Original Article

Value of CD5 and CD79 in Evaluation of GIT Lymphoma

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Abstract

Background: Primary gastrointestinal lymphoma is a rare tumor, accounting for less than 5% of all GIT lymphoma, 10%–15% of all non-Hodgkin lymphoma, and encompasses 30%–40% of total extranodal lymphoma its incidence is increasing. Approximately 60%–75% of cases occur in the stomach and then small bowel, ileum. The majority of all gastrointestinal lymphoma is B cell, and T cell is less common accounting for only 6%. DLBCL and MALT lymphoma are the most histological subtypes. Expression of CD5 and CD79 aids in supporting the diagnosis of GIT lymphoma. **Objective:** Our study was designed to assess CD5 and CD79 overexpression in Iraqi patients with GIT lymphoma. **Materials and Methods:** Samples included in this study represented 30 formalin-fixed paraffin-embedded biopsy tissue blocks of patients with GIT lymphoma age from 3 to 78 years. The collected pathological blocks were related to the period 2016–2023, which was evaluated in the pathology department in Baghdad Medical City. Tissue sections were stained immunohistochemically for expression by CD5 and CD79 markers. **Results:** GIT lymphoma is more common in patients more than 60 years old and commonly in males. DLBCL is the most common subtype, and CD79 expression in 96.7% and CD5 expression in only 33.3 % of cases. **Conclusion:** CD5 expression is negative in two-thirds of patients with GIT lymphoma. CD79 is highly expressed in patients with GIT lymphoma. H score of CD79 expression has a negative correlation with age, gender, and subtypes. There is no correlation between CD79 expression and CD5 expression.

Keywords: CD5, CD79,DLBCL, PGIL

Introduction

Primary gastrointestinal lymphoma (PGIL) is a malignant tumor originating from submucosal lymphoid tissue of the gastrointestinal tract and is the most common extranodal lymphoma accounting for approximately 30%–40% of all extranodallymphoma with the majority being non-Hodgkin type.[1] Although PGIL is a rare disease comprising only 1%–4% of gastrointestinal (GI) malignant tumors, its incidence is increasing.[2] Different regions of the GIT are involved in different subtype of PGIL with various frequency that reflects the diversity of the causative agents and the predisposing factors for each site and subtype of PGIL.[3] The stomach is the most commonly involved site (60%–75% in the gastrointestinal tract followed by the small intestine (20%–30%), large intestine (5%–10%), and esophagus <1%[4] The majority of all gastrointestinal lymphoma are B-cell lymphomas, whereas it is more responsive to chemotherapy and has a better prognosis. T-cell lymphoma is less common accounting for only 6% and Hodgkin lymphoma.[5]

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DOI: 10.4103/MJBL.MJBL_1160_23

Gastrointestinal tract lymphoma is usually secondary to the hematogenous widespread of nodal disease to extranodal tissue and PGIL is relatively rare.[6]

Dawson's criteria that were suggested six decades ago are used for the definition of PGIL, which include the following: (1) abscent of peripheral lymphadenopathy at the time of presentation, (2) lack of enlarged mediastinal lymph nodes (LN), (3) normal total and differential white blood cell(WBC), (4) predominance of bowel lesions at the time of laparotomy with only LNs affected in the immediate vicinity (LNs which are confined to the drainage area of the primary tumor site), and (5) no involvement of liver and spleen.[7]

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Submission: 08-Aug-2023 **Accepted:** 10-Oct-2023 **Published:** 28-Jun-2025

How to cite this article: Abdulwahid HM, Alkafaji HA, Al Maaroof ZW. Value of CD5 and CD79 in evaluation of GIT lymphoma. Med J Babylon. 2025;22:406-11.

High-grade DLBCL and low-grade MALT lymphoma are the most common histological subtypes. MALT lymphoma usually arises in the background of chronic inflammation in particular, infection with Helicobacter pylori, but its role in gastric DLBCL is uncertain[8]

PGIL is approximately two to three times more frequently seen in males compared to females and patients' ages with PGIL range 19–90) years with a median age of 55 years. The ratio and age can be varied depending on the sites of PGIL and pathological subtype; the patient with T-cell lymphoma (TCL) is usually 10–14 years younger compared to B-cell lymphoma (BCL).[9]

