



Successful treatment with olanzapine in severe hallucinatory-paranoid state during the course of treatment of inflammatory demyelination disease: a case report

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ABSTRACT

Inflammatory demyelination diseases (IDDs) frequently cause various psychiatric symptoms such as depression, but psychosis is uncommon. The patient was a 23-year-old man treated for IDDs with a steroid for 8 years. Somnolence, right femoral pain, dysuria, and walking difficulty had been observed, and these symptoms recovered after several rounds of steroid pulse therapy. He experienced severe psychotic symptoms, such as visual and auditory hallucinations and xenopathic experiences, even though the steroid dose was 5 mg/day. Successful treatment of the psychotic state was obtained using olanzapine (20 mg/day). The patient's Positive and Negative Syndrome Scale (PANSS) score decreased from 104 to 62. We concluded that the psychotic features may have been induced by IDDs and successfully treated by olanzapine in some patients.

Keywords: *Inflammatory demyelination diseases, steroid psychosis, multiple sclerosis, neuromyelitis optica, hallucinations, delusions*

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Introduction

The spectrum of the inflammatory demyelinating diseases (IDDs) of the central nervous system (CNS) includes multiple sclerosis (MS), neuromyelitis optica spectrum disorder (NMOSD), idiopathic transverse myelitis (ITM) and various other inflammatory syndromes [1]. MS is the most common autoimmune demyelinating disease affecting the CNS and is characterized by periods of relapse and remission, which over time can evolve into a progressive course with accumulating disability [2]. NMOSD is distinct from multiple sclerosis (MS), predominantly affecting the optic nerves and spinal

cord [3, 4]. The diagnosis of NMOSD is most likely when the aquaporin 4 antibody (AQP4) and MOG IgG antibody can be detected, while the distinction between MS and NMOSD is not easily determined by clinical features and MRI imaging.

Neuropsychiatric symptoms frequently occur in MS patients [5, 6]. Irritability and apathy are independent of disability and chronic disease and represent unique disease manifestations. However, psychotic features with MS are uncommon [5, 6]. A population-based survey indicated that the prevalence of psychotic disorders in MS patients is approximately 1.5% [7]. In addition, little information

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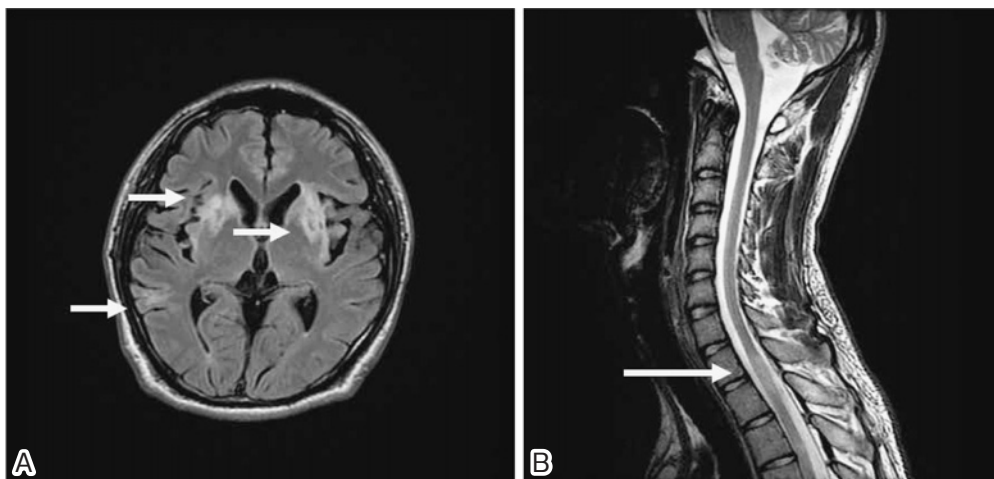


Figure 1. Structural MRI obtained from the patient. The axial Fluid-Attenuated Inversion Recovery (FLAIR) sequences image (A) reveals a large hyperintense lesion in both basal ganglia, insula and right temporal lobe. The sagittal spinal FLAIR image (B) demonstrates hyperintense lesion at the C7/8 level. White arrowheads indicate areas of abnormality.

exists regarding neuropsychiatric symptoms in NMOSD patients, although several reports have suggested that neuropsychiatric symptoms, such as paranoia [8], catatonia [9] and psychomotor agitation [10], occur in these patients. In particular, few reports on NMOSD have described a severe hallucinatory-paranoid state similar to that of schizophrenia.

