T/MYELOID MIXED PHENOTYPIC ACUTE LEUKEMIA (MPAL) WITH BZIP CEBPA MUTATIONS: A GENETICALLY AND BIOLOGICALLY DISTINCT SUBTYPE OF MPAL

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INTRODUCTION

CEBPA mutations are seen in AML which constitutes 10-15% of all AML and which has the most favorable outcome with standard AML-like treatment. Among MPAL, CEBPA mutation is predominantly seen in T/Myeloid subgroup and there is scarcity of literature in CEBPA mutated MPAL. At our centre, we have treated these cases predominantly like AML with few cases being treated like ALL. Hence, we analyzed their immunophenotypic, molecular features and compared the outcomes based on the type of treatment received.

METHOD

MPAL diagnosis was based on WHO criteria using a 5-tube, 10–13 color flow cytometry panel. MPO and cytoplasmic CD3 were used for lineage assignment. A targeted 137-gene NGS panel assessed genetic alterations. FISH for AML and ALL was performed in all cases. We analyzed diagnostic features, induction response, and outcomes. The primary outcome of this study was event free survival(EFS) which was defined as time from date of induction therapy until persistent MRD positivity, relapse or death. The secondary outcomes were response rates and overall survival. We treated all our MPALs with ALL like modified BFM-based induction therapy or AML-like induction and plan for allogeneic transplant in CR1. We analyzed the response to treatment based on AML-like versus ALL-like induction therapy.

RESULTS

Between November 2020 until June 2024, we diagnosed 44 cases of T/myeloid MPALs in adults out of which 12 cases had CEBPA abnormalities(27%) . One out of 12 cases had tri phenotypic (B/T and Myeloid) lineage at baseline. The median age of the cohort was 31 years and 80% were male. The median TLC count was 26.7 x 10^9/L. All cases were MPO positive by cytochemistry or flowcytometry. Cytogenetic evaluation by FISH and conventional karyotyping was normal for all cases except trisomy 21 abnormality which was seen in 4 cases and one patient had monosomy 7 abnormality. In comparison with 32 cases of T/myeloid MPALs, these 12 cases with CEBPA abnormality showed consistent MPO positivity, bright CD7expression, CD15 expression and negative for other T markers(CD2/CD5/CD1a/CD4/CD8). All patients had inframebZIP insertions except one patient who had TAD2 domain missense mutation and who also had triphenotypic disease (B/T/myeloid). GATA2 mutation was seen in 4 out of 12 patients (33%) which is commonly associated with AML.

Out of 12 patients, 4 were treated like ALL with modified BFM –90 induction out of which one patient died during induction, three of them were MRD positive post-induction. Out of 7 patients who received AML like therapy, four are doing well with MRD negative CR. The median follow up of the cohort was 19 months (range 3 months-2 years).One-year EFS for all 11 cases who received any treatment was 34.1 %. Patients who received AML like therapy had one-year EFS of 50% as opposed to 0% for those who received ALL like therapy (p=significant).

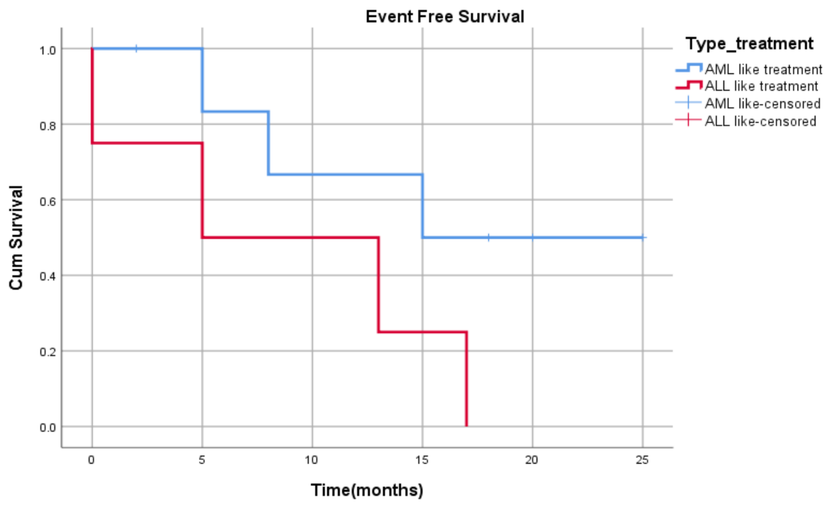

Figure-1: EFS based on type of therapy

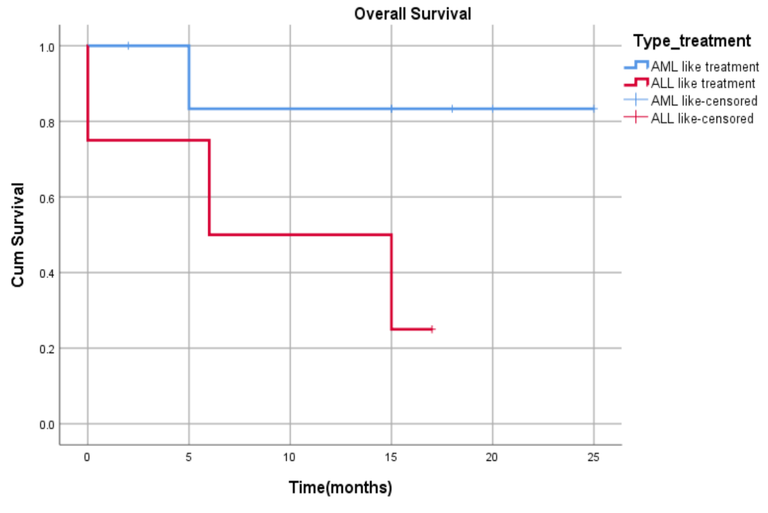

Figure-2: OS based on type of therapy

CONCLUSION

Our case series is the largest one among all T/myeloid MPAL with CEBPA abnormality with treatment and outcome data. Any T/myeloid MPAL should be screened for CEBPA abnormality and received AML like therapy if they have CEBPA bZIP domain mutation. The decision for allogeneic stem cell transplant can be considered based on donor type and comorbidity until more long-term data is available.

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