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Case Report

Demet Tosun, Nihal Akcay, Mustafa Ogur, Esra Sevketoglu

Bakırköy Dr. Sadi Konuk Research and Training Hospital, University of Health Sciences, Istanbul, Türkiye

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**Corresponding Author:** Demet Tosun, Bakırköy Dr. Sadi Konuk Research and Training Hospital, University of Health Sciences, Istanbul, Türkiye
Email: demettsn@gmail.com

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# A case of Acute disseminated encephalomyelitis treated with therapeutic plasma exchange

**Abstract**

**Aim:** Acute disseminated encephalomyelitis (ADEM), also known as postinfectious encephalomyelitis, is a demyelinating disease of the central nervous system typically associated with multifocal neurological symptoms and encephalopathy. High-dose intravenous corticosteroids, intravenous immunoglobulin, and therapeutic plasma exchange are used in the treatment, and more studies are still needed for optimal treatment.
**Material and Method:** Our patient, who was followed up in our pediatric intensive care unit and diagnosed with ADEM, was included in the study. Bakırkoy Dr. Sadi Konuk Training and Research Hospital Ethics Committee Approval were obtained.
**Results:** A 3.5-year-old, unvaccinated male patient had upper respiratory tract infection symptoms 10 days before his admission. He had complaints of fever, meningismus, altered consciousness, the inward shift in the left eye, and inability to walk. After the diagnosis of ADEM was made with the imaging of our patient, therapeutic plasma exchange was performed daily (TPE) for 7 days. On the 5th day of TPE, his muscle strength was 4/5 and he started walking with physical therapy support on the 7th day; In the control craniospinal MRI imaging of the patient whose gaze restriction did not disappear, on the 15th day of treatment, T2W sequences were normal and significant regression was observed in the findings.
**Conclusion:** Although there is limited data, TPE is thought to be beneficial in children with ADEM who show poor response to intravenous immunoglobulin (IVIG) and/or methylprednisolone treatment as the recommended immunotherapy, and a clinical response was observed in our patient after TPE application.

**Keywords:** Acute disseminated encephalomyelitis, childhood, MRI

## INTRODUCTION

Acute disseminated encephalomyelitis (ADEM), also known as postinfectious encephalomyelitis, is a demyelinating disease of the central nervous system typically associated with multifocal neurological symptoms and encephalopathy.

Although the etiology has not been fully elucidated, awareness of myelin oligodendrocyte glycoprotein antibodies (anti-MOG) has increased, and it is blamed as the cause and ADEM has a risk of recurrence (1,2). Imaging and laboratory tests should be performed to exclude ADEM's possible infectious, inflammatory, neoplastic, and genetic similarities.

The typical ADEM clinic is headache, vomiting, meningismus, behavioral changes, and changes in consciousness 1-2 weeks after infection. High-dose intravenous corticosteroids, intravenous immunoglobulin, and therapeutic plasma exchange are used in the treatment, and more studies are still needed for optimal treatment (3).

## CASE REPORT

A 3.5-year-old male refugee who had not received childhood vaccinations complained of fever and sore throat that began about 10 days ago; upper respiratory tract infection was considered. The patient, who had presented to an outside center 5 days ago with complaints of lower extremity pain, inability to stand on his feet, and fever, underwent brain tomography, which was

interpreted as normal. On follow-up, fever, vomiting, inability to defecate, and changes in consciousness were observed. When he presented to our pediatric emergency department, his fever was 37.5 C, GCS was 12, consciousness was lethargic, he had meningismus and restriction of outward gaze in the left eye, thus meningitis, neuromyelitis optica spectrum disorder, acute flaccid paralysis, and he was admitted to our pediatric intensive care unit with a provisional diagnosis of metabolic encephalopathy.

A lumbar puncture was performed on our patient; no cells were found; CSF pressure was normal. CSF protein: 20mg/dl, glucose: 70mg/dl. An oligoclonal band was sent from CSF and serum. Empirically, vancomycin, cefotaxime, and acyclovir were administered in a meningitis dose; dexamethasone was prescribed intravenously as an anti-edema. Our patient was evaluated for metabolic encephalopathy and neuromyelitis optica spectrum disorder. Serum amino acids, urinary organic acids, tandem MS, vitamin B12 levels, and copper levels were transmitted. With regard to autoimmunity, anti-TPO, anti-TG, anti-GAD antibodies, thyroid function tests, anti-MOG and aquaporin-4 levels, and an autoimmune panel in cerebrospinal fluid were sent. The test results can be found in Table 1.