The modern lymphoma classification is based on morphological, immunophenotype, genetic, and clinical features. Making the correct diagnosis according to WHO classification is critical because treatment can vary widely from a simple "wait and watch" approach to local radiation or surgery to high-dose chemotherapy with or without stem cell transplantation[10]

CD5 is a member of the scavenger receptor cycteine-rich family of extracellular domain-like structure and involved in signal transduction,[11] CD5 is weakly expressed on most immature T-cell precursors and is more intensely expressed on mature T lymphocytes. In addition, it is weakly expressed in a subset of normal B cells and B-cell lymphoma[12] The detection of unusual expression on a B-cell LPD is extremely helpful in the diagnosis process because it significantly narrows the differential considerably[13]

Numerous antigens that are expressed absolutely on B cells include CD79α, CD79β,[14] and CD79α. Its adisulfide-linked transmembrane heterodimer is not covalently associated with surface Ig-forming B-cell receptor complex[15] The expression of CD79 is largely restricted to B linage cells but may be co-expressed with CD3 in the proportion of T lymphoblastic leukemia/lymphoma.[16]

Objectives

The aim of this study was to investigate the Immunohistochemical expression of CD 5 and CD79 in gastrointestinal lymphoma cells.

Materials and Methods

This was a retrospective cross-sectional study done in the Department of Pathology and Forensic Medicine, Collage of Medicine at Babylon University. The study sample consists of tissue blocks fixed in formalin embedded in paraffin that were collected from archived material from Baghdad Medical City from 7 October 2022 to 20 April 2023. The paraffin block represents 30 cases of GIT lymphoma with patient age ranging from 3 to 78 years old. Three sections of 5 μm thickness were taken from each block, one stained with (Hα E) for histopathological revision, and the other section was stained immunohistochemically for CD5 and CD79 markers. CD5 and CD79 (monoclonal antibody) were used in the study with Envision FLEX target.

Data analysis

Statistical analysis was carried out using SPSS software program, version 27.0. Categorical variables are presented as frequencies and percentages, continuous variables are presented as mean, standard deviation, and range. Fisher's exact test was used to find the association between categorical variables. A value of $P \leq 0.05$ was considered as significant.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients' verbal and analytical approval before the sample was taken. The study protocol and the subject information and the consent form were reviewed and approved by a local ethics committee according to document number 6-2 in 6-7-2022 to get this approval.

Results

Demographic distribution of the patient

The patients' ages with GIT lymphoma ranged from 3 to 78 years with a mean age was (38.1±27.14) with a maximum age of 78 years and a minimum age of 3 years [Table 1]. The result shows that GIT lymphoma was more frequently diagnosed in the older age group with a higher incidence at the age group (≥60 years) and low incidence in ages of 20–40 years. The gender of patients group with GIT lymphoma includes 22 males (73.3%) and 8 females (26.7%). This study showed that the incidence of GIT lymphoma in males was higher than in females.

Table 1: Demographic distribution of patients with GIT lymphoma (*N* = 30)

Socio-demographic characteristics	Number	%
Age (years)		
<20	10	33.3
20–40	6	20
40–60	3	10
>60	11	36.7
Total	30	100
Gender		
Males	22	73.3
Females	8	26.7
Total	30	100.0

Distribution of patients with GIT lymphoma according to its subtypes

The present study showed that DLBCL is a more frequent type 16 cases (53.3) % while follicular lymphoma and T cell lymphoma are the least frequent types accounting for one case each at 3.3% [Table 2].

Table 2: Distribution of patients with GIT lymphoma according to its subtypes

Diagnosis	Frequency	%
Diffuse large B-cell lymphoma	16	53.3
Malt lymphoma	6	20.0
Burkitts lymphoma	6	20.0
Follicular lymphoma	1	3.3
T-cell non-Hodgkin's lymphoma	1	3.3
Total	30	100.0

Table 3: Immunohistochemical expression of CD5 and CD79 in GIT lymphoma ($N = 30$)

Study markers	Number	%
H score CD 5		
Negative (0)	20	66.7
+1	3	10.0
+2	7	23.3
Total	30	100.0
H score CD 79		
Negative (0)	1	3.3
+1	1	3.3
+2	6	20.0
+3	11	36.7
+4	11	36.7
Total	30	100.0

Distribution of patients with GIT lymphoma according to study marker: CD5 immunohistochemical expression was reported to be positive in 33.3% (10 out of 30) cases of GIT lymphoma, while CD79 immunohistochemical expression was reported to be positive in 96.7% (29 out of 30) cases of GIT lymphoma [Table 3].

