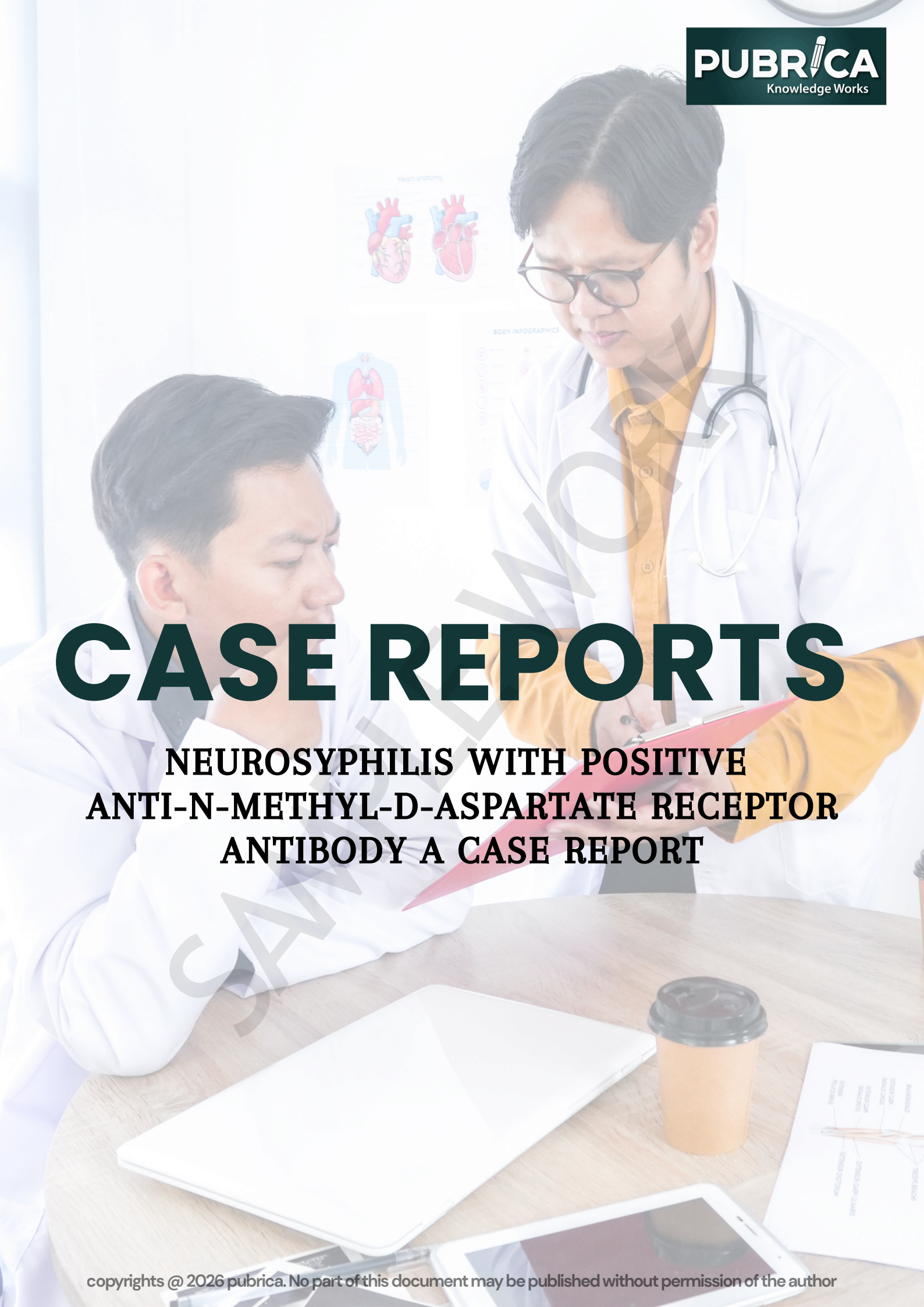

CASE REPORTS

NEUROSYPHILIS WITH POSITIVE ANTI-N-METHYL-D-ASPARTATE RECEPTOR ANTIBODY A CASE REPORT

Neurosyphilis with positive anti-N-methyl-D-aspartate receptor antibody: a case report

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Abstract

Introduction

Neurosyphilis may present with diverse neurological manifestations and can mimic acute ischemic stroke or autoimmune encephalitis. This report describes a rare case of neurosyphilis associated with positive anti–N-methyl-D-aspartate receptor antibodies, underscoring important diagnostic and therapeutic considerations.

