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Generalized Urticaria as Acute Transfusion Reaction in Children: A Case Report

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ABSTRACT

Introduction: Transfusions in children and neonates are less common than in adults. The risk of transfusion reactions in children is two times greater than in adults. The most common transfusion reaction is an allergic reaction. This paper aims to discuss a case of generalized urticarial responses in pediatric patients who received PRC transfusions.

Case Description: A 12-year-old boy, treated with beta-thalassemia since 5 years ago and gets regular transfusions. After receiving the second bag of PRC transfusion with a volume of 50 mL, the patient complained of itching and redness all over the body. The complaints were getting worse, and bumps appeared all over the body 15 minutes after the transfusion was stopped. Laboratory test results support thalassemia and several complications of repeated transfusions, such as increased ferritin levels and decreased liver function. The results of the pretransfusion test before and after the transfusion were B-positive blood type and compatible crossmatch results. The patient recovered after being treated as a moderate-severe transfusion reaction.

Conclusion: Allergic reaction is an acute transfusion reaction involving an immunological response. Fast responses to acute transfusion reactions are very helpful in improving patient conditions.

Keywords: Beta-thalassemia, generalized urticaria, packed red cell.
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INTRODUCTION

Blood transfusion in neonates and children patients is less common than in adults. The population of pediatric patients who receive blood transfusions is children who are treated in intensive care rooms, children who will undergo heart surgery procedures, children with hereditary diseases such as major thalassemia, and children who are undergoing intensive chemotherapy for leukemia or certain organ cancers. In clinical practice, transfusion techniques for neonates and children differ from those for adults. However, some special circumstances need attention. The potential risks and benefits of carrying out a transfusion must always be considered and can be adjusted according to research and transfusion guidelines.[1–3]

Transfusion science and technology have made blood transfusions safer for patients. However, there are still various complications or side effects (adverse events) which we call blood transfusion reactions. It is very important to recognize transfusion reactions because they can be fatal. A study mentioned there are five major symptoms of blood transfusion reaction in pediatric patients, including pruritus/itching (27.4%), fever (19.1%), chills (14.2%), urticaria (9.7%), and angioedema (7.7%). Based on the affected organ systems, most subjects with dermatological symptoms (56.6%). Pediatric patients had twice the transfusion reaction rate compared to adult patients.[4] The following will discuss a case with Generalized Urticaria as Acute Transfusion Reaction in a pediatric patient.

CASE DESCRIPTION

Male patient, 12 years old, with main complaints of itching and redness all over the body when receiving Packed Red Cell (PRC) transfusion. Indications of PRC transfusion in this patient were a hemoglobin (Hb) level of 6.40 g/dL, and the doctor planned 4 kolf of PRC transfusion. The patient complained of itching and redness all over his body after receiving the second bag of PRC transfusion with a volume of 50 mL. The complaints were getting worse, and bumps appeared all over his body 15 minutes after the transfusion was stopped. There were no other complaints such as shortness of breath, hoarseness, coughing, cold sweat, fever, nausea and vomiting. Bowel habit and urinary were normal. The patient was treated for beta-thalassemia 5 years ago and received routine transfusions.

Based on physical examination, vital signs were within normal limits, and the patient had anemia. From the local status, there was urticaria in his facial, trunk, antebrachii dextra et sinistra, femur dextra et sinistra, and tibia dextra et sinistra. As shown below, urticaria was also found in varying sizes (Figure 1). Laboratory results are also shown below (Table 1-2).

Based on Table 1, a complete blood count shows a decrease in RBC, hemoglobin, and erythrocyte index (MCV and MCH) before and after a blood transfusion.

Based on Table 2, the clinical blood chemistry test found increased ferritin, aspartate transaminase (AST), and alanine transaminase (ALT) levels. From the pretransfusion testing, there were concluded with B blood type and rhesus positive. Crossmatch results, major and minor auto control were negative. Blood from a donor was compatible with the patient. Based on anamnesis, physical examination and laboratory results, the patient was diagnosed with Generalized Urticaria caused by Acute Transfusion Reaction.

