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The diagnostic characteristics of a group of patients with primary gastric lymphoma: macroscopic, histopathological and immunohistochemical aspects

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Abstract

Primary gastric lymphoma is defined as the malignant lymphoproliferative disease with initial symptoms located in the stomach, or tumor mass located in the stomach. This paper aims to present the macroscopic, histopathological and immunohistochemical aspects encountered in a group of patients with primary gastric lymphoma, diagnosed between 2005 and 2010 in the Hematology Clinic of Craiova and the Hematology Clinic of "Fundeni" Institute in Bucharest. *Materials and Methods*: This study was performed on a group of 65 patients diagnosed with primary gastric lymphoma. The positive diagnosis in primary gastric lymphoma is established by the histopathological and immunohistochemical analysis of gastric biopsies, taken during the upper gastrointestinal endoscopy, or of gastric resection samples. We used the monoclonal antibodies CD20, CD10, CD5, k light chain, PCNA (proliferating cell nuclear antigen) and Ki67. *Results*: The average age of the patients enrolled in the study was 52.55 years. The most common macroscopic feature encountered was the mixed ulcerative-vegetative one. We found two histological types, represented by diffuse large B-cell lymphoma (with or without MALT component), and marginal zone lymphoma (MALT type). Both the MALT type lymphoma and the diffuse large B-cell lymphoma revealed B-cell phenotype. *Conclusions*: A correct diagnosis is very important in terms of therapeutic approach. The characteristics of the group of patients were: a higher number of the aggressive histological type; an excessive use of gastric resection; none of the cases was a T-lymphoproliferation.

***Keywords*:** primary gastric lymphoma, histopathology, immunohistochemistry.

Introduction

Non-Hodgkin's malignant lymphomas represent malignant proliferations of the immune system cells, which start and affect predominantly the lymphoid organs, but may have as a starting point or may involve during their evolution, any organ or tissue where these cells are. They can begin outside lymph nodes, in lymphoid organs (spleen), in non-lymphoid organs but which have an associated lymphatic tissue (small intestine), or even in organs that do not have their own lymphatic tissue (stomach containing a small number of B-lymphocytes on the IgM surface). Gastric lymphoma is considered to be primitive when the initial symptoms of the disease are located in the stomach, or when the tumor mass is located in the stomach. The gastrointestinal tract is a common location of non-Hodgkin's lymphomas with extranodal onset (30–40% of extranodal forms). Compared to all non-Hodgkin's lymphomas regardless of location, primary gastric lymphoma represents 4–20% of all cases of malignant non-Hodgkin's lymphomas [1], and MALT lymphoma represents 5–8% [2]. As for the gastric primary location, primary malignant non-Hodgkin's gastric lymphomas represent the most common malignancy of the stomach, after gastric adenocarcinoma. On the contrary, primary or secondary involvement of the stomach in Hodgkin's lymphoma is extremely rare [3].

Gastric lymphoma originates in the lymphoid tissue called "acquired" MALT. Lingering *Helicobacter pylori* infections lead to the accumulation of lymph follicles (reagents) in the gastric mucosa, surrounded by B-lymphocytes, as in the MALT tissue. The mechanism of action of *Helicobacter pylori* is indirect: initially it causes the development of a gastritis that is followed by the aggregation of T CD4+ lymphocytes and B-lymphocytes in the gastric lamina propria [4].

It is difficult to estimate the real increase of the incidence of gastric non-Hodgkin's lymphomas in the last 20 years because a correlation between this increase and the improvement of the means of investigation and diagnosis within the same period cannot be excluded [5].

The histological classification of non-Hodgkin's lymphomas was one of the most controversial issues in hematology.

Forms with extranodal onset are found as a distinct group of diseases in the REAL classification (*Revised European-American Lymphoma Classification*) published in 1994, the first to identify this category of lymphoproliferative diseases, correlating the information available at the time: morphological, immunophenotypical, genetic and clinical [6].

The WHO (*World Health Organization*) classification, released later and based on the REAL classification, identified over 30 types of lymphoproliferative diseases, representing a very heterogeneous group of disorders from the biological and clinical point of view, as well as regarding the response to treatment [7].

From a histological point of view, there are two more common types in the extranodal primary locations of malignant lymphomas: the diffuse large B-cell lymphoma and the marginal zone B-cell lymphoma (MALT type).

Follicular lymphoma, mantle-zone lymphoma and peripheral T-cell lymphoma are much more rarely encountered [8]. Table 1 shows the incidence of the various histological types of primary gastric lymphoma enrolled in the GIT NHL02/96 study [9].

