

## LETTERS TO THE EDITOR

### Treatment of paroxysmal symptoms in multiple sclerosis with bromocriptine

Paroxysmal symptoms are known to occur in multiple sclerosis and have a wide clinical range. We report two patients whose paroxysmal symptoms resolved with bromocriptine.

A 35 year old woman with a three year history of multiple sclerosis complained of paroxysmal upper and lower limb paresthesiae. She described these as "tingling sensations" beginning in her feet and ascending to her waist, and from her hands up to her shoulders, bilaterally. These sensations occurred in the upper and lower extremities simultaneously as well as independently. The symptoms lasted a few hours every day and remitted spontaneously. Occasionally, she complained of mild slurring of speech during these paroxysmal attacks. Neurological examination showed weakness of the hamstrings bilaterally and symmetric diffuse hyperreflexia.

Previous attempts to control her symptoms with carbamazepine, barbiturates and amitriptyline gave little relief. Bromocriptine at an initial dose of 2.5 mg twice a day was started, and led to appreciable reduction in the patient's symptoms. The dose was increased to 5 mg twice a day a week later, and the symptoms completely resolved. Discontinuation of bromocriptine six months later led to an immediate recurrence of her paroxysmal symptoms as described previously. Resumption of bromocriptine treatment was again successful in resolving her symptoms. Two further attempts to discontinue bromocriptine were unsuccessful, as the patient's symptoms recurred on each occasion. The patient tolerated bromocriptine well except for mild nausea.

She has since been maintained on 5 mg of bromocriptine twice a day and on follow up remains asymptomatic. Since the introduction of bromocriptine her dose of amitriptyline has been decreased from 75 mg to 30 mg at night.

A 38 year old man with multiple sclerosis for six years developed episodic numbness of the entire right half of his face. The numbness occurred daily, lasted a few hours, and remitted spontaneously. These paroxysmal attacks began two years ago. The patient had been unsuccessfully treated with amitriptyline. Neurological examination showed generalised hyperreflexia with mild impairment of tandem gait.

Bromocriptine at an initial dose of 2.5 mg twice a day was started and this was increased to 5 mg twice a day a week later; it resulted in resolution of his symptoms. The patient discontinued bromocriptine, and the paroxysmal facial numbness recurred within a day. Bromocriptine was resumed and this again resulted in resolution of his symptoms.

Six months later on follow up, the patient remained free of his paroxysmal attacks while taking bromocriptine at a dose of 5 mg twice a day.

This is the first report of bromocriptine in the treatment of paroxysmal symptoms in

multiple sclerosis. A placebo response cannot be excluded.

There is evidence that the hormone prolactin, which is secreted by the anterior pituitary, has a stimulatory role on the immune function as first shown by the pioneer work of Nagy and Berczi.<sup>1</sup> Later work showed that bromocriptine, a dopaminergic agonist, selectively inhibits prolactin release.<sup>2</sup> Hauser *et al* showed that bromocriptine inhibited both the secretion of prolactin as well as the severity of acute rat experimental allergic encephalomyelitis (EAE),<sup>3</sup> a commonly used animal model in the study of multiple sclerosis. In the same study, it was shown that the clinical course of EAE was also modified and late relapses of EAE were significantly reduced.

Although ephaptic spread from a demyelinated lesion is widely accepted as the most plausible explanation of paroxysmal symptoms in multiple sclerosis,<sup>4</sup> the exact mechanism of such symptoms remains poorly understood. Suppression of the ephaptic spread seems to be the most likely mechanism of action of carbamazepine and phenytoin, two drugs commonly used to treat paroxysmal symptoms in multiple sclerosis. Other drugs, such as acetazolamide, have also been used to treat paroxysmal symptoms in multiple sclerosis.<sup>5</sup> One of us (OAK) has already reported that ibuprofen can be used to successfully treat paroxysmal symptoms in multiple sclerosis.<sup>6</sup> It remains unclear as to how agents such as bromocriptine, that may suppress the immune system, may also suppress paroxysmal symptoms in multiple sclerosis.

Paroxysmal symptoms can be seen in multiple sclerosis. This report of two patients whose paroxysmal symptoms were successfully treated with bromocriptine is encouraging and suggests the need for a clinical trial to investigate the efficacy of bromocriptine in the treatment of paroxysmal symptoms in patients with multiple sclerosis.

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### Onset symptoms of multiple sclerosis

The date of the clinical onset of multiple sclerosis is routinely used for epidemiological studies of incidence and prevalence. To date there are no uniform criteria to be used

for that purpose, making comparisons between various studies difficult. Patients, and often their physicians, may date the onset of the disease to such non-specific symptoms as headaches, backaches, seizures, nervousness, or tremulousness. This article attempts to standardise the method of dating the clinical onset of the disease by establishing a list of definite and possible symptoms. These symptoms can be used only in cases that have been diagnosed as definite or probable multiple sclerosis.<sup>1</sup>

The proposed list of symptoms is based on the author's long clinical experience and that of the multiple sclerosis experts who were consulted.

With rare exceptions the date of symptomatic onset is obtained from the patient's history. In some instances, such as optic or retrobulbar neuritis, transverse myelitis, or acute monoparesis, the patient will almost certainly have sought medical attention at that time, so that documentation might be available. In other situations, the potential relevance of a particular symptom may not have been recognised by either the patient or the physician and may have been ignored or initially ascribed to another cause.

Because epidemiological studies must be based exclusively on patients who have been diagnosed as having definite or probable multiple sclerosis, the symptoms listed here are only a few of the constellation of symptoms and signs that develop later and form the basis for the diagnosis. Because the diagnosis of multiple sclerosis can never be established on the basis of the first episode, information about onset symptoms must be obtained retrospectively, and patients must be carefully questioned about these symptoms to determine their accuracy. The availability of medical records confirming the existence of these symptoms, perhaps when associated with abnormalities of the neurological examination, will greatly increase the value of the data.

The symptoms have been divided into *definite* and *possible* (table). *Definite* symptoms must have been present for a minimum of 24 hours. To be considered as *possible* symptoms of onset, a *definite* symptom must have appeared within two years.

To establish the importance of these symptoms, confirmatory information will have to be obtained by carefully questioning the patients.

Optic/retrobulbar neuritis is almost invariably preceded by pain in or behind the affected eye, associated with a decrease of monocular vision. Clearly, as with all the other symptoms listed, other causes must have been ruled out before the symptom is accepted as signifying the onset of the disease. Bilateral optic/retrobulbar neuritis is unusual in multiple sclerosis and, in this context, must be interpreted with caution.

Acquired monocular colour blindness, oscillopsia, and acute unilateral loss of hearing are extremely rare but, when present, practically pathognomonic for multiple sclerosis.<sup>2</sup> True binocular diplopia can be established only if the double image disappears when closing either eye. Tic douloureux must not be confused with simple facial pain. It is characterised by lightning pains usually occurring in series but each lasting for no more than one or two seconds.

Transverse myelitis, like optic/retrobulbar neuritis, may well be a symptom of an acute postinfectious or postvaccinal encephalomyelitis.