Association between H score CD 5 results and study variables:

The present study showed that there is no significant association between H score CD5 results including (negative 0. +1, +2), and study variables including (age, year, sex, diagnosis, and type of specimen; $P > 0.05$) [Table 4].

The association between H score CD 79 results including and study variables:

The association between CD79 results including (negative 0,+1, +2,+ 3,+ 4) and study variables including (age, years, sex, diagnosis, and type of specimen) showed that there was no significant association between H score CD 79 results and variable study ($P \leq 0.05$) [Table 5].

Association between H score CD 79 results and H score CD 5:

The present study showed there was no significant association between H score CD 79 results (negative 0, +1,+2,+3,+4) and H score CD 5 results (negative 0,+1,+2) at $P > 0.05$ [Table 6].

Table 4: Association between H score CD 5 results and study variables (N=30)

Study variables	H score CD 5 results			*P* Value
	Negative (0)	+1	+2	
Age (years)				0.474
<20 years	6 (30.0)	0 (0.0)	4 (57.1)	
20–40 years	5 (25.0)	1 (33.3)	0 (0.0)	
40–60 years	2 (10.0)	0 (0.0)	1 (14.3)	
≥ 60 years	7 (35.0)	2 (66.7)	2 (28.6)	
Total	20 (100.0)	3 (100.0)	7 (100.0)	
Gender				0.555
Male	13 (65.0)	3 (100.0)	6 (85.7)	
Female	7 (35.0)	0 (0.0)	1 (14.3)	
Total	20 (100.0)	3 (100.0)	7 (100.0)	
Subtypes				0.316
DLCBL	11 (55.0)	1 (33.3)	4 (57.1)	
Malt lymphoma	4 (20.0)	2 (66.7)	0 (0.0)	
Burkitts lymphoma	4 (20.0)	0 (0.0)	2 (28.6)	
Follicular lymphoma	1 (5.0)	0 (0.0)	0 (0.0)	
T-cell NHL	0 (0.0)	0 (0.0)	1 (14.3)	
Total	20 (100.0)	3 (100.0)	7 (100.0)	

Table 5: Association between H score CD 79 results and study variables (*N* = 30)

Study variables	H score CD 79 results					*P* Value
	Negative (0)	+1	+2	+3	+4	
Age (years)						0.216
<20 years	0 (0.0)	0 (0.0)	3 (50.0)	1 (9.1)	6 (54.5)	
20–40 years	1 (100.0)	0 (0.0)	0 (0.0)	3 (27.3)	2 (18.2)	
40–60 years	0 (0.0)	0 (0.0)	1 (16.7)	2 (18.2)	0 (0.0)	
≥ 60 years	0 (0.0)	1 (100.0)	2 (33.3)	5 (45.4)	3 (27.3)	
Total	1 (100.0)	1 (100.0)	6 (100.0)	11 (100.0)	11 (100.0)	
Gender						0.272
Male	0 (0.0)	1 (100.0)	6 (100.0)	8 (72.7)	7 (63.6)	
Female	1 (100.0)	0 (0.0)	0 (0.0)	3 (27.3)	4 (36.4)	
Total	1 (100.0)	1 (100.0)	6 (100.0)	11 (100.0)	11 (100.0)	
Diagnosis						0.12
DLCBL	1 (100.0)	0 (0.0)	2 (33.3)	9 (81.8)	4 (36.4)	
Malt lymphoma	0 (0.0)	1 (100.0)	2 (33.3)	2 (18.2)	1 (9.1)	
Burkitts lymphoma	0 (0.0)	0 (0.0)	2 (33.3)	0 (0.0)	4 (36.4)	
Follicular lymphoma	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (9.1)	
T-cell NHL	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (9.1)	
Total	1 (100.0)	1 (100.0)	6 (100.0)	11 (100.0)	11 (100.0)	

*$P \leq 0.05$ was significant

Table 6: Association between H score CD 79 results and H score CD 5 results (*N* = 30)

H score CD 5 results	H score CD 79 results					*P* Value
	Negative (0)	+1	+2	+3	+4	
Negative (0)	1 (100.0)	1 (100.0)	3 (50.0)	7 (63.6)	8 (72.7)	0.986
+1	0 (0.0)	0 (0.0)	1 (16.7)	1 (9.1)	1 (9.1)	
+2	0 (0.0)	0 (0.0)	2 (33.3)	3 (27.3)	2 (18.2)	
Total	1 (100.0)	1 (100.0)	6 (100.0)	11 (100.0)	11 (100.0)	

*$P \leq 0.05$ was significant.

