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Painful tonic spasms in a patient with neuromyelitis optica spectrum disorder: A case report

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Abstract

Painful tonic spasms initially described in association with multiple sclerosis are actually more common in patients with neuromyelitis optica spectrum disorder. Characterized by fierce pain and tonic posture of limbs, painful tonic spasms are common in patients during the recovery phase after the first episode of myelitis. A 68-year-old man presented with painful tonic spasm after 2 months of diagnosis of neuromyelitis optica spectrum disorder. Eventual use of eslicarbazepine resulted in significant control of spasms. Early recognition of painful tonic spasms and appropriate therapeutic medications can significantly decrease the impact it can have on the quality of life among neuromyelitis optica spectrum disorder patients.

Keywords

Painful tonic spasms, neuromyelitis optica spectrum disorder, myelitis

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Introduction

With primary attack to the spinal cord and optic nerves causing paralysis and blindness, neuromyelitis optica spectrum disorder (NMOSD) is a rare, autoimmune disease of the central nervous system (CNS).[1] Painful tonic spasms (PTSs) or paroxysmal dystonia were initially described in multiple sclerosis (MS)–associated cervical lesions as a part of movement disorder, delineated by fierce pain and tonic posture of limbs.[2,3] However, upcoming literature suggests the presence of PTS is less associated with MS, acute transverse myelitis as compared to neuromyelitis optica (NMO).[4]

Here, we report a case of a 68-year-old man admitted for PTS with NMOSD.

Case presentation

A 68-year-old man was admitted in hospital for acute onset of painful spasms, and burning and tingling sensations in bilateral lower limbs. His medical history was significant for NMOSD 2 months back. The patient, at that time, presented with bilateral optic neuritis, stiffening of bilateral lower limbs, and weakness of bilateral upper limbs and urinary retention. Spine magnetic resonance imaging (MRI) showed long segment altered signal activity in the cervical cord extending from upper border of C2 vertebrae to upper border of C6 vertebrae with patchy short segment in dorsal cord at D2 to D4 and D7 to D8, and also a syrinx formation from cervico-medullary to C2 vertebrae as shown in Figure 1. MRI of the brain revealed age-related small vessel disease and age-related cortical atrophy as shown in Figure 2. Immunofluorescence assay of serum showed positive anti-aquaporin-4 antibody and negative anti–myelin oligodendrocyte glycoprotein (MOG) antibody. Cerebrospinal fluid (CSF) analysis revealed glucose of 66 mg/dL, protein 54.5 mg/dL, total count 12 per mm^3 (monomorphs: 90%, polymorphs: 10%) without significant presence of oligoclonal bands. Renal function test, liver function test, serum angiotensin converting enzyme level, antinuclear antibody level, thyroid function test, and serum vitamin B12

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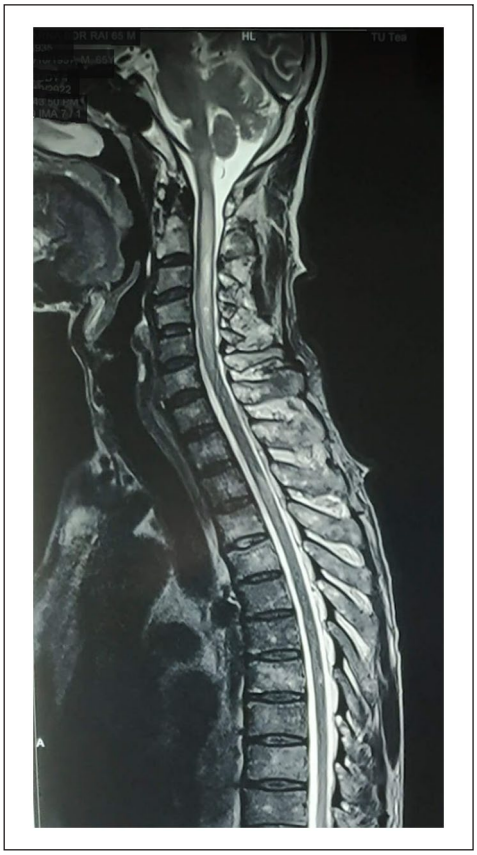

Figure 1. Sagittal T2-weighted image showing high signal intensity in cervical cord with syrinx formation from cervicomedullary to second cervical vertebral body, and patchy short segment altered signal intensity in second to fourth and seventh to eighth thoracic vertebral body levels.

