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Primary Digestive Lymphoma: Anatomical, Clinical and Epidemiological Study

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Abstract

Gastrointestinal lymphoma is a non-Hodgkin's lymphoma that develops from MALT (Mucosa Associated Lymphoid Tissue). It is a rare entity representing 1% of tumors of the gastrointestinal tract. In Madagascar, few studies have been performed on these lymphomas. Our objective is to report a series of digestive lymphoma in order to evaluate the epidemiological and anatomical-clinical aspects. This was a retrospective, cross-sectional, descriptive bicentric study conducted at the Department of Pathology at the Soavinandriana Hospital Center (CENHOSOA) and the Department of Pathology at the University Hospital Center of Andrainjato over a period of 4 years from January 1st, 2016 to December 31st, 2019. During the study period, we collected 14 cases of primary digestive lymphoma representing 16% of all lymphomas. We noted a female predominance with a sex ratio of 0.75. The mean age of the patients was 35.64 years with extremes of 3 and 78 years. The clinical signs were dominated by occlusive syndrome (57.14%), abdominal pain (21.44%), digestive hemorrhage (7.14%), intestinal invagination (7.14%) and lingual swelling (7.14%). Regarding the location, the ileum was the most frequently affected (42.85%), followed by the stomach (14.29%), the ileo-caecal area (14.29%), the sigmoid (14.29%), the colon (7.14%) and we also noted a lingual location (7.14%). The most frequent histological type was diffuse large B cell lymphoma (42.86%) followed by MALT lymphoma (35.71%), Burkitt's lymphoma (14.29%) and diffuse small cell lymphoma (unclassified) (7.14%). We did not observe a significant association ($p > 0.05$) between the site involvement and the histological subtypes. Among the 14 cases, 3 were confirmed by immunohistochemistry. Primary lymphomas of the gastrointestinal tract include several anatomic entities with different presentation and prognosis.

Pathological examination is essential for diagnosis. Immunohistochemical examination is a valuable aid for immunophenotyping despite its difficult access in Madagascar. A multidisciplinary collaboration is necessary for an optimal management of these rare lymphomas.

Keywords

Lymphoma, Gastrointestinal Tract, Madagascar

1. Introduction

Gastrointestinal lymphoma is a non-Hodgkin's lymphoma (NHL) [1] that develops from MALT (Mucosa Associated Lymphoid Tissue) which is a lymphoid tissue attached to the mucosa [2]. Gastrointestinal tract lymphomas are a rare entity [3] comprising only 1% to 4% of all malignant neoplasms of the gastrointestinal tract and it is the most common site of extranodal lymphomas worldwide, accounting for up to 40% of all extranodal non-Hodgkin lymphomas. Primary Gastrointestinal lymphomas are less common, accounting for approximately 10% to 15% of all non-Hodgkin lymphomas [4]. In Madagascar, few studies have been performed on these lymphomas. Our objective is to report a series of digestive lymphoma in order to evaluate the epidemiological and anatomical-clinical aspects.

2. Materials and Method

This was a retrospective, cross-sectional, descriptive bicentric study conducted at the Department of Pathology at the Soavinandriana Hospital Center (CENHOSOA) and the Department of Pathology at the University Hospital Center of Andrainjato over a period of 4 years from January 1st, 2016 to December 31st, 2019. We included all cases of digestive lymphoma diagnosed on biopsies (endoscopic or surgical) and on surgical operative parts with anatomopathological confirmation. We excluded incomplete records and did not include suspected gastrointestinal lymphoma lesions without histological or immunohistochemical confirmation and all non-contributory specimens. We studied the following parameters: gender, age, clinical information, lesion topography, and histological subtype. The data were collected in the liaison sheet and the results registers. All specimens were fixed in 10% buffered formalin, processed according to the conventional histological slide preparation technique, and stained with hematoxylin-eosin (HE). We used in some cases immunohistochemistry. The 2008 World Health Organization (WHO) classification was used for histological typing. The analysis was done on Epi info 7.2.2.6 and Microsoft Excel 2020. To investigate the relationship between two variables, we used the Chi-square test with Fisher's test. Differences were considered significant when "p" was less than 0.05. A descriptive analysis was performed; no other specific statistical tests were per-

formed. A descriptive analysis was performed; no specific statistical test was performed.

3. Results

During the study period, we collected 14 cases of primary digestive lymphoma, representing 16% of all lymphomas. We noted a female predominance with a sex ratio of 0.75 (Table 1). The mean age of the patients was 35.64 years with extremes of 3 and 78 years (Table 1). The clinical signs were dominated by occlusive syndrome (57.14%), abdominal pain (21.44%), digestive hemorrhage (7.14%), intestinal invagination (7.14%) and lingual swelling (7.14%). Regarding the location, the ileum (Figure 1) was the most frequently affected (42.85%), followed by the stomach (14.29%), the ileo-caecal area (14.29%), the sigmoid (14.29%), the colon (7.14%) and we also noted a lingual location (7.14%). The most frequent histological type was diffuse large B cell lymphoma (42.86%) followed by MALT lymphoma (35.71%), Burkitt's lymphoma (14.29%) and diffuse small cell lymphoma (unclassified) (7.14%). We did not observe a significant association ($p > 0.05$) between the site involvement and the histological subtypes. Among the 14 cases, 3 were confirmed by immunohistochemistry (Figure 2).

