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Therapeutic Plasma Exchange (TPE) in autoimmune encephalitis: a case report



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ABSTRACT

Introduction: Encephalitis is an inflammatory process of the brain parenchyma caused by viruses, bacteria, fungi, or autoimmunity. These rare cases result from antibody reactions to extracellular membrane antigens in the nervous system. The anti-n-methyl D-Aspartate Receptor (NMDA) test confirms autoimmune encephalitis diagnosis. The American Society for Apheresis (ASFA) recommends immunotherapy and Therapeutic Plasma Exchange (TPE) in autoimmune encephalitis, a medical procedure to remove pathogenic antibodies and replace them with substitute fluid. This study aimed to describe TPE in an autoimmune encephalitis patient.

Case description: An 18-year-old female with decreased consciousness GCS E2M4Vx. History of body seizures, frequency 4 times, duration 5-20 minutes, accompanied by fever. The patient had memory deficits and psychiatric disorders like hallucinations. A neurological physical examination revealed stiffness and weakness in all of the extremities. Radiology showed mesial temporal sclerosis, and abnormal electroencephalogram (EEG) results in a suspected structural lesion. Laboratory results showed leukocytosis, elevated inflammatory markers, and staphylococcus haemolyticus, which were detected from liquor cerebrospinal analysis. The patient met the criteria for the diagnosis of autoimmune encephalitis. TPE was performed 5 times as curative therapy. Neurological physical monitoring and routine blood tests, electrolytes (sodium, potassium, and chloride), and albumin as monitoring of TPE and therapeutic response.

Conclusion: The results of TPE were significant for the improvement of consciousness and improvement of motoric extremities in autoimmune encephalitis.

Keywords: autoimmune, encephalitis, NMDA, TPE.

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INTRODUCTION

Encephalitis is an inflammatory process in the brain parenchyma that viruses, bacteria, fungi or autoimmune can cause. The incidence of encephalitis is 32–75%, and the mortality rate worldwide is around 8–18.45%. Autoimmune encephalitis is a rare case. Autoimmune encephalitis results from an antibody reaction against extracellular membrane antigens in the nervous system. The clinical symptoms of autoimmune encephalitis are different from other encephalitis. General symptoms of encephalitis can include fever, headache and decreased consciousness, but hallucinations, psychosis and personality changes accompany autoimmune encephalitis.¹

Cases of autoimmune encephalitis occur due to immune complex deposits in the brain, which induce inflammation, causing unexplained neurological symptoms. Autoimmune encephalitis is diagnosed

based on history, physical examination and supporting examinations. Diagnosing encephalitis of autoimmune etiology is an immunoserological examination of the anti-n-methyl D-Aspartate Receptor (NMDA) to detect specific antibodies that attack brain cells. Therapy for this disease is the use of immunosuppressive drugs and steroid therapy to suppress the immune system response.^{2,3}

According to the American Society for Apheresis (ASFA), immunotherapy and Therapeutic Plasma Exchange (TPE) are recommended and provide significant results in cases of autoimmune encephalitis.^{2,3} TPE or plasmapheresis is a medical procedure used to remove a patient's plasma and replace it with a replacement fluid.⁴ TPE is important because it can eliminate pathological antibodies, increase macrophage/monocyte function, and replace lost plasma components.^{3,5,6}

TPE improves clinical symptoms of various medical conditions, including autoimmune conditions such as lupus, myasthenia gravis, and Guillain-Barre syndrome (GBS). In addition to eliminating circulating antibodies, TPE indirectly modulates the cellular immune system. TPE is associated with decreased B cells and activation of T cells, which play a role in the Th1/Th2 balance.^{2,5,6} Therefore, this study topic is interesting for discussing diseases related to autoimmune diseases. This study aimed to describe TPE in autoimmune encephalitis patient.

