CASE REPORT

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Allergic reaction in a Guillain-Barre Syndrome patient with therapeutic plasma exchange: a case report

Hayat Hamzah Dawi[1*], Rachmawati Adiputri Muhiddin[2], Uleng Bahrun[2], Hadia Angriani Machmoed[3], Faisal Muchtar[4]

ABSTRACT

Introduction: Guillain-Barre Syndrome (GBS) is a rare autoimmune disorder affecting the peripheral nervous system, often treated with therapeutic plasma exchange (TPE). While TPE is generally well-tolerated, it may cause complications, including allergic reactions, albeit rarely. This report highlights a case of an allergic reaction in a GBS patient following TPE, emphasizing the importance of recognizing and managing such adverse events.

Case Description: A 16-year-old female was diagnosed with the acute motor axonal neuropathy (AMAN) variant of GBS and underwent two TPE sessions. The first session was completed successfully with mild pruritus. However, during the second session, the procedure was discontinued during the seventh cycle due to generalized urticaria and pruritus, suspected to be a type I hypersensitivity reaction triggered by human serum albumin (HSA) used as a plasma replacement. Laboratory and clinical evaluations supported the diagnosis.

Conclusion: This case underscores the rare occurrence of a type I hypersensitivity reaction to HSA during TPE in a GBS patient. It highlights clinicians' need to remain vigilant and prepared to manage such rare but significant adverse events

Keywords: acute motor axonal neuropathy, Guillain-Barre Syndrome, human serum albumin, hypersensitivity reaction, therapeutic plasma exchange.

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[1]Clinical Pathology Resident, Faculty of Medicine, Universitas Hasanuddin, Wahidin Sudirohusodo General Hospital, Makassar, Indonesia;
[2]Department of Clinical Pathology, Faculty of Medicine, Universitas Hasanuddin, Wahidin Sudirohusodo General Hospital, Makassar, Indonesia;
[3]Department of Pediatrics, Faculty of Medicine, Universitas Hasanuddin, Wahidin Sudirohusodo General Hospital, Makassar, Indonesia;
[4]Department of Anesthesiology and Intensive Care, Faculty of Medicine, Universitas Hasanuddin, Wahidin Sudirohusodo General Hospital, Makassar, Indonesia.

*Corresponding author:
Hayat Hamzah Dawi;
Clinical Pathology Resident, Faculty of Medicine, Universitas Hasanuddin, Wahidin Sudirohusodo General Hospital, Makassar, Indonesia;
hayathamzahdawi901@gmail.com

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INTRODUCTION

Guillain-Barre Syndrome (GBS) is an autoimmune disorder affecting the peripheral nervous system, first reported by Guillain, Barre, and Strohl in 1916. GBS typically occurs after a patient experiences an infection in the upper respiratory tract or gastrointestinal system. Hyperactive immune responses, including the release of antiganglioside antibodies, the formation of antibody-dependent immune complexes, and macrophage activation, can lead to demyelination and axonal degeneration in GBS. Most patients with GBS are clinically characterized by tetraplegia, with or without sensory disturbances.[1]

Therapeutic plasma exchange (TPE) is accepted as a first-line treatment for several neuroimmune disorders, such as GBS, severe myasthenia gravis, chronic inflammatory demyelinating polyneuropathy, and fulminant Wilson's disease, according to the guidelines of the American Society for Apheresis (ASFA). TPE is a routine method to remove a particular blood volume from a patient and separate it into its components—erythrocytes, leukocytes, platelets, and plasma—extracorporeally. It removes the pathogenic substance-containing plasma and replaces it with albumin solution plus crystalloid or fresh frozen plasma (FFP).[2,3] The plasma volume removed is replaced with a substitute fluid of equal volume, such as donor or plasma substitutes. Common replacement fluids include 4.5–5% human albumin, FFP, and crystalloids. Albumin is sometimes combined with 0.9% saline in a 50:50 ratio. The choice of replacement fluid affects the procedure's effectiveness, oncotic pressure, coagulation, and susceptibility to side effects.[4]

TPE is generally a safe and well-tolerated technique, but it carries potential side effects that must be carefully managed due to its narrow safety margin. The reported complication rate ranges from 4–25%, with the occurrence of complications depending on factors such as anticoagulation and replacement fluids used, the volume exchanged, vascular access, plasma

