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Case report

Painful tonic spasms and brainstem involvement in a patient with neuromyelitis optica spectrum disorder



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ABSTRACT

Neuromyelitis optica (NMO) is an inflammatory-demyelinating disease of the central nervous system classically characterized by optic neuritis and severe myelitis. New diagnostic criteria defined neuromyelitis optica spectrum disorder as limited forms of NMO or diverse neurologic presentations in the presence of specific aquaporin-4 antibodies. We report the case of a 57-year-old woman admitted in our department for recurrent attacks of optic neuritis, tetraparesis with severe painful tonic spasms of the left limbs and brainstem involvement. Painful tonic spasms have been described as movement disorders associated with multiple sclerosis, but a growing number of reports describe them in cases of NMO.

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1. Introduction

Neuromyelitis optica (NMO) spectrum disorder (NMOSD) is a severe inflammatory and demyelinating disease of the central nervous system. The pathogenic process is attributed to destruction of aquaporin-4 water channels by specific auto-antibodies (NMO-IgG) [1]. NMOSD largely includes limited forms of NMO, such as optic neuritis (ON) and long extensive transverse myelitis, characteristic brain involvement as hypothalamus, corpus callosum, and brainstem lesions or Asian type of optic-spinal multiple sclerosis (MS) [2]. Painful

tonic spasms (PTS) or paroxysmal painful dystonia were first described as movement disorders associated with lesions of the cervical spinal cord, especially in MS [3]. The characteristics of painful tonic spasm are described as paroxysmal episodes lasting seconds or minutes, accompanied by intense pain and tonic postures of the limbs. Ephaptic transmission between abnormal demyelinated tracts could explain the spasms [4]. Recently, the presence of these manifestations seems to be associated to NMO rather than MS or idiopathic acute transverse myelitis [5]. Alongside with myelitis or isolated, brainstem involvement is found in almost 32% of the patients diagnosed with NMOSD [6].

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2. Case report

A 57-year-old woman admitted in our department for acute onset of painful spasms of the left limbs associated with gait and visual disturbances. The medical history is positive for a left ON diagnosed in 2001 that was partially responsive to intravenous (IV) methylprednisolone with normal MRI at that time. The patient was diagnosed at that moment with isolated ON syndrome, but no other diagnostic workup was followed. In December 2014, she presented bilateral decrease of visual acuity in both eyes and progressive numbness on the left arm followed by minor weakness with negative MRI findings for demyelinating disease, although two small unspecific lesions were described in the frontal white matter. Spastic gait and mild spasticity in the lower limbs were noted. A third episode of left ON occurred in April 2015, without any response to IV methylprednisolone and with subsequent amblyopia. After 2 weeks, the patient presented to the emergency room with sudden painful paroxysmal tonic flexion and adduction of the left upper limb, sparing the face, occurring every 5–10 min with duration of maximum 10–20 s. Inconsistently, they involved the left lower limb, were elicited by passive and voluntary movements of the left limbs, but the majority were observed as appearing spontaneously. There was no other history of cardiovascular pathology (arterial hypertension, cardiac arrhythmia, cardiac ischaemic disease, and dyslipidaemia),

autoimmune diseases or psychiatric diseases. Expanded neurologic examination showed spastic tetraparesis with left side predominance, bilateral plantar clonus, brisk reflexes, left eye blindness with absent pupillary reflex, decreased right eye visual acuity and bilateral nystagmus. The patient accused paraesthesia on the left hemibody without any clear sensory loss and accused imperious micturition. The patient needed bilateral assistance while walking. The general examination found a blood pressure of 110/80 mmHg, rhythmic heart beats with 76 bpm, but was otherwise normal. The acute presentation of tonic spasms raised the suspicion of epileptic seizures. The electroencephalogram was normal during and between the attacks, together with other neurologic findings making the epileptic tonic seizures less plausible. Brain MRI revealed several small frontal ischaemic lesions, T2 and FLAIR hyperintensities at the level of the medulla oblongata with bilateral corticospinal tracts involvement and contrast enhancement at the level of brainstem–spinal junction (Fig. 1). The lesion was not considered characteristic for anterior spinal artery infarction. An additional finding was a C5–C6 intervertebral disc protrusion with compression of the spinal cord and subjacent post-compressive ischaemic lesion. Laboratory studies showed positive serum and cerebrospinal fluid (CSF) NMO-IgG, elevated level of serum anticardiolipin antibodies, and slight CSF albumin elevation with borderline pleocytosis represented by lymphocytes. IgG quotient raised the suspicion of intrathecal IgG synthesis and oligoclonal