Here, we report a case of a severe hallucinatory-paranoid state during the course of IDD.

Case report

The patient was a 23-year-old man treated for IDD with steroid therapy for 8 years. The patient was admitted to the Department of Orthopedics of City Hospital 8 years prior to the study due to somnolence, right femoral pain, dysuria, and walking difficulty. Although no abnormal findings were observed on vertebral magnetic resonance imaging (MRI) and head computed tomography (CT), he was treated with steroid pulse therapy for myelitis. Subsequently, his lower limb pain improved, but he experienced left prepotent limb spastic paralysis and disorientation, and voiding disorders persisted. He was diagnosed with suspected MS by the Department of Neurology. Examination of the cerebrospinal fluid revealed that the oligoclonal band was negative. An MRI T2 enhanced image of the head showed multiple hyperintense lesions in the brain stem, thalamus, occipital dorsal fold, and parietal lobe. He experienced double vision and low vision,

but no ophthalmologic abnormalities were found.

Over the following years, the patient had 2 more episodes of myelitis that were treated with steroid pulse therapy. Due to the paralysis of the left leg and dysuria one year earlier, he visited the emergency room and was admitted to the Department of Neurology. MRI of the head showed a high fluid attenuated inversion recovery (FLAIR) signal in the left temporal lobe and left parietal lobe and accounted for the entire transmission of the MRI but was not obvious. Three cycles of steroid pulse therapy resulted in an improvement similar to that observed for MS relapse. After discharge, fingolimod-induced somnolence and a disturbance of consciousness, which caused the patient to speak quietly, were observed. Due to the suspicion of progressive multifocal encephalopathy, he received steroid pulse therapy and simple plasma exchange and recovered from these symptoms. Because the serum examination was negative for the aquaporin 4 antibody (AQP4) and MOG IgG antibody, the diagnosis remained IDD based on his clinical course and imaging findings (Fig. 1).

In addition, he described an experience of seeing and hearing ghosts and of being possessed by them for several weeks. He was influenced by these abnormal experiences. He and his family visited the Shinto shrine for purification many times. To exorcise the spirits, he recited Buddhist scriptures daily. Subsequently, he visited our department due to the suspicion of steroid-induced psychosis. The pre-

scribed prednisolone dosage decreased to 5 mg/day. We observed disorganized thinking and speech and distortions of self-experience in the patient, such as feeling as if his thoughts or feelings were not really his own and believing his thoughts were being inserted into his mind. Subsequently, his visual and auditory hallucinations and delusions were confirmed. His Positive and Negative Syndrome Scale (PANSS) score was 104. Although we advised admission to the Department of Neuropsychiatry, he declined. The Rorschach inkblot test showed mostly normal responses with a few exceptions. The Wechsler Adult Intelligence Scale-III showed the following results: Full-Scale IQ 59, Verbal IQ 64, Performance IQ 66, Verbal Comprehension Index 64, Working Memory index 67, Perceptual Organization Index 66, and Processing Speed Index 63. After the patient was treated with paliperidone (12 mg/day), no change in psychotic symptoms was observed. He was then switched from paliperidone to olanzapine (20 mg/day). At first, only the auditory hallucinations disappeared, but by 4 months after starting olanzapine treatment, all psychotic symptoms were ameliorated. His PANSS score decreased to 62. He then started working in an employment facility for persons with disabilities.

