

Case Report

# Dystonic Seizures and Intense Hyperperfusion of the Basal Ganglia in a Patient with Anti-N-Methyl-D-Aspartate Receptor Encephalitis

Hideyuki Matsumoto<sup>a</sup> Hideji Hashida<sup>a</sup> Yukitoshi Takahashi<sup>b</sup>

<sup>a</sup>Department of Neurology, Japanese Red Cross Medical Center, Tokyo, Japan;

<sup>b</sup>Department of Pediatrics, National Epilepsy Center, Shizuoka Institute of Epilepsy and Neurological Disorders, Shizuoka, Japan

## Keywords

Anti-N-methyl-D-aspartate receptor encephalitis · Acute juvenile female non-herpetic encephalitis · Dystonic seizure · Dystonia · Basal ganglia · Single-photon emission computed tomography

## Abstract

This report describes a rare case presenting with dystonic seizures due to anti-N-methyl-D-aspartate (NMDA) receptor encephalitis. The patient was an 18-year-old woman with repeated right-dominant dystonic seizures even under sedation. Single-photon emission computed tomography (SPECT) showed intense hyperperfusion of the caudate nuclei, putamen, globus pallidus, thalamus, and insula on the left side, suggesting encephalitis. Antibodies against NMDA receptors were detected in the sera and cerebrospinal fluids. Immune-mediated treatments were administered. Three months later, the dystonic seizures disappeared. We diagnosed her with anti-NMDA receptor encephalitis. SPECT suggested that the main region of encephalitis was the basal ganglia. Therefore, we propose that the patient's dystonic seizures may originate from the insula and be generated by intense hyperactivity of the basal ganglia.

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## Introduction

In 1997, Nishimura and co-workers reported 5 young adult female patients with acute non-herpetic encephalitis in Japan. The patients presented with specific clinical features such as severe prolonged coma, status epilepticus, and good prognosis [1]. Later, Kamei reported 11 similar patients in whom anti-glutamate receptor (GluR) antibodies were frequently detected. Since all of the patients were young adult women, Kamei proposed a new spectrum of disorders named acute juvenile female non-herpetic encephalitis (AJFNHE) [1]. In 2007, however, Dalmau and co-workers reported autoimmune encephalitis associated with antibodies against N-methyl-D-aspartate (NMDA) receptors, which they called anti-NMDA receptor encephalitis [2]. After anti-NMDA receptor encephalitis was proposed, anti-NMDA receptor antibody was analyzed in 4 patients with AJFNHE and detected in all 4 [3]. Thereafter, a nationwide survey in Japan revealed that the clinical features of AJFNHE are almost identical to those of anti-NMDA receptor encephalitis [1]. Although the co-identity of the two types of encephalitis remains controversial [4, 5], AJFNHE and anti-NMDA receptor encephalitis are currently assumed to be the same or nearly the same condition. Generally, in anti-NMDA receptor encephalitis, anti-NMDA receptor antibodies and anti-GluR antibodies such as anti-GluR $\epsilon$ 2 antibody and anti-GluR $\zeta$ 1 antibody can be simultaneously detected in the sera and cerebrospinal fluids [5–7].

Here, we describe a rare case of anti-NMDA receptor encephalitis presenting with dystonic seizures. In our case, intense hyperperfusion of the basal ganglia was observed on single-photon emission computed tomography (SPECT). On the basis of the SPECT findings, we propose that the patient's dystonic seizures may originate from the insula and be generated by intense hyperactivity of the basal ganglia.

## Case Report

The patient was an 18-year-old woman whose initial symptoms were fever and headache. Ten days later, she presented with rapid-onset mutism. With her mother, she visited our clinic and entered our hospital. Her past, family, and life histories were unremarkable.

On admission, her blood pressure was 100/70 Torr, with a pulse of 100 beats/min and a body temperature of 37.3°C. Neurological examinations revealed disorientation, mutism, and oral automatism. After intravenous injection of diazepam 10 mg, her symptoms temporarily diminished, suggesting aphasic seizure. Routine blood examinations were almost normal. Liquor examinations showed slightly increased cells (38 cells/mm<sup>3</sup>, only monocytes), increased protein (64 mg/dL), and increased immunoglobulin G index (0.81). Liquor polymerase chain reaction of herpes simplex virus was negative. Brain magnetic resonance imaging (MRI) showed no abnormal findings. Body computed topography (CT) and pelvic MRI did not show any tumors, including teratoma. Electroencephalography (EEG) showed diffuse slow waves on basic activity.

