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Review

Anti-NMDAR encephalitis followed by seropositive neuromyelitis optica spectrum disorder: A case report and literature review

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ABSTRACT

Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory central nervous system syndrome, and encephalitis associated with anti-N-methyl-D-aspartate receptor (NMDAR) antibodies is an autoimmune encephalopathy. A patient with both diseases, separately or simultaneously, is rare as a clinical phenomenon, but cannot be ignored. We report the clinical characteristics and imaging features of a special case with anti-NMDAR encephalitis followed by NMOSD. We subsequently reviewed the English language literature about demyelinating disorders with anti-NMDAR encephalitis. Details of the 34 patients identified are summarized and compared. There may be a connection between anti-NMDAR encephalitis and NMOSD.

Contents

1. Introduction

Encephalitis associated with anti-N-methyl-D-aspartate receptor (NMDAR) antibodies is an autoimmune encephalopathy that often develops as a multi-stage illness including psychosis, memory deficits, seizures, language disintegration, and even a state of unresponsiveness with catatonic features [1]. Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory central nervous system syndrome that is associated with serum aquaporin-4 immunoglobulin G antibodies (AQP4-IgG). The core clinical characteristics in patients with NMOSD include clinical syndromes or MRI findings related to optic nerve, spinal cord, area postrema, other brainstem, diencephalic, or cerebral presentations [2]. It is believed that the pathophysiologies of these two distinct diseases are both based on immune-mediated neuronal dysfunction. Here, we report the case of a 30-year-old man presenting anti-NMDAR encephalitis with subsequent NMOSD.

1.1. Case presentation

A 30-year-old man with no previous medical history was admitted to the Department of Neurology with dizziness and progressive cognitive decline for 1 month (February 2015). One month earlier, he had presented with fever and abdominal pain for 1 week without nausea or vomiting, with recovery after administration of traditional Chinese medicine. At his admission, a neurological examination showed anomic aphasia, memory loss, calculation disability, bilateral hyperreflexia, and a positive palm-jaw reflex. His score on the Mini-Mental State Examination (MMSE) was 9, and that on the Montreal Cognitive Assessment (MoCA) was 2. Brain magnetic resonance imaging (MRI, March 2015) showed multiple T_2 hyperintense signals in the right parietal-occipital and left frontal lobes, temporal lobe, inferior horn of the lateral ventricle, and temporal pole without gadolinium enhancement (Fig. 1). Anal-

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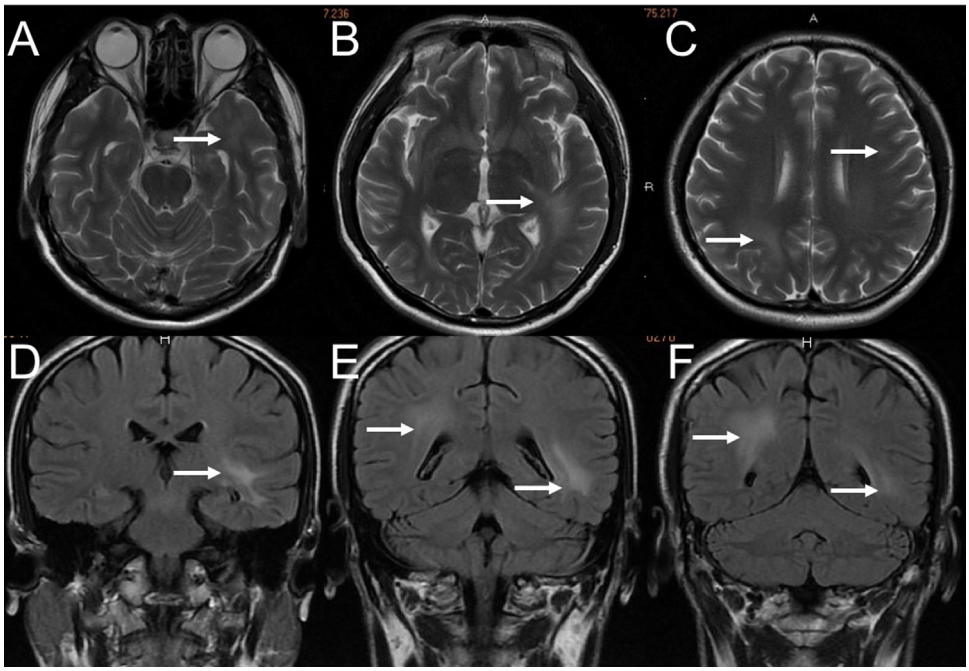

Fig. 1. Brain MRI in March 2015. Brain MRI showing multiple hyperintense T_2 lesions and T_2 FLAIR lesions within the left temporal pole (A) and right parietal-occipital lobe (C, E, F), left temporal lobe (B, D), left inferior horn of the lateral ventricle (B, E, F), and left frontal lobe (C).

