Short Communications

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Red Cell Alloimmunization in Repeatedly Transfused Sudanese Patients with Leukemia in Northern Sudan

Taj Alasfia Abdalkream Jawish[1], Hajir Mohamed Hessen[2], Mubarak Ahmed Alshafeea[3], Khalid Abdelsamea Mohamedahmed[3], Elhadi Abdella Ahmed[2], Gad Allah Modawe[4], Ibrahim Khider Ibrahim[5]*

Abstract

Background: Leukemia frequently causes anemia; thus patients need products containing normal blood or RBCs for treatment. Anti-red blood cell alloantibody formation is still a critical challenge in transfusion. **Objectives:** The current study aimed to investigate RBC alloantibodies in Sudanese leukemia patients who receive multiple blood transfusions at the cancer center in Dongola and Maroyee, Northern Sudan. **Materials and Methods:** At the Northern State oncology center in Dongola and Maroyee, Sudan, an across-sectional descriptive study design was used. In this study, 100 leukemic patients who had received blood transfusions three times or more were enrolled. From each participant, Peripheral blood was drawn in amounts of 3 ml in EDTA vacutainer tubes for ABO blood group and Rh factor testing and 3 ml in non-additive containers for antibody screening and Alloantibody identification. All individuals' ABO blood groups and Rh factors were determined using the slide method. Indirect Coombs test apply to detect alloantibodies by Polly Specific antihuman globulin reagents using tube method techniques. Alloantibody identification was performed by DiaMed-ID microtyping system. **Results:** Incidence of alloimmunization was 11%, with 11 alloantibodies found in 11 patients. The most common alloantibody was kell (36.4%), followed by Lea (27.2%; 3/11), then P (18.2%; 2/11) and M (18.2%; 2/11). **Conclusion:** Anti kell antibody was the most prevalent alloantibody among leukemic patients with multiple transfusions.

Keywords: Alloimmunization- blood group antigens- blood transfusion- Sudanese

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Introduction

Leukemia is a group of cancers that usually begin in the bone marrow and resulting inhigh numbers of abnormal white blood cells (Leukemia NCL, 2014). These white blood cells are not fully developed and are called blasts or leukemia cells. Symptoms may include bleeding and bruising problems feeling tired, fever, anemia and an increased risk of infection due to a lack of normal blood cells (National Cancer Institute, 2013). A combination of genetic and environmental factors (World Cancer Report, 2014), family history, smoking, ionizing radiation, and some chemicals (e.g. benzene) (Muniraj, 2015) are believed to play role as risk factors of leukemia. Leukemia belong to a broader group of tumors that affect the blood, bone marrow and lymphoid system and mainly divided into four types: acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL) and chronic myeloid leukemia (CML) (WHO Classification of Tumors of Hematopoietic and Lymphoid Tissues, 2008). Treatment of leukemia may involve some combination of chemotherapy and radiation therapy, targeted therapy and bone marrow transplantation. In addition to supportive care and palliative care as needed (Vardiman et al., 2009). Anemia commonly occurs in patients with leukemia resulting from decreasing number of erythrocytes precursor due to infiltration of bone marrow with leukemic cells. Moreover; Anemia is a frequently observed adverse effect appear in patients with cancer who receive chemotherapy or drugs designed to block specific oncogenic signaling pathway.These patient need normal whole blood or red blood cells product as therapy. The purpose of red blood cell transfusion (RBCs) is to increase oxygen distribution (Eldour et al., 2015). Transfusions can lead to erythrocyte alloimmunization with serious complications for the patient. These

