

Gastrointestinal lymphoma in Western Algeria: pattern of distribution and histological subtypes (retrospective study)

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Background: Primary gastrointestinal (GI) lymphomas (GIL) are uncommon diseases that can involve the whole GI tract. Considerable variation exists in the literature with respect to incidence of the various histological subtypes and sites of involvement. This study was undertaken to establish the anatomic distribution, histological subtypes and sites of GI lymphomas of patients from Western Algeria.

Methods: The case records of 58 consecutive patients with GIL diagnosed at the Pathologies Departments of Algerian west region (the Military Hospital of Oran city and the Central University Hospital of Sidi Bel Abbes city) from January 2006 to December 2013 were retrospectively evaluated for epidemiology and histopathology report. All lymphomas were reclassified according to the WHO 2008 classification.

Results: A total of 58 patients (39 male, 19 female) with mean age of 61 years and a range of 20–89 years were included in this study. Stomach was the most common site involved (70.7%). The commonest histological subtype was mucosa-associated lymphoid tissue (MALT) B cell lymphoma (46.6%), followed by diffuse large B-cell lymphomas (DLBCL) (43.1%). The frequency of *Helicobacter pylori* (HP) positivity differ between gastric and intestinal location $P=0.003$ and correlates with the histological type $P=0.01$.

Conclusions: This retrospective study of patients with GI lymphoma from Western Algeria illustrates the pattern of distribution of various common and rare histological subtypes. More studies are necessary to find a potential cause, risk factor or genetic mutation that can explain these specific characteristics of GIL.

Keywords: Gastrointestinal lymphomas (GIL); anatomic distribution; histological subtypes; Western Algeria

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Introduction

Lymphomas are considered to be tumors of lymphatic tissue. It has been shown recently that during the last two decades, incidence of lymphomas has increased at a rate of 4% per year (1). Approximately one-third of non-Hodgkin's lymphomas (NHL) arise in tissues different from the lymph node, they are usually termed extra-nodal lymphomas (EL) and may occur at any organ (2). However,

the gastrointestinal (GI) tract represents the most common site of EL presentation (3). GI tract lymphomas constitute 4–18% of primary extra-nodal (PE)-NHL and less than 5% of all GI malignancies (4,5). Several comprehensive studies of GI malignant lymphoma have been performed (6). The proportion and location of different types of lymphoma are different by the ethnic background of the patients studied (7). Epidemiologic studies have shown great difference in the patterns of GI tract NHL in different geographic parts of

Table 1 Histological classification and sites of lymphoma

Histological type	Gastric group (n=41, %)	Intestinal group (n=17, %)
Low-grad B-cell lymphoma		
MALT	20 (48.78)	7 (41.17)
Mantle	0	1 (5.88)
LLCB	1 (2.44)	0
High-grade B-cell lymphoma		
Diffuse large B-cell lymphoma	20 (48.78)	5 (29.41)
T-cell lymphoma	0	4 (23.52)

MALT, mucosa-associated lymphoid tissue; LLCB, B-cell chronic lymphocytic leukemia.

the world (8). Also, it seems that the epidemiologic pattern in GI tract lymphoma is changing (9). In our study, a series of GIL patients diagnosed at the Pathologies Departments of Algerian West hospitals were retrospectively analyzed in order to establish the anatomic distribution, histological subtypes, of all GI lymphomas (GIL).

Methods

This is a descriptive retrospective study evaluating histological subtypes of GIL diagnosed in Central University Hospital of Sidi Bel Abbes and Military Hospital of Oran over a 8-year period [2006–2013]. The data was collected from the pathology department of the two hospitals. The epidemiologic characteristics analyzed in this study were age, gender, site of location, histologic type and *Helicobacter pylori* (HP) infection. Histologic classification was based on the WHO 2008 classification; Giemsa (GS) stain was applied to determine the presence of HP bacteria. The data were analyzed using the Statistical Package Service Solution (SPSS) software version 20.0. Chi-squared tests was used where appropriate; a P value <0.05 was considered significant.

Results

Clinical and histological features

Fifty eight GIL patients were included in the current study. Median age of the patients was 61 years (range, 20–89 years). There were 39 (67.2%) male and 19 (32.8) female, male to female ratio: 2.05. The most common site of lymphoma was

stomach (group gastric) which was involved in 41 (70.7%) cases (29.3% antrum, 8.6% body, 24.1% fundus and pylore 8.6%) followed by the intestine (intestinal group) in 17 cases (29.3%).

Macroscopically, GIL showed wide spread lesions with ulcers in 29 cases (50%), infiltrate and polyp in 13 (22.4%), and 4 (6.9%) cases respectively. The exact macroscopic feature was unknown in 12 (20.7%) cases.

