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Case Report

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Separate (Asynchronous) Therapeutic Plasma Exchange (TPE) and Plasma Transfusion in the Patient with Severe TPE Complications: A Case Report

Saeid Anvari[1,2], Amirhossein Larijani[2,3], Nasim Ghorbannejad[4]

[1]Department of Hematology and Medical Oncology, Guilan University of Medical Sciences, Rasht, Iran
[2]Regenerative Medicine, Organ Procurement and Transplantation Multi-Disciplinary Center, Razi Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran
[3]Student Research Committee, Guilan University of Medical Sciences, Rasht, Iran
[4]Pediatric Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran

Corresponding Author: Saeid Anvari, Department of Hematology and Medical Oncology, Guilan University of Medical Sciences, Rasht, Iran
E-mail: drsaeidanvari@gmail.com

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ABSTRACT

Thrombotic thrombocytopenic purpura (TTP) is a medical condition characterized by a decreased activity of the ADAMTS13 protease for cleaving the von Willebrand factor. It contributes to thrombotic microangiopathy. In this report, we described a case of TTP followed by significant adverse effects during therapeutic plasma exchange (TPE) treatment. The patient received TPE with a time interval from plasma transfusion.

A 30-year-old female was evaluated for headaches and bruises on her arms and legs. Laboratory testing revealed thrombocytopenia and anemia. The identification of thrombocytopenia with severe schistocytosis was verified by the analysis of a peripheral blood smear. After confirming a diagnosis of TTP, TPE was performed as therapy. To avoid the complications arising during the previous TPE sessions, we conducted plasma exchange with albumin followed by FFP injection, with a six-hour interval between them. This strategy successfully alleviated the patient's symptoms.

Therapeutic plasma exchange (TPE) with a time interval from plasma transfusion can be successfully used in patients with severe TPE complications.

Keywords: Plasma exchange; Separate; Thrombotic thrombocytopenic purpura (TTP); Complications

INTRODUCTION

TTP is known as thrombotic microangiopathy, caused by the decreased activity of an enzyme called ADAMTS13, which cleaves the Von Willebrand factor. The activity level of ADAMTS13 is usually below 10% in people with TTP, leading to thrombocytopenia, the formation of platelet-rich thrombi in small blood vessels, and microangiopathic hemolytic anemia. Renal failure, cerebral problems, Furthermore, TTP is a severe medical emergency that can be fatal if not treated immediately. and/or low-grade fever may occur in patients. TTP may be classified into two main categories: immunological (including autoimmune and acquired) and hereditary disorders. Autoantibodies against ADAMTS13 are a sign of the immune form of TTP, while biallelic changes in the ADAMTS13 gene cause the inherited form.

However, more than 95 percent of patients survive with appropriate treatment. Various therapeutic

approaches are used in the management of TTP, including therapeutic plasma exchange (TPE), Glucocorticoids, Rituximab, and Caplacizumab. TPE is administered to all individuals having either clinical signs of TTP or a confirmed diagnosis of TTP according to significantly inadequate ADAMTS13 activity below 10%[1]. The standard plasma exchange volume is one estimated plasma volume or around 40 mL per kilogram of body weight. This process is carried out on a daily basis until the patient recovers or until the initial diagnosis is ruled out and a different diagnosis is determined. Plasma is used as the replacement fluid because it provides ADAMTS13. Plasmapheresis with a non-plasma replacement fluid is not adequate therapy. There are several types of plasma products available, including Fresh Frozen Plasma (FFP), Thawed Plasma (thawed FFP stored at 1-6°C for five days), cryoprecipitate-reduced plasma (Plasma containing removed cryoprecipitate, also known as cryo-poor plasma), and pathogen-inactivated products such as Solvent/Detergent (S/D)-treated or amotosalen-UVA-treated plasma[2]. Complications can arise from the central venous catheter and exposure to donor plasma, such as transfusion-related acute lung injury and allergic reactions. Major complications of TPE occur in approximately one-quarter of patients[3]. Plasma transfusion is not an adequate substitute for TPE in the treatment of immune TTP, and TPE should not be delayed. Plasma transfusion is not effective in removing the inhibitor to ADAMTS13. In addition, the amount of plasma and ADAMTS13 that can be delivered through this method is considerably lower compared to TPE. TPE may not be immediately available to all patients, and plasma transfusion may provide temporary benefit in some patients[4]. A retrospective analysis was conducted on 57 patients undergoing plasma transfusion (at a rate of 25 to 30 mL/kg per day) compared to therapeutic plasma exchange (TPE). The findings indicated that TPE was more effective than transfusion, although transfusion did show effectiveness in certain patients[5].