Table 1 – ***The distribution of the main histological types in 393 patients with primary gastric lymphoma enrolled in the German prospective multicentric study of gastrointestinal lymphomas (GIT NHL02/96) [9]***

Histological type	Incidence [%]
Diffuse large B-cell lymphoma	59
With MALT component	14
Without MALT component	45
Marginal zone lymphoma (MALT type)	38
Mantle-zone lymphoma	1
Follicular lymphoma	0.5
Peripheral T-cell lymphoma	1.5

The aim is to present the main macroscopic, morphological and immunohistochemical aspects that are common to a group of 65 patients diagnosed in the Hematology Clinic of Craiova and "Fundeni" Hematology Clinic in Bucharest, between 2005 and 2010.

Materials and Methods

Our study is based on a group of 65 patients with primary gastric lymphoma diagnosed between 2005 and 2010 in the Hematology Clinic of Craiova and Hematology Clinic of "Fundeni" Institute in Bucharest. The study is a retrospective one and attempts to identify the features of this rare type of malignant lymphoproliferative disease in the selected patients.

The inclusion criteria were:

- primary tumor location in the stomach with or without intra-abdominal structures involved;
- histopathological examination of gastric lesions which indicated the diagnosis of non-Hodgkin's malignant lymphoma;
- positive diagnosis established on the histopathological examination of the gastric tumor, even in the context of the existence of supradiaphragmatic lymph nodes or of the hematogenous bone marrow involvement.

The patients diagnosed by lymph node biopsy with histopathological and immunohistochemical examination, and who also presented gastric lesions in evolution were excluded from the study. In all patients, the diagnosis was based on the histopathological and immunohistochemical examination.

All patients were investigated by upper gastrointestinal endoscopy but only in 37% of cases gastric biopsy was practiced.

In those patients for whom the upper digestive endoscopy provided the biopsy material necessary for diagnosis, at least four and a maximum of eight gastric biopsies were performed for an accurate diagnosis. In the other cases, the material for histopathological and immunohistochemical examination was obtained by gastrectomy.

The histopathological and immunohistochemical examinations were performed in the Pathology Laboratory of the Emergency County Hospital of Craiova and of "Fundeni" Hematology Clinic, Bucharest.

The study is a retrospective one, the cases who received immunohistochemical tests involving the determination of the surface markers that allowed the identification of proliferating cell, and also the determination of the monoclonal nature of the proliferation by determining the kappa/lambda restriction (all cases being B-type lymphoproliferations), and the cell index proliferation by determining Ki67 and PCNA being selected for enrollment in the study.

Only the nuclei were stained, whereas the cytoplasm and cell membrane remained unstained by PCNA. The labeling indexes of the samples stained with anti-PCNA were determined by counting the number of positive nuclei per 1000 tumor cells and was calculated as the percentage of positive nuclei.

The cases were classified into three subgroups: low score group for which the PCNA labeling indexes were less than 30%, moderate score group for indexes between 31% and 50%, and high score group for more than 51%.

The same method was used for calculating the proliferation index by Ki67 immunolabeling.

Tissue sections obtained from gastric biopsies were investigated by routine histopathological examination following the standard technique for paraffin inclusion: fixation in 10% buffered formalin, washing with water or 80% alcohol, dehydration through successive alcohol baths, clarification in benzene, toluene, or xylene and paraffin embedding. The usual stain used was Hematoxylin–Eosin (HE).

For immunohistochemistry, the LSAB technique (Dako, code K0679, HRB) (LSAB – labeled Streptavidin Biotin; HRP – horseradish peroxidase) and the antibodies: CD20, CD10, CD5, k light chain, PCNA (proliferating cell nuclear antigen), and Ki67 were used.

The signal was detected with 3,3'-DAB (3,3'-diaminobenzidine) (Dako). The 4-μm sections were collected on special slides covered with a layer of poly-L-lysine. The antibody dilutions and pre-treatments are presented in Table 2.

Table 2 – *The antibodies, dilutions and pretreatments performed on the gastric biopsies or gastric resection samples*

Antibody	Source	Clone	Dilution	Antigen retrieval	Clonality
CD20	Dako	L26	1:100	Three cycles, citrate buffer	Monoclonal, mouse
PCNA	Dako	PC10	1:400	Seven cycles, citrate buffer	Monoclonal, mouse
Ki67	Dako	MIB-1	1:20	Seven cycles, citrate buffer	Monoclonal, mouse
CD10	Leica	56C6	1:100	Five cycles, citrate buffer	Monoclonal, mouse
CD5	Leica	NCL-L-CD5-4C7	1:100	Five cycles, citrate buffer	Monoclonal, mouse
K light chain	Dako	MHK-49	1:1000	Seven cycles, citrate buffer	Monoclonal, mouse

Results

The average age of the patients enrolled in the study was 52.55 years, the minimum age being 21 years and the maximum age 79 years. Age distribution by decades is shown in Table 3 and is graphically represented in Figure 1. Sex distribution is shown in Figure 2.