Case presentation

A 54-year-old man was admitted with acute memory impairment and disorientation. Acute ischemic stroke was initially suspected, and intravenous thrombolysis with recombinant tissue-type plasminogen activator was administered. However, intermittent episodic memory and orientation disturbances persisted. Brain magnetic resonance imaging revealed no diffusion restriction, while electroencephalography demonstrated frequent subclinical seizures. Serological testing showed positive rapid plasma reagin results. Cerebrospinal fluid analysis revealed pleocytosis and elevated protein levels, with positive rapid plasma reagin, Treponema pallidum particle agglutination assay, and Treponema pallidum antibodies. Anti-NMDAR antibodies were detected in both serum and cerebrospinal fluid. Based on these findings, neurosyphilis with positive anti-NMDAR antibodies was diagnosed. Treatment with intravenous penicillin G and levetiracetam resulted in clinical improvement and reduced cerebrospinal fluid leukocyte counts.

Discussion and conclusion

This case highlights the diagnostic complexity of neurosyphilis presenting with overlapping features of stroke and autoimmune encephalitis. The coexistence of anti-NMDAR antibodies may reflect immune activation secondary to infection rather than primary autoimmune disease. Comprehensive evaluation using clinical presentation, imaging, electroencephalography, and laboratory testing is essential to guide appropriate treatment and avoid unnecessary immunotherapy.

Keywords: neurosyphilis, encephalitis, anti-N-methyl-D-aspartate receptor (anti-NMDAR), epilepsy, case report

Introduction

Neurosyphilis, a central nervous system infection caused by Treponema pallidum, may present with heterogeneous and nonspecific neurological manifestations.[1] Anti–N-methyl-D-aspartate receptor encephalitis exhibits overlapping clinical features. The coexistence of neurosyphilis with anti-NMDAR antibody positivity is rare. We herein report a case highlighting this uncommon association.[2]

Case Presentation

A 54-year-old man was brought to the emergency department by his son because of acute memory impairment lasting approximately one hour. The patient was unable to find his way home or respond appropriately to questions and had no accompanying motor or sensory deficits. He had gone for his routine walk prior to symptom onset. His medical history was notable for hypertension, diabetes mellitus, smoking, and two prior ischemic strokes. The first stroke, eight years earlier, resulted in mild right lower-limb weakness and memory decline, though he remained functionally independent. A second stroke five years later caused transient worsening of right lower-limb weakness, with gradual recovery; however, progressive cognitive and executive dysfunction, personality changes, and irritability subsequently developed. He had been taking aspirin regularly.

The patient had no discernible signs of life upon examination. An emergency Computed Tomography scan showed evidence of multiple past strokes in the form of encephalomalacia. There was a suspicion that the patient had suffered from an Acquired Ischemic Stroke (AIS). Recombinant tissue-type plasminogen activator (rtPA) was then administered intravenously after the diagnosis was made. The patient regained orientation within 30 minutes following the administration of rtPA. Neurological examination at that time revealed delayed response time, impaired calculation, disorientation of left and right, impaired memory, mild weakness of the right lower extremity (5- out of 5), and a positive right Babinski sign. Other neurological examinations did not reveal any other notable findings. The score for the Mini-Mental State Examination was 15 out of 30.

The patient was admitted to the Neurology Inpatient Unit for additional diagnostics. A CT Angiogram of the head and neck demonstrated no significant stenosis. MRI of the head demonstrated chronic ischemic changes due to past strokes in the form of encephalomalacia or stroke-like lesions and the presence of lacunar strokes with no evidence of restricted diffusion. The patient subsequently had recurrent episodes of transient disorientation lasting between 10-30 minutes after the episodes occurred with amnestic results after the disorientation. There was a high suspicion that the patient was experiencing continuous non-convulsive status epilepticus. Although there were no electroencephalographic (EEG) events

detected during the course of EEG monitoring, there were more than 40 subclinical seizures recorded during the 16 hours of EEG monitoring.

