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Plasma Exchange as Rescue Therapy for Patient with Poorly Responsive Guillain-Barre syndrome

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Abstract

Background: Intravenous immunoglobulin (IVIg) has traditionally served as the primary treatment for Guillain-Barré syndrome (GBS), reserving plasmapheresis for severe cases or as an adjunctive therapy with uncertain outcomes. Currently, there is no robust recommendation supporting the utility of therapeutic plasma exchange (TPE) following IVIg treatment failure. *Case Report*: In this report, we present a case of severe GBS accompanied by respiratory failure necessitating mechanical ventilation. Nerve conduction studies and electromyography (EMG) findings indicated a profound hyperacute motor sensory axonal neuropathy phenotype of GBS. Despite an initial course of IVIg at a dosage of 0.4 g/kg administered over five consecutive days, the patient exhibited no improvement. However, a notable turnaround in the patient's condition was observed following TPE. *Conclusion*: This case report underscores the potential benefit of TPE as a viable treatment option for select patients who fail to respond to immunoglobulin therapy, shedding light on its effectiveness in such challenging cases of GBS.

Keywords: Guillain-Barre Syndrome, Intravenous immunoglobulins, Plasmapheresis, Respiratory Failure, Sensory Neuropathy.

Introduction

Guillain-Barré Syndrome (GBS) represents an inflammatory disorder of the peripheral nervous system, standing as one of the most prevalent causes of acute flaccid paralysis worldwide, with an estimated annual global incidence of approximately 1-2 per 100,000 person-years [1]. Patients commonly present with acute flaccid paralysis and/or sensory and autonomic nerve dysfunction. The diagnosis of GBS hinges upon a thorough evaluation of patient history and a combination of neurological, electrophysiological, and cerebrospinal fluid (CSF) examinations [2]. Distinguishing between axonal GBS and acute inflammatory demyelinating polyradiculoneuropathy (AIDP) typically requires an electrophysiological study performed around 3 to 4 weeks post-onset [3]. In the diagnostic context, the presence of albuminocytologic dissociation in the CSF holds particular significance and is observed in up to 90% of patients, most commonly emerging in the third week of the disease course [4]. Notably, some GBS patients experience rapid and severe deterioration, resulting in profound disability within a mere two-week period. Respiratory failure, necessitating mechanical ventilation, befalls around 20% of GBS patients, while autonomic nervous system involvement can trigger cardiovascular instability and account for mortality rates ranging from 3% to 10%, even with optimal clinical management [5]. Evidently, the therapeutic effectiveness of both intravenous immunoglobulin (IVIg) and therapeutic plasma exchange (TPE) in GBS treatment has been substantiated through extensive investigations [6]. Nonetheless, debates persist owing to the associated high costs, adverse events, and incomplete understanding of their underlying mechanisms [7].

To address these debates, an international randomized controlled trial (RCT) compared TPE, IVIg, and TPE followed by IVIg in a cohort of 383 adult patients with severe AIDP, revealing the equivalence of all three therapeutic modalities (Plasma Exchange/Sandoglobulin Guillain-Barré Syndrome Trial Group, 1997). However, there remains a compelling need for more comprehensive studies to establish the efficacy of TPE as a salvage therapy subsequent to IVIg failure [8].

Case Report

A 33-year-old woman presented with a three-day history of weakness in her limbs, drooping eyelids, limb pain, and difficulty speaking. There was no prior personal or family history of similar symptoms, and no recent infections were reported. Upon admission, her vital signs were mostly within the normal range, except for an elevated heart rate. Neurological examination revealed weakness in the muscles controlling her speech and profound, floppy weakness in all four limbs with no strength (graded at 0/5). Bilateral absence of deep tendon reflexes with flexor plantar responses was observed. The rest of her physical examination was unremarkable. Suspected to have Guillain-Barre Syndrome (GBS), she received intravenous immunoglobulin (IVIg) treatment at a dose of 0.4 g/kg for five consecutive days. However, just twelve hours after admission, she developed respiratory distress, requiring intubation, mechanical ventilation, and initiation of inotropic support due to low blood pressure.

A lumbar puncture revealed albuminocytologic dissociation with elevated protein levels (556 mg/L) in the cerebrospinal fluid (CSF). CSF analysis also showed oligoclonal IgG levels of 87 mg/L (normal: <34 mg/L). Tests for acetylcholine receptor antibodies, autoimmune profiles, and toxicology screenings were negative. Nerve conduction studies and electromyography (EMG) indicated a severe hyperacute axonal sensorimotor neuropathic process consistent with an acute motor sensory axonal neuropathy phenotype of Guillain-Barre syndrome.