Table 3 – *Age distribution of patients in the study*

Age [years]	No. of patients	%
20–29	5	7.69
30–39	9	13.85
40–49	12	18.46
50–59	17	26.15
60–69	13	20
70–79	9	13.85

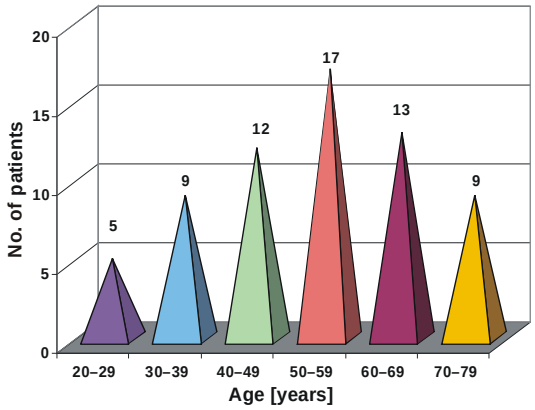

Figure 1 – *Graphic representation of age group distribution in the entire group of patients.*

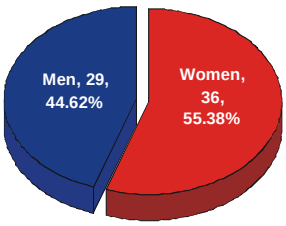

Figure 2 – *Gender distribution of patients in the entire group.*

Positive diagnosis was established by histopathological and immunohistochemical examination of the gastric biopsy fragments, obtained by upper gastrointestinal endoscopy, or of the gastric resection samples.

Endoscopic findings of primary gastric lymphoma are various and heterogeneous.

Upper gastrointestinal endoscopy shows macroscopic features similar to those of gastric cancer: infiltrative, polypoid or ulcerated lesions. The extension of lesions through the pylorus to the duodenum suggests a primary gastric lymphoma but it is not pathognomonic. Therefore, the histopathological diagnosis of lesions is required. Stomach lesions are usually multifocal. In primary gastric lymphomas, the mixed appearance of the lesion is suggestive for the diagnosis: a very irregular, protrusive lesion, surrounded by infiltrative mucosa and having a central ulceration.

The main macroscopic features encountered in our study are presented in Table 4.

Table 4 – *The main macroscopic features in the entire group*

Gastroscopy	No. of patients	%
Protrusive and ulcerative tumor	25	38.46
Ulcerative tumor	12	18.46
Protrusive tumor	9	13.85
Infiltrative tumor	8	12.31
Large folds	5	7.69
Nodules	3	4.62
Stenosing tumor	3	4.62

Figure 3 shows that the most common locations were the gastric body and pyloric antrum. The most frequent macroscopic aspects were protrusive and ulcerative tumor (Figure 4), and with a much less frequency, large folds (Figure 5), nodes (Figure 6) and stenosing tumor (Figure 7).

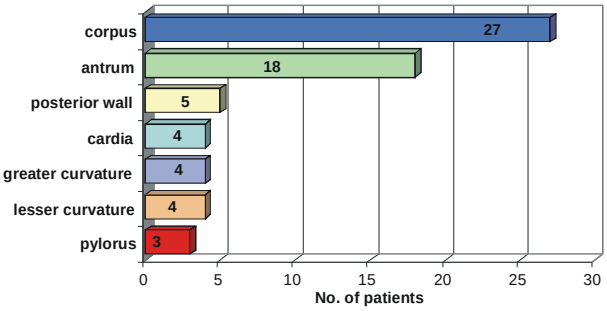

Figure 3 – *The main macroscopic features encountered during the endoscopic examination in the entire group.*

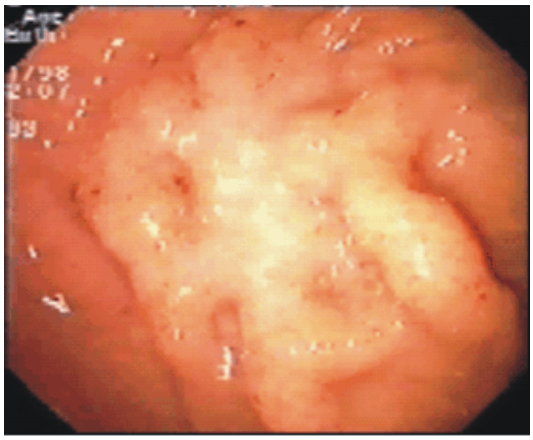

Figure 4 – *Diffuse large B-cell lymphoma. Protrusive and ulcerative tumor with many hemorrhagic lesions on the great curvature.*