On the second day from admission, the patient started to behave abnormally, exhibiting agitation and irritability, crying, and standing up abruptly. Although we started several anti-epileptic drugs such as carbamazepine, levetiracetam, and lamotrigine in an attempt to suppress her abnormal behavior, her symptoms deteriorated. On the eighth day, in a further attempt to suppress her abnormal behavior, she was intubated in the intensive care unit and intravenous anesthetics were administered. Despite the administration of intravenous anesthetics, a combination of midazolam and propofol, she started exhibiting repeated right-

dominant dystonic seizures as follows. First, the right wrist and elbow were flexed and elevated. Second, the neck was rotated to the left side. Third, the neck was returned to the original position. Fourth, the right arm was returned to the original position. A series of these faciobrachial dystonic seizures continued for approximately 30 s, with the seizures endlessly repeating separated by an interval of a few seconds. Her face was strongly grimaced during the seizures. Oral automatism appeared in the interval.

After thiopental was administered as a replacement for midazolam and propofol, her dystonic seizures were completely suppressed. SPECT with N-isopropyl (I-123)-iodoamphetamine (IMP) under sedation revealed intense hyperperfusion of the caudate nuclei, putamen, globus pallidus, thalamus, and insula on the left side in addition to mild hyperperfusion of the bilateral frontotemporal lobes (Fig. 1). EEG under sedation showed intermittent sharp waves on the left side in addition to diffuse slow waves. On the basis of the patient's age, gender, abnormal behavior, dystonic seizures, cerebrospinal fluid pleocytosis, EEG findings, and SPECT findings, we considered the possibility of autoimmune encephalitis, specifically, anti-NMDA receptor encephalitis. We tried various types of immune-mediated treatments such as steroid pulse therapy, intravenous immunoglobulin, plasma exchange, and rituximab. Whenever the patient's thiopental dosage was reduced, however, the dystonic seizures reappeared. During treatment, it was found that the patient's pretreatment sera and cerebrospinal fluids tested positive for anti-GluR $\epsilon$ 2 and anti-GluR $\zeta$ 1 antibodies. We tentatively diagnosed her with autoimmune encephalitis associated with anti-GluR antibodies, i.e., AJFNHE. Three months after her admission, the dystonic seizures disappeared even in the absence of sedation. Temporarily, she had several episodes of generalized convulsive seizures, although the seizures were well controlled with anti-epileptic drugs. Subsequently, she recovered with only rehabilitation, and EEG was also normalized. Five months after her admission, she was discharged without any medications or sequelae.

After discharge, it was found that the patient's pretreatment sera and cerebrospinal fluids tested positive for anti-NMDA receptor antibodies. Therefore, we diagnosed her with anti-NMDA receptor encephalitis. During the 2 years following disease onset, we repeated body CT and pelvic MRI to search for underlying tumors, although none were identified. Anti-leucine-rich glioma-inactivated 1 (LGI1) antibody was not examined.

## Discussion

Our young female patient acutely exhibited several clinical symptoms such as prodromal symptoms, disorientation, aphasic seizure-like episodes, abnormal behaviors, dystonic seizures, and generalized convulsive seizures. The clinical symptoms in our case are quite compatible with those of anti-NMDA receptor encephalitis. Dystonic seizures can be categorized into dyskinesia, involuntary movements, stereotypies, seizures, and others, as seen in previous papers on anti-NMDA receptor encephalitis. However, dystonic seizures are not well described in any previous publications. In addition, intense hyperperfusion of the basal ganglia on SPECT is also a unique finding. We cannot determine if the SPECT findings are a cause or a consequence of the dystonic seizures. However, we consider that this patient's dystonic seizures are strongly related to her SPECT findings, because the basal ganglia must have contributed to the pathophysiology of dystonia [8].

