

DIAGNOSTIC AND PROGNOSTIC VALUE OF NOTCH-2 MUTATIONS IN DIFFUSE LARGE B-CELL LYMPHOMA IN EGYPTIAN PATIENTS.

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Introduction

DLBCL is the most prevalent type of aggressive lymphoma in adults with Mean age of diagnosis between 45 and 65 years and accounts for 40% of NHL in favor for men by 1.5-3.5:1.The cause of DLBCL in most individuals is unknown, although there are related risk factors such as herbicides, pesticides, ultraviolet exposure, hair dyes and immunosuppression. Though Notch-2 gene mutations are more uncommon, they are likely biologically significant in DLBCL and it is believed that 4.3 - 8% of cases of DLBCL have mutations in Notch-2 gene. The therapeutic options for DLBCL in adult patients vary from standard chemotherapy to targeted therapies and bone marrow transplantation.

Aim of the work

The aim of the present study was to determine the diagnostic and prognostic implications of Notch-2 gene in DLBCL patients compared to its mutational status in healthy individuals.

Patients and Methods

This prospective study was conducted on 20 newly diagnosed cases of DLBCL patients and 10 healthy as control (Egyptians) in Hematology Unit at Alexandria Main University Hospital and clinics. Patients and controls were matched in the demographic criteria in the form of age (18 –59 years) and sex. The study was approved by the local Institutional Review Board, and informed consent was obtained from all study participants. Detailed clinical history and physical examination were obtained, and samples were taken for investigations from every participant. The Notch-2 mutational status was evaluated by Sanger Sequencing Analysis.

Results

The mean age at diagnosis of DLBCL patients was 47 years and the median was 49 years (and the lowest age was 33 years), 65% were males and 35% were female (Male: Female =1.85:1).The distinct feature of this study was to determine the Notch-2 mutation, hence it was found that One patient (5%) among all DLBCL patients sub classified in ABC subtypes had showed (p. Phe266Leu) missense mutation through substitutions.

Additionally, the DLBCL patients were classified into GCB-DLBCL-group and ABC-DLBCLR-group based on Hans algorithm using IHC markers (CD10, BCL6 and MUM1), thus 40% of our patients were in GCB subtype and 60% ABC subtype.

Table: Comparison between the two studied groups regarding laboratory investigations.

	Group		Test of significance p-value
	DLBCL (n=20)	Healthy (n=10)	
Hb (g/dl)			
-Min-Max	8.90-15.10	11.60-14.40	$t_{(df=28)}=1.862$
-Mean±SD	11.82±1.84	12.99±1.00	p= 0.073 NS
WBCs count (x10³/μL)			
-Min-Max	4.20-11.10	4.80-11.00	$t_{(df=28)}=0.609$
-Mean±SD	7.46±1.86	7.91±2.06	p= 0.547 NS
Platelets count (x10³/μL)			
-Min-Max	167.00-357.00	198.00-381.00	$t_{(df=28)}=1.205$
-Mean±SD	270.00±72.54	301.00±51.18	p= 0.238 NS
Serum Creatinine (mg/dL)			
-Min-Max	0.60-1.10	0.70-1.10	$t_{(w)(df=28)}=0.820$
-Mean±SD	0.97±0.14	0.92±0.15	p = 0.419 NS
Uric acid (mg/dL)			
-Min-Max	3.60-6.79	3.60-6.60	$t_{(w)(df=28)}=0.114$
-Mean±SD	5.12±0.81	5.08±1.04	p = 0.910 NS
Blood Urea (mg/dL)			
-Min-Max	20.30-39.00	19.00-39.00	$t_{(df=28)}=1.104$
-Mean±SD	32.39±4.39	30.10±6.94	p= 0.279 NS
AST (U/L)			
-Min-Max	21.00-38.00	12.00-33.00	$t_{(df=28)}=1.785$
-Mean±SD	28.15±5.00	24.30±6.62	p=.085 NS
ALT (U/L)			
-Min-Max	27.00-42.00	19.00-45.00	$t_{(w)(df=211.119)}=0.698$
-Mean±SD	33.90±4.12	31.90±8.58	p=.500 NS
PT (Sec)			
-Min-Max	10.00-13.80	12.20-13.30	$t_{(df=28)}=1.772$
-Mean±SD	12.19±0.91	12.73±0.38	p= 0.087 NS
PTT (Sec)			
-Min-Max	24.00-39.40	29.60-34.00	$t_{(w)(df=28)}=0.636$
-Mean±SD	32.84±3.90	32.01±1.67	p= 0.530 NS
LDH (U/L)			
-Min-Max	234.0-412.0	234-407	$t_{(w)(df=28)}=1.121$
-Mean±SD	312.2±54.88	289.30±48.01	p= 0.272 NS
B2 Microglobulin (mg/L)			
-Min-Max	0.40-2.60	0.60-2.50	$t_{(w)(df=28)}=0.572$
-Mean±SD	1.45±0.65	1.59±0.64	p= 0.57 NS

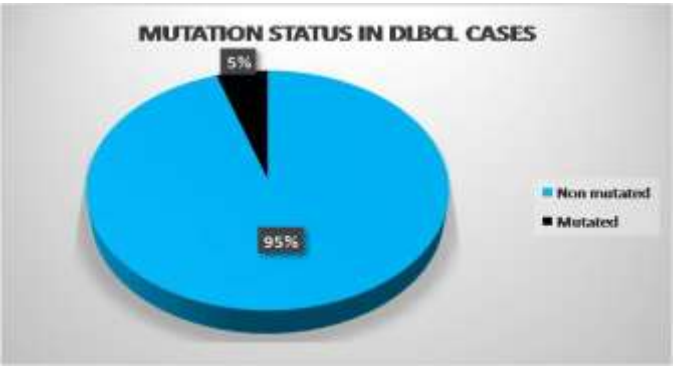


Figure 1:
Notch-2 mutational status in DLBCL patients.

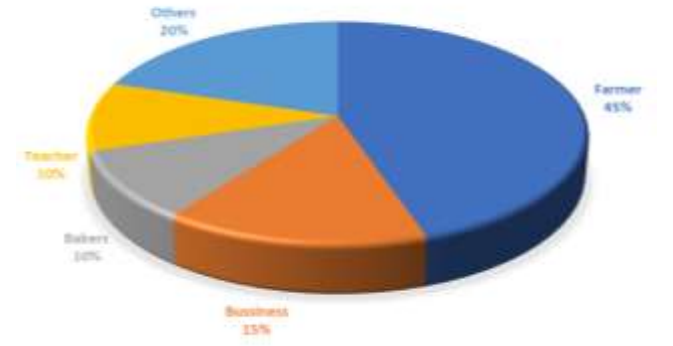


Figure 2:
Distribution of DLBCL patients according to their occupations.

Conclusion

In conclusion, Notch-2 was found to be mutated infrequently in DLBCL. It is associated with bad prognosis and usually occurs in ABC subtype. Besides this mutation occurred in about 5% of patients. In addition, in 45% of the patients they were found working as farmers. It is well known that farmers are exposed mainly to pesticides and to herbicides. In the 45% of patients with DLBCL in our study were exposed to both pesticides and herbicides during their work. The rest of the patients (55%) with DLBCL in the present work were not found to have definite pathogenetic factors and they didn’t show positivity for HCV.