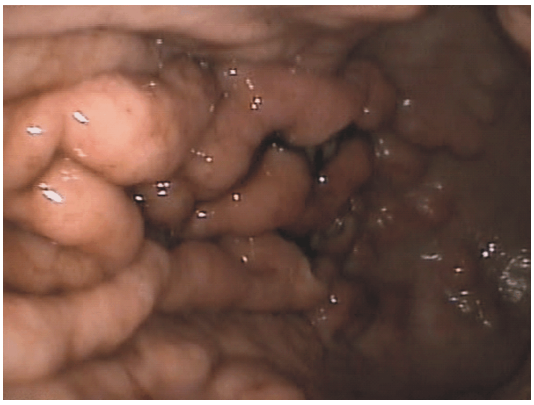

Figure 5 – ***Diffuse large B-cell lymphoma. The gastroscopy showed multiple gastric folds, different size, and many ulcerative lesions, in the gastric mucosa.***

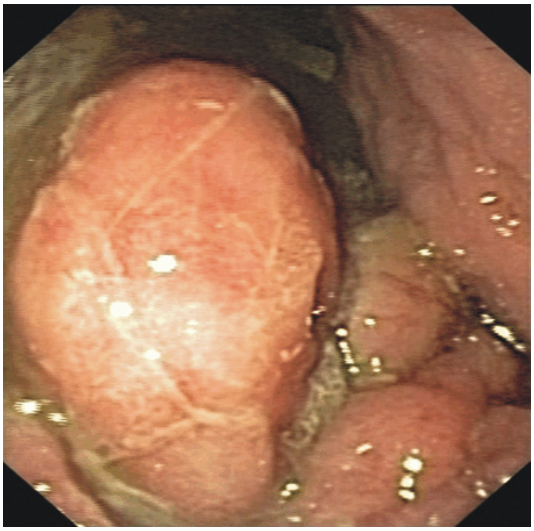

Figure 6 – ***Diffuse large B-cell lymphoma with protusive tumor in the gastric antrum and multiple nodules.***

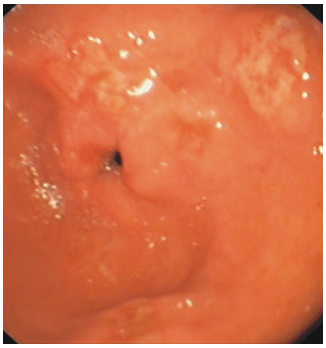

Figure 7 – ***Diffuse large B-cell lymphoma. Multiple papules, with local large erosions, located in the gastric antrum, with stenosing lesions.***

In terms of histopathology and immunohistochemistry, the group was divided into: the group of the patients with MALT lymphoma (low malignancy) and the group of patients with primary gastric diffuse large B-cell lymphoma (high malignancy) (Figure 8).

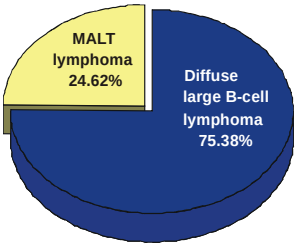

Figure 8 – ***Graphic representation of the encountered histopathological types.***

MALT lymphoma

The average age of patients with MALT lymphoma was 53.625 years, with a standard deviation of 11.026, as shown in Table 5.

Table 5 – ***The average age and the standard deviation of the group of patients with MALT lymphoma***

Age [years]	MALT
No. of patients	16
Mean	53.625
St. dev.	11.026
V.C. [%]	19.91
Min.	31
Quartile 1	47.25
Median	54.5
Quartile 3	61.75
Max.	71

Only one patient with MALT lymphoma was diagnosed after the age of 70 years and none in the age group under 30 years. In the studied group of patients, there were six men and 10 women.

The main macroscopic features encountered in the group of patients with MALT lymphoma are presented in Table 6.

Table 6 – ***The main macroscopic features encountered in the group of patients with MALT lymphoma***

Macroscopic features	No. of patients	%
Protrusive and ulcerative tumor	4	25
Ulcerative tumor	6	37.5
Protrusive tumor	1	6.25
Infiltrative tumor	2	12.5
Large folds	2	12.5
Nodules	1	6.25
Total	16	100

In more than half of the patients, we encountered an ulcerative or ulcerative-vegetative aspect of the lesions. The most common locations were the gastric pyloric antrum and body (12 of the 16 patients), as shown in Figure 9.