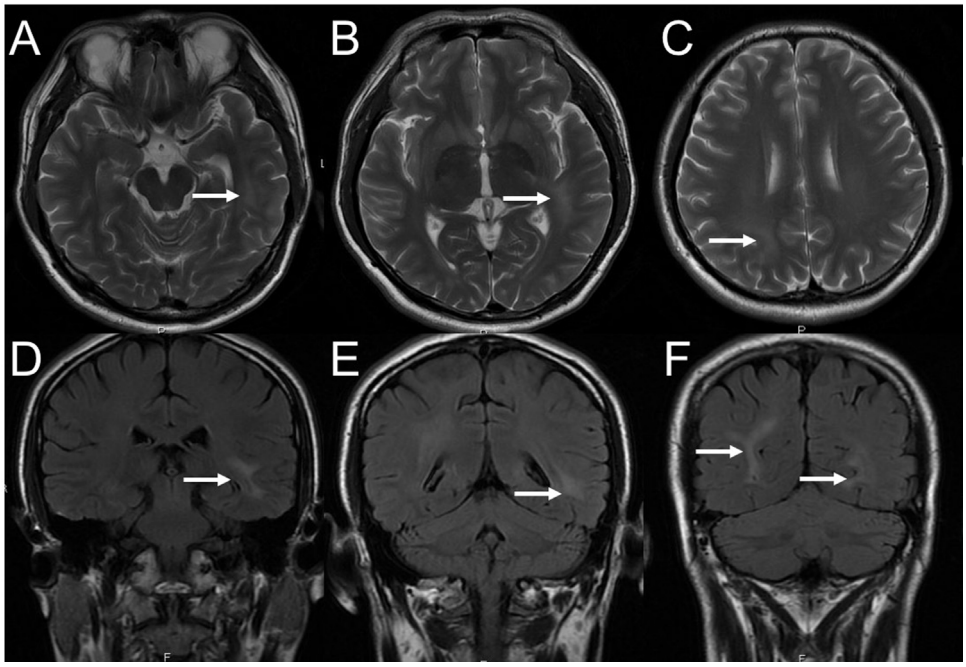

Fig. 2. Brain MRI in April 2015 showing diminution of the hyperintense T_2 and T_2 FLAIR lesion compared with the brain MRI in March 2015.

ysis of the cerebrospinal fluid (CSF) showed a white cell count of 8 cells/mm^3, mildly increased protein concentration (0.465 g/L), and intrathecal IgG synthesis (7.1 mg/dL). His serum and CSF were tested for anti-NMDAR antibodies; the CSF was positive. There was no evidence of a tumor (positron emission tomography scan, serum and CSF tests for classical onconeural antibodies were all normal). Intravenous methylprednisolone (1 g per day during 3 days) was given. Brain MRI follow-up (April 2015) showed diminution of the T_2-weighted hyperintense lesions (Fig. 2). There was a significant improvement in cognitive function (MMSE 15 points, MoCA 10 points).

Then, 10 months later, he developed acute and serious blurred vision in the left eye, with subsequent vision loss. Orbit MRI showed T_2-weighted hyperintense and diffusion-weighted hyperintense images (DWI) with gadolinium enhancement in the left optic nerve (Fig. 3, white arrow). An ophthalmological examination showed delayed P100 wave crests on both sides on visual evoked potentials, especially in the left eye. The test for anti-AQP-4 antibodies was positive in both the serum and CSF, and anti-NMDAR antibodies were positive in CSF and negative in serum. The titer of antinuclear antibodies is 1:100 in serum. Intravenous corticosteroids were ini-