With regard to the dystonic seizures, faciobrachial dystonic seizures in anti-LGI1 antibody-associated limbic encephalitis are well known. However, faciobrachial dystonic seizures characteristically precede limbic encephalitis. In addition, faciobrachial dystonic sei-

zures are typically brief (lasting less than 3 s, but occasionally more than 10 s), frequent (50 times per day), and patterned movements [9, 10]. Therefore, the dystonic seizures in our case seem to differ from the faciobrachial dystonic seizures in anti-LGI1 antibody-associated limbic encephalitis.

Recently, the term “dystonic-like seizures” has been used for a certain type of insular epilepsy [10]. Here, faciobrachial dystonic-like seizures in insular epilepsy seem to be analogous to the dystonic seizures in our case, because insular epilepsy shows a similar duration, from 30 to 60 s [10]. Since the insula is part of the limbic system, insular involvement is also possible in anti-NMDA receptor encephalitis. Actually, in our case, intense hyperperfusion on SPECT was observed in both the basal ganglia and insula. Therefore, the dystonic seizures in our case may originate from the insula.

Several papers have reported SPECT findings for similar cases of anti-NMDA receptor encephalitis and autoimmune encephalitis associated with anti-GluR antibodies. Hyperperfusion on SPECT has been observed in the frontal lobe [3, 11, 12, 14, 15], temporal lobe [3, 12–15], occipital lobe [13, 15], insula [13, 15], and basal ganglia [11, 14, 15]. Hypoperfusion, in contrast, has been observed in the frontal lobe [3, 15], temporal lobe [15], parietal lobe [15], insula [15], brainstem [15], and cerebellum [15]. Hyperperfusion is often observed in the acute phase, whereas hypoperfusion is often observed during the recovery phase. However, intense hyperperfusion of the basal ganglia on SPECT as seen in our case has not been previously reported. Since hyperperfusion of the basal ganglia on SPECT is well reported in medial temporal epilepsy presenting with dystonic posturing [16, 17], we propose that intense hyperactivity of the basal ganglia may generate dystonic seizures as well as dystonic posturing.

We described a rare case of anti-NMDA receptor encephalitis presenting with dystonic seizures. In our case, the main region of the encephalitis was the basal ganglia, which is a rare finding. We propose that the patient’s dystonic seizures may originate from the insula and be generated by intense hyperactivity of the basal ganglia.

### Statement of Ethics

The authors have no ethical conflicts to disclose.

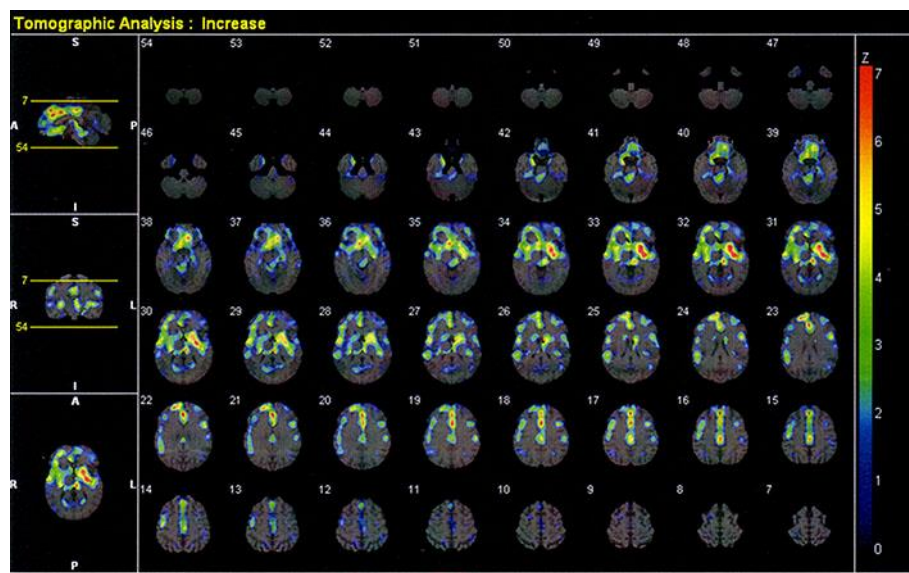
### Disclosure Statement

The authors have no potential conflicts of interest.

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**Fig. 1.** 3D-SSP analysis of SPECT with I-123 IMP. SPECT showed intense hyperperfusion of the caudate nuclei, putamen, globus pallidus, thalamus, and insula on the left side.