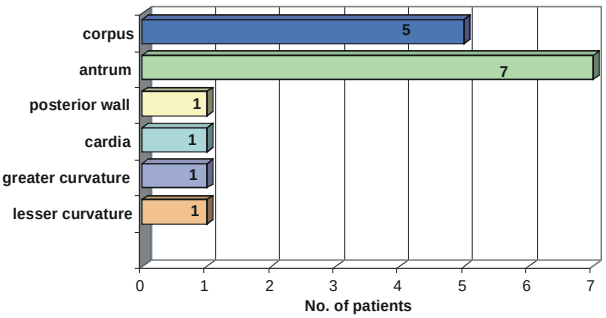

Figure 9 – ***The main locations in the different parts of the stomach in the group of patients with MALT lymphoma.***

Histopathological examination in MALT lymphoma revealed a heterogeneous cell population, with small atypical cells, similar to centrocytes but with more abundant cytoplasm, monocytoid B-cells, small lymphocytes and plasma cells. In the stomach, marginal zone cells infiltrate the epithelium, isolating glands and giving the appearance of "lymphoepithelial lesion" (Figure 10).

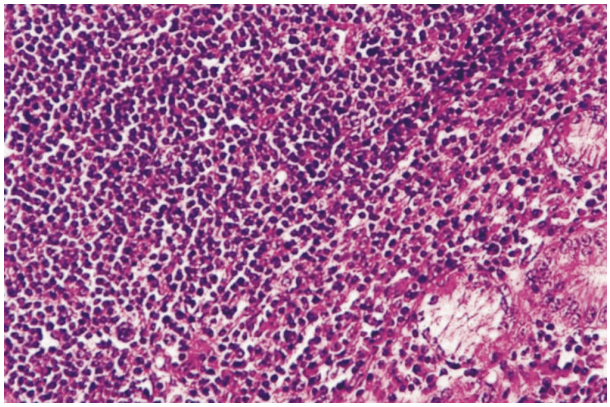

Figure 10 – ***Primary gastric MALT lymphoma. Centrocyte-like (CCL) cells: small or medium cells, with a small amount of cytoplasm, which is sometimes weakly colored and with a nucleus presenting an irregular shape, resembling the centrocytes (small cleaved cells), and lymphoepithelial lesions (HE stain, ×100).***

The most characteristic cells are small or medium, with a small amount of cytoplasm, which is sometimes weakly colored and with a nucleus presenting an irregular shape, resembling the centrocytes (small-cleaved cells). These cells do not resemble any cytological entity that is recognized in lymphoma classification and, due to their similarity to the centrocytes, they have been called centrocyte-like (CCL) cells.

Primary gastric diffuse large B-cell lymphoma (PG-DLBCL)

The average age of patients with primary gastric diffuse large B-cell lymphoma was 52.204 years, with a standard deviation of 15.412, as shown in Table 7, with age limits between 21 and 79 years. In the studied group of patients, there were no significant differences in terms of gender distribution (53.06% women *vs*. 46.94% men).

Table 7 – ***The average age and the standard deviation in the group of patients with primary gastric diffuse large B-cell lymphoma (PG-DLBCL)***

Age [years]	DLBCL
No. of patients	49
Mean	52.204
St. dev.	15.412
V.C. [%]	29.22
Min.	21
Quartile 1	40
Median	55
Quartile 3	65
Max.	79

The main macroscopic features encountered in the group of patients with primary gastric diffuse large B-cell lymphoma are presented in Table 8, almost half of the studied patients presenting a mixed appearance of the lesions.

Regarding the location of lesions, Figure 11 shows that in 33 of the 49 patients of the group the primary location of the lesions was in the gastric body and pyloric antrum.

Table 8 – ***The main macroscopic features encountered in the group of patients with primary gastric diffuse large B-cell lymphoma (PG-DLBCL)***

Macroscopic features	No. of patients	%
Protrusive and ulcerative tumor	21	42.86
Ulcerative tumor	6	12.24
Protrusive tumor	8	16.33
Infiltrative tumor	6	12.24
Large folds	3	6.12
Nodules	2	4.08
Stenosing tumor	3	6.12
Total	49	100

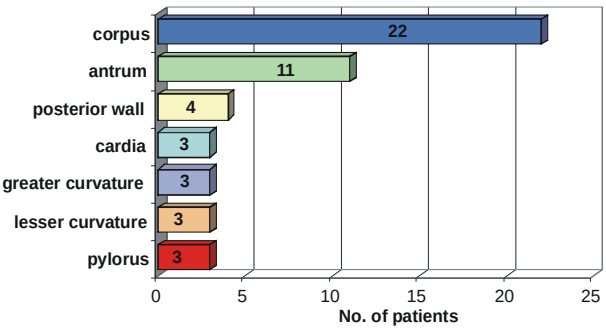

Figure 11 – ***The main locations in the different parts of the stomach in the group of patients with primary gastric diffuse large B-cell lymphoma (PG-DLBCL).***

As for diffuse large B-cell lymphoma with or without MALT component, a proliferation of large cells (the nucleus size is double in relation to the nucleus size of a normal lymphocyte) was described, prominent nucleoli, basophilic cytoplasm (Figure 12) and a moderately or highly increased nuclear proliferation index. In some cases, we noted a simultaneous low-grade MALT-component (Figure 13).

