CASE REPORT

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Anti-NMDA antibody autoimmune encephalitis post-HSV encephalitis: A rare case report

Neelam Sahu, Pushpendra Nath Renjen, Avinash Goswami, Shams Kanuga, Nidhi Goyal

ABSTRACT

Introduction: Autoimmune encephalitis is a group of neuropsychiatric disorder in which antibodies interact directly to their target antigen and produce neuronal dysfunction. Generally herpes simplex encephalitis is a monophasic illness although in few patients neurological worsening can develop some weeks later. This worsening is generally due to autoimmune encephalitis after herpes simplex encephalitis (AEaHSE).

Case Report: We report an interesting case report of 67 years old female patient who initially was diagnosed to have herpes simplex virus (HSV) encephalitis, showed improvement in her clinical status followed subsequently by deterioration in cognitive status. Anti-*N*-methyl-D-aspartate (NMDA) antibody was positive in cerebrospinal fluid (CSF) and serum. The patient was managed with intravenous immunoglobulin (IVIG) and subsequently showed improvement in her clinical state.

Conclusion: The discovery and clinical application of anti-NMDA receptor antibodies has helped to define the mechanism behind immune-based relapse of herpes simplex virus encephalitis (HSVE). This case illustrates the usefulness of testing for anti-NMDA receptor

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INTRODUCTION

Herpes simplex encephalitis (HSE) is considered to be one of the most common sporadic viral encephalitis. It has an annual incidence of 2–4 cases per million people worldwide, accounting for almost 20% of all encephalitis cases [1]. Most HSEs occur in children and the elderly and in these age groups herpes simplex virus-1 (HSV-1) has the major etiologic role [2].

CASE REPORT

A 67-year-old female, hypertensive and diabetic, developed abnormal involuntary movements of left limbs with altered sensorium and had fever around the same time. The patient was admitted, where she was intubated and put on mechanical ventilation. Cerebrospinal fluid (CSF) examination revealed white blood cells (WBC) – few cells protein – 133, sugar – 132 [corresponding random blood sugar (RBS) 101], and CSF HSV-1 realtime polymerase chain reaction (RT-PCR) was positive.

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The patient was managed with antibiotics, antiviral, antiepileptic and other supportive care. She was drowsy, arousable intermittently follows simple commands, The pupils were symmetrical and reactive measuring 2 mm. Muscle strength in right upper and lower limb was 2/51/5 and left upper and lower limb was 2/5 1/5, plantars were extensor bilaterally. Magnetic resonance imaging (MRI) brain FLAIR (fluid-attenuated inversion recovery) revealed evidence of ill-defined area of altered signal intensity predominantly involving the medial temporal lobe, which is extending along the anterior temporal lobe and extending superiorly along the internal and external capsule. Signal intensity alteration is also seen involving the right-sided thalamus with relative sparing of the basal ganglia. Mild similar changes are also seen involving the left temporal lobe and the capsular region (Figure 1A). Focal area of parenchymal bleed is seen in the right medial temporal lobe. The hemorrhage is also seen extending into the subarachnoid spaces along the right sylvian fissure. Bleed is also seen in the dependent part of bilateral lateral ventricle with fluid level (Figure 1B). Abnormal leptomeningeal enhancement is seen involving the sylvian and perisylvian regions on both sides, more prominently on right side. Abnormal enhancement is also seen along the convexity sulcal spaces in the right temporal region and along the interhemispheric fissure (Figure 1C). These findings are likely secondary to HSV encephalitis. The patient gradually improved to a conscious and alert stage with moving all 4 limbs and obeying commands. She was discharged after one month of hospital stay. Subsequently, the patient was admitted with complaints of cognitive decline, irrelevant talking, and altered sensorium started one month after discharge. The patient was not following verbal commands and comprehension was also impaired. Follow-up MRI brain revealed ill-defined area of FLAIR hyperintensity involving the right anterior and medial temporal lobe with evidence of volume loss prominent in the anteromedial temporal lobe including thinning of the right hippocampus. Interspersed magnetic susceptibility is seen in the sylvian fissure and in the medial temporal lobe: suggestive of hemorrhagic residua. The signal changes are seen extending superiorly along the internal and external capsule and involving the right frontal lobe, right periventricular and deep white matter including the corona radiata and centrum semiovale (Figure 2). Compared to the previous MRI there is mild increase in the extent of the FLAIR hyperintensity with interval encephalomalacic changes in the right temporal lobe. Similar ill-defined signal changes were also seen in the left perisylvian region, the periventricular and deep white matter including left corona radiata and centrum semiovale with mild increase in the left periventricular hyperintensity compared to the previous study. Persisting ill-defined FLAIR hyperintensity was also seen involving the right-sided thalamus with relative sparing of the basal ganglia with no significant change. There is near complete resolution of the hemorrhagic residua seen in

