

Red blood cell allo- and autoimmunization and microbes: Two sides of the same coin

Carlos A Gonzalez, Silvana Gonzalez

Developing antibodies against antigens on red blood cells (RBCs) is an important public health and health care problem. In fact, the clinical consequences include difficulty in finding compatible RBC units therefore causing a delay in transfusion and treatment, hemolytic disease of the newborn and hemolytic transfusion reaction, which can be fatal in some cases.

The explanation of why only a selected group of patients (respondents) develop RBC alloantibodies (due to transfusion or pregnancy) is complex and poorly understood.

A recent epidemiological study on risk factors of RBC alloimmunization shows that alloimmunization is more frequent in women than in men, in RhD negative than in RhD positive, and the primary diagnosis is associated with a greater or lower probability to be respondent [1]. The diagnosis of sickle cell disease, systemic lupus erythematosus, rheumatoid arthritis, and myelodysplastic syndrome was more common among respondents than among the non-responders.

This situation is not unexpected, as previous studies indicated the existence of a greater risk of alloimmunization when the transfusion receiver is in a proinflammatory state, such as autoimmune, infectious and oncohematological diseases [2]. This state of immune activation, caused by genetics and epigenetics, strengthens the response and is essential for the development of the humoral immunity to RBC alloantigens.

The host-microbe interaction is of immunohematological consequences. Some can be considered physiological (since they contribute to the

immune repertoire), some are temporary, and others are clinically significant, and may be fatal.

The first host-microbe interaction occurs during the first weeks of extrauterine life which generates a T-cell-independent immune response to carbohydrates and glycolipids present in bacterial membrane and the ABO antibodies are produced. In the next few months/years and as an integral part of the T-cell-independent immune response to bacteria, the "natural" blood group antibodies are generated (H, Le, and MNS) mostly IgM, low affinity IgG2/IgG4, and if they do not trigger complement, they tend to be clinically not significant [3].

A second kind of microbe-RBC interaction causes alterations in blood group antigens, whether by their potentiation (T, Tk, Th, and Tn); by their depression, such as Knops in Acquired Immunodeficiency Syndrome (AIDS) or A, B, H, I, K, M, and N in sepsis; or by acquiring them (B_{acq} , K_{acq} , Jk_{acq}). These phenomena are usually transient and remit spontaneously or due to medical treatment.

The third host-microbe interaction, not always clinically distinguishable from the previous ones, is produced by pathogenic carriers of sequences of peptides that are similar to blood group antigens, capable of generating a primary immune response (T-cell-dependent). This could explain the relationship between infection and the detection of alloimmune antibodies. Animal models strongly support this observation; as a matter of fact, viral infections or viral-like inflammation can potentiate alloimmunization [4].

Another phenomenon can be observed due to host-microbe interaction, which is the possibility of generating autoimmune responses in the context of certain infections. There is a strong relationship between infections and the development of anti-RBC autoantibodies. Several mechanisms, not mutually exclusive, have been proposed: (a) Molecular mimicry (an immune response to a microbial antigen which generates cross-reactive antibodies that recognize and destroy host antigens), (b) Escape from thymic deletion by autoreactive clones, and (c) T-B dysfunction which causes a decrease in Tregs cells, an increase in Th2; it may even generate a polyclonal B cell activation.

A situation that deserves our attention is Human Immunodeficiency Virus (HIV)-infected individuals, which by direct effect of the virus or by its associated infections are characterized by:

Carlos A. Gonzalez¹, Silvana Gonzalez²

Affiliations: ¹Servicio de Hemoterapia, Hospital Muñiz, Buenos Aires, Argentina; Dirección de Posgrado, Medical School, Pontificia Universidad Católica Argentina, Buenos Aires, Argentina; ²Medical School, Pontificia Universidad Católica Argentina, Buenos Aires, Argentina.

Corresponding Author: Dr. Carlos A. Gonzalez, Servicio de Hemoterapia, Hospital Muñiz, Buenos Aires, Argentina, Uspallata 2272, Buenos Aires, Argentina; Email: carlosgonzalez@buenosaires.gob.ar

Received: 20 May 2019
Published: 27 June 2019

Lower prevalence of anti-RBC alloantibodies:
One of the first consequences of the action of HIV is the decrease of alloimmune response upon exposure to allogeneic RBC [5] due to the qualitative and quantitative CD4 T cell declines, a vital subpopulation in the recognition, processing, and presentation of blood group antigens by antigen-presenting cells. Consequently, the incidence of irregular antibodies in HIV infected is 0–2% [2].

Higher prevalence of anti-RBC antibodies:
10% of HIV-infected patients present anti-RBC autoantibodies, reaching a prevalence of 85% in AIDS [6]. Autoimmune hemolytic anemia occurs in 3% of them, its risk 28 times higher than control group [7]. Even in those patients treated with antiretroviral therapy, the prevalence can be the same or even higher [8]. When studied properly, immune hemolysis can be drug induced [9].

In conclusion, infected patients constitute a heterogeneous group with different underlying conditions, microorganisms of diverse virulence, and a wide range of inflammatory capacity and response as a host; therefore, the immunohematological consequences of direct and indirect action of microbes in the host from not clinically significant to life-risking; the specialist must be alert in order to enable their early detection and differential diagnosis [10].

Keywords: Alloantibodies, Autoantibodies, Blood group antibodies, Immune response

How to cite this article

Gonzalez CA, Gonzalez S. Red blood cell allo- and autoimmunization and microbes: Two sides of the same coin. *Int J Blood Transfus Immunohematol* 2019;9:100045Z02CG2019.