CASE DESCRIPTION

An 18-year-old female patient was admitted to the hospital with decreased consciousness. Previously the patient experienced seizures throughout the body with a frequency of 4 times lasting around 5 to 20 minutes, which began with fever with a seizure pattern of hands and

Table 1. Routine blood examination results

Parameter	03/03/23	17/03/23	18/03/23	19/03/23	21/03/23	24/03/23	Units
WBC	13,5	10,4	10,0	9,3	8,6	8,6	10 ³ /μL
%Neu	83,3	74,7	69,9	82,8	74,0	68,7	%
%Lym	10,5	12,1	14,0	7,1	12,1	17,7	%
%Mono	5,1	9,1	10,9	7,7	8,2	9,7	%
%Eos	1,0	3,7	4,5	2,2	5,2	13,4	%
%Baso	0,1	0,4	0,7	0,2	0,5	0,5	%
RBC	4,50	3,77	3,49	3,36	3,12	3,81	10 ⁶ /μL
HGB	12,2	11,7	9,3	8,7	8,5	10,7	g/dL
HCT	34	31	30	29	27	32	%
MCV	76	83	85	85	85	85	fL
MCH	27	28	29	28	28	28	Pg
MCHC	36	33	34	33	33	33	g/dL
RDW-CV	11,9	13,8	14,6	14,7	15,4	14,5	%
PLT	188	143	133	118	105	188	10 ³ /μL
MPV	9,8	10,5	10,5	10,1	10,9	11,0	fL
PCT	0,00	0,00	0,00	0,00	0,00	0,00	%
PDW	11,1	12,0	11,8	9,6	10,6	14,6	%
ESR	10	4	9	6	102	5	mm/hour

Table 2. Blood chemistry examination results

Parameter	08/03/23	18/03/23	19/03/23	21/03/23	24/03/23	Units
RBG	125	92	101	72	132	mg/dL
Ureum	21		20	17	21	mg/dL
Kreatinin	0.43		0.45	0.47	0.74	mg/dL
Albumin	3.8	3.6	3.9	3.4	3.7	gr/dL
Natrium	130	138	136	141	138	mmol/L
Kalium	3.3	3.0	3.2	2.7	2.8	mmol/L
Clorida	96	110	110	107	105	mmol/L
Kalsium	8.6	8.9	8.7	9.1	9.3	Mg/dL

RBG: Random Blood Glucose

Table 3. Immunoserology examination results

Parameter	04/03/23	17/03/23	20/03/23	21/03/23	24/03/23	Units
Antibody HIV	NR					
Antigen HIV	NR					
CRP		1.5	17.4	90.4		mg/dL
Procalcitonin		<0.05	0.94	1.65	>50.0	ng/mL

NR: non-reactive, CRP: C-Reactive Protein

feet jerking, eyes rolling upwards, mouth open, saliva and foam coming out, during the seizure the patient is unconscious. Patients also experience memory deficits and psychiatric disorders in the form of hallucinations. Normal birth history, no history of growth and development according to age, no family history of similar complaints, no history of febrile seizures, no history of trauma.

Physical Examination

Physical examination of vital signs showed the impression of serious illness with Glasgow Coma Scale (GCS)

E2M4Vx, blood pressure 180/81 mmHg, breathing 28x per minute, pulse 90x per minute, temperature 37.2°C. Positive neck stiffness was found on meningeal stimulation. Neurological examination revealed weakness in all four extremities with motor strength (2/2) and decreased movement and muscle tone.

Supporting Examination

Complete blood counts were routinely performed on these patients (Table 1). The results showed leukocytosis, anemia, thrombocytopenia, and increased erythrocyte sedimentation

rate. On the last follow-up day, the blood count examination became normal. A blood chemistry examination showed hypokalemia (Table 2). Immunoserology examination results showed that the patient is not infected with HIV but has increased markers of infection and inflammation (Table 3). Cerebral fluid analysis showed results within normal limits. Meanwhile, *Staphylococcus haemolyticus* bacteria were found in cerebral fluid culture.

Several radiology examinations have been done on this patient. Thorax photo PA/AP (03/03/2023) showed no abnormalities in the photo. MSCT Brain Without Contrast (4/3/2023) showed mesial temporal sclerosis sinistra with hippocampal atrophy. MSCT Brain Without Contrast (5/4/2023) showed mesial temporal sclerosis sinistra with hippocampal atrophy and sinusitis sphenoidalis. Electroencephalogram (EEG) (10/03/2023) showed classification: Abnormal II (seeming bilateral intermittent slowing, which is more dominant in the right hemisphere) with impression: abnormal EEG is quite specific to suggest a structural lesion.