The histological classification and the localization site are shown in *Table 1*; the study sample comprised 27 (46.6%) patients who were classified as mucosa-associated lymphoid tissue (MALT) B-cell lymphomas, 1 (1.7%) as mantle B-cell lymphomas, 1 (1.7%) as B-cell chronic lymphocytic leukemia (LLCB), 25 (43.1%) as diffuse large B-cell lymphomas (DLBCL) and 4 (6.9%) as T-cell lymphomas.

HP infection

In both HE and GS stains, the microorganism was detected in 28 of 58 patients (48.3%). The frequency of HP positivity differ between gastric group (43.1%) and intestinal group (5.2%), P=0.003. The HP positivity also correlates with the histological type P=0.01. However, HP positivity did not show a correlation with aspect of tumors, nor with patient's age and sex (*Table 2*).

Relationship between clinico-pathological features and histological classification

Low grade B-cell lymphoma

MALT lymphoma

The 27 cases included 17 (63%) male and 10 female (37%), the age ranged from 20 to 83 years with a median of 56 years.

The macroscopic features: in more than half of the patients, we encountered an ulcerative aspect of the lesions (51.9%), an infiltrative and polypoid patterns in 29.6%, and 3.7% respectively, (unknown in 14.8%). The most common locations of tumor were the stomach and intestine in 20 (74.1%) and 7 (25.9%), respectively. Infection by HP was present in 19 cases (70.4%) (P=0.01) (*Table 2*).

Mantle-cell lymphoma

The single case of mantle-cell lymphoma occurred in a 61-year-old male. The tumor was located in the intestine and its macroscopic type was infiltrative tumor (*Table 2*).

LLCB

The single case of LLCB was observed in an 80-year-old male. The localization was fundic. This case was classified

Table 2 Histological classification and clinical feature

Characteristics	Low grade B-cell lymphoma			High grade B-cell lymphoma (n= 25, %)	T-cell lymphoma (n=4, %)
	MALT (n=27, %)	Mantle cell (n=1, %)	LLCB (n=1, %)		
Median age (years)	56	–	–	70	55.50
Age range (years)	20–83	–	–	35–89	43–59
Gender					
Male	17 [63]	1 [100]	1 [100]	20 [80]	0
Female	10 [37]	0	0	5 [20]	4 [100]
Macroscopic					
Ulcers	14 (51.9)	0	1 [100]	11 [44]	3 [75]
Infiltrate	8 (29.6)	1 [100]	0	3 [12]	1 [25]
Polypoid	1 (3.7)	0	0	3 [12]	–
Unknown	4 (14.8)	0	0	8 [32]	–
Localization					
Stomach	20 (74.1)	0	1 [100]	20 [80]	0
Intestinal	7 (25.9)	1 [100]	0	5 [20]	4 [100]
HP					
Positive	19 (70.4)	0	0	9 [36]	0
Negative	9 (29.6)	1 [100]	1 [100]	16 [64]	4 [100]

MALT, mucosa-associated lymphoid tissue; LLCB, B-cell chronic lymphocytic leukemia; HP, *Helicobacter pylori*.

as ulcer lesion (*Table 2*).

High grade B-cell lymphoma

Diffuse large B-cell lymphoma

The 25 patients had an age range from 35 to 89 years, with a median age of 70 years. There were 5 (20%) female and 20 (80%) male, male to female ratio: 4.

Macroscopic features: almost half of the studied patients presenting an ulcerative appearance of lesions (44%), 3 cases were polypoid lesions, 3 cases infiltrative lesions, [unknown in 8 cases (32%)]. Most of the cases had tumors located in stomach (80%). Infection by HP was detected in 9 cases (36%) (*Table 2*).

T-cell lymphoma

The median age of four patients with T-cell lymphoma was 55.5 years with age range between 43 to 59 years. All cases were female. Macroscopically, T-cell lymphoma showed wide spread lesion with ulcers in 3 (75%) cases, infiltrate in 1 case (25%). All cases were located in intestine (*Table 2*).

Relationship between clinico-pathological features and the site of lymphoma

Table 3 indicates the comparison of clinico-pathological features and site of lymphoma.

Male patients predominated in gastric group. The most frequent histological types were low grade B-cell lymphoma and high grade B-cell lymphoma in the gastric group, T-cell lymphoma in the intestinal group (P=0.008). The ulcers predominated in both gastric and intestinal groups (*Table 3*).