Case presentation

A 30-year-old woman was admitted to the hematology ward at Razi Hospital in Rasht, Guilan Province, located in the northern region of Iran. The patient was evaluated for headaches as well as bruising on her arms and legs. Two weeks before the patient's visit, she had bruises on both legs and one week later, she had bruises on both hands. The patient experienced a severe headache two days prior to the presentation. As a result, she sought an evaluation at the emergency department of another hospital. Subsequently, she was transferred to our hospital for further evaluation. The patient reported experiencing menorrhagia during their most recent menstrual period. Five years ago, she had rhinoplasty. She did not receive any medications and had no documented drug allergies. The patient resided in Astane town and worked as a housewife, living with her spouse and child. The individual in question has never engaged in tobacco smoking or the use of illicit substances. Furthermore, there is no history of such behaviors within their family. The patient presented with a headache upon admission. During the assessment, the patient's temperature was recorded as 37.2°C, blood pressure as 126/78 mm Hg, pulse rate as 95 beats per minute, respiratory rate as 18 breaths per minute, and oxygen saturation as 98% while inhaling ambient air. Upon assessment, it was found that the conjunctiva exhibited pallor, and petechiae were seen on the arms and legs. The results of other exams did not provide any notable findings. The laboratory analysis indicated a platelet count of 30,000 per microliter, which falls below the guideline range of 150,000 to 450,000. Additionally, the hemoglobin level was measured at 8.7 gr/dl, which is lower than the recommended range of 12-15 gr/dl. The analysis of a peripheral blood smear confirmed the presence of thrombocytopenia accompanied by a notable increase in schistocytosis. Table 1 displays supplementary laboratory test findings.

Table 1. Laboratory Data

Variable	During Admission, First Hospital	During Admission, This Hospital	Reference Range, Adults, This Hospital	Discharge time
Hemoglobin (g/dl)	9.5	8.7	12.3-15.3	9.1
Hematocrit (%)	28	26	34.5-44.6	30
Platelet count (per µl)	40000	30000	150000-450000	346000
White-cell count (per µl)	8500	9670	4-11	12900
Differential count (per µl)				
Neutrophils	55	53	50-70	60
Lymphocytes	39	30	20-40	32
Monocytes	5	7	5-8	6
Eosinophils	1	1	1-5	2
Reticulocytes (%)				
Sodium (mmol/liter)		142	135-145	141
Potassium (mmol/liter)		3.5	3.5-5.5	3.7
Chloride (mmol/liter)		105	98-108	
Urea nitrogen (mg/dl)		15	7-21	22
Creatinine (mg/dl)		1	0.6-1.3	0.84
Calcium (mg/dl)		9.4	8.6-10.3	9.1
Glucose (mg/dl)		99	70-99	
Troponin T (ng/liter)		Negative		
Albumin (g/dl)		3.8	3.5-5.5	
Erythrocyte sedimentation rate (mm/hr)		30	0-20	
C-reactive protein (mg/liter)		11	0-8	
Lactate dehydrogenase (U/liter)		1120	240-480	356
Uric acid (mg/dl)		5.6	3.4-7.2	
Creatine kinase (U/liter)		74	60-400	
Iron (µg/dl)		154	50-170	
Total iron-binding capacity (µg/dl)		295	250-450	
Ferritin (µg/liter)		330	10-124	
HIV Ab		Non-reactive		
HBS Ag		Non-reactive		
HCV Ab		Non-reactive		
Bilirubin total(mg/dl)		1.7	0.3-1.2	0.7
Bilirubin Direct(mg/dl)		0.3	0-0.2	0.2
PTT		34	28-40	35
PT		12.7	11-13.5	14
INR		1.1	1-1.3	1.3
ANA U/ml		1.7	0-12	
Anti ds DNA U/ml		0.9	0-25	
Amylase U/L		31	0-100	
Lipase U/L		20	0-60	
AST U/L		22	0-31	
ALT U/L		77	0-41	
Alkaline phosphatase (U/liter)		135	70-290	

Imaging studies were obtained. Brain and lung CT scans without contrast were unremarkable. Ejection Fraction in echocardiogram was 55%.

The patient received a diagnosis of TTP, and treatment with TPE was initiated. Following the beginning of the procedure, TPE was temporarily halted for a few minutes due to the occurrence of symptoms resembling hypocalcemia, including nausea, respiratory distress, and fatigue. The individual has experienced ongoing symptoms despite receiving prescription medication for symptom management. During the subsequent session of TPE, there was a recurrence of similar symptoms, and the same management course was implemented.