In terms of immunohistochemistry, the following markers were determined: pan B C19, CD20 and CD22 markers, the determination of the kappa/lambda restriction (Figure 14) in order to prove the monoclonal lymphoproliferation and to estimate the cell proliferation index by determining Ki67 (Figure 15) to some of the cases that were studied (18 cases representing 27.6%), and PCNA (in 16 cases), CD5 (for differential diagnosis with mantle cell lymphoma) and CD10 (for differential diagnosis with follicular lymphoma). We did not find any case positive for CD5 or CD10.

All of the MALT type lymphomas and diffuse large B-cell lymphomas revealed a B-cell phenotype as immunohistochemistry showed CD20 expression in almost all MALT cases (Figure 16).

Regarding the proliferation index, Ki67 positivity was usually observed in blastic cells. Moderate (10–20%) or high Ki67 index (over 20%, maximum found 45%) was observed in eight diffuse large B-cell lymphomas of 12 cases tested and in one MALT lymphoma of six cases tested, and low or moderate Ki67 index in five MALT cases of six cases tested (under 10%, minimum found 3%). Statistical analysis cannot be performed (detection of Ki67 only in 12 cases of diffuse large B-cell lymphoma).

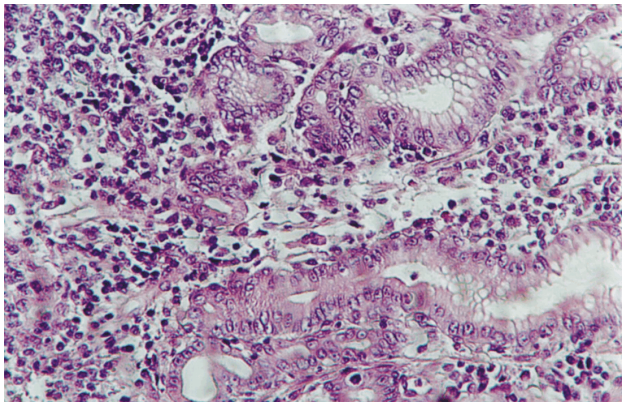

Figure 12 – ***Primary gastric diffuse large B-cell lymphoma. Infiltration with neoplastic large cells with reduced cytoplasm, basophilia with hypertrophic irregular nuclei, with multiple nucleoli, some of them attached to the nuclear membrane (HE stain, ×200).***

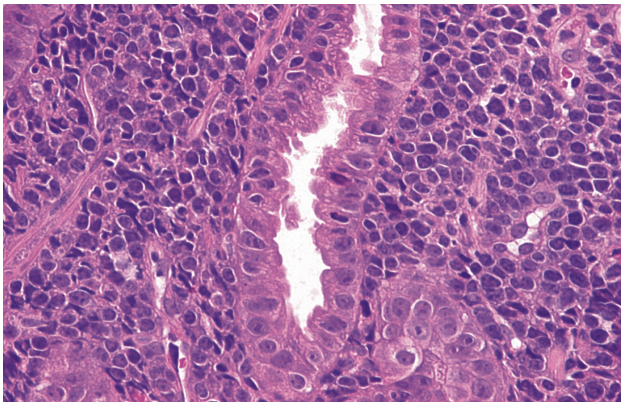

Figure 13 – ***Primary gastric diffuse large B-cell lymphoma with MALT component. Large cells, mostly with low quantitative cytoplasm, with round nucleus and central nucleoli (lymphoplasmocytic cells) or peripheral (centroblast-like cells), with discrete lymphoepithelial lesions (HE stain, ×200).***

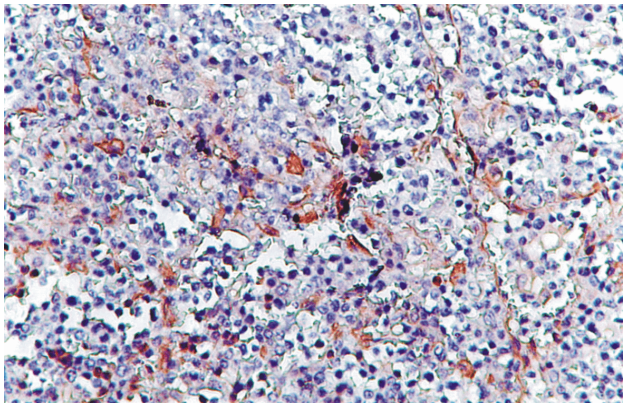

Figure 14 – ***Primary gastric diffuse large B-cell lymphoma with MALT component. Diffuse k light chain + (k light chain immunohistochemistry, ×200).***