Discussion

GIL represent approximately 1–10% of all GI malignancies (5). It is an uncommon heterogeneous disease in terms of site of involvement, histological type, and treatments offered (5,10). The incidence of non-Hodgkin lymphoma and primary GIL has been increasing both in men and women around the world (11).

Males were more affected than females in our study with a

Table 3 Comparison of clinico-pathological features and the sites of lymphoma

Characteristics	Gastric (n=41, %)	Intestinal (n=17, %)	P value
Mean age (years)	62	59	
Gender			0.1
Male	30 (73.2)	9 (52.9)	
Female	11 (26.8)	8 (47.1)	
Macroscopic features			0.3
Ulcers	21 (51.2)	8 (47.1)	
Infiltrate	10 (24.4)	3 (17.6)	
Polypoid	2 (4.9)	2 (11.8)	
Unknown	8 (19.5)	4 (23.5)	
Histology			<0.008
Low-grade B-cell	21 (36.2)	8 (13.8)	
High-grade B-cell	20 (34.5)	5 (8.6)	
T-cell	0	4 (6.9)	

male to female ratio of 2.05 which is higher than what has been reported from Thailand (1.4) (12); China (1.2) (13); and Japan (1.2) (14) and lower than another report from Jordan (2.8) (15); but it is close to the ratio reported from India (1.9) (16) and contrast to the study by Damaj *et al.*, which showed a female predominance (17). The median age of patients in our study was 61 years. It is similar to the published literature study by Al-Sayes (61.3 years) (18); Other studies revealed younger age of patients [e.g., mean age 21 and 34 years in two studies from India respectively (16) and of 35 years in Saudi Arabia (19)] reflecting the variable geographic characteristics of the disease. The most common macroscopic presentation was an ulcer, as observed in 29.3% of the patients and as reported in previous studies (20).

The site of involvement and the histological subtypes have been described as independent prognostic factors in many studies so it is important to determine the pattern of distribution and the various histological subtypes common in one particular region (10). Previous studies usually showed that stomach was the main involved site with a frequency ranging from 51.0% to 80.0% (14,21). However, other studies showed a lower frequency of gastric lymphoma with 37.8% and 44.6% (22). In our series of 58 patients, stomach was the main involved site, accounting for 70.7% cases.

Similar to the study in Japan, the MALT B-cell lymphoma was the commonest type followed by DLBCL (14), but different from others studies which report that the DLBCL was the commonest type followed by MALT B-cell lymphoma (12) and this may reflect another geographic variation (23). In fact as shown in *Table 1*, MALT B-cell lymphoma was the commonest histological subtype seen in stomach and intestine. Koch *et al.* reported that 40% of primary gastric lymphomas were of low grade MALT type (10). Similar to those findings, 34.5% of gastric lymphomas in our series were of low grade MALT type. The stomach was the most common site for MALT lymphoma (74.1%) as in the study of Wotherspoon *et al.* (85%) (24).

Environmental factors, especially *HP* infection, are considered to play a prominent role in the development of gastric lymphomas (25). A 2008 Canadian-North American study also showed *HP* infection in 20% of GI NHL, 44% in MALT lymphoma and 13% in DLBCL (26). In two Italian studies, *HP* has been reported to occur in 88% of low grade gastric MALT lymphoma identified by histological examination, while it occurred at lower frequency (52–63%) in high grade gastric lymphomas (27). Interestingly, both Italian studies revealed a statistically significant association between *HP* infection and low grade gastric lymphoma ($P < 0.0001$) (27). Similarly, a serologic study performed at a New York center showed *HP* seroprevalence up to 67% in gastric MALT, and increased seropositive rates were associated with increased age and country of birth outside the US or Canada ($P = 0.0001$) (26). Interestingly, *HP* infection in our study was seen in 70.4% of the gastric MALT and 36% of the gastric DLBCL, and we also noted higher frequency of *HP* infection in the low grade gastric MALTs compared to high grade gastric DLBCL.

Primary GI T-cell lymphoma are rare (28). In this study we were able to document that T-cell lymphoma accounted for 6.9% of the GIL. Koch *et al.* (10) and Shet *et al.* (28) have shown that T-cell NHL formed 1.5% and 3.5% respectively of all the GIL.

Conclusions

This retrospective study of patients with GIL from Western Algeria illustrates the pattern of distribution of various common and rare histological subtypes. More studies are necessary to find a potential cause, risk factor or genetic mutation that can explain these specific characteristics of GIL.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: Considering Decree No. 387 (article 25) dated 31 July 2006 about ethical trials in Algeria, we obtained the required access authorizations to the concerned health facilities in order to accomplish our study protocol. Furthermore, the authors obtained informed written consent from all participants and their treating physicians after the study protocol had been explained to them.

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