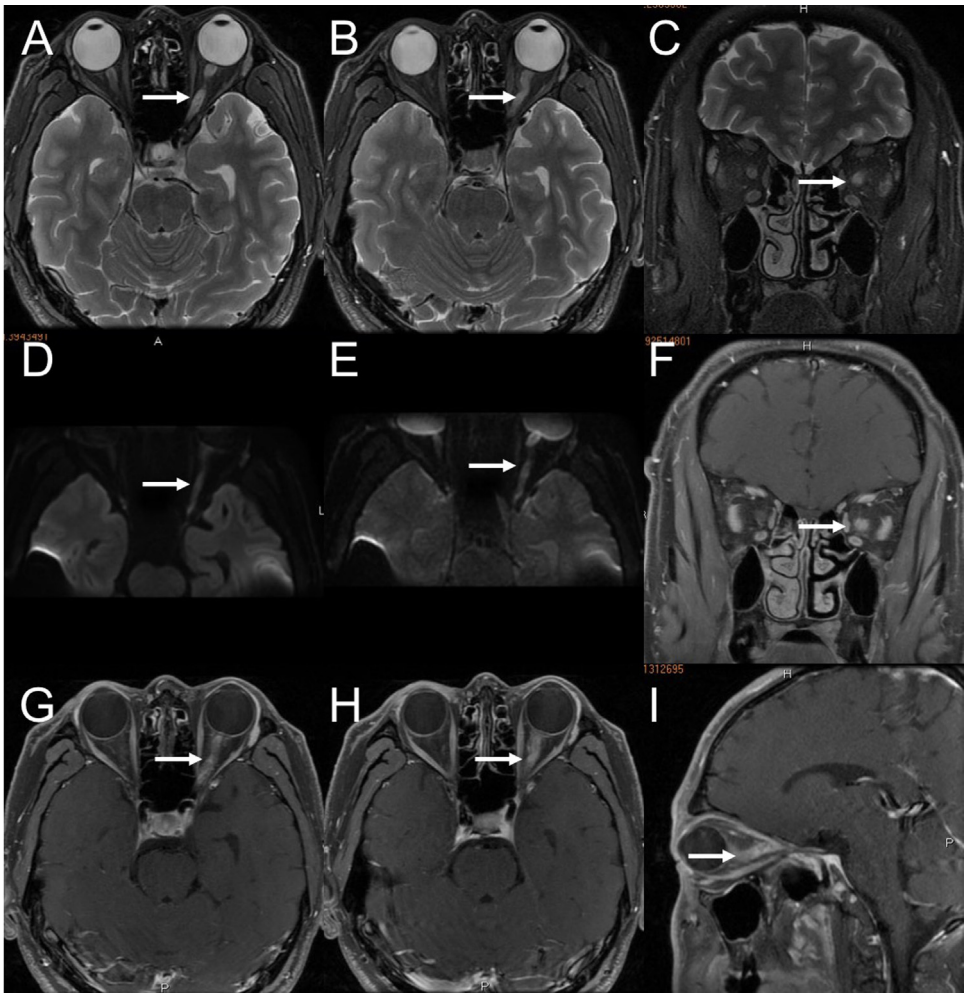

Fig. 3. Brain MRI in Jan 2016 showing hyperintense T_2 lesions (A, B, C) and hyperintense DWI signals (D, E) in the left optic nerve with gadolinium enhancement on a T_1 sequence (F, G, H, I).

tiated, combined with plasma exchange (PLEX). At 24 days after the onset of vision loss, his light sense in the left eye recovered partially.

One month later, after treatment, orbit MRI (March 2016) follow-up showed marked improvement in the lesion in his left optic nerve. The cerebral hyperintense T_2 and DWI lesions had disappeared (Fig. 4).

2. Discussion

Our patient may have presented with two distinct autoimmune diseases sequentially: anti-NMDAR encephalitis and NMOSD. In the first course, the patient presented cognitive dysfunction and positive anti-NMDAR antibodies at onset. Those clinical features are proofs of anti-NMDAR encephalitis [3]. However, there were still some features that did not support diagnosis of the disorder. According to previous report, only 33% patients of anti-NMDAR encephalitis have significant changes in brain MRI [4]. The lesions can occur in the hippocampi, cerebellar or cerebral cortex, fronto-basal and insular regions, basal ganglia, brainstem, or overlaying meninges [1,5,6]. Some of the patients even have demyelinating-like lesions which are usually transient [1]. Thus, the multiple white matter hyperintensities of T_2-weighted sequences in our patient were rare atypical symptoms of anti-NMDAR encephalitis. This leaded us to consider the possibility that the anti-NMDAR encephalitis was coexisting with demyelinating in our patient. Nevertheless, lesions within frontal lobe, parietal-occipital lobe, left temporal lobe, and left hippocampus are also atypical features in patients with NMOSD or multiple sclerosis [2]. And lesions adjacent to lateral ventricle in the inferior temporal lobe is even a red flag for NMOSD diagnosis [2]. Expect the anti-AQP-4 antibody, we had tested all of the autoimmune antibodies. The titer of antinuclear antibodies is 1:100 in serum, and all of other autoimmune antibodies were negative either in serum or CSF. Although there is no sufficient evidence for demyelination occurred simultaneously, the possibility cannot yet be excluded. In the second course, the optic neuritis (ON), combined with AQP-4 antibody positivity in serum and CSF, fulfilled the criteria for NMOSD [2].

