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CHARACTERISTICS AND OUTCOMES OF THERAPY-RELATED MYELOID NEOPLASMS (TR-MN) AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION (AUTO-HCT) FOR LYMPHOMA

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INTRODUCTION

Despite advancements in relapsed lymphoma treatment, high-dose chemotherapy (HDC) and auto-HCT remain a cornerstone of management, particularly in regions with limited access to novel therapies. Improved survival following auto-HCT has led to increased incidence of tr-MN, a leading cause of non-relapse mortality (NRM). In this study, we evaluate the characteristics and outcomes of patients developing tr-MN post auto-HCT for lymphoma at King Hussein Cancer Center (KHCC) in Jordan.

AIM

To evaluate the characteristics and outcomes of patients developing tr-MN post auto-HCT for lymphoma at King Hussein Cancer Center

METHOD

We conducted a retrospective review of all adult patients (≥18 years) who underwent auto-HCT for lymphoma at KHCC from 2003 to 2020. Data on demographics, prior therapies, auto-HCT, and subsequent tr-MN were collected.

Patient characteristics were compared using chi-square and Mann-Whiteny U tests, as appropriate. Time-to-event endpoints were estimated using Kaplan-Meier method. Statistical analysis was performed using SPSS V. 25.

RESULTS

- *We identified 407 patients with a median follow-up of 5.8 years (range 5-6.1). Median age was 34.6 years (range 19-71) and 223 (54.9%) were males.*
- *265 (65.3%) patients had Hodgkin lymphoma,167 (41.1%) were refractory to first-line treatment. DHAP was the most common salvage regimen (N=194, 47.8%), followed by GDP (N=84, 20.6%) with 173 (42.6%) patients receiving >1 salvage regimen.*
- *161 (39.7%) were in complete remission at auto-HCT.*
- *BEAM was the most common conditioning regimen (N=373, 91.9%). The 5-year overall survival was 64.4%.*
- *Thirteen patients (3.2%) developed tr-MN (5 AML, 8 MDS), with a median time-to-diagnosis of 3.25 years (range 0.3-4.9) post-auto-HCT. Median OS post-tr-MN diagnosis was 6 months (95% CI 5-6.9). Patients with tr-MN were older (median 55.7 vs. 34.1 years, p<0.001), more likely to have non-Hodgkin lymphoma (5.7% vs. 1.9%, p=0.039), and had more comorbidities (6.6% vs. 2%, p=0.02).*
- *Multivariate analysis identified age at transplant as the only significant predictor of tr-MN (HR=1.162, 95% CI 1.073-1.259, p<0.001). Among NRM cases (N=32, 7.9%), tr-MN accounted for 18.75%.*

Characteristics of patients with t-AML/MDS	
Parameter	t-AML/MDS (N= 13)
	Median (range) or N (%)
Median age at AutoSCT (Yrs), range	56 (24-65)
Median age at diagnosis (Yrs), range	59 (34-69)
Median time to development (years)	4.5 (1-17)
Sex (M)	7 (53%)
Lymphoma status at tr-MN diagnosis	
Remission	6 (46%)
Relapse	7 (53%)
Follow-up Time (months)	43.4
Time to Relapse Post-BMT (months)	6.2
Chemotherapy Lines prior to t-MN	4
Type of tr-MN	
MDS	8 (61.5%)
AML	5 (34.8%)
Median Hb (g/dL)	8.6 (6.7-10.9)
Median WBC	4.6 (1.3-58.7)
Median Platelet count	42 (11-159)
FISH	
Del 7	6 (46%)
Del 5	4 (30%)
Trisomy 8	1 (7%)
MLL-r	1 (7%)
Normal	4 (30%)
Karyotype	
Complex	2 (15%)
Aneuploidy	4 (30%)
Inv(3)	2 (14%)
Failed	5 (41%)
NGS	
TP53	2 (15%)
ASXL1	1 (7%)
TET2	1 (7%)
DNMT3A	1 (7%)
PTPN11	1 (7%)
None	2 (15%)
Missing	5 (42%)
R-IPSS	4.5 (4-9.5)
Treatment for t-MN	
Intensive induction	1 (8%)
Azacitadine/Venetoclax	2 (15%)
Azacitadine	7 (54%)
AlloSCT	1 (8%)
Best supportive care	2 (15%)
Response to treatment for t-MN	
Refractory	9 (69%)
CR	1 (8%)

CONCLUSIONS

tr-MNs are a significant complication following auto-HCT with a poor survival driving NRM, with age at auto-HCT being the primary predictor. Further research is needed to identify other risk factors and mitigate this risk.

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