neurological
symptoms improved except the vertical nystagmus, intention tremor and extensor plantar responses, and paroxysmal itching did not recur.

Discussion

Itching may occasionally be an important symptom of systemic disease, such as allergy, drug reaction, and intestinal and tissue parasites, but is a rare symptom in neurological diseases. Itching may occur in the pre-eruptive phase of herpes zoster, and may be an occasional feature of tabes dorsalis. In the three Japanese women described here with MS, laboratory and physical examinations showed that there were no systemic diseases, allergy, drug reaction, or emotional stress relating to their itching.

The common features of our three patients were as follows: (1) The attacks occurred and ended abruptly in all cases, (2) their duration ranged from several seconds to several minutes, (3) their frequency was five to six times a day and sometimes more, (4) the attacks often occurred during sleep, awaking the patient, (5) the distribution of the attacks involved the face, trunk and extremities: They were often symmetrical and segmental, (6) superficial sensory disturbances were present in the areas affected in all patients, (7) the attacks were sometimes provoked at the start of movement, (8) continuous pain changed to paroxysmal itching in one patient, and paroxysmal itching changed to trigeminal neuralgia in another, (9) carbamazepine was effective in two patients, (10) paroxysmal itching appeared as the first and only symptom at the onset of MS and a predictive symptom of exacerbation of MS in one patient.

These features are similar to those of other types of paroxysmal symptoms in MS. The duration of paroxysmal attacks such as tonic seizures and sensory seizures varies from a few seconds to several minutes. The duration of paroxysmal itching varied from several seconds to several minutes in our cases although the majority lasted less than a minute. Tonic seizures and painful tonic seizures were recognised to be closely correlated with Lhermitte's sign, and Osterman also suggested a correlation between paroxysmal itching and Lhermitte's sign, which is an indication of pathological processes affecting the posterior column of the cervical cord. Whether there is a correlation between the occurrence of paroxysmal symptoms and other neurological symptoms is in dispute. Osterman reported that neurological examination between bouts revealed only minor abnormalities, but Yabuki et al reported that tonic seizures tended to occur during exacerbations of MS. However, Osterman and Westerberg also reported that examination during the period of tonic seizures did not reveal any abnormality in two of five cases. Shibasaki and Kuroiwa reported that painful tonic seizures occurred in parallel with or in close proximity to clinical exacerbation of spinal cord lesions. In our cases, paroxysmal itching occurred as the first symptom at the onset of MS, and a predictive symptom just before exacerbation in one patient. It also occurred during the recovery course of MS (two patients) and prior to exacerbation (two patients).

Though the similarities of the various paroxysmal symptoms in MS suggest similar pathogenic mechanisms, there are various theories as to their causes. Osterman and Westerberg proposed that paroxysmal attacks in MS were caused by transversely spreading ephaptic activation of axons within a partially demyelinated lesion. Matthews and Yabuki also considered this idea compatible with the observation that many paroxysmal attacks in MS seem to be precipitated by sensory stimuli or movement. Paroxysmal itching was always provoked by having a hot bath in one of our patients, and the aggravation of symptoms of MS by raising body temperature has long been recognised. In this patient (case 1) paroxysmal itching tended to occur at night, when her body temperature rose 0.5 to 1.0°C compared with day time. Heat itself also produces itching, but itching in this patient was not due to a generalised skin reaction to a hot bath because the itching skin areas were localised. Paroxysmal itching also was provoked at the start of movement in two patients.

It is generally agreed that stimuli provoking itching give rise to impulses carried principally by unmyelinated, slow conducting fibres of the C groups to a central neuronal pool in the spinal cord via the posterior roots of the spinal nerves, and that pain fibres carry the sensation of itching in the sensory spinal nerve to the spinothalamic tract and thence to the thalamus. Some observers have suggested that itching is a sub-threshold pain sensation. C unit activity was recorded with microelectrodes from intact sensory fascicles in the human peroneal nerve by Torebjörk, who found that the sensations produced by stimuli inducing intense afferent C unit activity were reported as “burning or delayed pain”, whereas stimuli eliciting low frequency activity often were reported as “itch”. 
Osterman\(^\text{a}\) reported that one patient experienced both paroxysmal pain and paroxysmal itching within the same skin area. In our cases, one patient experienced both paroxysmal itching and continuous pain within the same skin areas, another patient experienced both paroxysmal itching and trigeminal neuralgia within the same area of her face. Clinically, these findings suggested that sensations of itching and pain were closely related.

**References**