Unusual presentation of more common disease/injury

Stretching the limbs? Tonic spasms in multiple sclerosis

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Summary

A 23-year-old man with a clinically isolated syndrome (right optic neuritis) diagnosed 6 months before, presented with recurrent, brief, painful, stereotyped, involuntary posturing movements of the left upper limb. The neurological examination was otherwise unremarkable (except for right optic atrophy). Intravenous methylprednisolone was initiated; the paroxysms persisted and worsened 7 days later, as the left lower limb and hemiface became affected. A video-EEG showed no epileptiform activity despite the movements. Brain MRI revealed new lesions affecting the right pyramidal tract, contralateral to the clinical manifestations. Valproate was prescribed and the paroxysms were completely resolved 5 days later. Tonic spasms are classically, although infrequently, seen in multiple sclerosis, and may clinically resemble primary paroxysmal dyskinesias or even focal motor epileptic seizures.

BACKGROUND

Apart from tremor, multiple sclerosis (MS) has rarely been associated with movement disorders.¹ Tonic spasms (TS), sometimes referred to as paroxysmal dystonia,^{1 2} are classically but infrequently seen in MS, although other demyelinating disorders have been associated with these phenomena, namely neuromyelitis optica (NMO).^{3 4} Recognising that motor paroxysmal phenomena can be observed in the MS clinical spectrum is important to avoid misdiagnosis, prevent excessive diagnostic testing and carry out the right therapeutic choices.⁵ We report a paradigmatic case illustrating the clinical presentation, differential diagnosis and treatment options for this unusual condition.

CASE PRESENTATION

A 23-year-old Caucasian man presented with recurrent (up to 10/h), brief (<60s), painful, stereotyped, involuntary posturing movements of the left upper limb, with abduction of the arm, mild flexion of the elbow, as well as abduction and athetotic movements of the fingers. This would be immediately followed by a mild extension of the ipsilateral lower limb (video 1). An undefined but clearly unpleasant ('almost painful') sensation in the arm or leg preceded the movements. No triggers could be identified for the paroxysms, which were completely non-kinesigenic in nature (eg, unrelated to the initiation of voluntary movement). Consciousness remained intact throughout the whole event. Neurological examination unveiled no abnormalities, apart from right optic disc atrophy.

Six months before, he had been admitted to the neurological ward due to acute, severe, painless, unilateral visual loss of the right eye (only light perception), accompanied by ipsilateral afferent pupillary defect. The neurological examination was otherwise unremarkable, including optic disc appearance. Thorough inquiry resulted negative for systemic or further neurological symptoms. Medical history and family history did not reveal any relevant

details. He denied alcohol consumption, and no toxic exposure could be identified, including illicit drugs. Routine blood tests were normal, as were the erythrocyte sedimentation rate, C-reactive protein, thyroid function tests, serum vitamin B₁₂ and folic acid. Antinuclear antibodies, anti-dsDNA, antiphospholipid antibodies, anti-SSa and SSb, anti-neutrophil cytoplasmic antibodies, HIV testing and venereal disease research laboratory test were negative. Cerebrospinal fluid (CSF) examination showed mild pleocytosis (22 cells/ μ l), with mild protein elevation (0.63 g/dl) and normal glucose levels. Borrelia, herpes simplex virus 1 and 2, cytomegalovirus and Epstein-Barr virus PCR tests were negative. Oligoclonal bands were present in CSF but not in the serum. NMO-antibody was negative.

Video 1 The left-sided limbs are involuntarily driven into tonic extension, more so the upper limb, accompanied by athetotic movements of the fingers. This is followed by mild dystonic posturing of the left hand as the left lower-limb relaxes back to primary position. Right-sided movement is strictly voluntary.

Brain MRI revealed multiple T2 hyperintense lesions, in the periventricular area and also in the infratentorial region, some with T1 hypointensity, but none displayed gadolinium enhancement. At this point, the diagnosis of a clinically isolated syndrome (optic neuritis) was made, and methylprednisolone (1 g per day, during 5 days) was prescribed, with no clinical response. A course of intravenous immunoglobulin was tried, followed by mild improvement. Disease-modifying therapy had been suggested to the patient, although not yet initiated.

Keeping in mind the patient's background and the clinical features of the new-onset paroxysmal motor manifestations, as well as further diagnostic testing (see Investigations), MS-related TS were diagnosed. Intravenous methylprednisolone was initiated (1 g per day, during 5 days) in the setting of day care hospital, assuming that these could be related to new demyelinating lesions, which proved correct after carrying out the brain MRI (see Investigations). Despite this therapy, the paroxysms persisted and worsened, as the left lower limb and hemiface became affected. The patient was severely distressed and was then admitted to the neurological ward.