Article ID: 100045Z02CG2019

doi: 10.5348/100045Z02CG2019ED

REFERENCES

1. Karafin MS, Westlake M, Hauser RG, et al. Risk factors for red blood cell alloimmunization in the Recipient Epidemiology and Donor Evaluation Study (REDS-III) database. *Br J Haematol* 2018;181(5):672–81.
2. Tormey CA, Hendrickson JE. Transfusion-related red blood cell alloantibodies: Induction and consequences. *Blood* 2019;133(17):1821–30.

3. Cooling L. Blood groups in infection and host susceptibility. *Clin Microbiol Rev* 2015;28(3):801–70.
4. Baine I, Bahar B, Hendrickson JE, Hudson KE, Tormey CA. Microbial pathogen primary sequence inversely correlates with blood group antigen immunogenicity. *Transfusion* 2019;59(5):1651–6.
5. Boctor FN, Ali NM, Mohandas K, Uehlinger J. Absence of D- alloimmunization in AIDS patients receiving D-mismatched RBCs. *Transfusion* 2003;43(2):173–6.
6. Lai M, d’Onofrio G, Visconti E, Tamburrini E, Cauda R, Leone G. Aetiological factors related to a positive direct antiglobulin test result in human immunodeficiency virus-infected patients. *Vox Sang* 2006;90(4):325–30.
7. Olayemi E, Awodu OA, Bazuaye GN. Autoimmune hemolytic anemia in HIV-infected patients: A hospital based study. *Ann Afr Med* 2008;7(2):72–6.
8. Yen YF, Lan YC, Huang CT, et al. Human immunodeficiency virus infection increases the risk of incident autoimmune hemolytic anemia: A population-based cohort study in Taiwan. *J Infect Dis* 2017;216(8):1000–7.
9. González CA, Guzmán L, Nocetti G. Drug-dependent antibodies with immune hemolytic anemia in AIDS patients. *Immunohematology* 2003;19(1):10–5.
10. Gonzalez CA, González S, Gonzalez J. The challenge of transfusion of patients infected with HIV/AIDS. *J Clin Case Rep* 2019;4(2):1–6.

Acknowledgments

I express my gratitude to Ana Maria Ahumada for her advice, support and time.

Author Contributions

Carlos A Gonzalez – Conception of the work, Design of the work, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Silvana Gonzalez – Conception of the work, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

The corresponding author is the guarantor of submission.

Source of Support

None.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

Copyright

© 2019 Carlos A Gonzalez et al. This article is distributed under the terms of Creative Commons Attribution

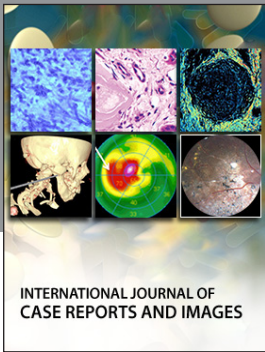
License which permits unrestricted use, distribution and reproduction in any medium provided the original author(s) and original publisher are properly credited. Please see the copyright policy on the journal website for more information.

Access full text article on
other devices



Access PDF of article on
other devices





INTERNATIONAL JOURNAL OF
CASE REPORTS AND IMAGES



VIDEO JOURNAL OF
CLINICAL RESEARCH



VIDEO JOURNAL OF
BIOMEDICAL SCIENCE



INTERNATIONAL JOURNAL OF
HEPATOBIILIARY AND
PANCREATIC DISEASES



INTERNATIONAL JOURNAL OF
BLOOD TRANSFUSION AND
IMMUNOHEMATOLOGY



EDORIUM JOURNAL OF
OPHTHALMOLOGY



Submit your manuscripts at
www.edoriumjournals.com



EDORIUM JOURNAL OF
MEDICINE



EDORIUM JOURNAL OF
CARDIOTHORACIC AND
VASCULAR SURGERY



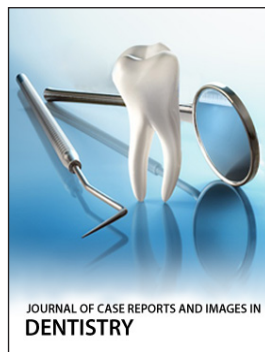
JOURNAL OF CASE REPORTS
AND IMAGES IN ORTHOPEDICS
AND RHEUMATOLOGY



EDORIUM JOURNAL OF
PSYCHOLOGY



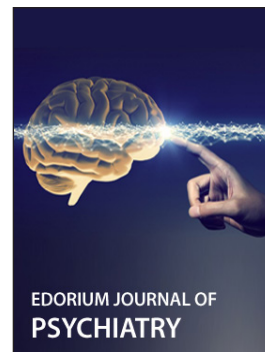
EDORIUM JOURNAL OF
CELL BIOLOGY



JOURNAL OF CASE REPORTS AND IMAGES IN
DENTISTRY



EDORIUM JOURNAL OF
CANCER



EDORIUM JOURNAL OF
PSYCHIATRY



JOURNAL OF CASE REPORTS AND
IMAGES IN INFECTIOUS DISEASES



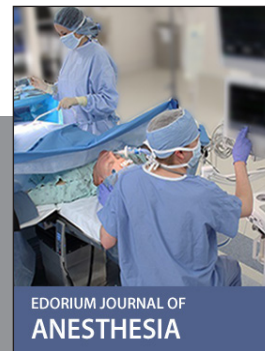
EDORIUM JOURNAL OF
ANATOMY AND EMBRYOLOGY



EDORIUM JOURNAL OF
SURGERY



JOURNAL OF CASE REPORTS
AND IMAGES IN PATHOLOGY



EDORIUM JOURNAL OF
ANESTHESIA