Table 1. Routine blood examination

Parameter	10/12/23	27/12/23	28/12/23	29/12/23	Units	References
Hematology						
WBC	2.7	3.0	5.0	4.3	10^3/ul	4.00-10.0
RBC	3.89	4.41	5.00	4.72	10^6/ul	4.00-6.00
HGB	9.3	11.2	12.6	12.0	g/dl	12.0-16-0
HCT	30	35	40	38	%	37.0-48.0
MCV	77	79	80	79	fl	80.0-97.0
MCH	24	25	25	25	pg	26.5-33.5
MCHC	31	32	32	32	gr/dl	31.5-35.0
PLT	89	136	95	86	10^3/ul	150-400
RDW-SD	46.5	49.1	50.8	49.5	fl	37.0-54.0
RDW-CV	16.6	17.4	17.8	17.2	%	10.0-15.0
PDW	10.8	00.0	13.5	13.3	fl	10.0-18.0
MPV	10.8	00.0	11.8	10.3	fl	6.5-11.0
PCT	0.00	0.00	0.00	0.00	%	0.15-0.50
NEUT	61.2	73.9	84.5	82.1	%	52.0-75.0
LYMPH	32.0	17.8	10.9	14.4	%	20.0-40.0
MONO	6.8	8.3	4.4	3.5	%	2.00-8.00
EO	0.0	0.0	0.0	0.0	%	1.00-3.00
BASO	0.0	0.0	0.2	0.0	%	0.00-0.10
ESR	-	48	45	2	mm/hours	Male<10 Female<20

WBC: White Blood Cell; RBC: Red Blood Cell; HGB: Hemoglobin; HCT: Hematocrit; MCV: Mean Corpuscular Volume; MCH: Mean Corpuscular Hemoglobin; MCHC: Mean Corpuscular Hemoglobin Concentration; PLT: Platelet; RDW-SD: Red Cell Distribution Width-Standard Deviation; RDW-CV: Red Cell Distribution Width-Coefficient of Variation; PDW: Platelet Distribution Width; MPV: Mean Platelet Volume; PCT: Plateletcrit; NEUT: Neutrophils; LYMPH: Lymphocytes; MONO: Monocytes; EO: Eosinophils; BASO: Basophils; ESR: Erythrocyte Sedimentation Rate.

Table 2. Clinical chemistry test results

Parameter	10/12/23	27/12/23	28/12/23	29/12/23	Units	References
Clinical Chemistry						
Albumin	3.3	-	4.7	3.6	g/dl	3.5-5.0
Calcium	-		7.6	7.4	mg/dl	6.8-10.2
Electrolyte						
Natrium	136	-	140	135	mmol/l	136-145
Kalium	3.9	-	3.9	3.9	mmol/l	3.5-5.1
Chloride	107	-	106	101	mmol/l	97-111

separation method, and the underlying disease. Common side effects include paresthesia, muscle cramps, hypotension, and urticaria. Most side effects are mild to moderate, and severe complications requiring discontinuation of TPE occur in only about 0.8% of cases.[4]

Allergic reactions to albumin are rare but have been reported in less than 1% to approximately 3% of cases. These reactions range from mild symptoms, such as itching and skin rash, to severe reactions, such as anaphylaxis. It is because albumin is routinely produced from human plasma. Albumin preparations have increased purity since their initial introduction; however, severe reactions can still occur despite these improvements.[4,5] This case report aimed to evaluate an allergic reaction in a GBS patient following TPE.

CASE DESCRIPTION

A 16-year-old female was referred to the Emergency Department of Wahidin Sudirohusodo Hospital in Makassar on December 10th, 2023, with complaints of difficulty moving her limbs, which had been experienced for the past month. The initial symptom was cramping in the lower limbs, progressing to difficulty walking. The patient also complained of headaches and experienced vomiting after every meal or drink. She had a history of hospitalization at the referring hospital with a diagnosis of GBS and had received treatment. Her medical history included an electromyography (EMG) examination with HSAil findings and a peripheral blood smear examination with HSAil findings. The patient had a history of epilepsy at the age of 5 years, which was declared resolved after two years of treatment. The patient had no known history of allergies.

