Postvaccinal Encephalopathy Presenting with Amnesia and Seizure After ChAdOx1 nCov-19 Vaccination: A Case Report

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Abstract

Purpose: Because of the COVID-19 pandemic and resulting widespread vaccination, many related neurological disorders, including autoimmune encephalopathy, have emerged. The pathophysiological mechanism underlying the COVID-19 vaccination and autoimmune encephalopathy remains unclear; more case reports and further investigation are required.

Case Report: We report a clinical case of a 38-year-old woman who presented with acute-onset amnesia, language disturbance, and seizure. We suspected autoimmune encephalopathy triggered by the ChAdOx1 nCoV-19 vaccine. Brain magnetic resonance imaging revealed a subacute infarction at the right internal capsule and irregular vascular contour, which indicated a vasculopathy, such as vasculitis. Cerebrospinal fluid analysis revealed inflammation without pleocytosis, and electroencephalography detected diffuse background slowing with sharp transients at the right temporal region. Although autoantibody tests were negative, we initiated steroid pulse therapy. The patient's symptoms improved rapidly. The patient was discharged without neurological deficit or sequelae.

Conclusion: Clinicians should be mindful of postvaccinal encephalopathy and suspect this condition in patients with acute onset of psychosis or mental change, higher cortical dysfunction, and seizure within 2 weeks of vaccination. Early diagnosis is key, and immune treatment, such as steroid pulse therapy or immunosuppressants, may dramatically improve patients' symptoms.

Keywords: ChAdOx1 nCoV-19 vaccine (AZD1222), postvaccinal encephalopathy, autoimmune encephalopathy.

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INTRODUCTION

Autoimmune encephalopathy is a complex form of brain inflammation in which the body's immune system attacks healthy cells and tissues in the brain, and it has diverse immunologic associations, clinical manifestations, and therapeutic outcomes. Three main subgroups of autoimmune encephalopathy have been identified: autoimmune encephalopathies with neural nonspecific serologic evidence of autoimmunity and without cancer, paraneoplastic encephalopathies, and central nervous system (CNS) vasculitis[(1)]. The diagnostic

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criteria for possible autoimmune encephalitis include (1) subacute onset (rapid progression of less than 3 months) of working memory deficits (short-term memory loss), altered mental status, or psychiatric symptoms; (2) a focal CNS sign, including seizures not explained by a previously known seizure disorder, cerebrospinal fluid (CSF) pleocytosis (a white blood cell count of more than five cells per mm^3), and magnetic resonance imaging (MRI) features suggestive of encephalitis; and (3) reasonable exclusion of alternative causes[2]. In 2014, the prevalence of autoimmune encephalitis was 13.7/100,000, and the incidence of autoimmune encephalitis, due to an increase in detection of autoantibody-positive cases, increased from 0.4/100,000 person-years (1995–2005) to 1.2/100,000 person-years (2006–2015; $p = 0.02$) [3]. Reported adverse neurological effects of vaccines are vaccine-related demyelinating diseases, Guillain-Barré syndrome, fever-induced seizure, encephalopathy, and autism[4]; postvaccinal encephalopathy, however, is rare. Here, we report a case of possible autoimmune encephalopathy after ChAdOx1 nCoV-19 vaccination with presentation of acute onset amnesia, focal CNS signs, and seizure, in which administration of steroid pulse therapy dramatically improved neurological symptoms.

CASE REPORT

A 38-year-old woman without systemic disease experienced acute onset of abnormal symptoms, such as amnesia, incoherent speech, and difficulty typing using communication software. Family members brought the patient to the emergency department, stating that she had received the first dose of ChAdOx1 nCov-19 vaccine 2 weeks prior. After receiving the vaccination, she experienced only fever and general malaise for 2 days. Her symptoms then seemingly resolved and she returned to work. The day before the patient arrived at the emergency department, her coworker noticed her abnormal behavior such as difficulty typing text messages via online social media. On arrival at the emergency department, the patient was conscious clear but demonstrated psychomotor slowing and confabulation. Neurological examination revealed high levels of cortical dysfunction including poor judgement; disorientation to time, place, and person; impaired short-term memory; failed abstract thinking; impaired calculation; and impaired language function (including partial incoherence, agraphia, and anomic aphasia). The language domains of fluency, reading, and repetition remained notably intact. No cranial nerve, motor, sensory, or coordination dysfunction were observed. Brain computed tomography revealed negative findings of hemorrhage and structural lesion. While waiting in the emergency room, the patient experienced a first-time seizure with a general pattern of a tonic–clonic seizure. The patient was prescribed lorazepam and levetiracetam, and the seizure subsided. The patient presented postictal confusion and agitation. She was admitted for examination and treatment.

