Case Report

Automated (Centrifugal) Therapeutic Plasma Exchange Option for Guillain-Barre Syndrome: A Report from Calabar, Nigeria

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ABSTRACT

Therapeutic plasma exchange (TPE) is performed frequently and effectively in developed countries, whereas the reverse is the case in developing countries. Guillain-Barre syndrome (GBS), synonymous with acute inflammatory demyelinating polyneuropathy, is an important indication for TPE, but this is rarely administered in the treatment of such patients in Nigeria due to lack of such automated facility, limited expertise, and high cost. This report therefore presents an uncommon case of GBS in which automated TPE was utilized in the management, with the aims of highlighting the current status and challenges of therapeutic apheresis services in Nigeria. A 42-year-old male presented with rapidly progressive (in an ascending fashion) paralysis of all four limbs within 24 h without any preceding history of fever or other symptoms. Clinical examination revealed a young man, afebrile, not pale, and also not dehydrated. Central nervous system examination showed a conscious man, alert, and oriented in time, person, and place. There were no signs of meningeal irritation and the cranial nerves were grossly intact. There was no power in the limbs: global hypotonia and areflexia were noted on examination. However, he had intact sensory perceptions to touch and pain. Following a diagnosis of GBS, he was treated with four sessions of plasmapheresis and TPE. The TPE session was done using a discontinuous flow apheresis machine which exchanged one plasma volume (3 L of plasma) and 5% albumin used for replacement. The patient made gradual but steady recovery as return of power to the upper limbs and trunk started by the 2nd week of treatment. TPE is an important treatment modality in the management of GBS as well as several other conditions, and it is becoming increasingly available in Nigeria. However, it is still grossly underutilized, thus the need for more therapeutic apheresis facilities and trained personnel, in addition to concerted efforts to subsidize the cost of accessing the treatment.

KEYWORDS: *Guillain-Barre syndrome, therapeutic apheresis, therapeutic plasma exchange*

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INTRODUCTION

Guillain-Barre syndrome (GBS), synonymous with acute inflammatory demyelinating polyneuropathy (AIDP), is a condition characterized by acute symmetrical ascending motor weakness and areflexia (or hyporeflexia), with variable sensory loss.[1] It is an immune-mediated inflammatory disease affecting the myelin and axons of peripheral nerves. The annual incidence of GBS, worldwide, is reported[2] to be 0.6–2.4 cases per 100,000 per year and with a male preponderance. Molecular mimicry and a cross-reactive autoimmune response play a crucial role in its pathogenesis.[3] Although the etiology is not fully understood, the majority of cases are triggered

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by infection which stimulates the production of antiganglioside antibodies.[1] The definitive treatment options include therapeutic plasma exchange (TPE) and intravenous immunoglobulins (IVIG).[4] Whereas both therapeutic approaches are equally efficacious,[5] TPE has been reported to be more cost-effective.[6] The TPE procedure removes antibodies and complement in the patient's plasma, resulting in less nerve damage and more rapid clinical improvement.[7]

TPE is a well-recognized treatment approach in a variety of neurological, hematological, renal, and autoimmune diseases including GBS. Based on the American Society for Apheresis guidelines for therapeutic apheresis, GBS is a category I indication for TPE,[8] which means that it is an appropriate first-line treatment for this disease. In spite of being an important therapeutic modality for several medical conditions, TPE is rarely done in Nigeria owing to limited availability of apheresis devices as well as expertise and high cost of the procedure (to an average Nigerian). However, a few centers in the country (to the author's knowledge) improvise by carrying out plasmapheresis procedures, in which <1 L of plasma is removed per session, and some even perform manual partial exchange blood transfusion in the management of GBS.[9]

By removing the patient's plasma, the goal of TPE is to remove pathological substances (such as pathological antibodies, immune complexes, and toxins) that are associated with a disease condition.[10] Indications for TPE include GBS, thrombotic thrombocytopenic purpura, myasthenia gravis, rapidly progressive glomerulonephritis, ABO incompatible solid organ transplant, cryoglobulinemia, hyperviscosity in monoclonal gammopathies, and paraproteinemic demyelinating polyneuropathies, among others.[8] Due to limited availability of therapeutic apheresis services, there is a paucity of publications on TPE in many developing countries. In Nigeria, there are isolated reports of filter membrane-based TPE[11] and "modified plasmapheresis"[12] in the management of lupus nephritis and myasthenia gravis, respectively. With gradual development of therapeutic apheresis services offered at certain centers in the country, TPE option is becoming increasingly available for patients in whom it is indicated.

This report therefore presents a case of GBS in which automated TPE was utilized in the management of the patient. The aim is to highlight the current status as well as challenges of therapeutic apheresis services in Nigeria.