Discussion

In the present study, the patients' age with GIT lymphoma ranged from 3 to 78 years, with a mean age of 38.1 ± 27.14 with maximum age was 78, and minimum age of child 3 years. GIT lymphoma is more frequently diagnosed in older age groups with the highest incidence in the age group of ≥ 60 corresponding to 11 cases (36.7)%. The results of this study were compatible with Xiang and Yao[5] who found that the median age was 63 years, while they were incompatible with Bidarizerehpoosh *et al.*[17] who showed that the incidence of GIT lymphoma is more common in the age group <60 years. These differences in age groups could be attributed to the differences in environmental risk factors and to the smaller sample size.

Our patients group with GIT lymphoma involved in this study included 22 males 73.3% and 8 females 26.7%; the incidence of GIT lymphoma in males was higher than in females. Similar results were carried out previously by several authors, who found it more common in males and the males are 2-3 times more affected than females, respectively.[18,19]

Distribution of patient according to its subtypes

The present study showed more than half of patients with GIT lymphoma (N=16, 53.3%) presented with Diffuse large B-cell lymphoma, Malt lymphoma, and Burkitt's lymphoma representing only 6 patients (20.0%), only one patient presented with Follicular lymphoma (3.3%) and only one patient presented with T-cell Non-Hodgkin's lymphoma. The present results agree with another study done in 2018,[20] which also shows that diffuse large B cell lymphoma is the highest one 59%, with low incidence in follicular and T cell lymphoma, and disagrees with a study in 2013[21] that show Maltoma is the most common type 60% this difference may be due to ethnic variation and smaller sample size.

Immunohistochemical expression of study marker

CD5

The criterion for detection of positive immunoreaction was a dark brown stain that precipitates as protein expression (cytoplasmic and nuclear) The intensity of the staining was measured by counting the percentage of positive cells for immune reaction in 300 malignant

cells on X40(400). The immunostaining was calculated as the percentage of immunoreactive cells per total number of malignant cells; the scoring for the result was calculated as the follows: Score 0: Negative, none of the cells exhibited positivity, as seen in Figure 1. Score +1: Mild staining (1%–25%) positive of cancer cells. Score +2: Moderate staining (25%–50%) of cancer cells positive for staining. Score +3: Strong staining (50%–75%) of cancer cells positive for staining. Score +4: Highly strong staining > 75% of cancer cells positive for staining.

In the present study, CD5 was negative in 66.7% of cases and positive in 33.3% H score CD5 was negative (0) in two-thirds of patients (N =20, 66.7%), H score CD5 (+1) representing three patients (10.0%) and H score CD5 (+2) represent seven patients (23.3%) included (DLBCL, MALT lymphoma, Burkitts lymphoma, and T-cell lymphoma).

These results have an agreement with another study done in 2003[22] that involved 34 cases of gastric B cell lymphoma and found expression was negative in MALT lymphoma and DLBCL and positive in T cell lymphoma, but not explained the intensity or H score of CD5 expression.

CD5 negative in DFL shown in 2021[23] that similar with our studies results that found the neoplastic cell in DFL show the immunophenotype similar to nodal FL by lack expression of CD5. The negative expression for CD5 in Burkitt's lymphoma agrees with the study conducted by Alvarez-Lesmes.[23]

Another study in 2013[24] showed CD5 positive in MALT lymphoma of the sigmoid colon this agrees with our study that CD5 positive in MALT lymphoma of the intestine.

Study done in 2018[25] that show CD5 positive in de nova DLBCL that has worse prognosis that CD5 negative DLBCL, this agree with our study that CD5 positive in DLBCL with some difference. So, none of the previous studiesies that showed CD5 positive expression does not explain the intensity of marker staining.