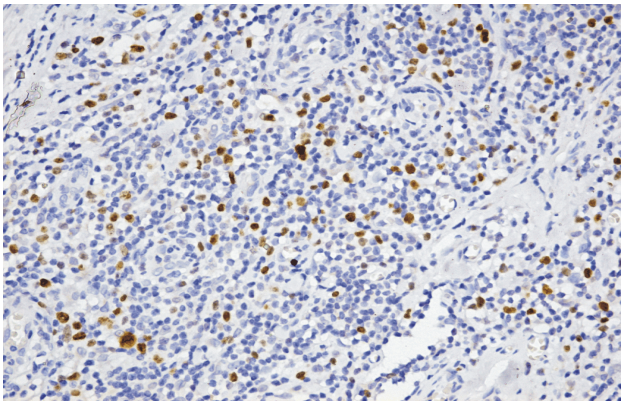

Figure 15 – ***Primary gastric diffuse large B-cell lymphoma with MALT component. Ki67 diffuse, intense positivity in many tumor cells (Ki67 immunohistochemistry, ×200).***

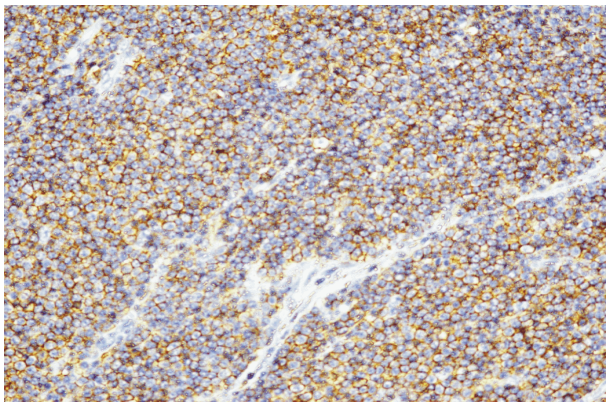

Figure 16 – ***Primary gastric diffuse large B-cell lymphoma with MALT component. Intense CD20+ common in tumor cells (CD20 immunohistochemistry, ×200).***

Discussion

The study group is relatively small in terms of number of patients, on one hand due to the low incidence of primary gastric lymphoma, and on the other hand, due to the selection of patients who received a full investigation in terms of positive diagnosis, the study being a retrospective one, and also due to the non-inclusion in the study of patients with gastric determinations, but diagnosed by histopathological and immunohistochemical examination of a lymph node.

The initial diagnosis and staging procedures should include a gastroduodenal endoscopy with multiple biopsies taken from each region of the stomach [10, 11].

At endoscopic examination, the ulcerative type is the most frequent presentation, although low-grade lymphoma is diagnosed on normal/hyperemic gastric mucosa in 9% of cases [12]. In our study, the most common feature was protrusive and ulcerative tumor; we did not find multiple polyps, very rarely in primary gastric lymphoma, but much more frequent in primary intestinal lymphoma [13].

In terms of the histopathological types, in studied group we found only two histological aspects according to the *WHO* classification of malignant lymphoproliferative diseases, namely the MALT lymphoma and the diffuse large B-cell lymphoma, although the literature also mentions other histological types (follicular lymphoma, mantle-zone lymphoma, and peripheral T-cell lymphoma) [7].

Compared to the literature, the number of cases diagnosed with MALT lymphoma is lower (24.62% *vs.* 40%) [9].

MALT lymphoma is characterized by the proliferation of small lymphocytes, monocytoid lymphocytes (with irregular nuclei, abundant cytoplasm), plasma cells and plasmacytoid cells who affect mainly the mucosa and glands. An important diagnostic feature of MALT lymphoma is the presence of lymphoepithelial lesions defined as the infiltration and distortion of epithelial structures by aggregates (usually three or more) of neoplastic lymphoid cells [14]. The lymphoma cells assume varied cytological appearances, often within individual samples. The most characteristic are the centrocyte-like cells, which are small to medium-sized cells with small irregular nuclei [15]. Alternatively, the neoplastic cells may have a monocytoid appearance with abundant pale cytoplasm and distinct cell borders, or may resemble the small mature lymphocytes. The most frequent problem in the diagnosis of gastric MALT lymphoma is its differentiation from *H. pylori*-associated gastritis. Among the histological features favoring MALT lymphoma there are: a dense lymphoid infiltrate occupying most of the biopsy fragment, prominent lymphoepithelial lesions, Dutcher bodies in plasma cells, infiltration of muscularis mucosae and moderate cytological atypia of lymphoid cells [16]. More recently, the incorporation of immunohistological and molecular genetic assessment alongside histological examination has resulted in an increase in the confidence with which a MALT lymphoma can be diagnosed or excluded in gastric biopsies.