Case Report

A 42-year-old businessman who resided in the Southern part of Nigeria was apparently well until 5 weeks before presentation, when (upon awakening) he suddenly noticed a shock-like sensation in both legs which was associated with difficulty in walking. These symptoms rapidly progressed (in an ascending fashion) to paralysis of all four limbs within 24 h and also affected his speech as well as ability to swallow. He had no difficulty in breathing or associated loss of consciousness. The symptoms were not predated by any history of fever, diarrhea, headaches, vomiting, trauma, or bone pains. Unfortunately, he did not initially seek medical intervention.

Clinical examination revealed a young man who was conscious, afebrile, anicteric, acyanotic, and not dehydrated. There was no pallor, digital clubbing, peripheral lymphadenopathy, or pedal edema.

The vital signs on presentation were as follows: temperature (36.5°C), pulse rate (112 beats/min), blood pressure (140/100 mmHg), and respiratory rate (28 cycles/min).

Central nervous system examination showed that he was conscious, alert, and oriented in time, person, and place. There were no signs of meningeal irritation and the cranial nerves were grossly intact. There was no power in the limbs, which had global hypotonia and areflexia. However, he had intact sensory perception to touch and pain.

An assessment of GBS (acute inflammatory demyelinating neuropathy) was made.

Several investigations were done including a full blood count: white blood cell count (8.6×10^9/L), lymphocytes (1.8×10^9/L), granulocytes (6.1×10^9/L), red cell count (5.18×10^{12}/L), platelet (131×10^9/L), hemoglobin concentration (15.8 g/dL), mean corpuscular volume (90 fL), mean corpuscular hemoglobin (MCH) (30 pg), and MCH concentration (33.8 g/dL). The peripheral blood film morphology was essentially normal. His erythrocyte sedimentation rate result was 75 mm in the first hour, while the clotting profile was normal (prothrombin and activated partial thromboplastin times were 15 and 35 s, respectively). Screenings for HIV 1 and 2 were nonreactive. Sinus tachycardia was noted on electrocardiogram. Renal function test and serum protein results showed no significant abnormality. Certain other investigations including cerebrospinal fluid examination/analysis, electrophysiologic studies, and skeletal survey were not done owing to either financial constraints or noncompliance issues.

His treatment consisted of sessions of plasmapheresis and TPE, physiotherapy, prophylactic anticoagulation (using low molecular weight heparin), multivitamins, and some symptomatic treatments. By the time of

treatment, the disease had apparently plateaued owing to his late presentation and the near absence of treatment options (particularly TPE and IVIG) in the country. He had three sessions of plasmapheresis (plasma collection) done on alternate days with approximately 0.55 L of plasma removed in each session (this was the best available option at that moment). However, he subsequently had one session of standard TPE in which 3 L (one plasma volume exchange) of plasma was exchanged, using 5% albumin and 0.9% saline as replacement fluids.

This centrifugation-based automated TPE was done using a discontinuous flow apheresis machine (Haemonetics MCS+). A 14 GA femoral catheter was inserted into the right femoral vein, for withdrawal and return of the patient's blood. The calculated plasma volume of the patient was approximately 3 L, and this was removed and replaced with 5% albumin (2250 ml) and 0.9% saline (750 ml). Anticoagulation was done using Acid Citrate Dextrose Adenine (ACDA) at an ACDA: blood of 1:11. Two tablets of oral calcium (Calcium Sandoz) were administered as prophylaxis for citrate-induced hypocalcemia. Except for occasional interruptions due to clotting around the catheter-tubing set connection, the procedure was otherwise uneventful and well tolerated by the patient. The preprocedure vital signs were temperature (36.5°C), respiratory rate (18/min), pulse rate (104 beats/min), and blood pressure (146/104 mmHg); whereas, the postprocedure vital signs were temperature (36.7°C), respiratory rate (22/min), pulse rate (116 beats/min), and blood pressure (131/98 mmHg).

A probable response to treatment was evident by a very gradual but steady return of power to the digits and limbs. After 3 weeks of hospitalization, he was discharged (due to financial constraints) to continue physiotherapy and prophylactic anticoagulation. Follow-up assessment at 1 month postdischarge revealed sustained improvement as the patient could move the upper limbs and sit without support.

Discussion

By definition,[8] TPE refers to a therapeutic procedure in which a patient's whole blood is passed through an apheresis device; the plasma component is removed and replaced with a colloid or colloid/crystalloid solution. On the other hand, a plasmapheresis procedure, which can be done on either a blood donor or a patient, removes a smaller volume (<15% of total plasma volume) without the use of replacement solution. For conditions where TPE is indicated, one total plasma volume or more is usually removed and replaced with colloids (albumin or plasma) or a combination of colloid and crystalloid (normal saline). The use of TPE in the treatment of GBS is well established and also reported[6] to be cost-effective. However, TPE as a treatment modality for both GBS and other conditions in which it is indicated is rarely available and is also underutilized in Nigeria.

