

THE CLINICOPATHOLOGIC SIGNIFICANCE OF MATRIX METALLOPROTEINASE 1 GENE EXPRESSION IN ACUTE MYELOID LEUKEMIA PATIENTS

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Introduction

The bone marrow (BM) microenvironment of acute myeloid leukemia patients is extensively altered, contributing to the severity of the disease as well as causing an antitumor immune surveillance. Matrix metalloproteinase 1 (MMP-1) is a secreted protein of collagenase groups in the bone marrow microenvironment that functions to remodel the extracellular matrix. Studies have demonstrated the role of MMP-1 as diagnostic and prognostic biomarker in esophageal, bladder and other solid tumors. Its value in hematological malignancies is yet to be elucidated.

Aim of the work

We sought to assess the differences in MMP-1 gene expression between AML patients compared to controls and its correlation with the patient’s clinical and laboratory characteristics.

Methods

MMP-1 gene expression from bone marrow aspirates of 60 newly diagnosed de novo AML cases and 40 controls with benign hematological conditions was assessed by real time polymerase chain reaction (PCR) method and the results of the relative gene expression statistically correlated with hematology, clinical chemistry results as well as flow cytometry and cytogenetic findings of the cases. A p value ≤ 0.05 was statistically significant.

Results

The median of the expression of the MMP-1 gene in the cases was 1.37 (range 0.43-3.11) and in controls it was 1.28 (range 0.74-1.85) and this difference was not statistically significant. The MMP-1 gene expression was higher in females than in males with p=0.023. The AML-M2 immunophenotype group showed significantly lower MMP-1 gene expression than AML-M1 with p=0.002. There was a statistically significant positive correlation between MMP-1 gene expression and bone marrow blast percentage with p=0.03. The mean age of the cases was 45 years. 25/60 (41.7%) of cases showed normal karyotype and were classified in intermediate risk group stratification, while 6/60 (10%) cases had a complex karyotype. There was a significant higher gene expression in the cytogenetic intermediate risk groups as compared to the favourable risk group. The median of the lactate dehydrogenase (LDH) of the cases 497.5 U/L (range 271-811) was significantly higher than the controls 194(range 155-216).

Table (1): Descriptive analysis of the studied cases and controls according to hematological laboratory parameters (n = 100)

Hematological data	Cases (n = 60)	Control (n = 40)	Test of Sig.	p
Hemoglobin g/dl				
Min – Max.	3.80 – 11.80	4.30 – 16.70	t=4.393*	<0.001*
Mean ± SD.	8.11 ± 1.89	10.04 ± 2.51		
Median (IQR)	8.10	9.75		
TLC 103/uL				
Min – Max.	0.86 – 338.0	1.18 – 16.70	U=240.500*	<0.001*
Mean ± SD.	59.85 ± 65.92	4.03 ± 3.19		
Median (IQR)	47.50 (9.19 – 81.20)	3.11 (1.81 – 4.90)		
Platelets 103/uL				
Min – Max.	4.0 – 564.0	11.0 – 341.0	U=924.000	0.052
Mean ± SD.	85.10 ± 105.4	84.05 ± 64.92		
Median (IQR)	50.0 (17.50 – 99.50)	66.0 (46.0 – 100.0)		
PB Blast %				
Min – Max.	5.0 – 94.0	0.0 – 0.0	U=0.000*	<0.001*
Mean ± SD.	61.22 ± 23.75	0.0 ± 0.0		
Median (IQR)	61.50 (42.0 – 80.50)	0.0 (0.0 – 0.0)		
BM blast %				
Min – Max.	18.0 – 98.0	0.0 – 5.0	U=0.000*	<0.001*
Mean ± SD.	70.25 ± 21.99	1.78 ± 1.12		
Median (IQR)	76.0 (55.0 – 89.50)	1.0 (1.0 – 2.0)		

Table (2) : Relation between MMP1 gene expression and FAB subtypes and with cytogenetics for cases (n = 60)

	N	Gene expression (MMP1)			Test of sig.	p
		Min. –Max.	Mean ± SD.	Median		
FAB subtypes						
M1	10	0.36 – 6.10	3.09 ± 1.90	3.43	H = 15.156*	0.002*
M2	22	0.02 – 6.32	1.67a ± 1.86	0.83		
M4	20	0.41 – 4.96	2.18 ± 1.32	2.10		
M5	8	0.03 – 1.03	0.41b ± 0.34	0.34	U= 331.50	0.185
M2	22	0.02 – 6.32	1.67 ± 1.86	0.83		
Others (M1 + M4 + M5)	38	0.03 – 6.10	2.05 ± 1.64	1.64		
Cytogenetic #						
Favorable risk	10	0.02 – 1.80	0.55 ± 0.53	0.39	13.783*	0.001*
Intermediate risk	34	0.02 – 6.32	2.57@ ± 1.77	2.53		
Adverse risk	8	0.03 – 4.11	1.73 ± 1.47	1.55		

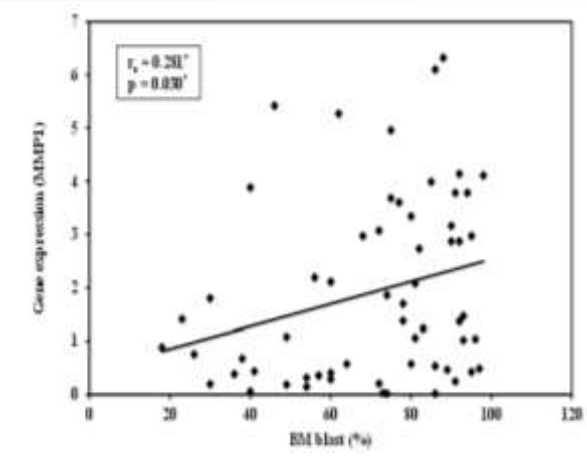


Figure (1): Correlation between MMP1 gene expression and BM blast (%) for cases (n = 60)

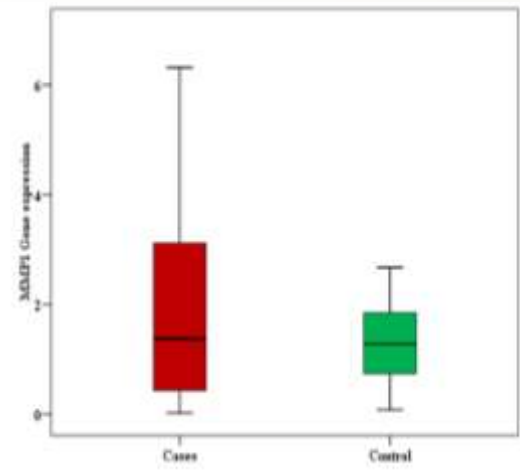


Figure (2): Comparison between the two studied groups according to MMP1 gene expression

Conclusion

The MMP-1 gene expression is increased in AML with high tumour burden of bone marrow blast counts at diagnosis, and it is also higher in intermediate cytogenetic risk groups hence showing prognostic role in AML. Follow up of patients to assess role of MMP-1 gene expression as a predictor of response to therapy and survival is recommended.