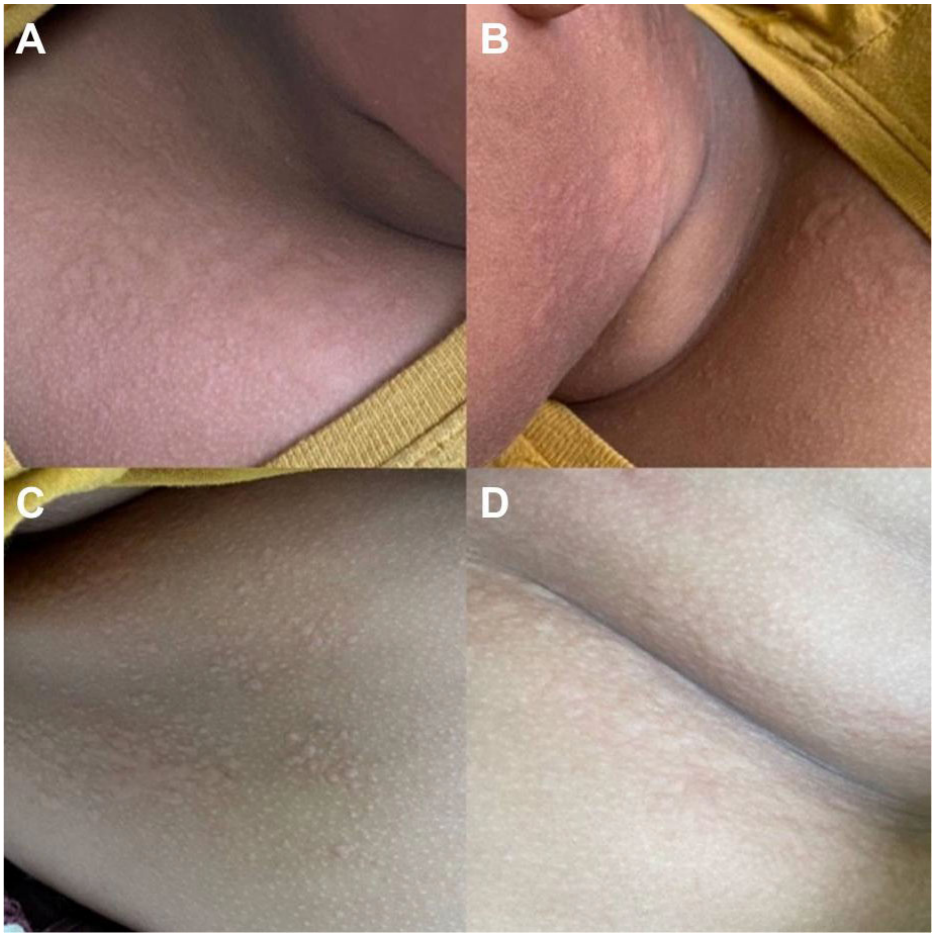

Figure 1. Patient's generalized urticaria.

Table 1. Hematology results

Laboratory test	Pra Transfusion	Post Transfusion	Reference
WBC	6.39	4.43	4.1-11.0 (10^3/µL)
Neutrophils	26.60	69.50	47-80 (%)
Lymphocytes	67.90	27.80	13-40 (%)
Monocytes	4.20	2.50	2.0-11.0 (%)
Eosinophils	1.10	0.00	0.0-5.0 (%)
Basophils	0.20	0.20	0.0-2.0 (%)
RBC	2.46	3.26	4.50-5.9 (10^6/µL)
HGB	6.40	8.70	13.5-17.5 (g/dL)
HCT	19.00	25.50	41.0-53.0 (%)
MCV	77.20	78.20	80.0-100.0 (fl)
MCH	26.00	25.00	26.0-34.0 (pg)
MCHC	33.70	34.10	31-36 (g/dL)
RDW	14.40	14.60	11.6-14.8 (%)
PLT	297.00	253.00	150-440 (10^3/µL)
MPV	11.50	10.80	6.80-10.0 (fl)
NLR	0.39	2.50	<3.13

DISCUSSION

Transfusion reactions can be distinguished by onset, pathogenesis, and symptomatology. Based on the onset, transfusion reactions can be divided into acute and delayed reactions. Based on the pathogenesis, transfusion reactions are divided into immunological reactions and non-immunological reactions. A classification based on the onset of events is preferred for clinical purposes. An acute transfusion reaction is a transfusion reaction that occurs less than 24 hours after the transfusion.[5–9]

Allergic reaction is one of the immunological acute transfusion reaction groups. It is the most common type of transfusion reaction. This reaction can occur because various elements act as allergens that can activate mast cells and basophils. In a five years' study, from January 2015 to December 2019, at the National Center for Children's Health in China, the incidence of transfusion reactions was 1.35%. Based on the blood products, 0.34% obtained a transfusion reaction using packed red cells (PRC), 3.21% using platelets, and 0.94% using fresh frozen plasma (FFP). The type of transfusion reaction was allergic reaction 86.67% and febrile non-hemolytic transfusion reactions (FNHTR) 4.24%.[2] Pathophysiology of allergic reactions occurs during or within 4 hours after transfusion, mediated by the release of substances due to mast cell activation, namely histamine. Histamine can cause blood vessel vasodilation, characterized by reddish skin color and urticaria. Other clinical symptoms are itching and facial, lips and mouth swelling. If the condition gets worse, the patient may suffer from shortness of breath.[10]

