MOLECULAR FEATURES ASSOCIATED WITH CNS DISEASE IN ACUTE MYELOID LEUKEMIA

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INTRODUCTION

Acute Myeloid Leukemia (AML) patients with central nervous system (CNS) involvement are commonly excluded from clinical trials, limiting our understanding of true incidence, presentation and optimal treatment. Due to this, there is a lack of information based on molecular features associated with CNS involvement. This retrospective analysis evaluated CNS involvement in adult AML.

AIM

The aim of this project was to obtain information regarding the presentation and associated clinical and molecular risk factors in patients with AML and CNS involvement.

METHODS

Medical records were analyzed from 2015-2023. We included patients aged ≥18 with newly diagnosed AML who received a lumbar puncture to assess for CNS involvement with symptoms or high-risk features per national guidelines. Data collected included demographics, CNS symptoms, monocytic/myelomonocytic phenotype, WBC count, cytogenetics, and next-generation sequencing. Patients were considered CNS+ with positive results on CSF cytology or CSF flow cytometry on screening LP.

RESULTS

138 patients were screened, 28 were CNS positive and 110 CNS-negative. Overall screening detection was 25%. We had 908 new AML cases from 2015 to 2023, Therefore our CNS-involvement incidence was 3% (28/908) during that period. The CNS+ group consisted of 14 males, with median age of 63 (range 23-85). Table 1 outlines the incidence rates by high-risk features for the CNS+ group. If patients had 2 or more risk factors for CNS involvement the detection rate increased to 86%.

The most common molecular mutations in CNS+ patients were FLT3, NPM1, NRAS/KRAS, DNMT3A, TET2, and ASXL1. Table 2 outlines frequency and detection rates of these in CNS+ patients.

Of NPM1+ patients who were CNS+ 75% had concomitant FLT3 mutations. There were no specific cytogenetic abnormalities associated with higher CNS+ rates.

Table 1: Incidence of CNS involvement by CSF screening indication

Detection rate in CNS positive group (n=28)	
CNS symptoms	35%
Hyperleukocytosis (WBC >40K)	27%
Monocytic/myelomonocytic phenotype	24%
FLT3 mutation	39%
2 or more risk factors for CNS involvement	86%

Table 2: Molecular features associated with CNS+ AML

Mutation (% in overall population)	Total number of screened patients with mutation	CNS + detection rate (%)
FLT3 ITD: (24%)	33	27
FLT3 TKD: (9%)	13	15
NPM1: (29%)**	44	18
NRAS/KRAS: (25%)	27	26
DNMT3A: (21%)	32	19
TET2: (18%)	20	25
ASXL1: (18%)	14	36

*** Of the 18% of patients with NPM1 that were CNS+, 75% had concomitant FLT3 mutations*

CONCLUSIONS

At our institution, 25% of screened patients were CNS+ and showed high detection rates for known risk-factors, and in patients with ≥2 risk-factors for CNS-involvement detection rate increased to 86%.

Furthermore, patients with NRAS/KRAS, TET2 and ASXL1 mutations showed high detection rates. Additionally, patients with FLT3 TKD had lower CNS detection rates compared to FLT3 ITD mutated patients.

Our data is limited by its small sample size and retrospective nature. Further studies should be performed to better evaluate outcomes and further delineate risk factors.

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