Brain MRI revealed a subacute infarction at the right internal capsule through diffusion-weighted imaging (Fig. 1A), and magnetic resonance angiography revealed an irregularity in vascular contour, indicating potential vasculopathy, such as vasculitis (Fig. 1B). No intracranial hemorrhage, mass lesion, or mesial temporal

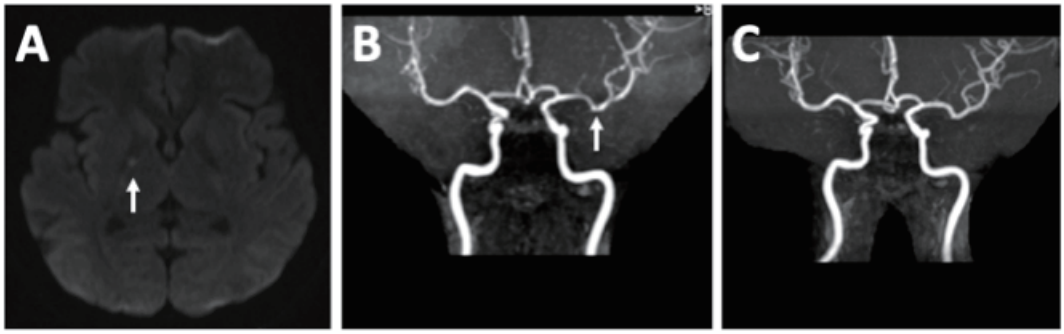

Fig. 1. Brain MRI (1A) revealing subacute infarction at the right internal capsule in the brain MR DWI (arrow); (1B) irregularity of vascular contour in magnetic resonance angiography of the brain (arrow) ; (1C) regressive change of previous irregularity of vascular contour after treatment

lobe enhancement was observed, and illicit drug screens were all negative. Basic blood and biochemistry profiles including renal function, liver function, electrolyte levels, complete blood count, and coagulation were within normal limits. Tumor markers and autoimmune tests, including erythrocyte sedimentation rate, free T4, TSH, anti-Tg, anti-TPO, rheumatoid factor, C3, C4, ANA, anti-ENA screen, anti-phospholipid IgG, anti-cardiolipin IgG, anti-β2 glycoprotein IgG, lupus anticoagulant LA1/LA2, anti-MPO(pANCA), anti-PR3(cANCA), LDH, hepatitis B virus, hepatitis C virus, and human immunodeficiency virus screening, were unremarkable. Electroencephalography (EEG) detected epileptiform discharges, which presented as a diffuse background slowing with intermittent low to moderate voltage sharp transients at the right frontotemporal region (Fig 2). CSF

