Role of Plasma Exchange in a Steroid- and IVIG-Refractory Patient with Acute Disseminated Encephalomyelitis: A Case Report

Parmatma Prasad Tripathi a Rekha Hans a Ratti Ram Sharma a
Divjot Singh Lamba a Preeti Paul a Naveen Sankhyan b Chandana Bhagwat b
Paramjeet Singh c

a Department of Transfusion Medicine, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India; b Department of Paediatric Medicine, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India; c Department of Radio Diagnosis and Imaging, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

Keywords
Acute disseminated encephalomyelitis · Steroid therapy · Intravenous immunoglobulin · Plasma exchange

Abstract
Background: Acute disseminated encephalomyelitis (ADEM) is a demyelinating disease usually affecting children and is treated with high-dose steroid therapy. Case Report: An 8-year boy presented with limbs weakness and complete loss of vision and was resistant to steroid therapy. He was further treated with plasma exchange and showed full recovery from the neurological deficit. Conclusion: Therapeutic plasma exchange appears to be effective in ADEM patients in reversing the neuropa thological process especially refractory to steroids and intravenous immunoglobulin.

Introduction
Historically, acute disseminated encephalomyelitis (ADEM) has been used as an umbrella term for noninfectious acute inflammatory demyelinating CNS disorder principally affecting the brain and spinal cord and particularly occurring in children. The median age of presentation of ADEM is 5–8 years with male predominance [1–3]. In some studies, the evidence of an infectious etiology was supported and associated with spring and winter seasonal peaks [4, 5]. ADEM is characterized by multifocal white matter lesions on neuroimaging. It is a monophasic disease with very low relapse rate. The exact incidence of ADEM is not known but, based on population studies in developed countries, its incidence is estimated to be 0.3–0.6 per 100,000 individuals per year [1, 6, 7]. Autoimmune attack via molecular mimicry may be triggered by infection on the CNS system [8]. Apart from infections (mostly viral), other immunological triggers, such as vaccinations and immunological disorders, have been related to ADEM [9–11]. Pathophysiological changes involve transient autoimmune response directed at myelin or other self-antigens, via nonspecific activation of autoreactive T-cell clones [4]. The authentication mark for pathological findings of post-infectious encephalomyelitis is areas of perivenous demyelination and infiltration of lymphocytes and myelin-laden macrophages, occasional plasma cells and granulocytes [12]. Inflammatory invasion, perivascular edema, hyperemia, endothelial swelling, and hemorrhage are other changes associated with pathological changes in ADEM [13–15]. Clinical features may be abrupt or progressed over a period of time. These include prodromal symptoms and mostly
neurological symptoms including altered mental status, cerebellar ataxia, optic neuritis, myelitis, brainstem syndromes, pyramidal dysfunction, and extrapyramidal syndromes [16]. Diagnosis is based on clinical history, CSF examination (pleocytosis and high protein), and MRI (white matter lesion) radiological correlation [17]. Treatment of ADEM includes specific high-dose intravenous methylprednisolone, intravenous immunoglobulin (IVIG), and plasma exchanges along with physical and rehabilitation therapy.

However, the role of plasma exchange in ADEM is helpful in those patients who are unresponsive or poorly respond to steroid therapy. According to ASFA 2019, therapeutic plasma exchange (TPE) for ADEM comes under category II (grade 2C) [18]. Hereby, we present the case of a ADEM patient who completely recovered post-TPE and as in follow-up.

**Case Report**

An 8-year-old boy developed progressive limbs weakness that progressed to a bedridden stage over 12 h. He was treated with steroid pulse therapy (injection methylprednisolone 750 mg/day for 3 days) and IVIG therapy (1 g/kg/day for 2 days). Later, the child also complained of transient loss of vision followed by bilateral complete loss of vision. On examination, there was complete loss of vision with no perception of light in the eyes. On CNS examination, deep tendon reflexes were elicited able with generalized hypotonia and left hemiparesis. The power strength in the right upper and lower limb was 4/5. Power strength in the left upper and lower limbs were 1/5 and 1/5, respectively. All routine investigations were within the normal range. Antibody testing for NMO-MOG (neuromyelitis optica-myelin oligodendrocyte glycoprotein) and aquaporin IgG4 were negative. MRI brain showed multiple subcortical hyperintense lesions of varying sizes on T2W and FLAIR images in both cerebral hemispheres, the largest one in the left parietal-occipital region as shown in Figures 1 and 2. This MRI finding was consistent with ADEM. The rest of the systemic examination was normal. Based on the clinical history and MRI radiological findings, a diagnosis of ADEM (tumefactive, necrotizing demyelination) was concluded. As the patient was a poor responder to steroids and IVIG, the next line of treatment for TPE was planned. On the third day of admission, the first session of TPE was initiated. In total, five sessions were given on every alternate day using a central femoral line dialysis catheter as vascular access on automated cell separators Cobe® Spectra and Optia® Spectra (Terumo BCT; Lakewood, CO, USA). A total of 4% of human serum albumin was used as replacement fluid during each session of plasma exchange. During each session, 1% calcium gluconate infusion was given through venular access to overcome any complications related to hypocalcemia. A detail of the plasma exchange is given in Table 1. All TPE procedures were uneventful.