The clinical picture of mild allergic reactions commonly includes morbilliform rash, urticaria, itching, localized angioedema, lips, tongue or

Table 2. Clinical chemistry results

Laboratory test	Result	Reference
Ferritin	9944.58	21.81-274.66 (ng/mL)
AST	85.1	5.00-34.00 (U/L)
ALT	165.20	11.00-50.00 (U/L)

uvula edema, periorbital edema, pruritus and conjunctival edema. A typical urticarial reaction is characterized by local hives with firm boundaries, accompanied by s erythema and pruritus. Systemic reactions or severe allergic reactions can be generalized urticaria (> 25% body area).[11]

Diagnosing allergic reactions to urticaria due to acute transfusion reactions can be easily recognized. Other causes of allergic reactions, such as food and drugs, must be elaborated to eliminate the possibility of allergies due to other causes. The onset of urticaria helps distinguish an allergic reaction from a medication or transfusion. It is highly recommended not to give drugs at the time or before transfusion. In mild cases of allergic reactions, there is no need for further examination to look for other causes of transfusion reactions. If the allergic reaction is severe, the manifestation is not typical or accompanied by fever (unusual in allergic reactions), further examination is needed to rule out acute hemolytic reactions and transfusion reactions due to bacterial contamination.[10]

Premedication before transfusion is common to prevent transfusion reactions. A study with 7900 transfusions in 385 pediatric oncology patients found no significant difference in allergic reaction between the patients who received premedication and those who didn't.[12]

In this patient, the main complaint was itching and redness all over the body when receiving a PRC transfusion. This condition is a clinical manifestation of systemic allergic reaction transfusion. Allergic reactions caused by IgE-mediated type 1 hypersensitivity cause mast cell activation and release histamine. Histamine will cause blood vessel vasodilation, characterized by reddish skin color and itching. The binding of complement and cytokines derived from macrophages can also cause allergy symptoms. Although the exact causative agent is usually unknown, these reactions occur when the patient is sensitized to the immunologically active compounds in the donor plasma. However, allergic reactions can also occur due to components in blood products such as IgA, haptoglobin, drugs such as penicillin, or chemicals left over from the blood supply process, such as ethylene oxide used for blood sterilization and latex.[8]

On hematological examination, RBC, hemoglobin, and erythrocyte indices (MCV and MCH) decreased before and after blood transfusion. Two factors can cause hypochromic microcytic anemia in beta-thalassemia. The first is reduced β-globin synthesis. It can cause the inadequate formation of HbA so that the MCHC (mean corpuscular hemoglobin concentration) per cell will decrease, and the cells will appear hypochromic. The second is an excess of α-globin chains. Unpaired α chains can form insoluble aggregates that precipitate in erythrocytes. This cell body makes the erythrocyte susceptible to phagocytosis. Due to membrane-damaging inclusion bodies, mature erythrocytes are susceptible to premature destruction and damage to erythroblasts in the bone marrow. These two factors caused this patient's RBC, hemoglobin and erythrocyte indices (MCV and MCH) to be low before and after transfusion.[13]

Clinical blood chemistry test results showed increased levels of ferritin, Aspartate Transaminase (AST) and Alanine Transaminase (ALT). The increase of ferritin in patients with beta-thalassemia was associated with a deficiency of ß-chain production which causes a deficiency of HbA (α2ß2). The excess α-chain will bind to the γ-chain. It can make Hb F form. Unbinding α-chain will be deposited on the erythrocyte membrane as Heinz bodies so that the erythrocytes are easily damaged (ineffective erythropoiesis). Iron levels in patients with beta-thalassemia will increase due to ineffective erythropoiesis and absorption of iron in the digestive tract. The iron increase is exacerbated by continuous transfusions every 2-3 weeks. An increase in serum ferritin levels characterizes excess iron.[14]

Increased Aspartate Transaminase (AST) and Alanine Transaminase (ALT) levels in this patient are associated with a history of repeated transfusions since 2017. Repeated blood transfusions in the patient with beta-thalassemia not only extend the life expectancy but also negatively impact excess iron, which can cause various damage to organs. One of its main targets is the liver. Excess iron will form free radicals that cause injury and death of liver cells and release aminotransferases into the blood, which is biologically described by increased activity of serum aminotransferases; alanine aminotransferase (ALT) or serum glutamic-pyruvic transaminase (SGPT) and aspartate aminotransferase (AST) or serum glutamic-oxaloacetic transaminase.[15,16]