From the histological point of view, most patients in our study are classified as with high malignancy (75.38%). Primary gastric diffuse large B-cell lymphoma is defined as a malignancy composed of large cells (nuclei at least twice the size of a small lymphocyte, usually larger than nuclei of tissue macrophages), prominent nucleoli, basophilic cytoplasm. The proliferation fraction is moderate to high. Lesions are characterized by an intense cellular infiltration of the lamina propria. In most cases, the predominant cells resemble either centroblasts (large noncleaved cells) or the immunoblasts; the most common appearance is that of a mixture of the centroblast-like and the immunoblast-like cells. In some cases, a simultaneous low-grade MALT-component is observed. The definition of these malignancies, previously called high-grade MALT-type lymphomas, has recently been incorporated under the term of diffuse large cell lymphomas [17]. The current *WHO* recommendation is that cases showing transformation to large-cell lymphoma should be diagnosed as DLBCL, and the presence of accompanying MALT lymphoma should be noted [18]. The term "high-grade MALT lymphoma" is confusing and should not be used. In the absence of at least a focus of unequivocal typical MALT lymphoma, the distinction between the transformed MALT lymphoma and the diffuse large B-cell lymphoma arising *de novo* is often impossible, particularly because the formation of lymphoepithelial lesions by DLBCL does not prove the transformation from MALT lymphoma.

In immunohistochemical terms, MALT lymphoma does not have a characteristic immunophenotype, the description of the above markers being the same as for the splenic marginal zone B-cell, the Payer plaques and the lymph node. The immunophenotype of the neoplastic cells of MALT lymphoma is virtually identical to that of non-neoplastic marginal-zone B-cells: CD20+, IgD-, IgM (>IgA>IgG)+, CD5-, CD10-, Bcl6-, cyclin D1- [19]. No specific immunohistochemical marker has yet been identified for MALT lymphoma, but the evaluation of a panel of immunostains is necessary for the assessment of the architecture of the lymphoid infiltrate, the lineage assignment, the identification of an aberrant phenotype or immunoglobulin light-chain restriction (it is extremely helpful in the exclusion of a reactive lymphoid infiltrate) and for the exclusion of other lymphomas. In approximately 50% of MALT lymphomas, there is aberrant co-expression of CD43 by CD20+ small B-cells, a phenotype strongly suggestive of lymphoma. Very often, MALT lymphomas may express CD5 or IgD [19, 20]; a careful review of these cases, particularly to exclude a mantle cell lymphoma, is important.

As with all other diffuse large B-cell lymphomas, the cells of primary gastric lymphoma express B-cell-associated antigens (CD19, CD20, CD22, and CD79a). They are CD45+/-, CD5-/+, and CD10-/+. In half of the cases, there is Bcl6 positivity and in 26% there is CD10 positivity, while CD38 immunoreactivity is observed in 47% of cases [21].

The high proliferation index was observed in the majority of diffuse large B-cell lymphoma: only in one MALT lymphoma of six cases Ki67 was over 20% (16.6%) *vs.* eight cases with Ki67 of 12 tested (66.6%). PCNA staining was performed in 16 cases (11 cases of diffuse large B-cell lymphoma and five cases of MALT lymphoma). Values over 51% (high proliferation index) were observed in seven cases of diffuse large B-cell lymphoma (63.6%) and in none of MALT lymphomas.

Some studies demonstrated that there is a significant relationship between PCNA score and histologic grade of gastric lymphomas. These findings suggest that PCNA immunoreactivity may be used as an operational marker of cell proliferation in gastric lymphomas [22]. Similar results were communicated by Nakamura S *et al.*, in a clinico-pathologic study on 233 cases, regarding Ki67/MIB-1 index [23]. We observed similar results for PCNA score and Ki67 score in our study.

Conclusions

A correct diagnosis is very important in terms of therapeutic approach and it requires a histopathological and immunohistochemical examination in order to allow the determination of the type of lymphoproliferation and its aggressiveness. The determination of the nuclear proliferation index is correlated with the histopathological type of lymphoma. Our study performs an analysis of the characteristics of a group of patients with gastric lymphoma, in terms of diagnosis, being useful to clinicians for dealing with this particular type of lymphoproliferation, with only a few studies on gastric lymphoma having been published in the last 10 years in

our country. The characteristics of the group of patients were: a higher number of aggressive histological types; an excessive use of gastric resection; none of the cases was a T-lymphoproliferation.

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