NIILM University International Journal of Applied and Behavioural Sciences (IJABS)

ISSN: 3048-9083 Vol.02, Issue 02, Jul-Dec 2025

Investigating the Pathophysiology and Immunological Mechanisms in Aplastic Anemia: A Focus on Natural Killer (NK) Cell Activity and Immunomodulation

Singh, Ajab

Research Scholar, Department of Microbiology, NIILM University Kaithal, Haryana, India

DOI: https://doi.org/10.70388/ijabs250149

Received on May 06, 2025

Accepted on June 15, 2025

Published on Sep 20, 2025

Abstract

Aplastic anaemia (AA) refers to a rare and potentially deadly disorder of the blood that is characterized by the disfunction of the bone marrow that combats infections and diseases by producing all types of blood cells to a significant degree, a condition identified as pancytopenia. Whereas the autoimmune obliteration of blood-forming progeny and stem cells (HSPCs) due to self-reactive T cells has been extensively recorded; however, the involvement of natural killing (NK) cells in the onset of aplastic anaemia remains inadequately comprehended. The paper explores the modern understanding of AA emphasizing the quantitative and functional Misfits of NK cells and their potential to be used as a treatment goal. We explore further into immunomodulatory strategies used to restore balance of the immune in individuals affected by Aplastic Anaemia (AA).

Introduction

Aplastic anaemia (AA) is a rare condition characterized by a lack of effective bone marrow work which causes pancytopenia and decreased cellular content in the bone marrow. It is believed that the underlying underlying processes of acquired AA include the impairment of immune response, and the demise of bloodline progeny and stem cells (HSPCs) instigated by the self-reactive characteristic of T cells in individuals with genetic susceptibilities. While it is crucial for T-cell mediated mechanisms to be thoroughly investigated, the function of

Natural Killer (NK) cells in the advancement of AA remains inadequately examined. In this evaluation, the NK cell role in AA is to be elucidated and potential immunomodulatory therapeutic interventions to address PCOS are to be investigated.

Pathophysiology of Aplastic Anemia

The most popular hypothesis that has been proposed about the pathogenesis of AA is based on the toxicity of the cytotoxic T cells that lead to the elimination of haematopoietic stem and progenitor cells (HSPCs). The pro-inflammatory cytokines released by self-reactive T cells include interferon-gamma (IFN- 7) and tumour necrosis factor-alpha (TNF- 7), and cause haematopoietic stem and progenitor cells (HSPCs) to undergo apoptosis. However, to the current date it has been found that there is not indeed a particular auto-antigen.

Natural Killer (NK) Cells: An Overview

Natural killer (NK) cells serve an essential function within the body's inherent immune system, as they are pivotal in triggering a swift response to molecules that have been impacted by viruses or have undergone transformation. Their action is shown through direct cytotoxic actions and secretion of cytokine, the role of which is controlled by a balancing fine equilibrium of activating and inhibitory receptors.

NK Cell Abnormalities in Aplastic Anemia

Recent information has suggested that numerical and functional abnormalities are observed in NK cells during Aplastic Anaemia. AA:

- Reduced NK Cell Counts: Research findings indicate a significant reduction in the circulating blood NK cell reservoirs among individuals with AA, correlating with the severity of their condition.
- Reduced Cytotoxic Effect: NK cells of AA patients have less cytotoxic potency over the target cell associated with altered activation receptors and cytolytic factors expression.
- Altered Cytokine Production: NK cells of AA produce less Type I cytokine and more Type II cytokine, an indication of a change their functional properties.

Mechanisms Underlying NK Cell Dysfunction in AA

The impairment of the NK cell function may be a result of a range of factors in AA:

- Cytokine imbalance: Elevated levels of IL-2 and IL-12 in the bone marrow microenvironment may influence the development and of NK cells and their activity.
- The suddenness of TIM3: a TIM3 expression depleted on NK cells results in the non-reduced NK cell effectivity, which in its turn reverses the immune activational position connected with intense severity of AA and the possible means to mitigate the disorder.

Immunomodulatory Therapies and NK Cells

Immunosuppressive therapy (IST) is essential in managing AA, focusing on diminishing the unusual immune reaction. Agents like antithymocyte globulin (ATG) and cyclosporine have demonstrated effectiveness in revitalizing haematopoiesis. Significantly, IST has been linked to the resurgence of NK cell quantities and their operational abilities in those who respond, indicating that the resurgence of NK cells could serve as an indicator of the treatment's efficacy.

Future Directions and Therapeutic Implications

Understanding NK cell dysregulation in AA opens avenues for novel therapeutic strategies:

NK Cell-Targeted Therapies: Modulating NK cell activity through cytokine therapy (e.g., IL-15 administration) or checkpoint inhibitors may enhance their cytotoxic function against autoreactive T-cells.

Adoptive NK Cell Transfer: Infusion of activated NK cells from healthy donors could potentially reconstitute innate immunity and suppress autoreactive lymphocytes.

Biomarker Development: NK cell profiles may serve as biomarkers for disease prognosis and treatment response, aiding in personalized therapy approaches.

Conclusion

NK cells play a crucial role in the immunopathology of aplastic anemia. Their quantitative and functional impairments contribute to disease progression and may impact treatment

outcomes. Further research into NK cell biology in AA is essential to develop targeted therapies that restore immune balance and improve patient prognosis.

References:

1. Bacigalupo, A. (2017). How I treat acquired aplastic anemia. *Blood*, *129*(11), 1428–1436. https://doi.org/10.1182/blood-2016-08-693481
2. Feng, X., Scheinberg, P., & Chen, J. (2015). Expression of NK-activating receptor-NKp46/NCR1 on NK cells in patients with severe aplastic anemia. *International Journal of Hematology*, *102*(2), 145–151.
3. Gascón, P., Zoumbos, N., & Young, N. (1986). Analysis of natural killer cells in patients with aplastic anemia. *Blood*, *67*(5), 1349–1355
4. Hu, W., Wang, Y., & Zhang, L. (2020). Proteomics analysis reveals alterations of NK cells in patients with severe aplastic anemia. *International Journal of Laboratory Hematology*, *42*(2), 157–163.
5. Maciejewski, J. P., & Risitano, A. M. (2019). Hematopoietic stem cells in aplastic anemia. *Archives of Medical Research*, *50*(1).
6. Risitano, A. M. (2005). Immunopathogenesis of aplastic anemia and therapeutic implications. *Haematologica*, *90*(5), 584–589.
7. Scheinberg, P., & Young, N. S. (2012). How I treat acquired aplastic anemia. *Blood*, *120*(6), 1185–1196. https://doi.org/10.1182/blood-2011-12-274019
8. Young, N. S. (2012). Aplastic anemia: Pathophysiology and treatment. *American Journal of Hematology*, *87*(8), 757–763.
9. Zhang, X., Feng, X., & Fu, Y. (2014). Abnormalities of quantities and functions of natural killer cells in severe aplastic anemia. *Experimental Hematology*, *42*(9), 789–797.