

# Therapeutic Plasma Exchange In Steroid Refractory Autoimmune Encephalitis - A Case Report

**Dr.Kuralarasi Priyadarshini<sup>1</sup>, Dr.Gopinathan Mathiyazhagan<sup>2</sup>,  
Dr.Ingersal Natarajan<sup>3</sup>**

<sup>1</sup>Registrar, Department of Transfusion Medicine, MGM Healthcare

<sup>2,3</sup>Consultant, Department of Hematooncology ,MGM Healthcare

## Abstract

A 63-year-old female with a known case of diabetes mellitus, hypertension, primary Sjögren's syndrome, carcinoma left breast on immunotherapy atezolizumab, presented with confusion, drowsiness (GCS E3VTM4), fever and respiratory distress. Neuroimaging studies did not reveal any structural abnormalities, and the paraneoplastic panel of neuronal antibodies were tested negative. The patient was clinically diagnosed to be a case of AE (Autoimmune Encephalitis). Due to persistent encephalopathy and unresponsiveness to steroid therapy, she was scheduled for a therapeutic plasma exchange (TPE), and after six sessions patient showed significant clinical improvement. This case report emphasizes the importance of TPE along with immunotherapy in the management of steroid-unresponsive Autoimmune Encephalopathy.

**Keywords:** autoimmune encephalitis, malignancy, plasma exchange

## Introduction

Encephalitis is a condition caused by inflammation of the brain parenchyma due to various infections and autoimmune condition. <sup>[1]</sup>

Its diagnosis depends upon the clinical course, serological evidence of autoantibodies, intrathecal inflammatory markers in the CSF (cerebrospinal fluid) and neuroimaging by MRI. <sup>[2]</sup>

According to the ASFA guidelines, steroids, immunotherapy and TPE are recommended and they provide significant clinical improvement in cases of autoimmune encephalitis. TPE is a medical procedure that involves removing the infected or diseased plasma of a patient and replacing it with replacement fluids such as healthy donor plasma or 5 % albumin. By doing so, it eliminates the pathological antibodies as well as modifies the cellular immune system to respond better to immunotherapy. <sup>[1]</sup>

Here, we present a suspected case of AE that was unresponsive to steroid, managed successfully using TPE along with immunotherapy.

## Case description

63yr old female with known case of diabetes mellitus, hypertesion, Sjögren's syndrome, carcinoma left breast on immunotherapy atezolizumab presented with drowsiness (GCS E3VTM4).

On examination patient was afebrile and vitals were stable.

CSF analysis showed increased protein, glucose and lactate levels. Neuroimaging (CT and MRI) did not reveal any parenchymal abnormality.

A paraneoplastic panel of neuronal antibodies such as anti-nuclear antibody (ANA), anti-Sm, anti-ds DNA, antiRNP, anti-Scl70, rheumatoid factor, anti-anticardiolipin IgM/IgG antibody, anti-neutrophil cytoplasmic antibody (ANCA) and anti-Jo-1 antibody, were tested negative.

CSF PCR assays for viral pathogens (varicella zoster virus, herpes simplex virus, human herpes virus-6), CSF cultures for bacterial (including tuberculosis) and fungal pathogens were negative.

Complete blood count gave a picture of bicytopenia with positive direct coombs test (DCT).

Despite IVIG and steroids, the patient's symptoms were worsening (**steroid refractoriness**).

Neurologically, she was diagnosed as ICI (immune checkpoint inhibitor) related Autoimmune encephalitis. Due to persistent encephalopathy and deterioration in her sensorium, a therapeutic plasma exchange (TPE) was scheduled.

The initial three procedures of plasma exchange were performed using dialysis equipment every alternate day, with minimal improvement and were continued on centrifugation apheresis.

Following this, a total of 06 sessions of TPE (one session every week) were performed using apheresis device (COM.TEC, Fresenius Kabi, Germany) along with RITUXIMAB immunotherapy.

Before procedure, prophylactic intravenous administration of calcium gluconate 2g, magnesium sulphate 2g, and chlorpheniramine 2ml was administered. During procedure, intravenous calcium gluconate at 10ml/hour over 2 hours was administered.

The first TPE session were performed using central venous catheter (CVC) placed in the right jugular vein, the next 2 sessions were using double-lumen femoral dialysis catheter placed in femoral vein and the remaining 3 sessions were performed using CVC under aseptic precautions, as there were repeated "low blood flow" alarm in the earlier procedures using femoral venous access. Throughout the procedure, patient vitals were monitored and recorded every 15 minutes.

