Case report

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Case report: Intensive care management of anti-NMDA receptor encephalitis in a young male patient presenting with behavioral disorders

Irham Hanafi[1], *Akhmad Yun Jufan*[1], *Bowo Adiyanto*[1]

Abstract

***Background*: Anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis is difficult to diagnose due to the variability of early symptoms. With an estimated incidence of only 1.5 per 1 million population per year (mean age: 23 years), this type of encephalitis is a very rare disorder. Given the limited number of patients, it is important to improve our understanding of pathophysiological mechanisms and therapeutic strategies to improve prognosis.**

***Case presentation*: We report the case of a 21-year-old man who presented to the emergency room after experiencing acute behavioral disturbances, auditory hallucinations, and panic attacks. Due to decreased consciousness and inability to maintain airway patency, the patient was intubated, and then a percutaneous dilatation tracheostomy was performed. The cerebrospinal fluid test results were positive for antibodies to NMDA receptors. After intravenous methylprednisolone and plasmapheresis, the patient's clinical condition gradually improved, and decannulation was performed 37 days after insertion. The patient was subsequently treated as an outpatient with complication sequelae in the form of dementia due to anti-NMDAR encephalitis.**

***Conclusions*: Anti-NMDAR encephalitis is difficult to diagnose because psychiatric symptoms predominate. There is no specific therapy for anti-NMDAR encephalitis, so further research is needed to find the most effective immunotherapy regimen. Because the diagnosis and recovery process of anti-NMDAR encephalitis takes a long time, supportive therapy in intensive care plays an important role in overall management to produce a good prognosis.**

Keywords: Anti-NMDAR encephalitis, autoimmune encephalitis, neuro-intensive care, plasmapheresis.

Background

Anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis is a rare autoimmune disease that often goes misdiagnosed. It most commonly affects children and young adults (less than 5% of patients over 45 years of age), with a median age of 23 years and a male-to-female ratio of 1:4. The origin of the disease is often paraneoplastic with approximately 50% of women over 18 years of age and only 9% of girls under 14 years of age have ovarian teratomas. In contrast, the presence of tumors is rare in men. (1,2) The benefit of this case report is to reflect a rare and frequently misdiagnosed case, providing insights to facilitate diagnosis and further management, particularly in ICU (Intensive Care Unit) settings.

Case presentation

A 21-year-old man was brought to the emergency room by his family with complaints of behavioral changes and recurrent seizures. Initial symptoms included fever, headache, and stiff hands and feet, which had been present for a month. In the following days, these were followed by psychological

[1] Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada – Sardjito Hospital, Yogyakarta, Indonesia

Address for correspondence:
Irham Hanafi
Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada – Sardjito Hospital, Yogyakarta, Indonesia
Tel: +6281328811447
Email: irham.hanafi.md@gmail.com

changes such as anxiety, panic attacks, and auditory hallucinations, as summarized in **Table 1,** which contained signs and symptoms. The patient was also uncommunicative and spoke incoherently. Physically, the patient's eyes constantly looked to the right, and her face twitched, as if in a seizure. The condition was initially diagnosed by a psychiatrist at a mental hospital as a behavioral disorder with symptoms of acute psychosis. It was treated with antipsychotic, anti-anxiety, and anti-seizure medications.

The patient then underwent inpatient treatment with a diagnosis of subacute onset with behavioral disorder, right lateralization, meningeal sign, right deviation conjugate, and facial myoclonus. On the fourth day of treatment, the patient's condition worsened with seizures, decreased consciousness, and respiratory distress. Endotracheal intubation was performed, and the patient was transferred to the ICU. Sedation and anticonvulsant medication were administered. On the first day of treatment in the ICU, the patient continued to experience restless movements and seizures, necessitating several medication changes (midazolam/propofol/dexmedetomidine/ketamine). During treatment, several supporting examinations were performed (**Table 2**) to determine the etiological diagnosis of the patient's disease, including brain magnetic resonance imaging (MRI) with contrast, cerebrospinal fluid (CSF) examination, and testing for infection markers (tuberculosis and toxoplasmosis, rubella, cytomegalovirus, herpes simplex [TORCH] viruses). Based on various examinations, the conclusion was obtained clinical diagnosis of cognitive impairment cum history of status epilepticus cum dyskinesia, topical diagnosis of temporal lobe, and etiological diagnosis of anti-NMDAR encephalitis.