A few case reports have described anti-NMDAR encephalitis associated with neuromyelitis optica (NMO) [7–10], myelitis [11,12], or acute demyelinating encephalomyelitis (ADEM) [13]. The cases reported previously, including clinical features, MRI, and CSF/serological findings, and the temporal relationship between anti-NMDAR encephalitis and demyelination syndrome episodes (DSEs), are summarized in Tables 1–3. We cataloged these cases by their initial appearances. Table 1 describes seven patients who presented with anti-NMDAR encephalitis at onset followed by demyelination episodes. Table 2 describes nine patients with symptoms of demyelination followed by anti-NMDAR encephalitis. Table 3 describes eighteen patients with anti-NMDAR encephalitis that occurred simultaneously with demyelination episodes. As for our patient presented above, the only thing we can confirmed is that the patient had anti-NMDAR encephalitis at the initial episode

Table 1
Clinical features of patients in whom anti-NMDAR encephalitis occurred at onset.

Source	Sex	Age of onset	Interval time (mo.)	Clinical characters of anti-NMDAR encephalitis at onset			Clinical characters of subsequent neurological event				
				Clinical features	MRI	NMDAR ab titer	Clinical features	MRI	OB	AQP-4 ab titer	NMDAR ab titer
Case presented in this article	M	30	10	Anomic aphasia, memory loss, calculation disability	Multiple T2 hyperintense signals in the right parietal-occipital and left frontal lobes, temporal lobe, inferior horn of the lateral ventricle, and hippocampus without Gb enhancement	CSF (+) S (+)	Acute and serious blurred vision in the left eye, with subsequent vision loss	T2-weighted and DWI hyperintense images with Gb enhancement in the left optic nerve	–	CSF (+) S (+)	CSF (+) S (−)
Kruer et al.	F	15	1	Encephalopathy, hypoventilation, dyskinesias, and seizures	A contrast-enhancing periatrial lesion	n.d.	More than 10 relapses with LETM and ON	Multifocal, contrast-enhancing gray and white matter lesions in brain and spine cord	+	CSF (−) S (−)	CSF (+) S (−)
Zoccarato et al.	F	50	5	Subacute short-term memory loss, confusion, and behavioral changes	T2-weighted, hyper-intense in medial temporal cortex	n.d.	R1 (5 mo.): drowsiness, cervical itching, impaired gait, paraplegia; R2 (14 mo.): left ON; R3 (17 mo.): weakness of the right limbs	Multiple T2- weighted hyper-intense lesions in the pons, hypothalamus, medulla oblongata, and cervical spine	+	CSF (−) S (1:100)	CSF (+) S (1:32)
Titulaer et al.	F	48	18	Behavioral dysfunction, seizures, memory deficit and mutism, bradycardia	Few scattered small increased T2/FLAIR signals	CSF (+) S (+)	Diplopia, abducens paresis; vertigo, diplopia	New increase of T2/FLAIR signal in pontomedullary junction with abnormal DWI signal, additional T2/FLAIR abnormalities in brachium pontis, putamen, and subcortical white matter with Gd enhancement	+	CSF (n.a.) S (−)	n.a.
	M	17	3	Behavioral dysfunction, insomnia, mutism, catatonia, dyskinesias	T2/FLAIR increased signal in right frontal/temporal lobes and left parietal/temporal region	CSF (+) S (n.d.)	Facial palsy, ataxia, ophthalmoplegia	Increased T2/FLAIR signals in internal capsula, pons (facial colliculus) and chiasm; additional brainstem and cerebellar increased T2/FLAIR in Th3 and Th9–10	–	CSF (−) S (n.d.)	n.a.
	M	34	3	Behavioral and speech dysfunction, orofacial dyskinesias, intubated	Increased T2/FLAIR signal in right cerebral peduncle	CSF (+) S (−)	R1: Diplopia, thoracic myelitis; R2: disorientation, fever	Several areas of increased T2/FLAIR signal: cerebellum, pons, periventricular with Gd enhancement	–	CSF (n.d.) S (−)	n.a.
	M	29	36	Seizures, dysarthria, hemiparesis	Frontotemporal increased T2/FLAIR signal with Gd enhancement	CSF (+) S (n.d.)	Hemiparesis, hypesthesia; later: ON, abnormal behavior, speech, and memory	Bilateral increased STIR signal and Gd enhancement of the optic nerve	–	CSF (−) S (n.d.)	n.a.

