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ELEVENTH ANNUAL MEETING

Association of leukocyte counts with somatic mutations and immunophenotype of tumor cells in acute myeloid leukemia.

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INTRODUCTION

Leukocyte counts at the onset of acute myeloid leukemia (AML) are known to be associated with certain genetic abnormalities in tumor cells. However, the relationship of these disease features with the immunophenotype of tumor cells have not been extensively characterized.

AIM

Evaluate the association of certain tumor cell immunophenotypes with leukocyte counts and mutational status of tumor cells in patients with AML.

PATIENTS AND METHODS

Laboratory data of 214 AML patients admitted to the National Medical Research Center for Hematology from 2010 to 2022 were included into retrospective study. Patients were divided into 6 groups according to immunophenotype: 1) CD34+ CD117+ MPO-CD13+ CD33+; 2) CD34+ CD117+ MPO+ (<70%) CD13+ CD33+; 3) CD34+ CD117+ MPO+ (>70%) CD13+ CD33+; 4) CD34-CD117+/- MPO+/- CD13+/- CD33+/-; 5) CD34- CD117+/-MPO+/- Lys^{high} CD13+/- CD33+/-; 6) myelomonocytic immunophenotype. Multivariate logistic regression with step-by-step selection, nonparametric Kruskal-Wallis rank criterion, Mann-Whitney U-criterion, and Pearson Chi-square were used for the statistical analysis.

RESULTS

Known associations of high leukocyte counts with *FLT3* mutations (OR=5.45, p<0.0001), *CBFB::MYH11* (OR=10.03, p=0.0009) were also observed in our study. *RUNX1::RUNXT1*, as well as adverse cytogenetic lesions like -5/del(5q); -7/del(7q); -17/abn(17p), complex or monosomal karyotype were statistically significantly associated with leukocyte counts less than 30 x 10^9/l at the onset of disease (p<0.0001).

NPM1, *FLT3*, *CEBPA*, *IDH1/2*, *DNMT3A*, and *TET2* gene mutations were associated with leukocyte counts elevated in following order: no mutations or only *DNMT3A/TET2/IDH1/2* → only *NPM1/FLT3/CEBPA* → *DNMT3A/TET2/IDH1/2* plus *NPM1/FLT3/CEBPA* (Fig.1). This regularity was observed in the groups with intermediate and unfavorable cytogenetic risk separately and in the general group.

The number of patients with a mature (CD34-) immunophenotype of blast cells increased in the same order (Fig.2). Mature (CD34-) immunophenotype was also significantly associated with the presence of *NPM1/FLT3/CEBPA* gene mutations (p<0.0001, Fig.2). Conversely, *RUNX1::RUNXT1* was associated with CD34+ immunophenotype (p<0.0001).

There were no statistically significant differences in leukocyte counts between six groups with different immunophenotypes, except groups #1 (CD34+ CD117+ MPO- CD13+ CD33+) and #5 (CD34- CD117+/- MPO+/- Lys^{high}CD13+/- CD33+/-). In the last group leukocyte counts were significantly higher (p=0,0017).

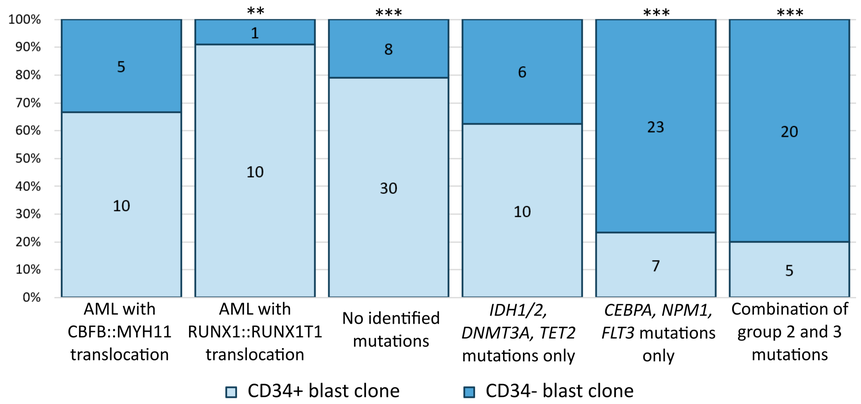


*Figure 2. CD34+/CD34- ratio of tumor clones in patients with different mutational status. ** - p-value < 0.01; *** - p-value < 0.001.*

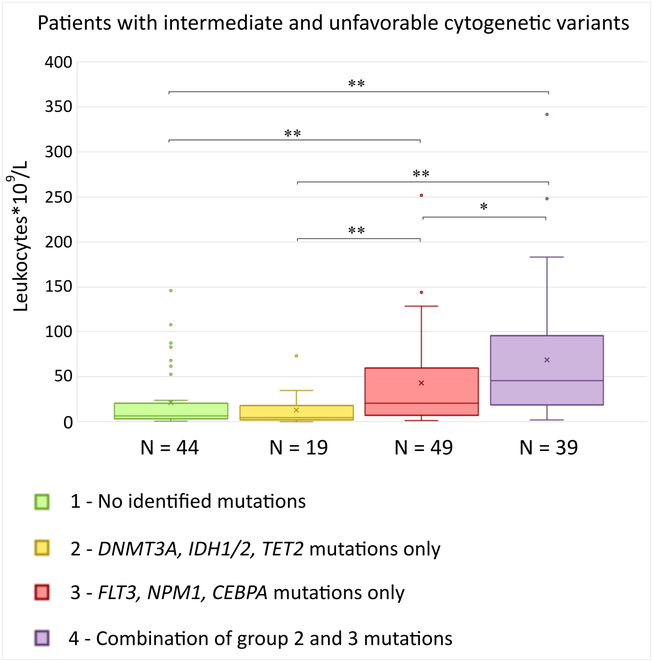


Figure 1. Differences in the level of leukocytes between groups of patients with different mutation landscape in patients with intermediate and adverse-risk cytogenetics.
** - p-value < 0,05,*
*** - p-value < 0,01.*

CONCLUSIONS

The genetic profile in AML and immunophenotype to a lesser extent are significantly associated with a high/low number of leukocytes. The highest leukocyte counts followed by combination of epigenetic and driver mutations (*DNMT3A / TET2 / IDH1/2* plus *NPM1 / FLT3 / CEBPA*) in both intermediate and unfavorable risk groups. We have also shown that patients with mutations *NPM1/FLT3/CEBPA* are characterized by an immunologically more mature immunophenotype (CD34-) of the tumor clone.

CONTACT INFORMATION

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