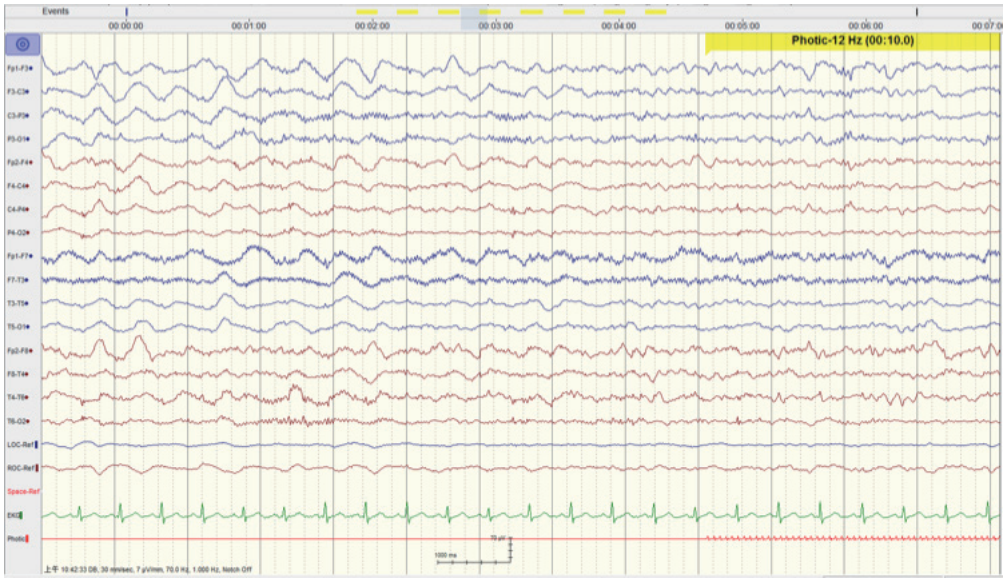

Fig. 2. EEG revealing diffuse background slowing with intermittent low to moderate voltage sharp transients at the right frontotemporal region

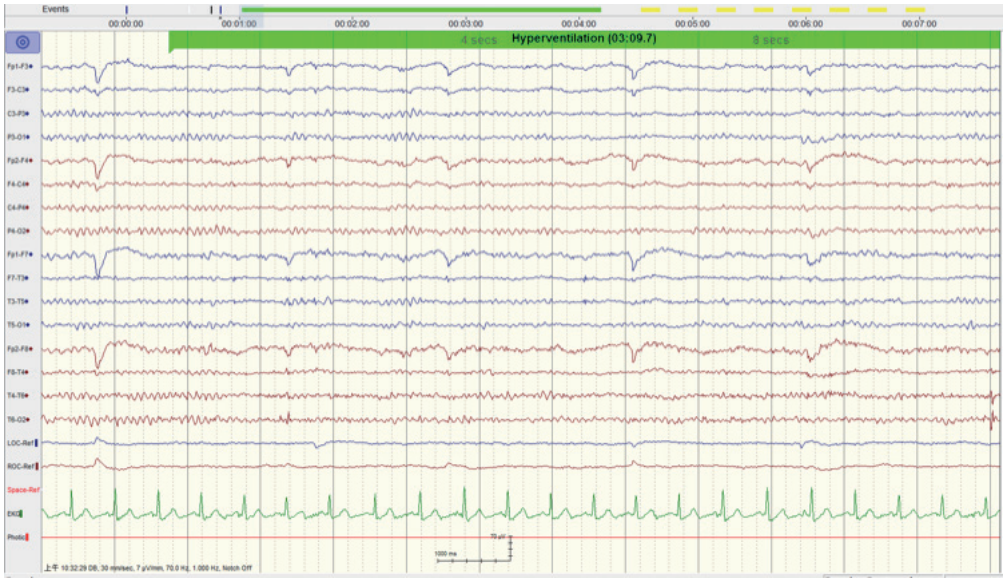

Fig. 3. EEG revealing regression of slow activities and epileptiform discharges

analysis revealed a composition of protein 59.3 mg/dL, glucose 90 mg/dL, and 1 leukocytes/μL, which indicates no pleocytosis but elevated levels of total protein and glucose. CSF panel tests for bacteria and viruses were all negative.

Qualitative serum tests for paraneoplastic neurologic syndrome, including anti-Tr(DNER), anti-GAD65, anti-Zic4, anti-titin, anti-SOX-1, anti-Recovertin, anti-Hu, anti-Yo, anti-Ri, anti-PNMA2(Ma2/Ta), anti-CV2, and anti-amphiphsyin, were all negative. Qualitative serum and CSF tests for limbic encephalitis, including anti-NMDAR, anti-AMPAR1, anti-AMPAR2, anti-GABABR, anti-LGI1, and anti-CASPR2, were all negative.