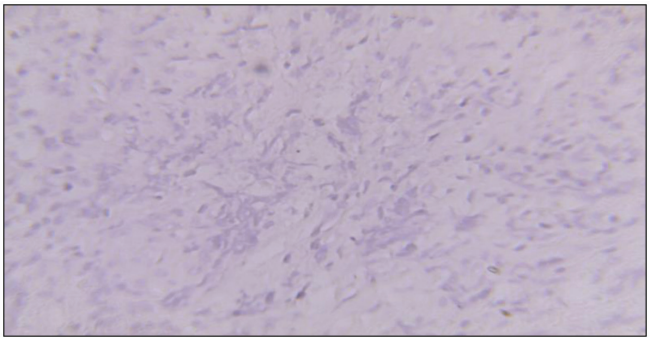

Figure 1: IHC staining showing no nuclear and cytoplasmic staining for CD5 (original magnification ×40)

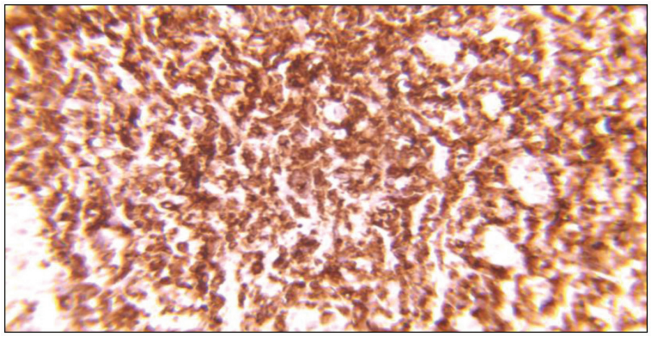

Figure 2: Diffuse, strong nuclear and cytoplasmic staining for CD79 (original magnification ×40)

CD79α

In this study, CD79α expressed in 96.7% (29 cases) [Figure 2] and was negative in 3.3% (One case) that was DLBCL. The H score for CD79α expression in GIT lymphoma was (+1) which represents only one patient who was diagnosed with MALT lymphoma (100%), while the H score for CD79α with (+2) represents patients that were diagnosed with DLBCL, 2 cases (33.3%), MALT, 2 cases (33.3%), and 2 cases (33.3%) of Burkitt's lymphoma. H score CD79α (+ 3) for DLBCL: 9 cases (81.8%) and MALT lymphoma: 2 cases (18.2%), CD79α H score with (+4) represents 11 cases, which include 4 cases (36.4%) DLBCL, 4 cases (36.4%) of Burkitt's lymphoma, and 1 case (9.1%) of MALT lymphoma.

These results agree with other studies done in 2007[26] that show T-cell lymphoma had an aberrant expression of B cell markers such as CD79α (CD79α-positive lymphoid cells were focally aggregated into small nodules in the area of massive infiltration of T lymphocyte these lymphoid cell were negative for T cell marker and we concluded that B lymphocyte aggregation was reactive. Inconsistent with the results of this study, CD79α reported to be expressed in T cell-type gastric lymphoma as mentioned in a previous study conducted by Sugita *et al.*[27]

CD79α was positive in gastric Burkitt's lymphoma shown by a study in 2017[28] that agrees with our study that shows positivity for B-cell markers CD79a, and other markers are required to differentiate BL from DLBCL in his study.

Another study in 2003[29] is similar to the present study that shows gastric MALT lymphoma and DLBCL positive for CD79 α. It is also in accordance with another study in 2022[22] that found gastric MALT stain positive for CD79 and in the case of the DLBCL diffuse proliferation of large lymphocyte cell stain positive for CD79 but not explained the intensity of expression [Figure 3].

The expression of CD79α in follicular lymphoma was compatible with the results of the study conducted by Charoenlap *et al.*[30] who found that the neoplastic cells

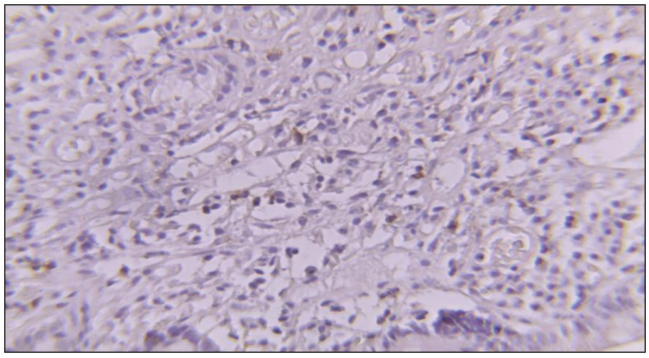

Figure 3: Low percentage of intense reaction for CD5 (original magnification ×40)

showed an immunophenotype similar to that of a low-grade nodal FL by expressing CD79α.[31,32]

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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