Routine laboratory investigations, autoimmune screening, thyroid function tests, tumor markers, and serological tests for hepatitis B and human immunodeficiency virus were unremarkable. Metabolic evaluation revealed hyperglycaemia and dyslipidaemia. Serological testing for syphilis was positive, with a serum rapid plasma reagin titer of 1:32. Further history revealed a prior diagnosis of syphilis eight years earlier, for which standard treatment had been administered. Given the progressive cognitive decline, personality changes, and seizures, neurosyphilis was suspected. Cerebrospinal fluid analysis showed pleocytosis with monocyte predominance, elevated protein levels, and positive rapid plasma reagin, Treponema pallidum particle agglutination, and Treponema pallidum antibody results. Oligoclonal IgG bands were present in cerebrospinal fluid but absent in serum. Autoimmune encephalitis antibody testing using a cell-based assay demonstrated anti-NMDAR antibodies in both cerebrospinal fluid and serum, with titers of 1:20 and 1:10, respectively; other neuronal antibodies were negative.

A final diagnosis of neurosyphilis with concurrent anti-NMDAR antibody positivity was made. The patient was treated with intravenous penicillin G for three weeks and levetiracetam, along with antiplatelet therapy, statins, and optimized control of blood pressure and blood glucose. Following treatment, episodic disorientation and cognitive impairment improved. Repeat electroencephalography showed no seizures, the MMSE score increased to 19/30, and cerebrospinal fluid leukocyte counts decreased substantially, although protein levels and anti-NMDAR antibody titers remained elevated. Five weeks later, serum rapid plasma reagin titers had decreased to 1:8.

Discussion

This patient had neurosyphilis with concurrent anti-N-methyl-D-aspartate receptor (NMDAR) antibody positivity, presenting with acute, nonspecific changes in mental status. While thrombosis was initially considered due to suspected acute ischemic stroke, diffusion restriction was absent on MRI, while multiple non-convulsive and subclinical seizures on EEG argued against evolving ischemic stroke in favor of non-convulsive status epilepticus.

Additionally, the patient's history of syphilis, progressive cognitive decline, seizure activity, and cerebrospinal fluid testing (rapid plasma reagin, Treponema pallidum particle agglutination, Treponema pallidum antibodies) confirmed a diagnosis of neurosyphilis. Clinical improvement following penicillin G and antiepileptic medications further corroborated neurosyphilis. Neurosyphilis is an infectious disease of the central nervous system

(CNS) characterized by a wide variety of clinical manifestations. The early forms of neurosyphilis are typically seen as either a meningitis or as a disease caused by the obstruction of blood flow due to an inflamed blood vessel; however, the late form of neurosyphilis may be characterized by the development of general paralysis of the insane with progressive dementia, psychiatric symptoms and personality changes. In this case, risk factors for vascular disease and previous cerebral infarctions complicate the determination of the underlying cause, although the presence of progressive cognitive decline supports the diagnosis of late neurosyphilis. Reportedly, about one-fourth of patients with neurosyphilis have seizures; however, there are very few reported cases of non-convulsive status epilepticus, which indicates the complexity of diagnosing this entity.[3,4]

This condition, known as Anti-NMDAR encephalitis, is an autoimmune condition of the brain with symptoms that include psychiatric symptoms, cognitive problems, seizures, and movement disorders.[5,6] Infections may act as triggers for this condition because they cause both damage to the neurons and expose them to an antigen.[7] There have been a few studies that found the marginal lobe to be involved with neurosyphilis, but there are almost no cases where neurosyphilis was present with the presence of antibodies for autoimmune encephalitis.[8,9] The limited number of reports available are variable in clinical presentation and treatment response. In the case we present, there was both anti-NMDAR antibodies in serum and CSF; however, because of the clinical course, imaging results, and laboratory work which were consistent with neurosyphilis and seizure related pathology, autoimmune encephalitis was not considered the primary cause. The improvement seen with antimicrobial and antiepileptic therapy without the use of any immunomodulatory agents demonstrates that the Anti-NMDAR antibodies in this patient may have been just a consequence of an immune response (i.e. a bystander immune phenomenon

Conclusion

The pathogenic significance of anti-NMDAR antibodies in neurosyphilis remains unclear. The presence of NMDAR antibodies alone should not be considered causative in the absence of a compatible autoimmune encephalitis syndrome and exclusion of alternative diagnoses. In patients with concurrent syphilis or neurosyphilis and NMDAR antibody positivity, treatment decisions should be guided by comprehensive clinical evaluation and diagnostic findings, with careful consideration of the risks and benefits of immunotherapy.

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