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STUDYING THE IMPACT OF CD38 EXPRESSION ON EXTRACELLULAR ADENOSINE AND ITS CONNECTION WITH THE PD1/PDL1 AXIS IN MATURE B CELL LYMPHOMA PATIENTS

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INTRODUCTION

Expression of CD38 by cancer cells is hypothesized to mediate immune-suppressive effect via Adenosine (ADO) production. Extracellular ADO favors the onset of neoplasia by signalling through G-protein-coupled cell surface receptors through several pathways, one of which is increasing PD1 expression and interaction with its ligand (PD-L1) in the tumour microenvironment, leading to CD8+ cytotoxic T cells suppression and eventual exhaustion.

AIM

In this study, we aim to analyze the effect of CD38-ADO-mediated production and its link with the PD1/PD-L1 axis in Mature B-cell lymphoma patients

METHOD

Eligible 90 newly diagnosed Mature B-cell lymphoma patients were recruited into the study. They were **firstly** subcategorized into the CLL patients' group (n=48) and the B-NHL patient group (n=42). Regarding the CD38 positivity (cut-off >20% by IPT), the patients were **secondly** subcategorized into the CD38 positive group (n = 48) and CD38 negative group (n = 42). Immunophenotyping was done to assess the CD38 surface expression. Assays of serum soluble PD1 (sPD1), PD-L1 (sPD-L1), and ADO (sADO) were assayed by a commercially available sandwich ELISA kit.

RESULTS

Our data revealed a statistically significant positive correlation in Mature B-cell, lymphoma patients between sPD-L1, sPD1, sADO, and the degree of CD38 expression. Also, sPD-L1, sPD1, and sADO serum levels were significantly higher in the CD38-positive Mature B-cell lymphoma group when compared to the CD38-negative group. Furthermore, sADO showed a statistically highly significant negative correlation with both Hb level and Platelets count in Mature B-cell lymphoma patients; besides, we found a statistically significant decrease in the mean Hb level and median platelets count in the CD38 positive B-NHL patients compared to CD38 negative B-NHL. Finally, CD38-ADO-mediated production was positively related to the risk stratification in all Mature B-cell lymphoma patient.

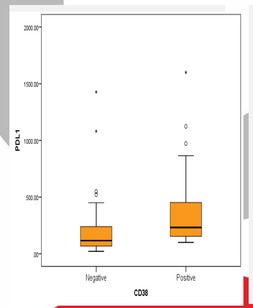
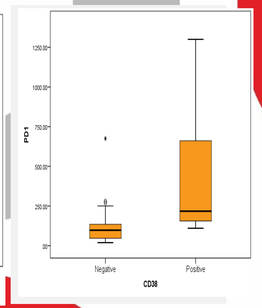


Figure (1):showing h the difference between cd38 positive and cd38 negative lymphoma patients as regard PDL1



)figure (2): showing the difference between cd38 positive and cd 38 negative lymphoma patients as regard PD1.

Mature B-cell lymphoma		Negative CD38	Positive CD38	Test value	P-value
		No. = 42	No. = 48		
sPD-L1 (ng/L)	Median (IQR)	116.7 (68.25 - 240)	232.35 (153.75 - 452.75)	-4.416‡	0.000
	Range	21.51 - 1427	100.9 - 1600		
sPD1 (ng/L)	Median (IQR)	97.74 (47 - 135)	217.5 (156 - 661)	-6.143‡	0.000
	Range	19.38 - 680	110 - 1300		
sADO (ng/ml)	Median (IQR)	530 (343 - 614)	835.5 (723 - 1332)	-7.399‡	0.000
	Range	73 - 777	553 - 1700		
Prognosis (Risk)	Low	13 (31.0%)	9 (18.8%)	4.701*	0.095
	Intermediate	18 (42.9%)	16 (33.3%)		
	High	11 (26.2%)	23 (47.9%)		

CONCLUSIONS

This research highlighted the pathophysiology of the increased CD38-ADO-mediated production in Mature B-cell lymphoma and its link with the PD-1/PD-L1 axis pathways. We also emphasized how ADO enhances the neoplastic process. Finally, targeting the CD38-ADO-mediated production should be considered a promising therapeutic immune target with multiple mechanisms considering the PD-1/PD-L1 immune checkpoint inhibition, improving associated thrombocytopenia, and impairing tumour angiogenesis in Mature B-cell neoplasm.

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