BAALC expression and FLT3 Internal tandem duplication mutations in acute myeloid leukemia

Thesis

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Abstract

Brain ***A***nd ***A***cute ***L***eukemia ***C***ytoplasmic (BAALC) overexpression has been reported in acute myeloid leukemia (AML). In the present study, BAALC overexpression was investigated by reverse transcriptase- polymerase chain reaction (RT-PCR) in 30 patients with de novo AML as well as 20 normal subjects as a control group. Internal tandem duplication mutation of ***F***ms – **l**ike ***t***yrosine kinase ***3*** (FLT3/ITD) and length mutation of FLT3 (FLT3/LM) were also analyzed. BAALC overexpression was detected in (46.6%) of the patients while FLT3/ITD was detected in (63.4%) and FLT3/LM (30%). All the control subjects were negative for the three types of mutations. In BAALC positive patients, the mean total leucocytic count is much lower than BAALC negative patients but the difference did not reach a statistically significant level. BAALC positive overexpression was significantly associated with higher blast percentage in peripheral blood and bone marrow blasts. BAALC overexpression was seen in FAB subtypes M1, M2, M4 and M5 and was absent in M3. Most of BAALC positive patients (57%) had normal karyotyping and 56% coexpress FLT3/ITD. The coexpression of both genes showed the worst prognosis, as none of the patients achieved complete remission and 62% of the patients died. Thus, it can be stated that BAALC alone or in conjunction with FLT3/ITD show the worse response to induction chemotherapy.

Key words: Acute myeloid leukemia (AML), Brain And Acute Leukemia Cytoplasmic (BAALC), Internal tandem duplication (FLT3/ITD), length mutation (FLT3/LM) and reverse transcriptase- polymerase chain reaction (RT-PCR).

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List of Abbreviations

Abbreviation	**The Full Term**
aa	Amino acid
ABL	Abelson strain of murine leukemia virus
ALL	Acute lymphoblastic leukemia
AMbL	Acute myeloblastic leukemia
AMgL	Acute megakaryocytic leukemia
AML	Acute myeloid leukemia
AMoL	Acute myelomonocytic leukemia
ANLL	Acute non lymphoblastic leukemia
AP	Acid phosphatase
ARA-C	cytarabine
ATRA	All trans retinoic acid
BAX	Bcl_2- associated protein
Bcl_2	B-cell lymphoma/leukemia-2 oncogene.
BCR	Break point cluster region
BM	Bone marrow
bp	Base pair
CBF	Core binding factor
CBFα	Core binding factor alpha subunit.

CBFβ	Core binding factor beta subunit.
CD	Cluster of differentiation
cDNA	Complementary DNA
CEPBA	CCAAT/enhancer binding protein-α
CNS	Central nervous system
CR	Complete remission
del	Deletion
DFS	Disease free survival
DIC	Disseminated intravascular coagulopathy
DNA	Deoxyribonucleic acid
dNTPs	Deoxynucleoside triphosphate
DW	Distilled water
ECM	Extracellular matrix
EDTA	Ethylene diamine tetra-acetic acid
EM	Electron microscopy
ETO	Eight twenty one
EVI1	Ectopic virus integration 1
FAB	French American British
FLT3	Fetal liver tyrosine kinase 3
FLT3/ITD	Internal Tandem duplication
FLT3/LM	FLT3/length mutation.
FLT3-L	Fetal liver tyrosine kinase 3 ligand