Based on the results of the examination, the patient was diagnosed with autoimmune encephalitis (NMDA-r encephalitis) + bacterial encephalitis + status epilepticus. The patient then received the following therapy: (1) RL infusion 20 dpm; (2) Oxygen 4 lpm via nasal cannula;

Table 4. TPE evaluation

TPE	Total Blood Volume (TBV)	Total Plasma Volume (TPV)	Input (Substitution)	Output (Extracted)
TPE 1	2400 mL	1656 mL	1604	1604
TPE 2	2400 mL	1584 mL	1604	1606
TPE 3	2400 mL	1656 mL	1602	1602
TPE 4	2400 mL	1704 mL	1640	1640
TPE 5	2400 mL	1704 mL	1643	1645

Table 5. Follow-up on TPE results

TPE cycle	Consciousness	Motor strength	Muscle tone
TPE 1	GCS E2M4Vx	2/2	Decrease
TPE 2	GCS E3M5V3	3/3	Decrease
TPE 3	GCS E3M5V3	3/3	Normal
TPE 4	GCS E4M5V4	4/4	Normal
TPE 5	GCS E4M6V5	5/5	Normal

(3) Citicoline 500mg/12 hours/oral (if systolic blood pressure >110mmHg); (4) Methylprednisolone 8 Ampoules per 24 hours per syringe pump (for 3 days); (5) Phenytoin 100 mg/8 hours/intravenous; (6) Vancomycin 1 gram/12 hours/intravenous; (7) Mecobalamin 500mg/24 hours/NGT; (8) Diazepam 10 mg/extra/slow bolus for seizures; (9) Gabapentin 300 mg/12 hours/oral; and (10) Therapeutic Plasma Exchange (TPE). Monitoring of TPE actions for 5 cycles is shown in Table 4. The patient's total blood volume (TBV) is calculated based on gender, height, weight and hematocrit. Calculation of total plasma volume (TPV) is the need for replacement plasma following guidelines from the ASFA. Table 5 shows significant changes in consciousness, motor strength, and muscle tone after undergoing 5 TPE procedures.

DISCUSSION

An 18-year-old female patient was admitted to the hospital with decreased consciousness. Previously, the patient experienced seizures throughout the body with a frequency of 4 times lasting around 5 to 20 minutes, which began with fever with a seizure pattern of hands and feet jerking, eyes rolling upwards, mouth open, saliva and foam coming out, during the seizure the patient is unconscious. Patients also experience memory deficits and psychiatric disorders in the form of hallucinations. Normal birth history, no history of growth and development according to age, no family history of similar complaints, no history of febrile

seizures, no history of trauma. A physical examination of vital signs showed the impression of serious illness with GCS E2M4Vx, blood pressure 180/81 mmHg, breathing 28x per minute, pulse 90x per minute, and temperature 37.2°C. Positive neck stiffness was found on meningeal stimulation. Neurological examination revealed weakness in all four extremities with motor strength (2/2) and decreased movement and muscle tone. Thus, encephalitis was suspected based on the clinical history and physical examination.

Supporting examinations for this patient include laboratory examinations, radiology and EEG examinations. Laboratory examination revealed leukocytosis and increased inflammatory markers. A brain fluid analysis examination was conducted to identify microorganisms, with culture results showing the bacteria *Staphylococcus haemolyticus*. An MSCT radiological examination without contrast found the impression of left mesial temporal sclerosis accompanied by hippocampal atrophy. The EEG showed bilateral intermittent slowing, which was more dominant in the right hemisphere, an abnormal impression specific to the suspicion of a structural lesion. Based on the results of the history, physical examination and supporting examinations, the patient falls within the diagnostic criteria for autoimmune encephalitis and bacterial encephalitis.