**Table 1. Detailed plasma exchange procedure**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Session 1</th>
<th>Session 2</th>
<th>Session 3</th>
<th>Session 4</th>
<th>Session 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, kg</td>
<td>27</td>
<td>27</td>
<td>27</td>
<td>27</td>
<td>26</td>
</tr>
<tr>
<td>Total blood volume, mL</td>
<td>1,890</td>
<td>1,890</td>
<td>1,890</td>
<td>1,890</td>
<td>1,820</td>
</tr>
<tr>
<td>Plasma volume, mL</td>
<td>1,070</td>
<td>1,158</td>
<td>1,266</td>
<td>1,266</td>
<td>1,219</td>
</tr>
<tr>
<td>Red cell volume, mL</td>
<td>684</td>
<td>596</td>
<td>623.7</td>
<td>623.7</td>
<td>600.6</td>
</tr>
<tr>
<td>Any complication</td>
<td>Shivering, vomiting, hypotension</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Plasma volume exchanged, mL</td>
<td>1,482</td>
<td>1,412</td>
<td>1,355</td>
<td>1,432</td>
<td>1,654</td>
</tr>
</tbody>
</table>

Fig. 1. MRI finding (T2W image) on pre plasma exchange.

Fig. 2. MRI finding (FLAIR image) on pre plasma exchange.
Plasma Exchange in a Patient with Acute Disseminated Encephalomyelitis

except for the first one where the patient complained of shivering followed by vomiting and hypotension which was managed conservatively with intravenous fluid 0.9% normal saline bolus. After completion of the TPE sessions, the patient showed improvement in vision and started to regain his power. He was discharged on day 18 of hospital stay and had a motor power in the right lower limb of 4/5, in the left lower limb of 3/5, in the left upper limb of 3/5, and in the right upper limb of 3/5.

**Follow-Up**

During follow-up, the patient looked healthy and able to walk independently. The first visit was after 1 month of discharge, where a second dose of pulse cyclophosphamide was given. Vision improvement is shown in Table 2. During the second visit, 2 months after discharge, the patient gave history of full recovery from neurological deficits, and the third dose of cyclophosphamide was given. He was able to play and able to do normal daily routine activities. His vision improved. Left eye vision improved fully with vision 6/6. The patient still complained of blurring of vision in the right eye. But he was able to recognize faces and appreciate hand movement from the right eye with vision 6/9. For this, an ophthalmologist consultation was advised. At 3 months of follow-up, the child was able to walk independently and vision also improved to 6/6 in both eyes as shown in Table 2.

**Discussion**

ADEM is a rare disease in the pediatric age group and related to immune-mediated pathogenesis. Treatment is based on immunomodulatory agents, out of that, steroids are the most important ones. Apart from this, the evidence for other treatment modalities like plasma exchange is based only upon short case series or case reports [19, 20]. The diagnosis of ADEM was made on the basis of clinical, radiological, and CSF findings. In our case, the child showed no improvement, even after initial steroid and IVIG treatment, and his symptoms became more progressive. In steroid- and IVIG-resistant cases, TPE can be used as best therapy [19, 21, 22]. There are case reports and series in which TPE was used in those patients who are refractory to steroids [19, 23, 24]. The effectiveness and ability of plasma exchange is to remove offending circulating antibodies [25]. According to the latest ASFA guidelines 2019, a plasma volume of 1–1.5 needs to be exchanged with a replacement fluid every alternate day for a minimum of 5 procedures, as further suggested by Tselis [26]. A case report by Miyazawa et al. [23] showed the effectiveness of TPE in an 11-year-old child with ADEM who was treated with 4 procedures of TPE. As in our case, we also performed 5 TPE procedures to treat the patient. There could be individual variation in volume, frequency, and duration of TPE based on the clinical response of the patient. TPE can be used in patients who are refractory or not affordable for steroids and IVIG, especially in patients with myelopathy. Borras-Novell et al. [27] found clinical improvement in all their patients after plasma exchanges in ADEM cases which are comparable to our study. It can be used alone as a second line of treatment or in conjunction with immunomodulatory therapies. Criteria for using TPE in cases of ADEM have been established in the 2007 ASFA guidelines [28] as category III, but upgraded as category II (2C) in the 2010 ASFA guidelines [23]. Good tolerance of TPE without any significant adverse effects and progressive neurological improvement recognized in several reports suggest that TPE is an effective therapeutic tool in pediatric ADEM patients when performed in an experienced center.

**Conclusion**

ADEM presentation and MRI lesions in cerebral hemispheres may be the messengers of prolonged illness and lack of response to steroid therapy. TPE may be an effective regimen or at least adjuvant therapy along with steroids in these patients.

**Statement of Ethics**

We are thankful to the father of the child who gave informed consent for publishing this case report. This study was approved by the Institutional Review Board.

---

Table 2. Improvement in vision during and after plasma exchange

<table>
<thead>
<tr>
<th>Duration</th>
<th>Right eye (vision) follow-up</th>
<th>Left eye (vision) follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>After 2nd plasma exchange</td>
<td>Light perception +</td>
<td>Light perception +, pupil restriction +</td>
</tr>
<tr>
<td>After 4th plasma exchange</td>
<td>Light Perception +, pupil restriction +</td>
<td>Light perception +, shadows +/–, pupil restriction +</td>
</tr>
<tr>
<td>After 5th plasma exchange</td>
<td>Light perception +, flashes + pupil restriction +</td>
<td>Light perception +, shadows +/–, pupil restriction +, inconsistent response to finger counting at half a meter and color identification</td>
</tr>
<tr>
<td>During 1st visit after discharge</td>
<td>Vision 6/36</td>
<td>Vision 6/36</td>
</tr>
<tr>
<td>During 2nd visit after discharge</td>
<td>Vision 6/9 with the blurring of vision</td>
<td>Vision 6/6 within normal limit</td>
</tr>
<tr>
<td>During 3rd visit after discharge</td>
<td>Vision 6/6 within normal limit</td>
<td>Vision 6/6 within normal limit</td>
</tr>
</tbody>
</table>

Plasma Exchange in a Patient with Acute Disseminated Encephalomyelitis

DOI: 10.1159/000504987
Disclosure Statement

The authors have no conflicts of interest to disclose.

Funding Sources

No funding was received for this research.

References