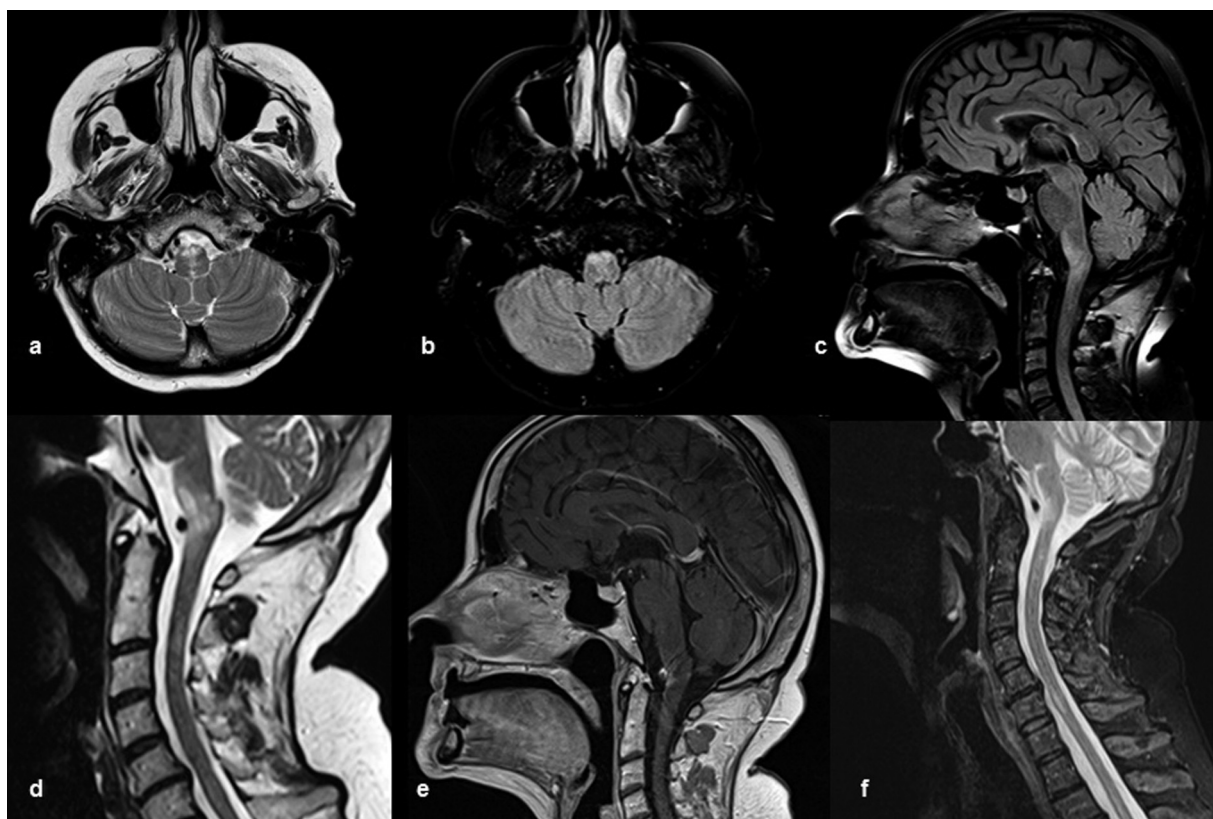


Fig. 1 – (a) T2 axial sequence showing hyperintense lesion of the corticospinal tracts and paramedian structures of the medulla oblongata. (b) FLAIR sequence with lesions at the same level. (c) Sagittal FLAIR with hyperintensities at the level of medulla oblongata and brainstem–spinal junction. (d) Sagittal T2 showing extensive lesion of medulla oblongata. (e) Discrete gadolinium enhancement at the level of brainstem–spinal junction. (f) C5–C6 disc protrusion with subjacent myelopathy.