Regular blood transfusion is one of the management in patients with beta thalassemia. Examination of blood type and crossmatching is required before blood distribution. The test is needed to see the compatibility of the donor and the patient's blood. A compatible crossmatch is required so that recipients get appropriate and safe blood transfusions.[12] Blood products were given to this patient after a blood group examination and crossmatching. The blood type was found to be O Rhesus (+), and blood donors were compatible with the patient. An ABO incompatibility did not cause the transfusion reaction in the patient.

Based on the anamnesis and physical examination, the patient was diagnosed with generalized urticaria related to an acute transfusion reaction. A critical transfusion reaction diagnosis can be established based on complaints that appear less than 24 hours after the transfusion with generalized urticarial manifestations all over the patient's body. Etiologies other than allergic reactions can be ruled out because the patient's manifestations are only found in one organ system, the integumentary system (skin), without other complaints such as fever, tightness and bleeding manifestations. Because the patient's blood group and rhesus have been examined and crossmatch has been matched, the etiology of ABO incompatibility can also be ruled out.[15,16]

The transfusion should be stopped immediately in the patient with suspected acute transfusion reactions, and the blood bag label should be rechecked according to the patient's identity. The needle should be withdrawn immediately if a severe reaction or mistaken identity is found. If the response is mild, the intravenous line is kept open by administering 0.9% NaCl. In this patient, the treatment was given accordance with the initial management of category 2 of moderate to severe transfusion reactions. The physical examination was followed by discontinuation of the transfusion, infusion of 0.9% NaCl 30 drops per minute, epinephrine 1:1000 0.01 mg/kg body weight/ times 0.3 mg intramuscular, methylprednisone 0.3-0.5 mg/ kilogram body weight/ times 15-25-20 mg intravenous, and diphenhydramine 1-2 mg/ kilogram body weight/ times 50 mg intravenous. The patient was also given ursodeoxycholic acid 250 mg every 8 hours orally as a hepatoprotective agent and exjade 20 mg/kg body weight/ times 1000 mg every 24 hours to treat iron overload. Antihistamines are also given before the transfusion to prevent allergic reactions.[17,18]

The prognosis of patients who suffer from allergic reactions was related to the symptoms and clinical signs. Most of the prognoses of allergic reactions are minor.[19] In this case, the patient was recovered. Two days after treatment, the patient was discharged from the hospital.

CONCLUSION

An allergic reaction is an acute transfusion reaction involving an immunological response. In this case, a pediatric patient with beta-thalassemia suffered from generalized urticarial reactions after receiving PRC transfusions. The patient recovered after being treated as a moderate-severe transfusion reaction.

PATIENT CONSENT

The patient signed informed consent and agreed that the case would be published in an academic journal.

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DISCLOSURE OF CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTION

All authors equally contributed to the preparation of the article.

