Case Report

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Successful whole-blood exchange transfusion in a patient with paroxysmal nocturnal hemoglobinuria: A case report and literature review

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Abstract

Objective: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare acquired clonal disorder of the hematopoietic stem cells that involves all blood cells. The primary aim of this study was to assess the role of whole-blood exchange (WBE) in treating patients with PNH.

Methods: A 32-year-old male patient was admitted our hospital because of severe anemia. His clinical test results indicated serious hemolysis, with positive anti-I on pretransfusion antibody screening tests. Because immunosuppressive therapy was ineffective and red blood cell (RBC) transfusion may aggravate hemolytic symptoms, the COBE Spectra blood cell separator was used for WBE.

Results: We performed WBE, where 1789 mL of the patient's blood was removed and replaced with 12 U of packed RBCs, along with 150 mL of frozen plasma and 200 mL of normal saline (total volume, 1883 mL), representing an exchange of 42.5% of the patient's total blood volume (approximately 4209 mL). The WBE treatment was considered successful. Rapid improvement in clinical signs and symptoms were observed after the WBE transfusion. The patient was discharged from the hospital on the third day after treatment.

Conclusion: Whole-blood exchange may be an applicable emergency treatment for rescuing PNH patients with severe or life-threatening hemolysis.

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Introduction

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare acquired disease with an estimated incidence of 1.5 to 2 cases per million per year.[1] The cause of PNH has now been confirmed as a somatic mutation in the X-linked phosphatidylinositol glycan complementation class A gene (PIG-A), which blocks the synthesis of the glycosylphosphatidylinositol (GPI) anchor on erythrocyte membranes and results in the deficiency of GPI anchored proteins[2] (including the complement regulatory proteins, complement decay-accelerating factor (CD55), and the MAC-inhibitory protein, which is also known as CD59). Therefore, the erythrocytes become susceptible to uncontrolled complement-mediated intravascular hemolysis. PNH is clinically characterized by intravascular hemolysis, bone marrow failure, and thrombosis. Historically, before eculizumab was used, the prognosis of PNH patients was poor; approximately 25% of patients died within 10 years after diagnosis.[3]

Until a decade ago, the treatment options for PNH were mainly symptomatic treatment and prophylaxis of complications, or stem cell transplantation. Symptomatic treatment includes red blood cell transfusions, folic acid and iron supplements, corticosteroids, and antithrombotic anticoagulant prophylaxis.[4] However, symptomatic treatment and prophylaxis provide unsatisfactory long-term disease control. The development of eculizumab, a humanized monoclonal antibody directed against the terminal complement protein C5,[5] has resulted in dramatic improvements in survival and a reduction in complications. However, eculizumab is still associated with high morbidity and mortality rates and it is reserved for highly selected patients, especially those with severe associated aplastic anemia. Additionally, eculizumab is not available in our hospital and this treatment is expensive.

If the condition of a PNH patient with acute hemolytic crisis becomes life-threatening, traditional treatments cannot promptly control the disease progression. Whole-blood exchange (WBE) transfusion is an innovative treatment that can physically remove hemolyzed RBCs, plasma, and complement on the cell surface of sensitized RBCs from the circulation and replace them with healthy RBCs and frozen plasma. In a previous study,[6–8] WBE was used to successfully treat several extremely severe hemolytic patients, thereby demonstrating that this therapy is appropriate to treat patients with severe hemolysis. To the best of our knowledge, no data are available concerning the use of WBE in PNH treatment. In this study, we report, for the first time, the case of a PNH patient with acute severe hemolysis who was successfully treated with WBE.

Case presentation

A 32-year-old man was admitted to the emergency intensive care unit at Xiangya Hospital because of severe anemia.