the dependent part of bilateral lateral ventricle in the previous study. Also, there is near complete resolution of the leptomeningeal enhancement seen in the previous study. The ventricular system is appearing mildly more prominent from the previous study. Lumbar puncture revealed CSF glucose-79 (RBS144), protein - 74.9, cells -5 with negative rapid meningitis panel, negative aerobic, anaerobic, fungal cultures, and negative gram, AFB, KOH, and India ink stains. Cerebrospinal fluid autoimmune encephalitis panel was positive for anti NMDA antibodies. Positron emission tomography-computed tomography (PET-CT) of the whole body revealed an ill-defined hypodense area involving the right temporal lobe with reduced F-fluorodeoxyglucose (FDG) uptake. Reduced uptake was also seen in bilateral periventricular regions and the right frontal lobe. The patient was managed with 140 grams of IVIG over a period of five days, antiepileptic drug and other supportive care. Subsequently she showed improvement in her neurological state and discharged in a hemodynamically stable condition.



Figure 1: (A) MRI brain FLAIR revealed evidence of ill-defined area of altered signal intensity predominantly involving the medial temporal lobe, which is extending along the anterior temporal lobe and extending superiorly along the internal and external capsule. Signal intensity alteration is also seen involving the right sided thalamus with relative sparing of the basal ganglia. Mild similar changes are also seen involving the left temporal lobe and the capsular region. (B) MRI brain SWI revealed focal area of parenchymal bleed is seen in the right medial temporal lobe. The hemorrhage is also seen extending into the subarachnoid spaces along the right sylvian fissure. Bleed is also seen in the dependent part of bilateral lateral ventricle with fluid level. (C) MRI brain with contrast revealed abnormal enhancement is also seen along the convexity sulcal spaces in the right temporal region and along the interhemispheric fissure.

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Figure 2: Follow-up MRI brain showing ill-defined area of FLAIR hyperintensity involving the right anterior and medial temporal lobe with evidence of volume loss prominent in the anteromedial temporal lobe including thinning of the right hippocampus. The signal changes are seen extending superiorly along the internal and external capsule and involving the right frontal lobe, right periventricular and deep white matter including the corona radiata and centrum semiovale.

DISCUSSION

N-methyl-D-aspartate receptor (NMDAR) encephalitis is an autoimmune encephalitis syndrome characterized by variable combinations of neuropsychiatric and behavioral changes, seizures, movement disorders, amnesia, aphasia, other neuropsychiatric symptoms and autonomic dysfunction [3]. Immunoglobulin G (IgG) antibodies to the NR1 subunit of the NMDAR contribute to pathogenesis and affect neuronal function [3]. A subset of patients with anti-NMDAR encephalitis has certain group of tumors, an ovarian teratoma, and pathogenesis in these cases is thought to be paraneoplastic [4]. In patients without tumors, the pathogenesis is generally assumed to be autoimmune [5, 6]. Early hypotheses for the mechanisms underlying post-HSVE-AE considered the possibility of molecular mimicry between HSV surface molecules and NMDARs [7]. Although the exact mechanisms underlying the synthesis of anti-NMDAR antibodies following HSV infection remain unknown, it is hypothesized that the virus induced neuronal destruction may expose neuronal antigens to the systemic immunity, initiating a primary autoimmune response [8]. In their important analysis, the authors describe 4 distinct imaging patterns in MRI brain: normal MRI findings (type 1, 53% of patients), isolated hippocampal involvement (type 2, 13%), other brain lesions without hippocampal involvement (type 3, 13%), and other brain lesions with hippocampal involvement (type 4, 21%) [9, 10].

CONCLUSION

The discovery and clinical application of anti-NMDA receptor antibodies has helped to define the mechanism behind immune based relapse of HSVE. This case illustrates the usefulness of testing for anti-NMDA receptor antibodies following worsening few weeks after treatment of herpes simplex encephalitis.

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Author Contributions

Neelam Sahu – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all Edorium J Neurol 2024;9(1):1–4. www.edoriumjournalofneurology.com

aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Pushpendra Nath Renjen – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Avinash Goswami – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Guarantor of Submission

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Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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