levels were within normal limits. The patient was diagnosed with NMOSD, and intravenous (IV) methylprednisolone 1 gm was given for 5 days after which oral prednisolone and azathioprine were started. His symptoms of limb weakness showed significant response to IV methylprednisolone, and the patient was discharged after 10 days on oral prednisone and azathioprine with residual stiffening of bilateral lower limbs. After 2 months of discharge, the patient presented to the emergency department with paroxysmal, painful flexion and adduction of bilateral lower limbs sparing the upper limbs and face for 20 days which was progressive in duration and frequency. They were mostly spontaneously occurring but also were elicited by passive and voluntary movements of lower limb and trunk. Maximum duration was 10–12 s, and they occurred every 4–6 min. There was no history of hypertension, diabetes mellitus, ischemic cardiac disease, dyslipidemia, other autoimmune diseases, and cardiac arrhythmia. The patient required bilateral support for ambulation. Neurological examination revealed spastic paraparesis, brisk reflexes, and bilateral plantar clonus. Power was in bilateral upper limbs which had remained static since last 2 months. The patient also complained of burning and tingling sensations over bilateral lower limbs without any sensory loss.

General examination revealed blood pressure of 110/70 mm Hg, heart rate of 98 beats per minute, respiratory rate of 16 breaths per minute, temperature of 98.9°F, and oxygen saturation of 96% in room air. Blood investigations showed white blood cell (WBC) count 3800 per mm^3, hemoglobin 11.2 g/dL, and platelets 50,000 per mm^3. Urine investigations were normal. Electroencephalogram (EEG) was normal both during and in between the attacks. Repeat brain imaging and CSF analysis were not performed. Visual evoked potential study showed bilateral delayed P100 latency for both eyes with normal N75-P100 amplitude suggestive of bilateral conduction defect. Patient was then started on oral gabapentin 900 mg three times daily, and tizanidine 4 mg thrice daily was added the next day. Injection diazepam 5 mg thrice daily was added on the third day, and oral baclofen 20 mg three times a day was also added on the fourth day. Finally, after 7 days of admission, eslicarbazepine 200 mg once a day was added after which significant reduction in amplitude and frequency of spasms with eventual disappearance was seen.

Discussion

The cardinal pathogenic process in NMOSD is ascribed to demolition of aquaporin-4 water channels by immunoglobulin G (IgG) autoantibodies.[5] Initially described in MS, PTS is found to be more common among NMOSD patients with about 23% prevalence among these patients and relatively higher age at onset as shown by a study from China.[6,7] PTSs refer to recurring, stereotypical, and localized muscle spasms in the trunk and/or one or more limbs, lasting between 20 s and 3 min, associated with dire pain.[7,8] In our case, these spasms occurred every 4–6 min and lasted for the maximum duration of 10–12 s. The origin of the spasms could be explained by the ephaptic transmission between abnormal demyelinated tracts.[3] Various simulations such as passive or active movements, sensory stimulation, and emotional undulations can induce PTSs but usually have spontaneous onset.[8] PTS of our patient was mostly spontaneous onset but occasionally elicited by active and/or passive movements of limbs.

Exact pathogenesis of PTSs in NMO is not clear till date. The origin of the spasms could be explained by the ephaptic neurological transmission between abnormal demyelinated tracts in the spinal cord.[3] However, as the majority of PTSs occur after 2 weeks of initial myelitis, remyelination of spinal cord rather than demyelination has also been implicated as the origin of these spasms.[4] Our patient presented with PTS after 2 months from initial diagnosis of NMO. A study by Kanamori et al. revealed that tonic spasms associated with NMO have more dire and enfeebling pain as compared to those with MS.[9] Demyelination in MS is caused by direct destruction of oligodendrocytes while NMO is associated with primary astrocytopathy with secondary demyelination, and this difference in pathogenesis could lead to variable expression of pain in these diseases.[10] This may be further elucidated by the fact that NMO often causes transverse myelitis with severe demyelination and