He was diagnosed with PNH at the age of 27 years based on the following clinical signs: (1) evidence of hemolysis, such as decreased hemoglobin (Hb) level (77 g/L), elevated indirect bilirubin level (total bilirubin, 91.0 μmol/L; direct bilirubin, 13.4 μmol/L) and lactate dehydrogenase (LDH) level (921 U/L), decreased haptoglobin level (<0.0706 g/L), and positive Ham test results. (2) Flow cytometry analysis of peripheral blood cells revealed that 58.14% of leucocytes and 59.23% of erythrocytes demonstrated CD55 deficiency, while 64.71% of leucocytes and 78.06% of erythrocytes demonstrated CD59 deficiency. (3) A bone marrow aspiration revealed hypercellular marrow with relative erythroid hyperplasia. Through immunosuppressive therapy with an average daily prednisone dose of 20 mg, the patient showed complete clinical remission. From 28 to 29 years of age, the patient experienced clinically evident hemolytic anemia twice (Hb concentration, 40–50 g/L). After treatment with prednisone, the patient showed complete remission. During these years, the patient did not have a blood transfusion. Upon admission, the patient presented with dark-colored urine, fatigue, and dizziness, with a decreased Hb level (27 g/L), increased plasma LDH activity (3956 U/L), and increased total bilirubin level (120.1 μmol/L; Table 1), which indicated that the hemolysis was very severe. Based on the patient's severe anemia-induced hypoxia, RBC transfusion treatment was administered. Clinical experimental data showed that the patient's blood group was O, D+ C+ E+ c+ e+, M-N+. A pretransfusion antibody screening tests revealed anti-I positivity (the titer was128 at 4°C and the titer was 8 at 37°C). Half a unit of RBCs (type O, D+ C+ E+ c+ e+, M-N+) without irradiation (one "unit" in China corresponds to the production that can be derived from 200 mL of whole blood, which is approximately 120 ± 12 mL including RBC, preservatives, and additives) was issued from the Department of Blood Transfusion with positive cross-matching test results (1+). However, there was no change (26 g/L) when compared with the pretransfusion concentration (Table 1). Moreover, the hemolytic activity related to PNH was not alleviated with prednisone treatment (10 mg/day) for 5 days.

WBE was selected after evaluating the clinical situations described below. First, RBC transfusion might aggravate hemolytic symptoms, because an anti-I titer value of 128 was detected. However, WBE can remove large amounts of sensitized RBCs as well as soluble antibodies (anti-I), and consequently alleviate RBC destruction. Second, immunosuppressive therapy was ineffective. Although glucocorticoids were administered, the symptoms of hemolytic anemia were not alleviated. Third, the Coombs test was positive. After approval from the ethics committee and informed consent for WBE treatment was obtained, the patient started to receive the special therapeutic procedure. The procedure was

Table 1. The patient's laboratory results.

	Admitted	Before WBE	After WBE	Discharged	Normal values
Hb (g/L)	27	26	101	92	130–175
TB (μmol/L)	120.1	100.1	70.6	58.2	1.7–17.1
DB (μmol/L)	7.3	8.5	8.6	7.2	0–6.8
LDH (μ/L)	3956	4165	–	–	109–245

Hb, hemoglobin; TB, total bilirubin; DB, direct bilirubin; LDH, lactate dehydrogenase; WBE, whole-blood exchange.

previously reported by our group.[6–8] Briefly, using a blood cell separator (COBE Spectra, Terumo BCT, Lakewood, CO, USA), 1789 mL of the patient's blood was removed and replaced with 12 U of packed RBCs along with 150 mL of frozen plasma and 200 mL of normal saline (total volume, 1883 mL), representing an exchange of 42.5% of the total blood volume (approximately 4209 mL). The time taken to complete the procedure was 1 hour and 18 minutes. To avoid a hemolytic transfusion reaction associated with anti-I, we warmed the donor's blood during the WBE procedure. Additionally, the patient was treated with large doses of glucocorticoids (500 mg). The WBE was successful, and there was no evidence of transfusion reaction or citrate toxicity.

On the first day post-treatment, the patient showed a dramatic clinical improvement and a rapid increase in Hb levels (101 g/L) as well as a decreased total bilirubin concentration (70.6 μmol/L; Figure 1, Table 1). Prednisone administration was continued (500 mg/day) for 3 days. The patient was discharged from the hospital on the third day post-treatment with no sign of hemolytic activity related to PNH. One month later, the patient reported feeling very well with no symptoms of anemia and his Hb concentration was 110 g/L. One year later, the patient has not had any further hemolytic crises, and his Hb concentration was around 90 g/L. Additionally, his general clinical condition had improved, and he experienced a dramatic improvement in his quality of life.