Autoimmune encephalitis is a rare inflammatory disorder that attacks the central nervous system. This case is more

common in young women with an average age of 20 without any previous medical history. Initial complaints of encephalitis include prodromal symptoms such as fever, nausea, vomiting, myalgia and lethargy. Subsequently, the patient experienced repeated seizures and symptoms typical of autoimmune encephalitis, namely, accompanied by psychiatric disorders, including hallucinations and memory deficits.^{2,3}

In the initial process, autoantibodies in autoimmune encephalitis will result in central nervous barrier dysfunction. The activation of the innate immune system involves the recruitment of immune cells such as monocytes and macrophages. Next, the cellular immune system is activated, mediated by lymphocytes, resulting in the formation of antibodies. The ongoing inflammatory process and antibody formation induce the release of pro-inflammatory cytokines and chemokines. Immune complex deposits in the brain parenchyma will then cause damage, especially to the mesial temporal lobe, which plays a role in cognitive function and memory.⁵⁻⁷

Autoimmune encephalitis is diagnosed based on history, physical examination and supporting examinations. The diagnosis of autoimmune encephalitis is carried out by examining anti-NMDA immunoserology to detect specific antibodies that attack brain cells. In this patient, the diagnosis was made based on a clinical approach, namely meeting the following diagnostic criteria: (1) Subacute onset with changes in consciousness, memory impairment and psychiatric manifestations; (2) At least one of the findings such as focal lesions in the central nervous system based on MRI results, unexplained seizures, pleocytosis in cerebrospinal fluid (CSF); (3) Other etiologies of encephalitis have been excluded.⁵⁻⁷

According to ASFA, immunotherapy and TPE are recommended and provide significant results in autoimmune encephalitis cases. Therapy for this disease is the use of immunosuppressive drugs and steroid therapy to suppress the immune system response. Laboratory monitoring of autoimmune encephalitis patients receiving TPE should be performed regularly to monitor the patient's response

to therapy and minimize the risk of side effects. Several laboratory parameters need to be monitored during TPE therapy. Complete blood count to monitor the possibility of anemia thrombocytopenia during TPE. Albumin levels to monitor the possibility of hypoalbuminemia due to protein loss during TPE. Electrolyte, glucose and kidney function levels to monitor the possibility of electrolyte disturbances, hypoglycemia and kidney damage due to TPE side effects. The levels of inflammatory markers such as C-reactive protein (CRP) and Procalcitonin can increase when inflammation occurs during the TPE process.⁸⁻¹⁰

TPE therapy in autoimmune cases, including encephalitis, plays an important role, namely eliminating pathogenic antibodies, correcting the imbalance of T-helper cells, increasing T cells and reducing B cells, thereby suppressing antibody production, increasing the activity of regulatory T cells and suppressor T cells, eliminating cytokines thereby suppressing inflammation, increasing macrophage/monocyte function and replacing lost plasma.⁹⁻¹¹

Bacterial encephalitis is inflammation of the nervous system caused by bacteria.¹² The results of the brain fluid culture examination found *Staphylococcus haemolyticus* bacteria. Organisms enter the body through the skin, respiratory tract and digestive tract. Furthermore, pathogenic organisms will spread throughout the body, both hematogenously and through neurons. Hematogenous spread occurs through intracerebral arteries, resulting in symptoms of encephalitis.¹³ This study's limitation is that it does not evaluate the antibodies of this patient related to TPE therapy in autoimmune encephalitis. Therefore, a more comprehensive study is needed.

CONCLUSION

An 18-year-old female with decreased consciousness (GCS E2M4Vx) with a

history of seizures, fever and hallucinatory disorders. The patient was diagnosed with autoimmune encephalitis, and then TPE was carried out 5 times. Neurological physical monitoring and routine blood tests, electrolytes (sodium, potassium and chloride) and albumin were carried out as monitoring during the TPE process and response to therapy. The results of TPE 5 times in this patient were very significant, namely marked by an improvement in consciousness from GCS E2M4Vx to GCS E4M6V5 and improvement in neurological physique in the form of an increase in extremity motor skills to 5/5. A good response to TPE indicates an improvement in immune function in the patient.

DISCLOSURES

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There is no external funding for this study.

Conflict of Interest

All authors stated that there is no conflict of interest in this study.

Author Contribution

All authors stated equal proportions and contributed to this study.

Ethical Consideration

The patient has provided informed consent and has agreed to this writing.

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