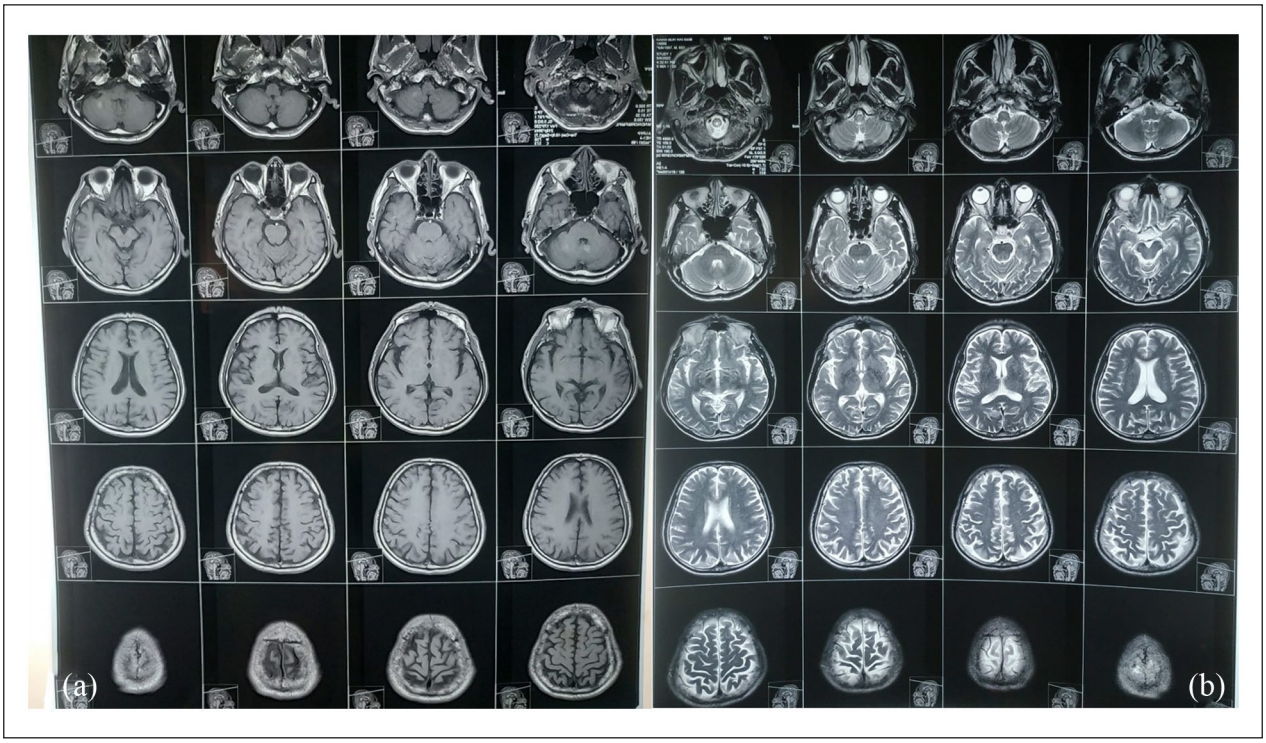

Figure 2. T1-weighted axial (a) and T2-weighted axial (b) brain magnetic resonance imaging showing multiple discrete confluent T2 high signal intensity noted in bilateral periventricular white matter and centrum semiovale along with prominent extra axial cerebrospinal fluid space with proportionate dilatation of ventricles giving impression of age-related small vessel disease and age-related cerebral atrophy.

tissue necrosis due to induction of complement-dependent cytotoxicity elicited by anti-aquaporin 4 antibodies belonging to the IgG1 isotype, opposed to MS.[11] In addition, recruitment of neutrophils and eosinophils into perivascular spaces with ultimate neutrophil degranulation caused by cytokines such as interleukin (IL)-17, IL-8, and granulocyte colony stimulating factor leads to death of astrocyte.[11]

PTS usually tends to be partnered by pruritus which may be because of elicitation of itching sensation as a result of involvement of dorsal horn caused by inflammation of the spinal cord in NMO.[6,12] Although our patient had a burning and tingling sensation in bilateral lower limbs, he had no pruritus. MRI of our patient showed long segment cervical and dorsal cord lesions, which is in line with the fact that PTS is associated with substantial cervicothoracic lesions in MRI.[7]

The initial choice of drug in PTSs is carbamazepine; however, due to its frequent adverse effects such as exfoliative dermatitis or rash, medications such as gabapentin or oxcarbazepine are preferentially given together with drugs such as baclofen, pregabalin, levetiracetam, or others.[6,7,13] In our case, gabapentin and baclofen were used together with diazepam and tizanidine which resulted in only minimal improvement of spasms initially and then addition of eslicarbazepine led to significant improvement without any associated adverse effects. Our patient had decreased hemoglobin, WBC, and platelet counts probably due to the azathioprine therapy he was receiving, and hence we chose not to use carbamazepine when spasms were not improved with initial medications. We then started our patient on low-dose eslicarbazepine due to its comparative low toxicity and better tolerability, after which considerable improvement in the spasms were noticed.

Conclusion

In order to decrease the impact on patients' quality of life, PTS should be recognized early, regarded as a paroxysmal symptom, and treated with appropriate therapeutic medications from various available treatment options.

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Author contributions

Roshan Aryal: Collected all the required case information, reports; reviewed the literature and contributed in writing and editing the manuscript.
Sushan Homagain: Reviewed the literature, and contributed in writing and editing the manuscript.
Suraj Shrestha: Contributed in writing and editing the manuscript.
Bikram Prasad Gajurel: Involved in the patient care team and contributed to the collection of case information.
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Ashish Shrestha: Involved in the patient care team and contributed to the collection of case information.
Sumit Shahi: Involved in the patient care team and contributed to the collection of case information.
Rajeev Ojha: Involved in the patient care team and contributed to the collection of case information, conceptualization, and editing the manuscript.
All authors read and approved the final manuscript.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declaration of conflicting interests

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Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

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