*[1]Ministry of Health, Northern State, Dongola, Sudan. [2]Department of Medical Microbiology, Faculty of Medical Laboratory Science, University of Gezira, Wad Medani, Sudan. [3]Department of Hematology and Immunohematology, Faculty of Medical Laboratory Science, University of Gezira, Wad Medani, Sudan. [4]Department of Biochemistry, Faculty of Medicine and Health Sciences, Omdurman Islamic University, Omdurman, Sudan. [5]Department of Hematology, Faculty of Medical Laboratory Sciences, Al Neelain University, Khartoum, Sudan. *For Correspondence: ibrahimkh82@gmail.com*

antibodies are often directed against antigens expressed on RBCs of white persons, which represent the majority of donors (Mohsin et al., 2013). All immunization consists of the induction of immunity in response to foreign antigens encountered through exposure to cells or tissues from a genetically different member of the same species (Abedelrahman and Mirghani, 2017). Multiple blood transfusion may result in red cells alloimmunization with low-incidence or private minor blood groups. Hence this study to detect RBCs alloantibodies concern minor blood group in leukemic patients with multiple blood transfusion. The aim of present study was to detect RBC alloantibodies in Sudanese leukemic patients with multiple blood transfusions at Dongola and Maroyee, oncology Center, Northern Sudan.

Materials and Methods

Across sectional hospital based study aimed to detect RBCs alloantibodies among 100 leukemia patients with multiple blood transfusion in Dongola and Maroyee City, Northern State, Sudan. The data collected by using well designed constructive questionnaire and results of the laboratory investigations. The SPSS computer software version 21 was used for statistical analysis. The ethical clearance was obtained from the Ministry of Health, Northern State. The informal consent was obtained from any participant. About 6 ml of peripheral blood was collected from each patient by qualified phlebotomies. Peripheral blood was drawn in amounts of 3 ml in EDTA vacutainer tubes for ABO blood group and Rh factor testing and 3 ml in non-additive containers for antibody screening and Alloantibody identification.

Results

The gender of the patient might influence the rate of red cell alloimmunization. The association of alloantibody development and gender of patients was studied. In the present study, the rate of red cell alloimmunization in females was found higher (12.5 %) than males (10 %) (Table 1).

One third (36.3%) of red cell alloantibodies belonged to the K system, 27.2% were directed against lewis blood system and 18.1 % directed against P blood system as well as for M antigen. No other clinically significant red cell alloantibodies were detected in the present study (Table 2).

The most frequently alloimmunized individuals were those with the O^+ blood group (6; 13.9%), followed by those with the A^+ blood group (4; 14.2%). A statistically significant correlation between the types of ABO and Rh blood groups and alloimunization (P value = 0.025) (Table 3). There were 6 O^+ blood group members who tested positive for 2 anti-Kell antibodies, 2 anti-M antibodies, 2 anti-P antibodies, and 1 anti-Le-a antibody. There were 2 anti-Kell antibody positives, 1 anti-P antibody positive, and 1 anti-Le-a antibody positive among the 4 A^+ blood group individuals.

Table 1. Positive and Negative Alloantibody Screening Test among Gender

Gender	Total	Alloantibody positive	% of positivity
Male	60	6	10%
Female	40	5	12.50%

Table 2. Distribution of Alloantibodies According to the Blood Group System

Blood group system	Antibody (n)	%
Kell	4	36.3
Le	3	27.2
P	2	18.1
M	2	18.1
Total	11	100

Table 3. Association between Types of Blood Group (ABO and Rh) and Alloimuniztion among Study Cases

Blood group	Screening test		Total
	Positive	Negative	
A^+	4 (14.2%)	24 (85.7%)	28 (100.0%)
A^-	0 (0%)	1 (100%)	1(100.0%)
B^+	1 (5.2%)	18 (94.7%)	19 (100.0%)
AB^+	0 (0.0%)	8 (100.0%)	8 (100.0%)
O^+	6 (13.9%)	37 (86.0%)	43 (100.0%)
B^-	0 (0%)	1 (100%)	1 (100.0%)
Total	11 (11%)	89 (89%)	100 (100.0%)