Because the patient was predicted to undergo a long treatment period, a percutaneous dilatational tracheostomy was performed on the fourth day of treatment in the ICU. Other drug therapy, particularly anticonvulsants, was administered to control restlessness and abnormal movements; antibiotics were administered according to culture results; and other symptomatic medications were used (**Table 3**). Empirical antibiotic therapy initiated on the day of treatment was subsequently replaced, based on culture results, with definitive antibiotics, as shown in **Table 4**. Plasmapheresis was prepared via double-lumen catheter access, along with other causative and supportive therapies. The plasmapheresis program and its implementation are presented in **Table 5**.

Following treatment and three rounds of plasmapheresis, the patient showed clinical improvement, with increased consciousness and the ability to follow commands. He was discharged from the ICU after 13 days and then discharged home for a total of 29 days in the hospital. He was discharged with a tracheostomy tube in place due to his cough and swallow reflexes being questionable for decannulation.

Patient experienced pneumonia and respiratory distress for seven days at home and then underwent inpatient treatment again with a diagnosis of somnolence cum lateralization of the right et causa anti-NMDAR encephalitis, suspected pneumonia, and then given antibiotics until his condition improved, fully conscious, and decannulation was performed. Subsequently, the patient continued to make outpatient visits with complaints of repetitive speech, often forgetting what had just been done, and talking in his sleep. The patient was diagnosed with dementia due to anti-NMDAR encephalitis and non-rapid eye movement sleep disorder and received donepezil as medication.

Discussion

Anti-NMDAR encephalitis is an autoimmune disease characterized by the presence of antibodies against the NMDA receptor. Anti-NMDAR antibodies bind to the NR1 subunit, leading to receptor internalization and synaptic dysfunction, ultimately leading to complex neuropsychiatric symptoms. Autonomic dysfunction is an important indication for intensive care and a major risk factor for poor outcomes. (3)

Symptoms of anti-NMDAR encephalitis are preceded by a non-specific prodromal stage (experienced by 70% of patients) that may include nonspecific influenza-like symptoms, such as headache, low-grade fever, diarrhea, or upper respiratory tract infection. (1,4,5) Subsequently, acute psychiatric symptoms appear, including behavioral disturbances, agitation, delusions, visual or auditory hallucinations, anxiety, paranoia, emotional lability, and disorganized thinking. The most common motor disorders are orofacial dyskinesia, choreoathetosis, and dystonia. These disorders can progress to catatonia or mutism, followed by changes in consciousness. (1,4) Neurological symptoms typically develop after 1–3 weeks and include abnormal movements, seizures, and autonomic nervous system disturbances with tachycardia, bradycardia, hyperhidrosis, and hypersalivation. Seizures can be focal or may present as status epilepticus. Clinical features that often indicate the need for intensive care include altered consciousness, swallowing difficulties, and respiratory distress. (1,4)

The diagnosis is confirmed by the detection of

NMDA receptor antibodies in serum and CSF. (1) In this case, the diagnosis was based on the finding of anti-NMDAR antibodies in the CSF. Prodromal symptoms of fever, headache, and stiff extremities appeared one month before hospital admission. Two weeks later, psychiatric symptoms emerged, including anxiety and panic attacks, auditory hallucinations, and slurred speech. Neurological symptoms, including automatisms, eyelid twitching, and oral dyskinesia, emerged and became more pronounced during hospitalization. Altered consciousness, resulting in hypoventilation and airway obstruction, necessitated intensive care with the installation of an endotracheal tube and a ventilator.

First-line therapy consists of intravenous (IV) glucocorticoids, IV immunoglobulin, and plasmapheresis. Several therapeutic regimens for initial treatment have been recommended, including those in **Table 6**. Other recommendations suggest combination therapy, namely IV methylprednisolone 1 gram for 3–5 days and IV immunoglobulin (0.4 g/kg/day for 5 days) or IV methylprednisolone and plasmapheresis. (4,6)

If there is no clinical improvement, second-line treatment with rituximab (375 mg/m^2/week for 4 weeks), cyclophosphamide (750 mg/m^2/month for 4–6 months), or a combination of these agents is recommended for patients aged>16 years. In patients with severe and refractory conditions, bortezomib or tocilizumab is used as third-line therapy. (1,4) In the ICU, the patient received immunosuppressive treatment with IV methylprednisolone 250 mg every 6 hours for 5 days. In addition, plasmapheresis was performed three times: on the fourth, sixth, and seventh days of the patient's treatment.