The patient received a total of five days of IVIg therapy, but over the subsequent ten days, there was no improvement in limb strength, and she remained dependent on mechanical ventilation. In light of the lack of progress, she was referred to our facility for therapeutic plasma exchange (TPE) as a rescue therapy after ten days of IVIg treatment and supportive care. The patient underwent six cycles of TPE over twelve days, using membrane plasma separation with continuous renal replacement therapy (CRRT) machines. Heparin (5000 units) was used initially for filter priming, followed by enoxaparin (20 mg). Each TPE session aimed for a filtration fraction of less than 20 percent, a mean blood flow of 150 mL/min, a mean plasma removal rate of 20 ml/min and a mean therapy time of 180 minutes for a total exchange volume of 3600 mL. Vascular access was achieved through a double-lumen femoral catheter (11.5 Fr), and exchange volumes ranged from 1 to 1.5 plasma volume exchanges per session. Replacement fluids consisted of 5 percent albumin and normal saline, with sessions conducted on alternate days during the twelve-day course.

Before initiating TPE, a comprehensive set of laboratory investigations were performed, including full blood count, prothrombin time, partial thromboplastin time, fibrinogen, D-dimer, immunoglobulin levels, urea and electrolytes, calcium, phosphate, and magnesium. Additional checks for serum calcium, magnesium, albumin, urea, electrolytes, and coagulation profiles were carried out after each TPE session. Remarkably, following the second TPE session, significant clinical improvement was observed, with upper limb strength improving to grade 2/5. After the third TPE session, the patient regained movement in her upper limbs, achieving a strength grade of 3/5. She was successfully weaned from controlled ventilation and transitioned to oxygen therapy via a non-rebreathing mask, followed by a simple mask,

and eventually room air. The patient also regained the ability to swallow both liquids and solids. After the fourth TPE session, she regained movement in her lower limbs with a power grade of 2/5, while her upper limbs reached a strength grade of 5/5. Reflexes in both the upper and lower limbs became elicitable, and she experienced neuropathic pain, which was managed with analgesics and carbamazepine.

Following the completion of TPE sessions, the patient achieved a power grade of 5/5 in the upper limbs but remained at 3/5 in the lower limbs. Over the course of her three-week hospital stay, she continued to demonstrate clinical improvement, gaining the ability to support her trunk and requiring only minor assistance when transitioning from a supine position.

Discussion

In the United States, intravenous immunoglobulin (IVIg) and therapeutic plasma exchange (TPE) are the cornerstone therapies for 92% of Guillain-Barré Syndrome (GBS) patients [9]. While IVIg is the recommended initial treatment, a subset of patients may experience ongoing deterioration or symptom fluctuations following the initial course of IVIg, potentially necessitating a trial of a second IVIg administration. However, the efficacy and benefit of a second IVIg course remain to be firmly established. When considering the use of TPE after IVIg treatment failure, the existing evidence supporting such an approach is limited [10]. Physicians faced with treatment failures may either repeat the same treatment or opt for an alternative therapeutic approach, yet there is currently a lack of evidence-based guidelines supporting the superior outcome of these alternate therapies [11].

A thorough review of the literature reveals varying perspectives, with some articles favoring IVIg, others advocating for plasma-pheresis/ plasma exchange, and some reporting no significant difference between the two therapies [12]. A meta-analysis published in 2016 found no compelling evidence for the superiority in efficacy or safety of either IVIg or plasmapheresis in managing GBS [11]. In contrast, a Cochrane review concluded that TPE stands as the first and only treatment proven to be superior to supportive treatment alone in GBS [13]. Clinical trials further suggest that TPE can be particularly beneficial when initiated within 4 weeks from the disease onset, while IVIg is most effective when administered within the first 2 weeks [14]. As such, TPE emerges as the preferred therapy for patients who present later in the disease course. Some experts even recommend a combination of both treatments, commencing with an IVIg dose followed by TPE in refractory cases that fail to respond. Such an approach could potentially expedite recovery, reduce the patient's hospital stay, and minimize the time spent on mechanical ventilation [15]. In practice, TPE is strongly endorsed for GBS cases requiring mechanical ventilation support, especially due to its potential advantages in reducing the duration of mechanical ventilation in pediatric GBS cases.

Future large-scale randomized controlled trials (RCTs) are imperative to address treatment complexities associated with variant forms of GBS, treatment-related fluctuations, cases presenting late in the disease course, and situations where patients fail to show improvement or even progress after initial treatment.

Conclusion

It is essential to reinforce GBS guidelines for cases that do not respond to first-line therapy through well-designed randomized controlled trials (RCTs). This case report highlights the potential for future research endeavors to explore the impact of TPE as a salvage therapy after IVIg failure in severe GBS cases, further contributing to our understanding and management of this complex disorder.

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