P value = 0.025

Discussion

Due to recurrent anemia, leukemia patients typically get blood as part of their treatment regimen. Leukemia patients frequently develop anemia due to a decrease in erythrocyte precursors brought on by the invasion of leukemic cells into the bone marrow or as a direct side effect of chemotherapy and radiotherapy (Kennedy, 2014). Out of 100 cases,11 patients(11%)developed alloantibodies, of those 4 patients (36.3%) were positive for anti-Kell blood group system alloantibodies which is the most important blood group,antigen is strongly immunogenic, and is frequently found in sera from transfused patients,some bind complement. Anti-Kell caused HTRS on numerous occasions, both immediate and delayed. Both have been implicated in HDN.Study was carried out on 100 patients with leukemia under treatment and the results were revealed that the most frequent antibody was anti-Kell and this finding is agree with Azza and her team who concluded the same finding (Ahmed, 2010). Also agree with Ahmed in Elobied City, Sudan in 2015 who found the most detected anti-K, flowed by anti-E, anti-c and anti-Kidd (Agab et al., 2015), but inconsistent with study carried out in India by (Joseph et al., 2014) who found the most antibody was anti-Rh system followed by anti-M, and anti-Lewis. Also disagree with study done in Iran by Ghasemi et al., (2016) who found the most common antibodies against Rh. Also the findings in the study disagreed with Agab et al., (2015) who did a study in Northern Kordfan among sickler transfusion dependent patients and found anti-K,

Anti-c, anti-E, anti-Kidd, and Anti-Le b.Three patients (27.2%)were positive for anti-Lewis "a", person whose RBCs phenotype is Le (a-b$^+$) make anti Le (a), because small amount of unconverted Le (a) are present in their saliva and plasma.These antibodies also react in37°C but it much weaker than seen at room temperature,and also may be detected weakly at the anti-human globulin (AHG) phase if poly specific is used, the antibody can bind complement and cause hemolysis. Lewis antibody cannot cross the placenta, don't make HDN,and antigens are poorly developed at birth. Lewis antibodies in recipients serum are readily neutralized by Lewis blood group substance in donor plasma, for this reason Lewis Abs rare cause in vivo hemolysis (Roebuck et al., 2008).Two patients (18.1%) were positive with anti-Pcell detected, these antibody react optimally at 4°C but occasionally at 37°C, rarely may cause in vitro hemolysis, it always IgM, it there aren't cross the placenta and has not cause HDN.Antibody is weakly react at room temperature. Anti-P1 has rarely cause hemolysis in vivo,strength of P1 antigen varies among different RBCs sample, and antigen strength has been diminishing when RBCs are stored (Roback et al., 2008). Two patient were position with M cell (18.1%), This anti-M naturally occurring, agglutination at room temperature, it is predominantly IgM, but rare have been found that are partly or wholly IgG, rarely clinically significant, that react at 37°C or AHG, and it has rarely related with HDN or HTR. Azerkerkevan etal., (2015); found the most common antibodies (E/e/C/c/Cw) then anti-K, anti-D in multi transfusion thalassemic patients. Abdelrazik et al., (2016) found the most common antibodies was anti-D followed by anti-C in thalassemic patients with multi transfused blood in Egypt. Other study results for alloimmunization frequency in other countries is 30% (Kuwait), 19.5% (Egypt), 7.4% (Hongkong) and 3.7% (Greece) (Ragab et al., 2013). The study recommended that, the screening of minor blood grouping alloantibodies in leukemic patients with multiple blood transfusion is important in order to reduce the risk of alloimmunization.

In conclusion, The study found that in leukemic patients receiving multiple blood transfusions at the Maroyee and Dongola Oncology Centers in Sudan, Anti-Kell was the most common alloantibody. Additionally, the study found that in order to decrease the risk of alloimmunization, antibody screening needs to be implemented as a standard pre-transfusion test for each patient who depends on blood transfusions.

Author Contribution Statement

Concept: Taj Alasfia Abdalkream Jawish, Hajir Mohamed Hessen, Experimental Studies: Taj Alasfia Abdalkream Jawish, Statistical analysis: Mubarak Ahmed Alshafeea, Khalid Abdelsamea Mohamedahmed, Manuscript preparation: Elhadi Abdella Ahmed, GadAllah Modawe Ibrahim Khider Ibrahim. All authors read and approved the final manuscript.

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Ethics Committee Approval

The study protocol was approved by Institutional Ethics Committee of Ministry of Health, Northern State, Dongola, Sudan.

Declaration of competing interest

The authors declare that they have no competing financial or any other interests that could have appeared to influence the work reported in this paper

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