REFERENCES

1. Agrawal A, Rai P, Kelly S. Unique aspects of red blood cell transfusion in pediatric patients. Int J Clin Transfus Med. 2016;43. Available from: https://doi.org/10.2147/IJCTM.S70541
2. Goel R, Cushing MM, Tobian AAR. Pediatric Patient Blood Management Programs: Not Just Transfusing Little Adults. Transfus Med Rev. 2016 Oct;30(4):235–41. Available from: https://doi.org/10.1016/j.tmrv.2016.07.004
3. McCormick M, Delaney M. Transfusion support: Considerations in pediatric populations. Semin Hematol [Internet]. 2020;57(2):65–72. Available from: https://www.sciencedirect.com/science/article/pii/S0037196320300214
4. Vossoughi S, Perez G, Whitaker BI, Fung MK, Stotler B. Analysis of pediatric adverse reactions to transfusions. Transfusion [Internet]. 2018 Jan 1;58(1):60–9. Available from: https://doi.org/10.1111/trf.14359
5. Bolton-Maggs PHB, Cohen H. Serious Hazards of Transfusion (SHOT) haemovigilance and progress is improving transfusion safety. Br J Haematol. 2013 Nov;163(3):303–14. Available from: https://doi.org/10.1111/bjh.12547
6. Carman M, Uhlenbrock JS, McClintock SM. CE: A Review of Current Practice in Transfusion Therapy. Am J Nurs. 2018 May;118(5):36–44. Available from: https://doi.org/10.1097/01.naj.0000532808.81713.fc
7. Dasararaju R, Marques MB. Adverse Effects of Transfusion. Cancer Control [Internet]. 2015 Jan 1;22(1):16–25. Available from: https://doi.org/10.1177/107327481502200104
8. Li K, Xu Y. Citrate metabolism in blood transfusions and its relationship due to metabolic alkalosis and respiratory acidosis. Int J Clin Exp Med. 2015;8(4):6578–84. Available from: www.ijcem.com/ISSN:1940-5901/IJCEM0006754
9. Yelima J, Ufelle DS, Milgwe DD, Oyeleke K, Denue B, Chikwendu C. Complications of Blood Transfusion and Management Definitions and History of Blood Group Systems. Eur J Biol Med Sci Res. 2019;44(8):1689–99. Available from: https://doi.org/10.37745/ejbmsr.2013
10. Hirayama F, Yasui K, Matsuyama N, Okamura-Shiki I. Possible Utility of the Basophil Activation Test for the Analysis of Mechanisms Involved in Allergic Transfusion Reactions. Transfus Med Rev. 2018 Jan;32(1):43–51. Available from: https://doi.org/10.1016/j.tmrv.2017.09.002
11. Rujkijyanont P, Monsereenusorn C, Manoonphol P, Traivaree C. Efficacy of Oral Acetaminophen and Intravenous Chlorpheniramine Maleate versus Placebo to Prevent Red Cell Transfusion Reactions in Children and Adolescent with Thalassemia: A Prospective, Randomized, Double-Blind Controlled Trial. Anemia. 2018;2018:9492303. Available from: https://doi.org/10.1155/2018/9492303
12. Oktari A, Handriani R, Musbihah SS. Optimization Concentration Control Cell Coombs (CCC) for Validity Tests on Crossmatching Examination. J Phys Conf Ser [Internet]. 2021;1764(1):12016. Available from: https://dx.doi.org/10.1088/1742-6596/1764/1/012016
13. Adewoyin AS, Adeyemi O, Davies NO, Ogbenna AA. Erythrocyte Morphology and Its Disorders. In: Tombak A, editor. Rijeka: IntechOpen; 2019. p. Ch. 2. Available from: https://doi.org/10.5772/intechopen.86112
14. Susanah S, Rakhmilla LE, Ghozali M, Trisaputra JO, Moestopo O, Sribudiani Y, et al. Iron Status in Newly Diagnosed β-Thalassemia Major: High Rate of Iron Status due to Erythropoiesis Drive. Chen H, editor. Biomed Res Int [Internet]. 2021;2021:5560319. Available from: https://doi.org/10.1155/2021/5560319
15. Ayyash H, Sirdah M. Hematological and biochemical evaluation of β-thalassemia major (βTM) patients in Gaza Strip: A cross-sectional study. Int J Health Sci (Qassim). 2018;12(6):18–24. Available from: ijhs.org.sa/ISSN: 1658-3639
16. Salama KM, Ibrahim OM, Kaddah AM, Boseila S, Ismail LA, Hamid MMA. Liver Enzymes in Children with beta-Thalassemia Major: Correlation with Iron Overload and Viral Hepatitis. Open access Maced J Med Sci. 2015 Jun;3(2):287–92. Available from: https://doi.org/10.3889/oamjms.2015.059
17. Kohorst MA, Khazal SJ, Tewari P, Petropoulos D, Mescher B, Wang J, et al. Transfusion reactions in pediatric and adolescent young adult haematology oncology and immune effector cell patients. EClinicalMedicine. 2020 Sep;26:100514. Available from: https://doi.org/10.1016/j.eclinm.2020.100514
18. De Pascale MR, Belsito A, Sommese L, Signoriello S, Sorriento A, Vasco M, et al. Blood transfusions and adverse acute events: a retrospective study from 214 transfusion-dependent pediatric patients comparing transfused blood components by apheresis or by whole blood. Ann Ist Super Sanita. 2019;55(4):351–6. Available from: https://doi.org/10.4415/ann_19_04_08
19. Vladimirovna K, S.Yu Z, O.N M, Ya.V K, A.P S, T.V S, et al. Impact estimation of long regular exercise on hemostasis and blood rheological features of patients with incipient hypertension. Bali Med J. 2017;6(3):514. Available from: https://doi.org/10.15562/bmj.v6i3.630
20. Ackfeld T, Schmutz T, Guechi Y, Le Terrier C. Blood Transfusion Reactions-A Comprehensive Review of the Literature including a Swiss Perspective. J Clin Med. 2022 May;11(10). Available from: https://doi.org/10.3390/jcm11102859