In order to mitigate the risk of complications, a sequential approach was considered during TPE. Initially, plasma exchange was conducted using albumin as the primary replacement fluid. Subsequently, FFP transfusion was administered at a six-hour interval. This approach aims to enhance the safety and effectiveness of the TPE procedure. The implemented strategy proved to be effective, leading to the completion of seven rounds of TPE. As a result, the patient's symptoms were resolved, and laboratory tests, including platelet count, LDH, bilirubin, and others, returned to normal levels. Afterward, the patient was discharged. After several months of follow-up, the disease did not return, and the patient remained asymptomatic.

DISCUSSION

Plasma exchange is a process in which plasma is removed from the patient's bloodstream, and the replacement plasma is returned to the recipient's body from another donor. This procedure is used by the cell separator machine using a centrifuge mechanism to separate different blood cells, which is done as a standard continuous multi-step protocol without a time interval. In this way, the harmful substances that caused the disease, such as autoantibodies and immune complexes, and toxic substances are removed from the body and replaced with healthy plasma. In some special cases, this process is used to replace missing factors. In our patient, due to the special circumstances that occurred due to the complications caused by the plasma exchange, we had to change the standard protocol in such a way that the process was divided into two stages. Initially, plasma exchange was conducted primarily using albumin. Subsequently, a transfusion of FFP was administered, with a six-hour interval between the two procedures. While this approach is not commonly used in references and does not have supporting studies, Coppo et al. propose that a high dose of 30ml/kg/d may be considered as a safe method for managing thrombotic microangiopathy in patients not undergoing early plasma exchange[6]. In a study conducted by Escolar et al. (2022), it has been shown that performing plasma exchange with a smaller volume can be as effective as the usual dose in controlling the symptoms of various patients, including Alzheimer's[7]. Given the nature of the plasma exchange procedure, it is important to acknowledge the potential complications that may arise. These complications include sensory abnormalities resulting from hypocalcemia, hypotension, muscle spasms, headaches, and urticarial reactions. Additionally, plasma transfusion carries a variety of complications, such as allergic reactions and transfusion-related lung injuries[8]. It is worth noting that these complications can also be attributed to metabolized citrate in restored plasma or the utilization of crystalloids during the plasma exchange process[9]. In a systematic review conducted by Wang et al. (2023), it was shown that treatments other than plasma exchange in TTP patients were as effective as plasma exchange and the mortality rate of patients did not increase[10]. In another study conducted by Welker et al. (2020), it was reported that caplacizumab was effective in mild, moderate, or even severe TTP cases. It caused a rapid increase in platelets and normalization of hemolysis tests, and even no plasma exchange treatment was needed to perform in all cases[11]. In a case report by Chandler et al. (2019) on a TTP patient who refused to undergo plasma exchange, it was explained that although the main treatment is still plasma exchange, in certain cases, it is possible to use caplacizumab along with glucocorticoid and rituximab[12]. There are studies and reports that in cases where the patient refuses to receive the product due to religious reasons, treatments other than plasma exchange can be used,

such as the use of vincristine in the study of Dabak et al. (2007)[13] or using plasma exchange with albumin without using FFP along with rituximab and prednisolone in the study of George et al. (2017)[14]. There are many other articles about not performing plasma exchange and using alternative treatment, such as caplacizumab, rituximab, and glucocorticoid, or performing plasma exchange with albumin instead of FFP, such as Tran's study (2023)[15], Baseri et al. (2019)[16], Warr (2020)[17], Lim et al. (2020)[18], Cardesa-Salzmann et al. (2022)[19], and Sukumar et al. (2021)[20]. Based on the assumption that performing this process asynchronously can mitigate complications, we have devised and implemented a method in this particular case to minimize early complications associated with plasma transfusions, such as symptoms resembling hypocalcemia, chills, respiratory distress, and lethargy. Fortunately, our approach has proven effective, and it can be used as an alternative treatment method in specific conditions similar to our patient.

CONCLUSION

Therapeutic plasma exchange (TPE) with a time interval from plasma transfusion can be successfully used in patients with severe TPE complications. We recommend conducting additional research in centers that perform a high volume of TPE with more patients and considering the control group. Standard TPE may not be suitable for certain patients due to similar complications. Utilizing this alternative method and comparing it with the standard approach can provide a more comprehensive assessment and the best and most effective treatments with the least possible adverse effects.

Ethics approval and consent to participate

Ethical code: IR.GUMS.REC.1402.001

Consent for publication

Not applicable

Availability of data and materials

Not applicable

Competing interests

There is no conflict of interests

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