Received: 9 July 2021 | Revised: 24 September 2021 | Accepted: 25 September 2021

DOI: 10.1002/npr2.12214

NEUROPSYCHOPHARMACOLOGY REPORTS

WILEY

CASE REPORT

Suicide attempt induced by drug-induced leukoencephalopathy: A case report

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Abstract

Background: Leukoencephalopathy is identified during the administration of anticancer drugs. Symptoms vary from neurological symptoms to psychiatric symptoms depending on the site of damage. There have been no previous reports of suicide attempts due to drug-induced leukoencephalopathy.

Case Presentation: The patient was diagnosed with diffuse large B-cell lymphoma (DLBCL) infiltrating the pharyngeal lesion. Rituximab + methotrexate + oncovin + procarbazine (R-MPV) therapy, a methotrexate-containing chemotherapy, was initiated. At the end of the fifth course, the patient attempted suicide by hanging with an appliance cord, which was associated with delusion. A head MRI scan showed no evidence of lymphoma recurrence, but white matter lesions around the ventricles showed progression.

Conclusion: We report the case of a patient in whom drug-induced leukoencephalopathy related to methotrexate led to a suicide attempt. In addition to monitoring brain tumors, daily monitoring of psychiatric and neurological symptoms is important for patients with methotrexate-induced encephalopathy.

KEYWORDS

leukoencephalopathy, methotrexate, MRI, suicide attempt

1 | INTRODUCTION

Drug-induced leukoencephalopathy, including that induced by methotrexate, is an encephalopathy caused by abnormal brain metabolism during the administration of anticancer drugs or immunosuppressive drugs.[1] Symptoms vary from neurological symptoms to psychiatric symptoms depending on the site of damage.[2] Methotrexate has a higher affinity for intracellular dihydrofolate reductase than folic acid and indirectly inhibits the metabolism of folic acid into tetrahydrofolate (THF), which is necessary for nucleic acid synthesis.[2,3] Inhibition of nucleic acid synthesis also inhibits the production of methionine, which is necessary for myelination in central nervous tissue, resulting in cerebral white matter lesions. Several factors are thought to be involved in the pathogenesis of drug-induced leukoencephalopathy, such as increased stimulation of N-methyl-D-aspartate (NMDA) receptors by elevated homocysteine, extracellular adenosine accumulation, and abnormal biopterin metabolism.[2,3]

We report the case of a patient who experienced leukoencephalopathy during treatment with methotrexate, the most frequent cause of drug-induced leukoencephalopathy, and attempted suicide.

2 | CASE PRESENTATION

We present the case of a 77-year-old Japanese male patient who was a former police officer. He presented after a suicide attempt and had no previous psychiatric history. Three years earlier, the patient was diagnosed with diffuse large B-cell lymphoma (DLBCL) of the pharynx after visiting a local doctor due to the symptoms of nasal obstruction and sore throat. After six courses of rituximab + cyclophosphamide + doxorubicin + vincristine + prednisolone (R-CHOP) therapy, the patient achieved remission. One year before the patient presented to us, right-sided paralysis and fluctuating aphasia arose, and he visited the Department of Neurology at our hospital in the same year. The patient had cognitive impairment evidenced by a score of 18 points on the Mini-Mental Scale Examination (MMSE). A head MRI scan revealed a mass lesion compatible with recurrent lymphoma in the left thalamus (Figure 1). Although the radiologist determined the white matter changes to be chronic cerebral ischemia, we thought that leukoencephalopathy caused by both CHOP and R-MPV could be considered. Rituximab + high-dose methotrexate + vincristine + procarbazine (R-MPV) chemotherapy was initiated. At the end of the fourth course, the patient's right paralysis had improved, but his aphasia remained. Subsequently, he began to make delusional statements such as “my house is going to burn down” and “my wife is being cheated by a gang.” Furthermore, amnesia became prominent, including symptoms such as forgetting the details of previous conversations. One month prior, the patient began to show a decrease in activity. He had attempted suicide by hanging with an appliance cord because of his delusion. The patient was a former police officer and had a gang-related delusion that if he did not die, his family would be killed by the gang. The patient presented at the Department of Psychiatry and was admitted on the same day. According to the results of the interview, the patient did not have any visual hallucinations. Hence, we concluded that he was paranoia. The pathological picture appeared to be paranoia related to life history. A chest X-ray showed a cardiothoracic ratio of 47.4%, no abnormal shadows in the lung fields, and an acute diaphragmatic angle of the ribs. Electrocardiogram (ECG) showed sinus rhythm, QTc of 0.414 s, and no ST change. Blood tests showed no electrolyte abnormalities or abnormalities in liver and kidney function. Thyroid function was within normal limits, and HbA1c was 7.2%. Electroencephalography (EEG) showed symmetrical 10-Hz occipital-dominant alpha waves, alpha-blocking by eye opening, no light-driven activation, and no slow waves or spiny slow waves. A head MRI scan on the 7th day showed no evidence of lymphoma recurrence in the left thalamus, but white matter lesions around the ventricles showed progression (Figure 1). We discussed the clinical course and the head MRI scan (Figure 1) findings with a physician in the Department of Hematology at our hospital and came to the diagnosis of drug-induced leukoencephalopathy, including methotrexate-induced encephalopathy. Symptoms of person misrecognition, such as not being able to recognize his wife as his wife when she visited him, and other forms of misrecognition, such as mistaking the ECG monitor for a radio, also appeared. On the 29th day, the patient experienced insomnia and was given 0.25 mg of brotizolam, which caused restlessness, agitation, and disturbance of consciousness on the following day. On the 31st day, we diagnosed the patient with delirium, which was improved after the administration of 4 mg of perospirone and 25 mg of trazodone; however, the