The patient appeared moderately ill but fully conscious on physical examination, with a Glasgow Coma Scale score of 15 (E4V5M6). Vital signs included a blood pressure of 90/60 mmHg, a respiratory rate of 24 breaths per minute, a heart rate of 78 beats per minute, a body temperature of 36.8°C, and an oxygen saturation (SpO_2) of 99%. The patient weighed 52 kg, was 160 cm tall, and had a head circumference

Table 3. Estimated Blood Volume, Total Plasma, Plasma Output, and Plasma Input in Milliliters (ml)

Time	Total Blood Volume (ml)	Total Plasma Volume (ml)	Input (*Substitution*)	Output (*Extracted*)
I (28/12/23)	3,780	2,028	2,032	2,032 ml
II (29/12/23)	3,120	1,872	1,389	1,389 ml

of 54.8 cm, chest circumference of 73 cm, abdominal circumference of 68 cm, and mid-upper arm circumference of 21.8 cm.

The head and neck examination revealed non-anemic conjunctivae and non-icteric sclerae with grade T1-T1 hyperemic tonsils. No lymph node enlargement was noted in the neck. Thoracic examination showed symmetrical chest movement with normal vesicular breath sounds and no retractions, rales, or wheezing. Heart sounds S1 and S2 were clear and regular, with no murmurs detected. The abdomen appeared flat with normal bowel sounds, and the liver and spleen were not palpable.

The extremities were warm, with a capillary refill time of less than two seconds, and no edema was observed. Cranial nerve examination showed intact olfactory function, pupils that were round and reactive to light, and regular extraocular movements in all directions. Corneal reflexes were intact, and no facial nerve palsy was present. The hearing was normal, though the balance assessment was inconclusive. Swallowing reflexes were intact, and there was no deviation of the tongue. Motor examination revealed decreased muscle strength in the lower extremities.

The patient had undergone laboratory and EMG examinations at the referring hospital, with the following findings: cerebrospinal fluid (CSF) analysis suggested an inflammatory etiology, possibly viral infection; a peripheral blood smear revealed microcytic hypochromic anemia suspected to be caused by iron deficiency, leukopenia with signs of infection likely of viral origin, and mild thrombocytopenia. The EMG examination indicated GBS, specifically the acute axonal motor neuropathy (AMAN) variant. At Wahidin Sudirohusodo Hospital, laboratory investigations showed pancytopenia and an elevated erythrocyte sedimentation rate (ESR) on routine blood tests (Table 1). Clinical chemistry and electrolyte tests were within normal limits (Table 2).

On December 12th, 2024, a Nerve Conduction Velocity (NCV) and EMG examination was performed at Wahidin Sudirohusodo Hospital, revealing symmetrical axonal demyelinating motor neuropathy, primarily affecting the lower extremities, suggestive of GBS, specifically the AMAN subtype.

The patient received initial treatment from the Neurology Department at the Emergency Unit, which included an infusion of Ringer's lactate at 20 drops per minute, intravenous Methylprednisolone 50 mg every 12 hours, Ranitidine 50 mg every 12 hours, and Citicoline 7.5 mg every 12 hours. Subsequently, the patient was admitted to the pediatric ward at Wahidin Sudirohusodo Hospital and referred to the Clinical Pathology Department for further management with TPE. The patient underwent two TPE sessions on December 28th and December 29th, 2023 (Table 3).

The second TPE procedure was stopped during the seventh cycle due to the onset of clinical manifestations across the entire body, including urticaria and pruritus. Several laboratory tests can be recommended for this patient, such as allergen provocation tests (e.g., Prick test, Patch test), to identify the cause of the allergic reaction.

DISCUSSION

Based on the anamnesis, physical examination, and NCV and EMG tests, a diagnosis of GBS, specifically the AMAN variant, was established for this patient, indicated by symmetrical axonal demyelinating motor neuropathy predominantly in the lower extremities. GBS is a rapidly progressive, immune-mediated polyneuropathy with an etiology and pathogenesis that remain not fully understood. Autoantibodies against nerve gangliosides are thought to play a central role in the pathogenesis in many cases. GBS can be classified into several variants based on clinical presentation and neurophysiological findings. The classic variants include Acute Inflammatory Demyelinating Polyneuropathy (AIDP) and AMAN, characterized by rapidly progressive symmetrical weakness ascending proximally and diminished or absent proprioceptive reflexes.[5]

GBS is considered an immune-mediated neuropathy that follows infection. Its pathophysiology involves molecular mimicry, where pathogens trigger B cells to produce antibodies against the pathogen. The pathogen's outer membrane (lipo-oligosaccharide) shares structural similarities with proteins on nerve cells, known as gangliosides (e.g., GM1 and GD1a), components of peripheral nerves. As a result, the antibodies mistakenly target proteins in the myelin sheath or the nerve axons themselves.[6,7]