Discussion

A patient experienced a severe hallucinatory-paranoid state during the course of treatment for IDD. This patient showed typical psychotic features similar to those of schizophrenia. These symptoms were ameliorated following treatment with olanzapine but not with paliperidone, both of which are second-generation antipsychotics. Olanzapine has an affinity for several neurotransmitter receptors, while paliperidone has selective affinity for D2 and 5-HT_{2C} receptors [11]. Therefore, the broad pharmacological properties of olanzapine may make it more effective for the treatment of the psychotic features of IDDs.

According to the DSM-5, the patient fulfilled Criterion A of schizophrenia, but not Criterion E, which states that the disturbance is not attributable to the direct physiological effects of a substance (e.g., a drug of abuse or medication) or another medical condition [12]. In addition, the patient showed almost no unusual responses characteristic of schizophrenia during the Rorschach inkblot test. In addition, because steroid-induced psychiatric symptoms typically develop at the dosage of 40 mg/day, ad-

ministration of a small dosage (5 mg/day) of prednisolone is unlikely to have caused the psychotic symptoms in this case [13].

Although IDDs may be differentiated, significant overlaps could lead to diagnostic uncertainty based on the clinical, imaging, and laboratory findings. In this case, the serum examination was negative for AQP4 and MOG IgG antibodies. Patients clinically diagnosed with NMOSD do not always test positive for these antibodies. In fact, a study shows that expert clinicians frequently disagree on the diagnosis of AQP4-Ab-negative NMOSD/MS overlapping patients [14], indicating that there are distinctions in the diagnosis of NMOSD from optic neuritis-predominant MS patients. The accurate diagnosis of our patient may require longitudinal follow up observations. Further studies to subdivide AQP4-Ab-negative NMOSD and to provide a clinical diagnosis support system in patients with indefinite diagnosis is required.

Several surveys have demonstrated that psychosis-associated MS is rare [5, 6, 7, 15, 16]. In addition, little information exists regarding neuropsychiatric symptoms in NMOSD patients. However, a population-based survey indicated that the prevalence of psychotic disorders in patients with MS is approximately 1.5% [7]. In particular, the prevalence of psychosis-associated MS in younger individuals (15-24 years) increased to 4.0% compared to other ages. Psychosis in MS can be successfully treated with atypical antipsychotic drugs [17], which is consistent with our case.

Three previous case reports have described psychiatric symptoms in patients with NMOSD. First, a 40-year-old Asian man with no previous psychiatric history presented with new onset obsessionality, paranoia and severe insomnia [8]. After 6 months of treatment with risperidone and paroxetine, his symptoms resolved. Second, a 16-year-old Antiguan female presented with psychiatric symptoms. Her parents reported a 1-week history of confusion, incoherent speech, hallucinations, left-sided numbness and urinary incontinence [9]. She had minor hand rigidity, visual hallucination, nihilistic delusions, a feeling that her body was dead, and slowed, halting speech. Her catatonia was treated with lorazepam (1.5 mg/day). Finally, an 84-year-old Japanese woman suddenly began to cry loudly and became aggressive toward her husband [10]. She became violent and occasionally slapped him. Olanzapine

was not effective in treating these symptoms. Trazodone (25 mg/day) and risperidone (2 mg/day) were effectively used to treat the psychiatric symptoms, including delirium.

In conclusion, the present case suggest that psychotic features may have been induced by IDD and successfully treated by olanzapine in some patients.

Declarations

• *Ethics approval and consent to participate*

The patient provided written informed consent after receiving a full description of the study.

• *Consent for publication*

The patient consented to the publication of the report.

• *Competing interests*

Norio Yasui-Furukori has received grant/research support or honoraria from and has been a lecturer for Asteras, Dainippon, Eli Lilly, GSK, Janssen-Pharma, Meiji, Mochida, MSD, Otsuka, Pfizer, Takeda and Yoshitomi. The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript. The remaining authors have no conflicts of interest to declare.

• *Authors' contributions*

NYF is a doctor in charge of the case in the Department of Neuropsychiatry. TN and TK are doctors in charge of the case in the Department of Neurology. NT gathered and reviewed the relevant literature. KN and MS supervised the case.

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