Ab = antibodies; AQP-4 = aquaporin-4; CSF = cerebrospinal fluid; DSE = demyelination syndrome episode; DWI = diffusion weighted image; F = female; FLAIR = fluid-attenuated inversion recovery; Gd = gadolinium; LETM = longitudinally extensive transverse myelitis; mo. = months; M = male; MRI = magnetic resonance imaging; n.a. = not available; n.d. = not done; NMDAR = N-methyl-D-aspartate receptor; OB = oligoclonal bands; ON = Optic neuritis; S = serum.

Table 2
Clinical features of patients in whom symptoms of demyelination occurred at onset.

Source	Sex	Age of onset	Interval time (mo.)	Clinical characters of DSE				Clinical characters of subsequent anti-NMDAR encephalitis		
				Clinical features	MRI	OB	AQP-4 ab titer	Clinical features	MRI	NMDAR ab titer
Titulaer et al.	F	8	84	Bilateral ON, LETM	n.a.	+	CSF (1:160) S (1:10,240)	Fluctuating level of consciousness, seizures, paranoia, dystonia, and orofacial dyskinesias, coma, autonomic symptoms, spasticity	Multifocal increased T2 signal in putamen, internal capsula, subcortical insula, hippocampi, and temporal regions, bilateral optical and cervical atrophy	CSF (+) S (+)
	F	13	11	Recurrent LETM	T2/FLAIR increased signal from medulla to C5	n.d.	CSF (1:160) S (n.d.)	Seizures, altered behavior, memory and speech dysfunction	Transient mild FLAIR increased signal	CSF (+) S (n.d.)
	F	37	30	Recurrent ON	n.d.	+	CSF (1:320) S (1:10,240)	Depression, behavioral, memory, and sleep dysfunction, autonomic symptoms	Several areas of increased T2/FLAIR signal in right caudate, right temporal lobe and frontal lobes	CSF (+) S (−)
	F	55	38	n.a.	White matter lesions NMOSD in brain and spinal cord	n.d.	CSF (−) S (1:20)	Seizures, blurry vision, encephalopathy; behavioral, memory, speech, and sleep disorder, lower level of consciousness	Unchanged	CSF (+) S (n.d.)
	F	27	48	R1: hemihypesthesia; R2: diplopia; R3: hemiparesis, dysphagia; R4: numbness, involuntary movements; R5: aphasia and dysphagia	Multiple areas of increased T2/FLAIR signal in midbrain and pons; new lesion in midbrain; new lesions in left parietal lobe and medulla	+	CSF (n.d.) S (−)	Confusion, behavioral dysfunction, stupor, orofacial dyskinesias [between R3 and 4]	Increased FLAIR signal in cortical area of right frontal lobe	CSF (+) S (n.d.)
	M	10	96	Hemiparesis, bilateral visual impairment	Multiple areas of increased T2/FLAIR signal in white matter of parietal, temporal, occipital lobes, focal Gd enhancement	–	CSF (n.d.) S (−)	Seizures, fever [multiple episodes]	Increased T2/FLAIR signal in the gray matter of frontal lobes	CSF (+) S (−)
	M	38	22	R1: Hemidysesthesia, ptosis, diplopia, convergence deficit, absent light reflex; R2: diplopia	T2/FLAIR abnormalities in thalamus, hypothalamus, and mesencephalon, slight Gd enhancement	–	CSF (n.d.) S (−)	Character change, psychosis, RBD; mild memory change, severe psychosis; cognitive changes, mild psychosis	T2/FLAIR lesion in right parietal cortex and temporal subcortical white matter	CSF (+) S (−)
Hacohen et al.	M	18	13	Onset: Brainstem encephalitis R (day 60): encephalopathy, psychiatric, movement disorder, dysautonomia	New midbrain, mesial temporal lobe, and posterior periventricular diffuse white matter changes	n.d.	CSF (−) S (−)	Encephalopathy, psychiatric, movement disorder, dysautonomia	Brainstem signal change	CSF (n.d.) S (1:500)
	F	10	60	Onset: Brainstem encephalitis R1 (day 21): encephalopathy, seizures, movement disorder, hyperpyrexia	Onset: no imaging, R1: widespread cortical signal change	n.d.	CSF (−) S (−)	Encephalopathy, worsening seizures	Diffuse posterior white matter changes	S (1:1000) CSF (1:20)