INVESTIGATIONS

Routine blood workup was normal. A video-EEG showed no epileptiform activity despite the movements. Brain MRI revealed previously absent white matter lesions, as compared with previous imaging, affecting the right pyramidal tract (cerebral peduncle, internal capsule and corona radiata, the latter displaying gadolinium enhancement), contralateral to the clinical manifestations (figures 1 and 2).

Figure 1 Brain MRI (3 T) displaying one gadolinium-enhancing lesion (T1-weighted contrast-enhanced sequence) in the right semioval centre.

Figure 2 A hyperintense lesion on the right cerebral peduncle (T2-weighted sequence) affecting the right pyramidal tract, contralateral to the TS.

DIFFERENTIAL DIAGNOSIS

Secondary paroxysmal dystonia (MS-associated TS). Focal motor epileptic seizures, primary paroxysmal dystonia and functional dystonia have also been considered.

TREATMENT

Valproate (1000 mg/day intravenously) was prescribed until remission (5 days), followed by the same dose by oral route. Serum levels have been repeatedly shown to be within the therapeutic range.

OUTCOME AND FOLLOW-UP

The frequency of paroxysms decreased after the intravenous perfusion of valproate was started, and complete remission has been observed 5 days later. No recurrences have been noticed after tapering valproate, a few months later. Meanwhile, interferon β -1b has been initiated. MS diagnostic criteria had now been fulfilled at this point.^{6 7}

DISCUSSION

Paroxysmal dyskinesias have been classified under the rubric of movement disorders, although some early reports considered that these could be epileptic phenomena.⁸ Most cases are considered primary, but secondary causes can be found in up to 22% of cases.⁹ An ephaptic activation of the axons within a demyelinated lesion is still the main pathophysiological explanation in MS.¹⁰ It is postulated that the movements can be related to lesions virtually anywhere along the motor pathway¹⁰ but it is probably generated only in sites where the motor fibres are close enough to allow radial spreading of the ectopic impulse (such as the posterior limb of the internal capsule or the cerebral peduncle).¹¹

The inflammatory milieu will probably cause changes in neuronal channel function towards hyperexcitability,² thus initiating the process in demyelinated axons. This suggests that TS might be a sign of disease activity (eg,

relapse), a notion also supported in this case by the findings in brain MRI. Therefore, in this case immunosuppressive therapy was first tried. The initial lack of improvement may reflect ionic channel dysfunction,² which forms the rationale for using antiepileptic drugs in TS, such as carbamazepine or valproate.^{1 2 8} To the best of our knowledge, the use of valproate in TS has been reported only once,¹² but the multiple mechanisms of action of this compound (including the effect on sodium channels) support this choice.¹³

In this case, the paroxysmal and stereotyped nature of the movements brought some diagnostic challenges, namely with regard to a possible epileptogenic origin. Tonic seizures consist of a unilateral or, more frequently, bilateral sustained muscle contraction, lasting >3 s, leading to posturing of the limbs and/or trunk. Consciousness is commonly maintained, at least in the initial moments.^{14–16} These can usually be seen in extra-temporal seizures, mainly in frontal lobe epilepsy, with tonic semiology arising as the seizure spreads to the supplementary sensorimotor area.^{15 16} Most frequently, they occur within a seizure sequence, and other epileptic features support the nature of the paroxysms. Of note, they may be preceded by a somatosensory aura, especially in frontal lobe epilepsy.¹⁶ Curiously, some patients with MS TS report an ‘unpleasant aura’ before the event. This might be related to subtle muscle contractions preceding the spasm, at this point of insufficient magnitude to produce movement.¹¹ They may be confused with epilepsy-related auras. In the present case, the unilateral stereotyped painful manifestations, with athetotic elements, associated with preserved consciousness, a normal ictal video-EEG and no other features suggestive of seizure activity pointed to a non-epileptic disorder.

Primary paroxysmal dystonia would be improbable, based on the age at the onset of the symptoms, and in the absence of a positive family history; moreover, classical triggers could not be identified.^{8 17} No elements in the history or clinical features (namely variability, or reportedly self-induced episodes) were suggestive of functional paroxysmal dyskinesia,^{18 19} so this diagnosis has not been pursued from the start.

Improvement and remission (only) after prescribing an ion channel-acting drug (valproate), and the absence of recurrence after stopping the drug, supports a transient channel dysfunction in the setting of an active demyelinating lesion as the primary pathogenic mechanism.²

Competing interests None.

Patient consent Obtained.

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Learning points

- Tonic spasms are seen in multiple sclerosis (MS) and neuromyelitis optica.
- In MS, the emergence of tonic spasms may represent a form of disease relapse, and may be associated with a new onset of the white matter demyelinating lesions, so an intravenous course of corticosteroids should be considered.
- Antiepileptic drugs (eg, carbamazepine, valproate) remain useful for symptomatic control.
- Differential diagnosis includes focal motor seizures and primary paroxysmal dystonia.

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