Conclusion

Anti-NMDAR encephalitis presents a significant diagnostic challenge because the dominant symptoms are psychiatric. A CSF examination should be performed as soon as possible. There is no specific therapy for anti-NMDAR encephalitis; therefore, further investigation into the most effective immunotherapies and plasmapheresis regimens is necessary. Because of the lengthy recovery process, supportive therapy in the ICU is an important part of overall management.

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Table 1. Signs and symptoms of the patient

Onset time	Signs and symptoms
1 month	Fever Headache Stiffness in the hands and feet Anxiety, restlessness, and panic attacks Auditory hallucinations
2 weeks	Eyes darting to the right Face moving as if convulsing Slurred and incoherent speech

Table 2. Diagnostic examinations in the ICU

Examination	Results
Blood culture	Staphylococcus hominis ssp hominis (MRCONS)
Urine culture	No microorganisms found
Sputum culture	Staphylococcus aureus
CSF culture	Staphylococcus hominis ssp hominis (MRCONS)
ETT culture	Acinetobacter baumanii
CSF examination	Clear, lymphocytic pleocytosis cell count 10 cells/µl, PMN 0%, MN 100%, total protein 0.0997 g/dl, glucose 98.9 mg/dl, Pandy test positive, Nonne test negative
Viral immunoserology (IgM)	Anti-toxoplasma, anti-rubella, anti-CMV, anti-HSV1, anti-HSV2: non-reactive
anti-NMDAR immunoserology	Positive
CSF tuberculosis	Negative
MRI with contrast	No signs of infarction, hemorrhage, infection, or intracranial mass

Legend: ICU=intensive care unit; ssp=subspecies; MRCONS=methicillin-resistant coagulase-negative Staphylococci; CSF=cerebrospinal fluid; ETT=endotracheal tube; PMN=polymorphonuclear; MN=mononuclear; IgM=immunoglobulin M; CMV=Cytomegalovirus; HSV=Herpes simplex virus; NMDAR=N-methyl-D-aspartate receptor; MRI=magnetic resonance imaging.

Table 3. Pharmacological therapies in the intensive care unit

Antibiotic based on culture results
Anticonvulsants titration doses: propofol/midazolam/dexmedetomidine/ketamine
Fentanyl titration doses
Phenobarbital 100 mg every 8 hours
Diazepam 15 mg if needed
Methylprednisolone 250 mg every 6 hours
Ipratropium bromide-salbutamol sulfate every 8 hours
N-acetylcysteine 200 mg every 8 hours

Table 4. Antibiotic therapies during treatment

Antibiotic	Rationality
Ceftazidime 2 g every 8 hours	Empirical
Meropenem 1g every 8 hours	Sputum culture sensitive (S. aureus)
Cefoperazone-sulbactam 1 g every 12 hours + vancomycin 1 g every 12 hours	ETT culture sensitive (A. baumanii)
Ampicillin sulbactam 1.5 g every 6 hours + cotrimoxazole 960 mg every 12 hours	ETT culture sensitive (A. baumanii)
Cefixime 200 mg every 12 hours + cotrimoxazole 960 mg every 12 hours	Oral preparations for discharge

Legend: S. aureus=Staphylococcus aureus; ETT=endotracheal tube; A. baumanii=Acinetobacter baumanii.

Table 5. Plasmapheresis program and implementation

Therapy program: • Right femoral vein access • Planned number of procedures: 3–4 • Exchange volume: 1,800–2,000 ml • Replacement fluid: 5% albumin 1,000 ml + 0.9% sodium chloride (800–1,000 ml) • Post-therapy laboratory tests: routine blood work, albumin, electrolytes Plasma exchange I (day 4 post-diagnosis), volume 2,051 ml Plasma exchange II (day 6 post-diagnosis), volume 2,010 ml Plasma exchange III (day 7 post-diagnosis), volume 2,012 ml

Table 6. First-line therapy (1,3,7)

IV methylprednisolone (1 g/day for 5 days); or IV immunoglobulin (400 mg/kg/day for 5 days); or Plasmapheresis

Legend: IV=intravenous.

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