Ab = antibodies; AQP4 = aquaporin-4; CSF = cerebrospinal fluid; DSE = demyelination syndrome episode; DWI = diffusion weighted image; F = female; FLAIR = fluid-attenuated inversion recovery; Gd = gadolinium; LETM = longitudinally extensive transverse myelitis; mo. = months; M = male; MRI = magnetic resonance imaging; n.a. = not available; n.d. = not done; NMDAR = N-methyl-D-aspartate receptor; OB = oligoclonal bands; ON = optic neuritis; RBD = rapid eye movement sleep behavioral disorder; S = serum.

Table 3
Clinical features of patients in whom anti-NMDAR encephalitis and demyelination episodes occurred simultaneously.

Source	Sex	Age of onset	Clinical features	MRI brain/spinal cord	CSF WBC/mm^3	OB	NMDAR ab titer	AQP4 ab titer
Pennington et al.	F	35	Decreased appreciation of light touch and pin prick up to L1 level, with impaired distal proprioception, memory and concentration problems, low mood, and sleep talking and walking, complex partial seizures, secondary generalized seizure, emotional lability, hostility and impaired memory and concentration	A few focal T2 hyper-intense lesions perventricularly and in the adjacent white matter; multiple small focal and larger segmental areas of high signal on the T2-weighted scans within the cord below C5	11	+	CSF (2) S (+)	n.a.
Outteryck et al.	F	65	Walking difficulties related to moderate paraparesis, moderate superficial and deep sensory dysfunction of the lower limbs and urinary retention, slight dysfunction of mental processing	T2 hyperin-tensities within the insular regions, medial temporal lobes and thalamus associated with Gd enhancement of the meninges and ventricles; longitudinally extensive myelitis from C5 to T10 with Gd enhancement	53	n.a.	CSF (+) S (+)	CSF (n.a.) S (−)
Lekoubou et al.	F	34	Recurrent psychomotor agitation, incoherent speech, loss of judgment, insomnia and aggressiveness associated with progressive walking difficulties	Widespread and multifocal white matter lesions, a right frontal Gb enhancing lesion; cervical and lumbar extensive myelitis on T2-weighted imaging	19	+	CSF (+) S (n.a.)	n.a.
Titulaer et al.	F	37	Fluctuating level of consciousness, change of behavior	Periventricular [3th and 4th ventricle] increased FLAIR abnormalities	76	–	CSF (+) S (−)	CSF (>2) S (1:80)
	F	32	Psychiatric symptoms, depression, irritability, apathy, behavioral changes, attention and language deficit, dysphasia, and mild distal myoclonus	Multiple increased T2 signals in cerebellar peduncles, pons, midbrain, pyramidal tracts, thalamus, internal capsules, and lenticular nuclei, with 2 small periventricular areas of Gd enhancement/increased T2 signals	<5	+	CSF (+) S (n.d.)	CSF (−) S (20)
	F	16	Headache, diplopia, anisocoria, vertigo, ataxia, intention tremor, memory deficit, anxiety, depression, insomnia; Later hemihypesthesia, dyskinesias, and dysarthria; afterward hemiballismus, hemiparesis, vomiting and flushing	Multiple increased T2/FLAIR signals in the right mesotemporal lobe, cerebellum and thalamus/normal	5	–	CSF (+) S (−)	CSF (−) S (20)
	F	32	Memory and behavioral dysfunction, depression	Increased FLAIR signal in hippocampi and caudate nuclei	<5	+	CSF (+) S (+)	CSF (−) S (40)
	F	47	Speech disturbance, behavioral change, orofacial dyskinesias, decreased level of consciousness, seizures, tachycardia, and hypoventilation	Multifocal periventricular, subcortical white matter T2/FLAIR increased signal	25	n.d.	CSF (+) S (+)	CSF (n.d.) S (20)
	F	4	Seizures, hemiparesis; later: mutism, chorea, orofacial dyskinesias	Multifocal areas of T2/FLAIR increased signal: periventricular, basal ganglia, cerebellum, and pons	<5	+	CSF (+) S (n.d.)	CSF (n.d.) S (−)
	M	6	Irritability, personality change, hypersomnia	Multifocal areas of increased FLAIR signal: cortex, subcortex, thalamus, basal ganglia, cerebellum, brainstem, cervical, thoracic cord, with small areas of Gd enhancement	43	+	CSF (+) S (−)	CSF (n.d.) S (−)
	F	13	Confusion, behavioral dysfunction, stupor, orofacial dyskinesias	Multifocal areas of increased FLAIR signal: cortex, subcortex, thalamus, basal ganglia, cerebellum, brainstem, cervical, thoracic cord, with small areas of Gd enhancement	18	–	CSF (+) S (+)	CSF (n.d.) S (−)
	F	18	Behavioral and speech dysfunction, orofacial dyskinesias, intubated	Single area of “demyelination” in the right frontal region [discovered 2 months before onset encephalitis]	40	+	CSF (+) S (+)	CSF (n.d.) S (−)