Discussion

PNH is a chronic and life-threatening disorder. The persistent occurrence of manifestations such as hemolysis severely impairs the patient's quality of life. Hemolysis has been shown to be intravascular and is characterized by chronic mild hemolysis, nocturnal exacerbations, and hemolytic precipitation that was induced by infection, transfusion, and operation.[9] The mechanism of hemolysis in PNH results from the deficiency of cell surface CD55 and CD59. The absence of CD55 and CD59 in particular accounts for the occurrence of intravascular hemolysis, which results from the failure to inactivate the late components of complement.[10,11] Hemolysis results in the production of erythrocyte debris, liberates free hemoglobin, and induces severe anemia. Careful monitoring is,

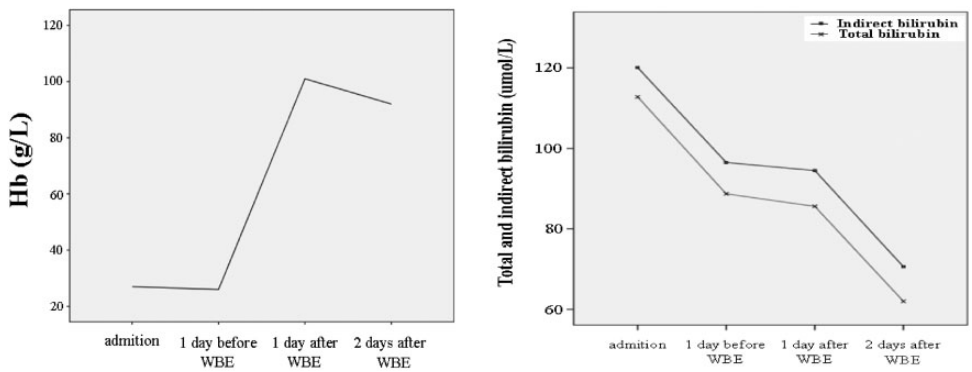

Figure 1. Changes in Hb, total bilirubin, and free bilirubin concentrations with whole blood exchange transfusion.

therefore, required to prevent hemolysis. Corticosteroids have been widely used for years in the treatment of PNH, but there is no clear evidence of their benefits.[12] Hemolysis in this patient was extremely severe, and conventional treatments were ineffective. Moreover, anti-I, with a titer value of 128 was detected, making it difficult to obtain matched RBCs. It was, therefore, very important to develop a special therapy for this patient. In a previous study, Li and colleagues[6–8] successfully demonstrated that WBE was an appropriate method for treating patients with severe hemolysis.

To the best of our knowledge, this is the first study in which WBE has been used to successfully treat a patient with PNH with acute severe hemolysis. As an effective method, WBE could physically remove hemolyzed RBCs from the circulation and replace them with healthy RBCs. Additionally, elimination of sensitized RBCs could also remove its activated antibodies and complement on the RBCs' surface.[13] In this case, WBE also removed plasma including large amounts of soluble antibodies such as anti-I and complement, which consequently inhibited RBC destruction; thus, renal and liver function might also be protected indirectly because of the reduction of destructive RBCs and bilirubin concentration. Additionally, the patient benefited from WBE because toxic compounds and white blood cells such as lymphocytes and monocytes were removed during the procedure, which could prevent excessive antibody production and antibody rebounding. It is generally believed that B lymphocytes can produce a large number of antibodies that activate antigens to attack and destroy RBCs using antibody-dependent macrophage-mediated cytotoxicity. Removing the autoreactive lymphocytes and memory cells could create a new balanced microenvironment.[14,15]

Conclusion

We reported, for the first time, the case of a patient with PNH who was successfully treated with WBE. By removing whole blood and replacing it with non-hemolyzed RBCs and frozen plasma, we demonstrated that WBE may be an applicable emergency treatment for rescuing PNH patients who have severe or life-threatening hemolysis or in whom drug therapy has failed. However, a large-scale study is required to further confirm this result.

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Zhimin Zhang performed was involved in treating the patient and wrote the manuscript. Yamei Shen and Xiangwu Shu were involved in treating the patient. Bijuan Li designed the treatment program and was involved in treating the patient. Ning Li designed this treatment program, analyzed the data, and revised the article.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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