Our patient had a high C-reactive protein in acute phase reactants in laboratory values, and bacterial infection was ruled out as a preliminary diagnosis due to procalcitonin negativity. There was no significant elevation in liver and kidney function tests. The absence of cells in the CSF evaluation and the negative PCR tests in the meningitis panel excluded the preliminary diagnosis of meningitis. No features were found in the autoimmune tests sent by our patient. Viral respiration and viral markers were negative. Immunoglobulin tests were within normal ranges for his age. Metabolic tests were unremarkable. The autoimmune meningitis panel was negative. Although anti-MOG and NMO positivity were observed in the diagnosis of ADEM, our patient was negative, but imaging findings that may be specific to ADEM and the clinical and radiological response after treatment led us to the diagnosis of ADEM.

EEG and Craniospinal MRI were performed in our patient; T2 hyperintensity was observed in the whole medulla spinalis starting from the T4 level and inflammation demyelinating foci in the spinal cord were found to be compatible with ADEM in the foreground. The images of the patient are shown in Figure 1. On the 2nd day of his hospitalization, the patient was agitated, his lower extremity muscle strength was 3/5, and his left eye continued to turn inward. Meningismus had disappeared. Our patient was started on exercises by physical therapy.

Considering the diagnosis of ADEM, therapeutic plasma exchange (TPE) was started in our patient. The plasma volume of our patient was calculated as 0.065x patient weight x (1-hematocrit), and a therapeutic plasma session lasting 3 hours per day was performed. A Prismaflex TPE filter (Gambro Lundia AB) was used. 5% albumin replacement and therapeutic plasma exchange were performed. Pulse Methylprednisolone (30mg/kg max 1g/kg) was diagnosed after each cure. On the 5$^{th}$ day of TPE, the ocular findings regressed, the patient received a clinical response, and TPE treatment was applied for 7 cycles. He started walking with support on the 7$^{th}$ day. Our patient had assisted walking on the 12$^{th}$ day of his intensive care hospitalization and was transferred to the pediatric service. A control craniospinal MRI was performed during the service follow-ups, On the 15$^{th}$ day of the patient's treatment, T2W sequences were normal in the control craniospinal MRI imaging, and significant regression was observed in the findings. Our patient was discharged from our hospital without any sequelae. He was included in the missed vaccine opportunity program implemented by the Ministry of Health and was followed up in the outpatient clinic of healthy children.

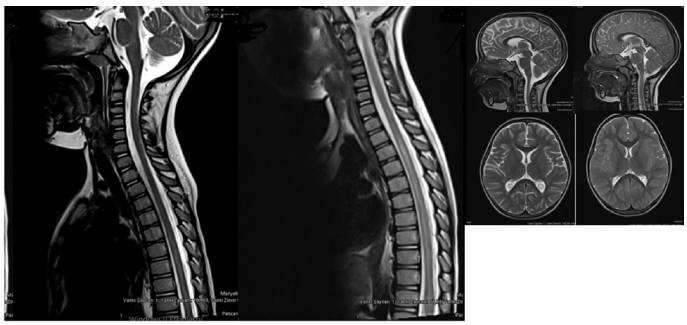

**Figure 1.** T2 flair hyperintense foci were observed in deep gray matter and white matter levels in both cerebral hemispheres, and large areas of involvement were observed in posterior part of pons and in both cerebral hemispheres. T2 hyper intensity was observed in the whole medulla spinals starting form T4 level and inflammation-demyelinating foci in the spinal cord were found to be compatible with ADEM in the foreground. Spinal and Cranial MR images of patient on first day and 15th day of hospitalization shown from left to right.

## DISCUSSION

MRI is the best imaging modality to evaluate a patient with a prior diagnosis of ADEM. MRI of the cervical and dorsal spinal cord can also be performed to confirm the degree of inflammation. Our patient's imaging was specifically evaluated by a pediatric radiologist. The imaging results were consistent with his clinical symptoms.

The use of plasma exchange has been reported in only a small number of cases, typically in severe cases where steroid therapy has failed. Six pediatric ADEM cases treated with plasma exchange have been reported in the literature. Four of these patients recovered completely, and residual left hemiparesis was reported in one of them, and there is no clinical data for the other case (4).

Although information about the treatment in ADEM is limited, it has been reported that intravenous immunoglobulin and/or methylprednisolone treatment is effective in children with ADEM who poor, and better clinical response is observed with early-onset TPE (5). Based on the beginning of the neurological clinic, TPE was started in our patient on the 2nd day of his hospitalization in the pediatric intensive care unit.