Table 3 (*Continued*)

Source	Sex	Age of onset	Clinical features	MRI brain/spinal cord	CSF WBC/mm^3	OB	NMDAR ab titer	AQP4 ab titer
	M	19	Recurrent seizures, fever	Recurrent left parietal T2/FLAIR abnormality with Gd enhancement	36	+	CSF (+) S (n.a.)	CSF (−) S (n.a.)
	F	62	Seizures, dysarthria hemiparesis.	Extensive areas of increased T2/FLAIR signal in temporal and frontal lobes	88	n.d.	CSF (+) S (n.a.)	CSF (−) S (n.a.)
Hacohen et al.	M	5	Brainstem encephalitis	Multiple cranial nerve enhancement	n.a.	–	CSF (1:1000) S (1:20)	–
	F	11	Hyperventilation, dizziness, and double vision	Numerous lesions in subcortical white matter and body of the corpus callosum, no significant change on repeat imaging	n.a.	–	S (1:100) CSF (n.d.)	–
	F	6	Bilateral ON	Normal	n.a.	n.d.	CSF (n.d.) S (1:150)	–
	M	9	Bilateral ON	Normal	n.a.	n.d.	CSF (n.d.) S (1:150)	–

Ab = antibodies; AQP4 = aquaporin-4; CSF = cerebrospinal fluid; DSE = demyelination syndrome episode; DWI = diffusion weighted image; F = female; FLAIR = fluid-attenuated inversion recovery; Gd = gadolinium; LETM = longitudinally extensive transverse myelitis; mo. = months; M = male; MRI = magnetic resonance imaging; n.a. = not available; n.d. = not done; NMDAR = N-methyl-D-aspartate receptor; OB = oligoclonal bands; ON = Optic neuritis; S = serum.

with or without demyelinating process simultaneously. Taking into account all the symptoms, we preferred to classified the patient into Table 1, not into Table 3.

Kruer et al. and Zoccarato et al. separately described two females who initially presented with anti-NMDAR encephalopathy with subsequent ON or a course of longitudinally extensive transverse myelitis (LETM) in addition to multifocal, contrast-enhancing gray and white matter lesions. AQP-4 antibody testing was positive in Zoccarato's patient, but negative in Kruer's patient [7,9]. Titulaer et al. reported 23 patients with anti-NMDAR encephalitis with overlapping clinical syndromes of NMOSD and/or MRI features of demyelinating disorders. Of these, 12 patients developed anti-NMDAR encephalitis and demyelination episodes at separate times, eight had infratentorial or spinal cord abnormalities, and four had ON [8].

We summarized seven patients who occurred anti-NMDAR encephalitis followed by demyelinating episode in Table 1. Besides the areas of lesion reported previously, they had shown multiple lesions in brain MRI, including parietal-occipital lesion, periatrial lesion with enhancement, periventricular lesion with enhancement, right cerebral peduncle lesion. And hyper-intensity in the medial temporal cortex was only detected in three of the seven patients. These atypical lesions which are rarely detected in patient with anti-NMDAR encephalitis may be a prompt of overlapping or subsequent demyelination episode.

In a study by Titulaer et al., seven patients had demyelination symptoms that preceded anti-NMDAR encephalitis. Moreover, Hacohen et al. also described two pediatric patients with demyelination episodes followed by neurologic events associated with the anti-NMDAR antibody (Table 2) [14]. Of the abovementioned