Table 1 – Serum and CSF parameters.

Test	Patient values	Range values
NMO-IgG (serum)	1:320	<1:10
NMO-IgG (CSF)	1:32	<1:10
IgG serum	824 mg/dl	700–1600 mg/dl
IgG CSF	4.41 mg/dl	<4.0 mg/dl
Oligoclonal bands CSF	Weak detection	Negative
Q-IgG	5.35	<5.0
CSF albumin	0.65 g/L	0.15–0.45 g/L
CSF cellularity	11-small lymphocytes	<10
Anticardiolipin antibodies	>120 U/ml	<10 U/ml
Antinuclear antibodies	Negative	Negative
Antityroperoxidase antibodies	Negative	<5.6 U/ml
Antityroglobulin antibodies	0.64 U/ml	<4.1 U/ml

bands were detected in CSF. All other tests showed normal values (Table 1). The patient fulfilled the criteria for NMOSD with brainstem involvement associated with PTS and compressive cervical myelopathy. IV methylprednisolone was reinitiated 1 g daily for 5 days, followed by azathioprine 50 mg bid with good recovery of the motor deficit and gait, but without any visual improvement of the left eye. PTS were reduced in amplitude and frequency until disappearance after oral administration of carbamazepine 400 mg/day and baclofen 20 mg/day. In August 2015, the patient was treated with IV methylprednisolone followed by plasma exchange with further improvement of symptoms.

3. Discussion

Brainstem involvement, with or without transverse myelitis, is rarely seen in the classic type of NMO, and thereby, it fulfils the extended criteria for NMOSD [2]. Other unspecific lesions are seen in the hypothalamus, thalamus, *splenium* of corpus callosum, but virtually all over the brain although distributed in a different manner from MS. PTS were first described in MS, but recent studies showed a higher incidence in cases with NMO and their presence, associated with ON, should rise the suspicion of NMO [5]. Although our patient presented episodes of ON, the MRI scan until December 2014 showed no specific NMOSD lesions. PTS occurred relatively sudden, consecutive to the lesions in the brainstem corticospinal tracts. PTS must be differentiated from psychogenic attacks, tonic epileptic seizures, paroxysmal kynesigenic dystonia, facio-brachial dystonic seizures of LgI1 autoimmune encephalitis and carpopedal spasm due to hypocalcaemia [5]. In our case, the most important differential diagnosis was represented by focal epilepsy with tonic seizures and brainstem ischaemia caused by upper occlusion of anterior spinal artery. In a recent study, brainstem involvement in NMOSD is present in almost 15% of cases, while other authors find it in up to 32% of the cases [6,7]. The most characteristic brainstem lesion involves *aria postrema*, but in almost 2% of the cases, the involvement of brainstem corticospinal tract may be distinctive for NMO [7]. Carbamazepine is recognized as the first choice for PTS, but other drugs can be considered,

as levetiracetam and gabapentine. Recently, it has been demonstrated that patients with MS and NMO can express positive anticardiolipin antibodies which may not be related to the antiphospholipid syndrome, but can predict a worse outcome regarding the advanced age of the onset [8]. In spite of all these, one must consider that NMO patients can develop other systemic autoimmune diseases such as systemic lupus erythematosus and myasthenia gravis in up to 30% of the cases [9]. The long-term therapy is represented by immunosuppressive therapy, out of which the most used are azathioprine, mycophenolate and rituximab. The relapse treatment is IV methylprednisolone and if it fails to improve the neurological status, plasma exchange must be considered. New studies even suggest combining IV methylprednisolone with plasma exchange in patients with severe disease [10]. In the earliest stages of the disease, the clinical presentation of NMOSD can overlap or mimic other inflammatory diseases of the CNS such as MS. A correct diagnosis (based on criteria, NMO-IgG titre, MRI scan) can prevent further disability through a correct therapeutic management as some immune therapies can aggravate the course of NMO such as interferon or fingolimod [11].

In conclusion, PTS associated with a history of ON may be distinctive for NMO or NMOSD and must be early recognized in order to follow a proper diagnostic workup and therapeutic management.

Conflict of interest

None declared.

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None declared.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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