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Relapsed Multiple Myeloma-Driven Hemophagocytic Lymphohistiocytosis Post-Autologous Stem Cell Transplantation: A Case Linking Cytokine Overload to Immune-Cancer Crosstalk

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BACKGROUND

Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening hyperinflammatory syndrome typically associated with infections, lymphomas, or autoimmune disorders. Its occurrence in multiple myeloma (MM), especially following autologous stem cell transplantation (ASCT), is exceedingly rare and mechanistically undefined. This case explores the unique interplay between MM relapse and HLH in the post-transplant setting, challenging the conventional understanding of HLH triggers.

PURPOSE

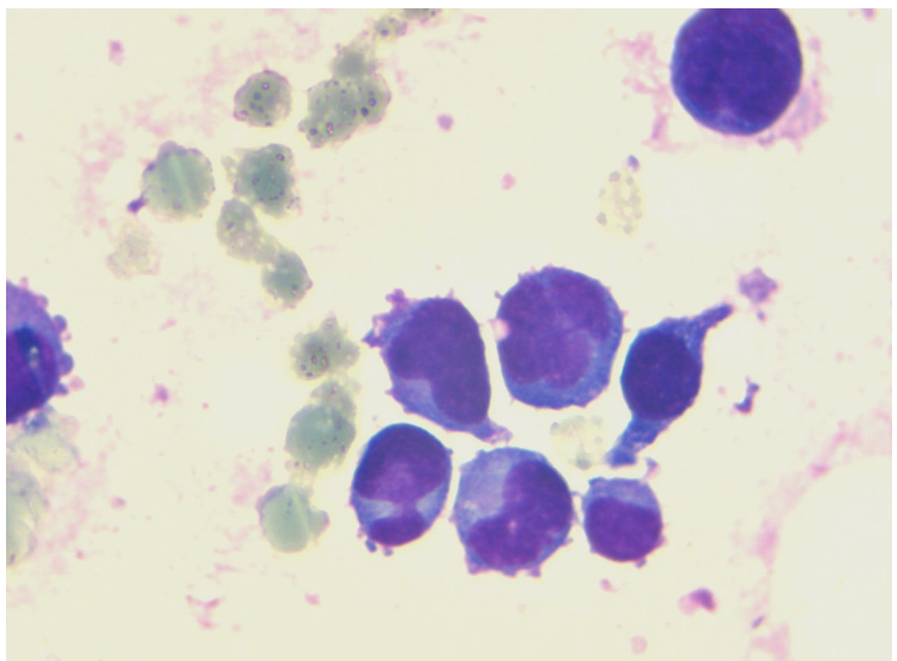
To delineate the pathophysiological mechanisms by which relapsed MM drives HLH development post-ASCT, with a focus on cytokine-mediated immune dysregulation and organ injury. It further evaluates the efficacy of combined HLH-directed and anti-myeloma therapies in disrupting this lethal synergy.

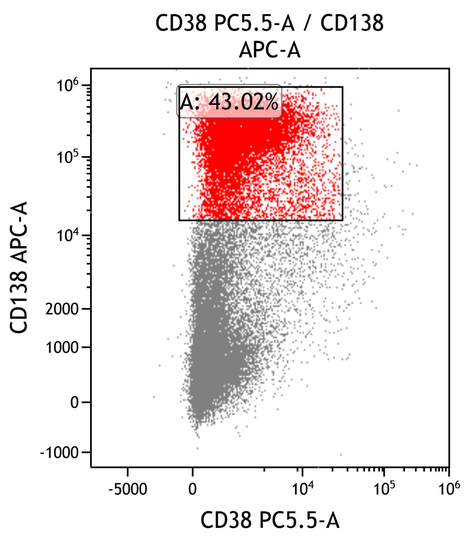
METHODS

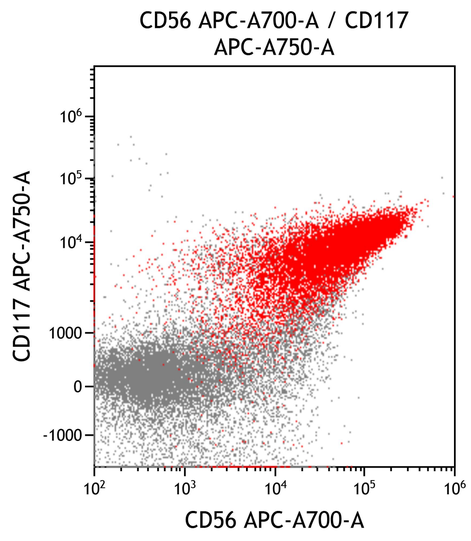
A 60-year-old female with relapsed MM (ISS III) post-ASCT after induction KRD chemotherapy. At 232 days post-ASCT, she presented with fever, pancytopenia, and multi-organ dysfunction. Diagnostic evaluation included serial cytokine profiling (IL-6, IL-10, sCD25), bone marrow tests, infectious investigation (tNGS/viral PCR), and HLH-2004 criteria application.

RESULTS

Cytokine profiling revealed a storm (IL-6:171.38 pg/mL, IL-10:764.32 pg/mL) coinciding with active MM (56% bone marrow plasma cells) and treatment with DRD led to rapid HLH remission, evidenced by ferritin reduction to 2,937 ng/mL and improved cytopenia within two weeks. Mechanistically, post-ASCT immune paresis ($CD8^+$ large granular lymphocyte expansion, hyponatremia) and MM-derived IL-6/TNF-α overproduction were identified as synergistic drivers of macrophage hyperactivation, exacerbated by renal dysfunction impairing cytokine clearance.







CONCLUSION

This case establishes relapsed MM as a direct instigator of HLH through a cytokine-driven cascade, diverging from classical infection-associated paradigms. Key findings include: (1) MM relapse fuels a self-sustaining inflammatory loop via IL-6/IL-10 overproduction, priming histiocyte activation; (2) Post-ASCT immune paresis and renal failure amplify cytokine accumulation, creating a permissive microenvironment for HLH; (3) Dual-pathway suppression targeting both hyperinflammation and MM clones is critical for therapeutic success. These insights advocate for proactive cytokine monitoring in high-risk ASCT recipients and beware of HLH.

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