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| Table 1. Biochemical and Hematologic Findings of the Patient | |
|---|---|
| White blood cell (per µL) | 16530 |
| Lymphocyte (per µL) | 2590 |
| Neutrophil (per µL) | 12750 |
| Platelet (per µL) | 229000 |
| Hemoglobin (g/dL) | 11.1 |
| C reactive protein (mg/L) | 116 |
| Procalcitonin (ng/mL) | 0.75 |
| Urea (mg/dL) | 15.6 |
| Creatinine (mg/dL) | 0.29 |
| Aspartate aminotransferase (unit/L) | 24.9 |
| Alanine aminotransferase (unit/L) | 10.8 |
| Lactate dehydrogenase (unit/L) | 240 |
| pH | 7.47 |
| $pCO_2$ | 28.6 |
| Lactate(mmol/L) | 1.9 |
| HCO3 | 22.6 |
| PRO-BNP (pg/ml) | 351 |
| D-dimer(ng/mL) | 0.28 |
| APTT (sec) | 29.8 |
| INR | 1.19 |
| CSF | No cell |
| CSF Glucose (mg/dl) | 70.5 |
| CSF Protein (mg/dl) | 20.1 |
| Homocysteine µmol/L | 6.6 |
| IgA( g/L) | 0.57 |
| IgM( g/L) | 1.32 |
| IgG( g/L) | 7.54 |
| SARS Cov-2 Total Antibody(serum) U/mL | 0.4 |
| SARS Cov-2 Total Antibody(CSF) U/mL | 0.4 |
| CSF culture | sterile |
| TSH | 0.53 |
| Free T4 (ng/dl) | 1.26 |
| Folic acid (µg/L) | 7.3 |
| C3c (g/L) | 1.82 |
| C4 | 0.33 |
| Anti-TPO (IU/ml) | 12.8 |
| Anti-TG (IU/ml) | 10.8 |
| Anti- Rubella IgM COI | 0.263 |
| ANTI TOXOPLASMA IGG (IU/mL) | 0.18 |
| Toxoplasma Antibody. IgM COI | 0.212 |
| ANTI CMV IGG (Microparticle Immune Assay) U/mL | 242 Pos |
| ANTI CMV IGM (Microparticle Immune Assay) COI | 0.179 |
| PR3 ANCA u/mL | 0.88 |
| Anti-GAD antibody IU/ml | 1.81 |
| MPO ANCA (U/mL) | 0.2 |
| ANTI NUCLEAR ANTIBODY ANA IFA | <1/100 TITER NEGATIVE |
| Anti ds DNA IFA | <1/10 TITER NEGATIVE |
| ANCA IFA | <1/20 TITER - NEGATIVE |
| EBV VCA IGG | 3.33 Pos |
| EBV VCA IGM | 0.01 |
| Parvovirus B19 IGG | 0.43 |
| Parvovirus B19 IGM | 0.5 |
| Mycoplasma pneumoniae IgG (U/mL) | 1.1 |
| Mycoplasma pneumoniae IgM (U/mL) | 2.3 |
| Copper (serum/plasma) (ug/dL) | 96.6 (normal) |
| HSV-2 RT PCR (CSF) | Not Detected |
| VZV DNA (CSF) | Not Detected |
| HSV-1 RT PCR (CSF) | Not Detected |
| HHV 7 DNA (CSF) | Not Detected |
| HHV 8 DNA (CSF) | Not Detected |
| Respiratory swab panel includes: Influenza A. Adenovirus. Coronavirus OC43. M. pneumonia. Parainfluenzavirus 4. Sars-Cov-2. Influenza H1N1. Coronavirus 229E. Enterovirus. Parainflenzavirus 1. Parechovirus. Influenza H3N2. Coronavirus HKU1. H.Bocavirus . Parainfluenzavirus 2. Rhinovirus. Influenza B. Coronavirus NL63. H.Metapneumovirus. Parainfluenza 3. RSV A/B. | Negative |
| CSF PCR panel; C.neoformans. CMV. Enterovirus. Escherisha Coli K1. H.influenza. Herpes simplex virus 1-2. HHV-6. VZV. H.parechovirus. L.monocytogenes. N.meningitidis. S.galactiae. S.pneumoniae. | Negative |
| Autoimmune meningitis panel<br>Anti-NMDA-R-Ab<br>AMPA-R1-Ab<br>AMPA-R2-Ab<br>CASPR Ab (VGKC)<br>LGI1 Ab (VGKC)<br>GABA-R Ab | Negative |
| NMO (AQUAPORIN-4) | Negative |
| Anti MOG | Negative |

TPE is increasingly being used to treat patients with severe or life-threatening demyelination, such as patients with myelitis or brainstem involvement. Side effects that may develop due to Plex invasiveness include electrolyte imbalance, catheter-related sepsis, and coagulopathy. The possible benefit of TPE depends on the therapeutic removal of systemic blood-circulating autoantibodies and immune complexes from the blood (6).

## CONCLUSION

TPE may be effective in helping to clear antibodies that cause demyelination in ADEM. However, it is performed as a last resort treatment, considering the need for specialist personnel, venous intervention, and catheter-related complications. More research is needed in terms of the timing of TPE therapy for pediatric cases of ADEM.

**Conflict of interests**
*The authors declare that there is no conflict of interest in the study.*

**Financial Disclosure**
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