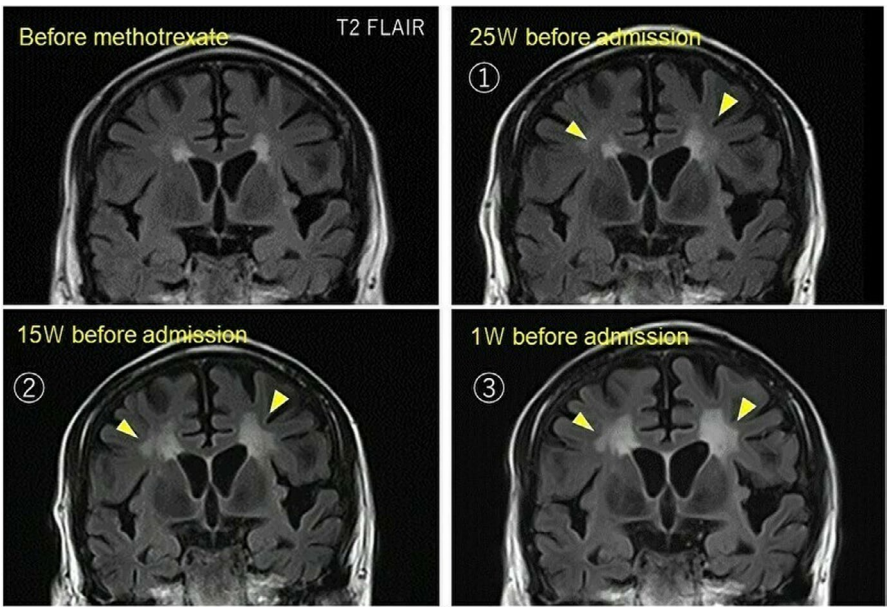

FIGURE 1 Comparison of MRI images with T2 FLAIR. This figure shows a comparison of MRI images. Arrows indicate white matter lesions. Comparing the image in (2), which was taken after the completion of 5 doses of methotrexate, with the image taken before methotrexate, the white matter lesion clearly progressed. In addition, comparing the image in (2) with the image in (3), which was taken after admission to our hospital, revealed that the white matter lesions had progressed even after methotrexate administration was completed. The image taken after one dose of methotrexate also shows mild progression of white matter lesions

patient's cognitive impairment did not improve. It was decided that it would be difficult to discharge the patient from the hospital to his home. The patient was moved to a nursing home on the 85th day.

3 | DISCUSSION AND CONCLUSIONS

There have been no previous reports of suicide attempts due to drug-induced leukoencephalopathy. The patient developed progressive leukoencephalopathy during R-MPV therapy for recurrent brain metastases of DLBCL, and after the fifth course of R-MPV therapy, a head MRI was performed to evaluate the effect of the therapy. After four courses of R-MPV therapy, symptoms such as cognitive decline and delusions appeared, and it is highly likely that the patient had already developed methotrexate-related encephalopathy at that time. However, due to aphasia caused by the brain metastases, it was not possible to detect methotrexate-related encephalopathy at the early stage. Since it has been reported that clinical symptoms of methotrexate-related encephalopathy appear before imaging findings,[4] we cannot expect to detect this complication early using imaging. In addition, since there are no disease-specific findings in blood tests or spinal fluid tests, daily monitoring of psychiatric and neurological symptoms is important. Careful monitoring of symptoms is especially necessary for patients who already experience neuropsychiatric symptoms due to brain metastases, as in this case.

In addition to the mute, motionless, and comatose states, the symptoms in this patient were consistent with the symptoms of methotrexate encephalopathy, such as delusion of victimization complaints and incoherent speech and behavior related to unpredictable dangerous behavior.

In some patients, encephalopathy symptoms appeared immediately after methotrexate was administered, while in other cases, encephalopathy symptoms appeared approximately 6 months after methotrexate was administered.[5] In acute cases where encephalopathy occurs within approximately 2 weeks of administration, withdrawal of the drug may result in significant improvement in symptoms within 1 week of symptom onset, whereas in slow-onset cases, symptoms often persist.[5,6] In this case, encephalopathy symptoms appeared at the end of the fourth course, indicating the slow onset of symptoms, and the detection of symptoms was delayed due to the presence of aphasia.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

RM, YK, and MI were involved in the clinical investigations. NYF wrote the manuscript. KM, NYF, and KS were involved in the literature review and revisions. All authors read and approved the final manuscript.

APPROVAL OF THE RESEARCH PROTOCOL BY AN INSTITUTIONAL REVIEWER BOARD

The ethics committee is not required to review case reports.

INFORMED CONSENT

The patient has consented in a written form to the submission of the case report for submission to the journal.

REGISTRY AND THE REGISTRATION NO. OF THE STUDY/TRIAL

Not applicable.

ANIMAL STUDIES

Not applicable.

DATA AVAILABILITY STATEMENT

The data are not publicly available due to privacy restrictions.

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How to cite this article: Maehara R, Kawamata Y, Ichikawa M, Mitani K, Yasui-Furukori N, Shimoda K. Suicide attempt induced by drug-induced leukoencephalopathy: A case report. Neuropsychopharmacol Rep. 2021;41:551–553. https://doi.org/10.1002/npr2.12214