ASSESSMENT OF ABL-1, ALK, BCL2, BRAF AND CCND-1 MUTATIONS IN ADULT EGYPTIAN PATIENTS WITH ACUTE MYELOID LEUKEMIA

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Introduction

Next-generation sequencing (NGS) is a type of DNA sequencing technology that uses parallel sequencing of multiple small fragments of DNA to determine sequence and here are select genes in AML:

ABL1: a protooncogene that encodes a protein tyrosine kinase involved cell division, adhesion, differentiation, and response to stress.

ALK: a receptor tyrosine kinase playing an important role in the development of the brain and exerts its effects on specific neurons in the nervous system. BCL2: its family proteins play an important role in intrinsic apoptosis. Overexpression of BCL-2 proteins in acute myeloid leukemia can circumvent resistance to apoptosis and chemotherapy.

BRAF: a key component of the RAS-RAF-MAPK signal transduction pathway. Broadly, signaling through the MAPK cascade leads to phosphorylation and activation of transcription factors in the nucleus, thereby regulating key cellular processes including proliferation, differentiation, and apoptosis.

CCND1: The protein encoded by this gene forms a complex with and functions as a regulatory subunit of CDK4 or CDK6, whose activity is required for cell cycle G1/S transition.

Aim of the work

The aim of this work was to study the following genes ABL-1, ALK, BCL2, BRAF AND CCND-1 in a cohort of newly diagnosed Egyptian AML patients using NGS technique as well as their relation with other clinico-pathological features.

Patients

Twenty-four newly diagnosed AML patients of both sexes admitted to Alexandria Main University Hospitals (Hematology Department) or attending at Hematology clinic.

Methods

Patients were diagnosed as acute leukemia after performing a complete blood count, bone marrow aspiration and immnunophenotyping. Targeted Next Generation Sequencing for ABL-1, ALK, BCL-2, BRAF and CCND1 using peripheral blood or BMA.

Results

Table (1): Comparison between the two studied groups according to FAB classification

FAB classification	Group I (n = 2)		Group II (n = 22)		c^2	^{MC}p
	No.	%	No.	%		
FAB M1	0	0.0	5	22.7	6.053*	0.022*
FAB M2	2	100.0	2	9.1		
FAB M3	0	0.0	0	0.0		
FAB M4	0	0.0	6	27.3		
FAB M5	0	0.0	9	40.9		

Table (2): Comparison between the two studied groups according to different genes

	Group I (n = 2)		Group II (n = 22)		Test of sig.	p
	No.	%	No.	%		
DNMT3A	2	100.0	3	13.6	c^2=8.291*	^{FE}p=0.036*
FLT3	2	100.0	7	31.8	c^2=3.636	^{FE}p=0.130
KRAS	2	100.0	3	13.6	c^2=8.291*	^{FE}p=0.036*
NPM1	1	50.0	3	13.6	c^2=1.745	^{FE}p=0.312
PHF6	1	50.0	1	4.5	c^2=4.959	^{FE}p=0.136
SF3B1	2	100.0	1	4.5	c^2=15.273*	^{FE}p=0.011*
SRSF2	1	50.0	1	4.5	c^2=4.959	^{FE}p=0.163
TP53	2	100.0	1	4.5	c^2=15.273*	^{FE}p=0.011*

Table (3): Descriptive analysis of group I (+ABL1 fusion genes) according to variant location (n = 173 variants)

Location	N	Percent
Intronic	111	64.2
Exonic	50	28.9
Utr-3	8	4.6
Splice site 3	4	2.3
Total	173	100.0

Conclusion

The discovery of novel variants through NGS enhances our understanding of mutations, opening new research avenues enabling personalized treatments. Molecular profiling of the ABL1 fusions offers insights into the genetic landscape, enabling personalized treatments and improved outcomes.