The diagnosis of GBS relies heavily on clinical findings since treatment should be commenced as soon as diagnosis is suspected. Our patient had a rapidly evolving ascending paralysis with areflexia, in the absence of fever or other systemic symptoms. Although he did not recall any antecedent gastrointestinal or respiratory tract infections, GBS in many cases is preceded by a history of such infections occurring a few weeks before onset of AIDP symptoms. Organisms implicated in such infections include *Campylobacter jejuni, Haemophilus influenza, Mycoplasma pneumonia*, Epstein-Barr virus, influenza, and cytomegalovirus.[3] Detailed investigations including cerebrospinal fluid examination/analysis and electrophysiologic studies were not carried out due to either financial constraints, sheer noncompliance, or limited availability of some investigations in our setting. The challenge of high cost and relative unavailability of IVIG lead to the decision to use TPE, which is equally efficacious.[5]

There are two fundamental assumptions in TPE and other therapeutic apheresis procedures.[13] First is that the disease state is causally related to the presence of a substance found in the blood. Second is that the pathogenic substance in the patient's blood/body can be removed efficiently enough to permit disease resolution or remarkably decrease disease morbidity. TPE for the treatment of GBS significantly removes pathological antibodies as well as complement in the patient's plasma, thereby limiting nerve damage and facilitating faster clinical recovery.[7] It has been shown[14] that TPE administered early in the course of GBS results in better outcome, with a protocol consisting of four to six exchange procedures over 10–14 days. With each procedure, 1–1.5 plasma volumes are exchanged and replaced with 5% albumin and saline.[13] Following the onset of disease symptoms, the patient unfortunately spent about 4 weeks elsewhere before seeking medical attention. This underscores the level of health-seeking behavior and enlightenment of some of our patients. Initially, on admission, he received four sessions of plasmapheresis, with each procedure removing less than a liter of his plasma. At that moment, it was the only available option as the apheresis machine needed a different programming to be able to perform TPE. Subsequently, a one-plasma volume TPE was

administered (3 L of plasma exchanged) and he requested to be discharged home due to financial constraints. It was the first automated TPE to be carried out in this part of Nigeria and was well tolerated by the patient.

He was given calcium tablets before the procedure to prevent hypocalcemic episodes (which can be a side effect of the citrate that was used as anticoagulant during the TPE procedure) and there was none. A combination of 5% albumin and 0.9% saline was used for the replacement, with the saline making up just 25% of the total replacement fluid so as not to jeopardize the oncotic pressure. We encountered some interruptions toward the end of the approximately 4-h long procedure due to clotting within the tubing. The adverse effects that can be observed during TPE procedures include symptoms of hypocalcemia (paresthesias and carpopedal spasms), hypotensive and vasovagal reactions (diaphoresis and bradycardia), allergic reactions, and certain blood transfusion reactions (febrile, allergic, and anaphylactic).[13] The common adverse reactions are usually mild and easily treated, while potentially life-threatening events have been reported to occur in 0.12% of TPE procedures.[15,16] In this case, clots were observed around the connection of the femoral catheter to the TPE tubing set and subsequently flushed off with 0.9% saline. Our protocol recommends the use of a central line or femoral catheterization to ensure that the vessel remains patent at all times, especially during withdrawal of blood.

Therapeutic apheresis is still an emerging aspect of transfusion medicine practice in Nigeria. There are scant publications on therapeutic apheresis in Nigeria. Arogundade *et al*.[11] published two cases of lupus nephritis that had filter membrane-based automated TPE in 2011; whereas, Bazuaye and Iheanacho[17] in 2015 reported the first automated red cell exchange in the country. Conversely, therapeutic apheresis is a frequently utilized treatment modality in many developed countries where it has been in use for several decades. Data from the Canadian Apheresis Study Group revealed that 5907 plasma exchange procedures were carried out in Canada in 1987 and the figures have steadily increased.[18] Until recently, the management of GBS in our environment has been largely supportive. Very few patients can afford IVIG owing to high cost and limited availability. Automated TPE was hitherto not available and some centers applied various maneuvers such as partial exchange blood transfusion,[9] and plasmapheresis techniques that remove arguably insignificant quantities of plasma as well antibodies.

Conclusion

TPE is an important treatment modality in the management of GBS, and it is becoming increasingly available in Nigeria. There is a need for more therapeutic apheresis facilities and trained personnel, in addition to concerted efforts to subsidize the cost of accessing the treatment.

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Conflicts of interest

There are no conflicts of interest.

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