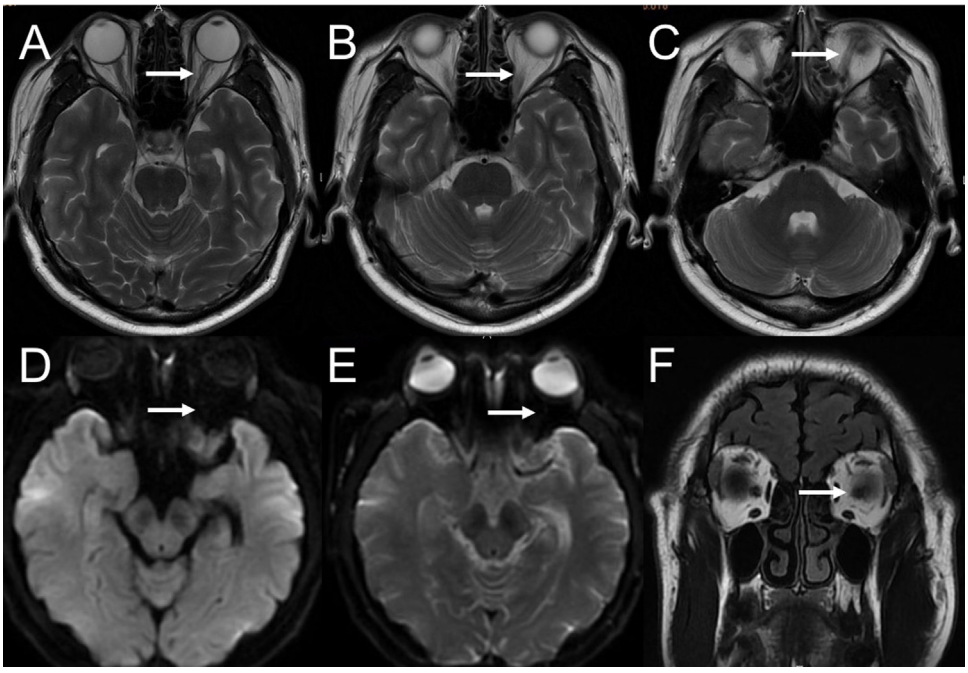

Fig. 4. Brain MRI in March 2016 showing that the optic nerve hyperintense T_2 and DWI lesions had resolved.

patients, four were positive for AQP-4 antibodies and were diagnosed as definite NMOSD.

Pennington et al. and Outteryck et al. separately reported two females presented as myelitis with typical features of anti-NMDAR encephalitis [11,12]. Similarly, Lekoubou et al. reported a female with anti-NMDAR encephalitis whose MRI features were suggestive of acute disseminated encephalomyelitis (ADEM) [13]. In the study by Titulaer et al., 11 patients had anti-NMDAR encephalitis occurring simultaneously with a demyelination-like syndrome episode and/or MRI abnormalities in which five patients also had AQP-4 antibodies, but none experienced ON [8]. The study by Hacohen et al. reported four patients with anti-NMDAR antibody in serum and CSF, whose MRI showed demyelination changes [14] (Table 3).

Considering these reports and our patient, we suggest that there may be a connection between anti-NMDAR encephalitis and NMOSD. According to previous report, the mechanism underlies the anti-NMDAR encephalitis is that NMDAR antibodies mediate capping and internalization of surface NMDARs by Fab fragments, and the subsequent crosslinking with anti-Fab antibodies cause a selective decrease in NMDAR surface density and synaptic localization [15]. NMDA receptors are present on various cells, such as neurons, oligodendrocytes, and astrocytes, at many excitatory glutamate synapses in the central nervous system [16]. In NMOSD, AQP4-antibody-mediated complement-dependent cytotoxicity (CDC) may play a major role in the pathogenesis [17]. These two diseases may have immunological influences on patients leading to susceptibility to other autoimmune-associated disorders. Titulaer et al. suggested that patients with NMDAR encephalitis were more prone to having AQP-4 antibodies than the general population [8]. Several reports have shown that 30–75% of patients with NMO presented with clinical and serological findings of coexisting autoimmune conditions [18–21].

To our knowledge, our patient is the first reported male patient with anti-NMDAR encephalitis followed by seropositive NMOSD. Based on the data we summarized in Tables 1–3, the male:female distribution was 2:7 in patients who suffered from anti-NMDAR encephalitis and demyelinating episode simultaneously. According to previous reports, the male:female ratio for NMOSD is 1:8–9 [22], and about 80% of patients with anti-NMDAR encephalitis are women [1]. Our data suggest that patients with anti-NMDAR encephalitis associated with demyelination are predominantly female, as are patients with NMOSD or anti-NMDAR encephalitis.

3. Conclusions

Our patient suffered from anti-NMDAR encephalitis followed by NMOSD, as evidenced by NMDAR antibodies and AQP-4 IgG in serum and CSF. After reviewing case reports about the two diseases, we suggest that there may be a connection between anti-NMDAR encephalitis and NMOSD.

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