A total of 06 sessions of TPE were performed using the apheresis device (COM.TEC, Fresenius Kabi, Germany) One standard TPE procedure had 1.2–1.3 TPV (total plasma volume) exchanged using 5% albumin and FFP as a replacement fluid. After the 06 sessions, patient's clinical condition, sensorium improved significantly, she moved all her four limbs, tolerated oral feeds and responded to oral commands.

The early suspicion of ICI related Autoimmune Encephalitis and the early intervention of TPE despite screening negative for panel of neuronal antibodies, played a significant outcome in the management of AIE.

## Discussion

Though our AE patient presented with features of bicytopenia and positive DCT, the paraneoplastic panel of neuronal antibodies were negative and this type of finding is similar to the article published by **Pandey PK**.<sup>[3]</sup>

In our study, the patient was unresponsive to steroids but showed significant clinical improvement soon after the third cycle of TPE using apheresis device (COM.TEC, Fresenius Kabi, Germany), which is supported by other studies **Badly et al** <sup>[4]</sup> and **van den Berg et al**.<sup>[5]</sup>

According to ASFA guidelines TPE has been recommended as a standalone secondary treatment (Category II) for Acute Disseminated Encephalomyelitis (ADEM) after high-dose IV corticosteroid failu-

re. [6]

In our study, the initial three procedures of plasma exchange was done using dialysis with minimal improvement, followed by 06 procedures using apheresis device (COM.TEC, Fresenius Kabi, Germany) performed over 6-8 weeks with significant clinical improvement, compared to the study **van den Berg et al.** [5]

In our study, we performed one standard TPE procedure as **1. 2–1. 3 TPV** exchanged using replacement fluid using 5% albumin and FFP but Pathak et al. performed TPE on patients every alternate day with 1.0 TPV exchanged volume using 5% albumin as replacement fluid and the number of procedure ranging between 4 to 6 sessions depending upon their improvement. [2]

Aggressive treatment (>1.0 TPV exchange) of Autoantibody mediated encephalitis using TPE which has showed improved survival of the patients emphasizing the role of plasmapheresis in various forms of AE [7] Simabukuro [8] Abdulhafeez M. Khair [9] and Gastaldi, M.

By eliminating antibodies, correcting the imbalance of T-helper cells, and reducing B cells, TPE therapy in autoimmune cases plays an important role as it suppresses antibody production, increases the activity of regulatory T cells and suppressor T cells.

TPE also increase the macrophage/monocyte function.

The strength of the study is clinical Assessment of the patient with complete blood counts, electrolyte levels (Table:01), and a neurological assessment (GCS) (Table: 02) after every TPE cycle.

Major limitations of therapeutic plasma exchange include, increased bleeding risk, total body volume shifts, need for central line placement with its associated risks and it is less suitable for agitated patients.

### Conclusion

Therapeutic Plasma exchange for autoimmune encephalitis can have a successful outcome if an early diagnosis could be made and the TPE is initiated on time, along with immunotherapy. The compliance to TPE was excellent in our case as the patient showed improvement in her sensorium, biochemical parameters, blood counts and motor extremities. Despite a category I and II recommendation of TPE for encephalitis from the American Society for Apheresis, therapeutic plasma exchange remains underutilised.

**Table 01: Patient parameters Pre and Post TPE procedure**

| Parameters                            | Pre- Procedure | Post-Procedure |
|---------------------------------------|----------------|----------------|
| Hb (g/dl)                             | 7.9            | 9.1            |
| PCV (%)                               | 23.3           | 31.8           |
| Platelet Count (x10 <sup>3</sup> /ul) | 54             | 175            |
| Sodium (mmol/L)                       | 155            | 127            |
| Potassium (mmol/L)                    | 5.82           | 3.44           |
| Urea (mg/dl)                          | 87.2           | 63.3           |
| Creatinine(mg/dl)                     | 0.71           | 0.91           |

| TPE Cycle No: | Blood Vol Processed (ml) | Plasma Vol Processed(ml) | TPV Exchanged | Replacement Fluid Vol(ml) | Consciousness |
|---------------|--------------------------|--------------------------|---------------|---------------------------|---------------|
| TPE-01        | 4535                     | 3031                     | 1.2           | 3000                      | GCS<br>E3M4VT |
| TPE-02        | 5014                     | 3504                     | 1.2           | 3500                      | GCS<br>E3M4VT |
| TPE-03        | 5376                     | 2998                     | 1.3           | 3000                      | GCS<br>E4M6VT |
| TPE04         | 4984                     | 2997                     | 1.2           | 3000                      | GCS<br>E4M6VT |
| TPE-05        | 4760                     | 2999                     | 1.2           | 3000                      | GCS<br>E4M6VT |
| TPE-06        | 4704                     | 3710                     | 1.2           | 3000                      | GCS<br>E4M6VT |

**Table 02: Therapeutic plasma exchange procedure details**

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