This patient was referred to the Clinical Pathology Division for TPE. According to the American Society for Apheresis (ASFA), TPE for the AMAN variant of GBS is classified as category I, grade IA, meaning it is a first-line therapy, either as monotherapy or combined with other treatments. TPE was performed on this patient one month after symptom onset. Indications for discontinuing TPE include serious allergic reactions, severe hypotension, worsening medical conditions, coagulopathy, or ineffectiveness of TPE. The first TPE session was conducted on December 28th, 2023, with mild pruritus as a side effect, but the procedure was completed successfully. During the second TPE session on December 29th, 2023, the patient developed more severe side effects, including pruritus and generalized urticaria, necessitating the discontinuation of the procedure after the seventh cycle.[8]

Immunomodulatory therapy with plasmapheresis or IV immunoglobulin (IVIG) has proven effective in GBS by accelerating recovery from weakness. Plasmapheresis has been used as a treatment modality in various

autoimmune disorders, including neurological conditions like GBS and Chronic Inflammatory Demyelinating Polyneuropathy (CIDP). The American Society for Apheresis (ASFA) publishes its guidelines on therapeutic apheresis every three years based on evidence, assisting physicians in medical and technical aspects of apheresis consultation. The ASFA guidelines endorse TPE as an acceptable first-line therapy for GBS and CIDP, either as monotherapy or combined with other treatment modalities.[8,9]

TPE is generally a safe and well-tolerated procedure, though complications can occur in 4–25% of cases, including death in critically ill patients. Potential complications in critically ill patients undergoing TPE include hemodynamic instability, coagulopathy, or electrolyte disturbances, which may result in fatal outcomes. Other possible complications include allergic reactions (pruritus, urticaria, and anaphylaxis), catheter-related hematomas, and acute myocardial infarction.[8,9]

In this case, the side effects were suspected to be an allergic reaction, precisely a type I hypersensitivity reaction, manifesting as itching and urticaria across the patient's body. Type I hypersensitivity is mediated primarily by Immunoglobulin E (IgE). The binding of antigens to IgE on mast cells and basophils triggers degranulation, releasing inflammatory mediators such as histamine and prostaglandins. These mediators cause vasodilation, increased capillary permeability, and fluid transudation, resulting in clinical manifestations of itching and urticaria. This reaction was suspected to have been caused by human serum albumin (HSA) and its components used as a plasma exchanger.[9,10]

HSA is the most abundant protein in plasma, functioning as a monomeric multidomain macromolecule and the principal determinant of plasma oncotic pressure and fluid distribution among body compartments. HSA is a commonly used colloid for volume expansion and albumin replacement during plasmapheresis. Colloids rarely cause anaphylaxis, and hypersensitivity reactions to HSA are infrequent. Albumin is produced using variations of the Cohn fractionation technique involving ethanol precipitation. This procedure may cause albumin to aggregate into polymers, creating macromolecules that could be antigenic. This process can result in macromolecules or structural changes in the albumin molecule that the immune system may recognize as foreign, potentially inducing an immune response.[10,11]

The type of albumin used as the plasma substitute in this patient was Octalbin 5%, comprising HSA, distilled water as a solvent, caprylate, and acetyl tryptophan. Studies have shown that stabilizing agents like caprylate, added during albumin production, can trigger the formation of specific antibodies, making caprylate a potential allergen in humans. In other words, albumin and its components introduced during TPE can be identified as antigens, eliciting an exaggerated immune response.[11] This study's limitation is the short follow-up time after the therapy. Further evaluation of the effectiveness and safety is warranted on a larger scale and over a more extended observation period to provide more comprehensive insights.

CONCLUSION

This case highlights a rare occurrence of a type I hypersensitivity reaction in a 16-year-old female diagnosed with GBS, likely triggered by HSA and its components used during TPE. This finding emphasizes the need for awareness of such uncommon adverse effects in clinical practice. Continued cross-specialty research and collaboration is critical to optimizing care for these patients.

DISCLOSURES

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The authors declare no external funding for this study.

Conflict of Interest

The authors declare no conflict of interest.

Author Contribution

HHD, RAM, and UB contributed to the manuscript preparation, revising, and drafting. RAM, UB, HAM, and FM contributed to the design of this study and supervision.

Ethical consideration

The patient's family has agreed regarding using cases in this case report.

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