Natural Killer Cell Impairment as a Mechanism of Immune Evasion in Myelodysplastic Syndromes

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Introduction

•Myelodysplastic syndromes (MDS) are clonal hematopoietic disorders with risk of leukemic progression.
•Immune evasion is a hallmark of MDS progression and treatment resistance.
•NK cells are key innate immune effectors that recognize and eliminate abnormal hematopoietic clones.
•In MDS, NK cell dysfunction enables malignant clones to escape immune surveillance.
•Understanding NK impairment offers potential for immunotherapeutic targeting.
•This review highlights clinical evidence of NK dysregulation in MDS.

Objectives

To synthesize data on NK cell phenotypic and functional abnormalities in MDS.
Evaluate how NK dysfunction contributes to immune evasion and disease severity.
Identify potential biomarkers and targets for NK-directed therapy in MDS.

Methods

•Narrative review of observational studies (2010–2024) on NK cells in MDS.
•Included studies with peripheral blood and bone marrow NK profiling.
•Key outcome measures: NK cell counts, subset distribution, receptor expression, and cytotoxicity.
•Clinical endpoints included blast count, survival, and IPSS/IPSS-R classification.

Figure 1: NK Cell Dysfunction and Immune Evasion in MDS

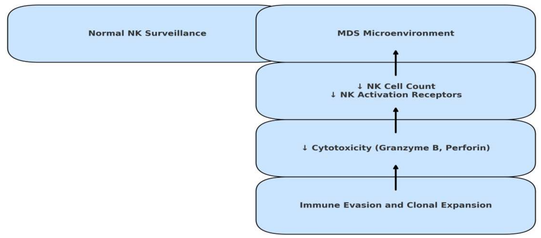


Figure 2: Expression of Key NK Cell Molecules in MDS vs Healthy

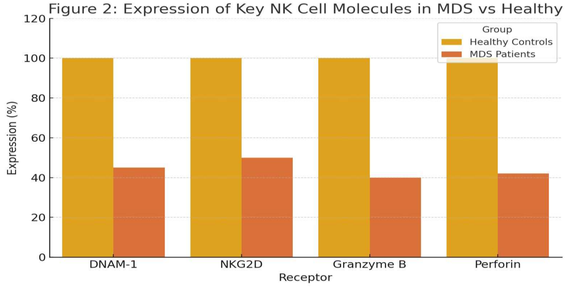
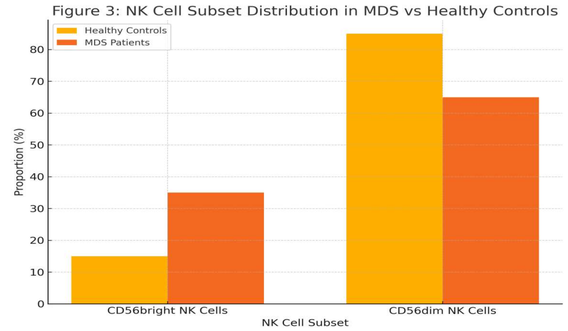


Figure 3: NK Cell Subset Distribution in MDS vs Healthy Controls



Results

•NK cell counts are significantly reduced in MDS (about 50% lower than in healthy individuals).
•Severe depletion seen in higher-risk MDS categories.
•NK cells exhibit immature phenotype with expansion of CD56^bright^ and reduction of CD56^dim^ cytotoxic cells.
•Functional cytotoxicity is impaired due to decreased granzyme B and perforin.
•Key activating receptors (NKG2D, DNAM-1) are downregulated in marrow NK cells.
•Decreased receptor expression correlates with higher blast counts and worse prognosis.
•NK cells with MDS-associated mutations show intrinsic functional deficits.
•Patients with NK cells <8% had significantly worse overall survival (independent of IPSS-R).

Conclusion

•MDS is characterized by both quantitative and qualitative NK cell defects.
•These impairments contribute to immune evasion and correlate with disease severity.
•NK dysfunction may serve as both a biomarker and therapeutic target.
•Future strategies should explore enhancing NK activity or reversing inhibitory phenotypes in MDS.

References

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