Although autoantibodies were all absent detected, seronegative autoimmune encephalopathy triggered by the ChAdOx1 nCov-19 vaccination was highly suspected. In addition to levetiracetam, we initiated steroid pulse therapy at the start of treatment. The regimen was methylprednisolone 1000 mg IV daily for 5 days, which was subsequently changed to prednisolone 30 mg PO daily starting from day 6 of admission. The patient's symptoms dramatically improved from day 3 of admission. The patient was discharged without neurological deficit or sequelae. One week after discharge, the patient received repeat EEG, which revealed resolved slow waves without epileptiform discharges (Fig. 3). Three months later, repeated brain MRI revealed regressive change of previous irregularity of vascular contour. (Fig. 1C)

DISCUSSION

Vaccine-related autoimmune encephalitis or encephalopathies have sporadically been observed after large-scale distribution of the COVID-19 vaccination. Because of the rarity of such cases, large pooled data from observational epidemiologic studies are lacking. In 2021, Zuhorn et al[5]. reported a case series that presented three cases of postvaccinal encephalitis that were temporally correlated with ChAdOx1 nCov-19 vaccination. These patients reported no previous somatic or psychiatric diseases, and they developed symptoms including headache, fever, difficulties with concentration, aphasia, seizure, and opsoclonus–myoclonus syndrome. The vaccination to onset time ranged from 5 to 8 days. Brain MRI revealed normal status of the parenchyma in all patients. CSF analyses revealed lymphocytic pleocytosis ranging from 7 to 115 leukocytes/μL in all patients. EEG recording indicated diffuse abnormally slow theta and delta rhythms without epileptiform activity in all three patients. In two cases, the patients received immunosuppressive therapy with pulse steroid therapy and exhibited considerable symptomatic improvement. In the third case, the patient refused immunosuppressive therapy with steroids; however, the patient's neurological symptoms gradually improved. Residual neurological deficits, such as mild cognitive slowing without functional impairment, or low-grade tremor, were observed. Subsequent, brain MRI several months after treatment revealed no evidence of structural lesions. The relationship between vaccines and autoimmune encephalitis or encephalopathies and the trigger mechanism of autoimmune diseases remains unclear; however, several studies have suggested that it may be related to a component of the vaccine (such as an inactive viral or bacterial agent or an attenuated living microorganism) or to a wild, superimposed infectious agent in people with a genetic predisposition[6].

In our case, the patient initially presented with rapidly progressing cognitive impairment, psychobehavioral disturbance, atypical aphasia, and seizure. Brain MRI revealed subacute infarction at the right internal capsule, which does not explain the symptoms the patient presented with. Brain MRI further revealed an irregular vascular contour, which indicated a vasculopathy, such as vasculitis. The lacunar infarction was suspected to be related to vasculitis. We examined a series of autoantibodies for vasculitis, and all results were negative. CSF analysis revealed inflammation without pleocytosis. EEG detected diffuse background slowing with sharp transients at the right temporal region, and qualitative serum tests for paraneoplastic neurologic syndrome and limbic encephalitis were all negative. We administered pulse steroid therapy, which led to dramatic improvement in the symptomatology. The patient met the criteria for possible autoimmune encephalitis (subacute onset of working memory deficits, altered mental status, or psychiatric symptoms; with seizures not explained by known seizure disorder) and presented a similar clinical course after ChAdOx1 nCov-19 vaccination as that reported in a case series by Zuhorn et al.,[5] although our case lacked CSF pleocytosis. Our patient with seronegative postvaccinal

encephalopathy responded favorably to pulse steroid therapy.

CONCLUSION

Because of the COVID-19 pandemic and resulting widespread vaccination, clinicians should be mindful of postvaccinal encephalopathy and suspect this condition in patients who exhibit rapidly progressing cognitive impairment, psychobehavioral disturbance, higher cortical dysfunction, and seizure within 2 weeks of vaccination. Early diagnosis is key, and immune treatment, such as steroid pulse therapy or immunosuppressants, may dramatically improve patients' symptoms.

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