4. Discussion

The primary location of lymphoma in the gastrointestinal tract constitutes 1% to 4% of malignant tumors of the gastrointestinal tract, 10% to 15% of non-Hodgkin's lymphomas and 30% to 40% of extranodal lymphomas, making the gastrointestinal

Table 1. Correlation between age groups and gender.

Gender \ Age	<10	[10 – 20]	[20 – 30]	[30 – 40]	[40 – 50]	[50 – 60]	≥60
Female	2	1	1	0	1	1	2
Male	1	1	0	0	4	0	0

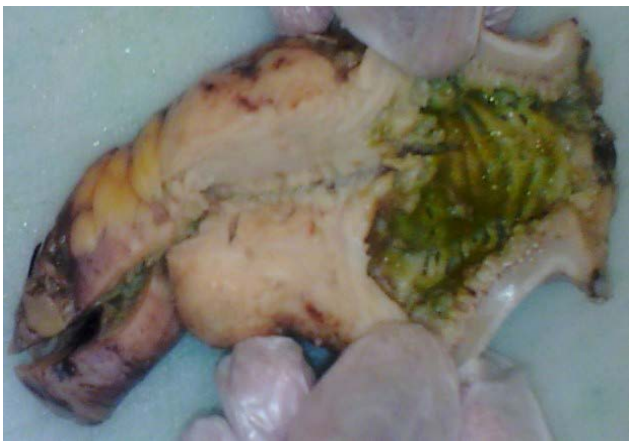

Figure 1. Ileum: Macroscopic appearance of a lymphoma surgical specimen. Source: Department of Pathology of Soavinandriana Center Hospital.

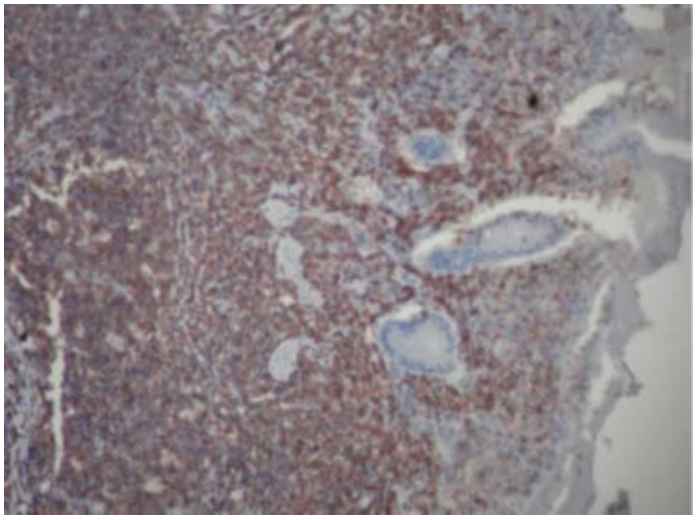

Figure 2. Small intestine: diffuse large B cells lymphoid proliferation, immunohistochemistry (CD 20), Gx100. Source: Department of Pathology of Soavinandriana Center Hospital.

tract the most frequent site of extranodal lymphomas [4]. Nevertheless, primary lymphoma of the digestive tract remains a rare entity [3]. Our results are similar with these statements, since lymphoma of the digestive tract represents 16% of all lymphoma cases in both laboratories.

Regarding gender, our data diverge with those of the literature since we observed a female predominance (**Table 1**) representing 57.14% of cases. On the other hand, authors such as Raina V *et al.* [5] and Xiang Y *et al.* [6] have observed a male predominance in their series.

The mean age was 35.64 years in our study, which is identical to the result of Raina V *et al.* [5] who found 32 years in their series unlike Xiang Y and al whose mean age was later (63 years) [6]. This difference could be explained by the variation in geographical areas, environmental factors and study populations considered.

In our series, the presenting signs were mainly dominated by the occlusive syndrome. The results of Shirwaikar Thomas A, performed in Texas, showed that about 45% - 65% of all cases of gastrointestinal lymphoma clinically presented with abdominal pain [7]. These signs could be explained by the fact that digestive lymphoma often presents as a mass that can stenosis or obliterate the digestive lumen explaining the pain and/or obstructive syndrome.

The site 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 [8].

In our study, the main location of primary lymphoma of the gastrointestinal tract was the ileum (42.85%) followed by the stomach (14.29%). In their series, Ruskoné-Fourmestraux A *et al.* [3] and Papaxoinis G *et al.* [9] reported that the stomach was the primary location of lymphoma.

The frequency of gastric localization of lymphoma is explained by the pathogenesis of gastric lymphoma of the MALT type with the involvement, in recent years, of a bacterium, *Helicobacter pylori*. *Helicobacter pylori* infection induces the formation of a mucosa-associated lymphoid tissue or "MALT" whose evolution can induce a B tumor clone and then lymphoma [10]. In Madagascar, the seroprevalence of *Helicobacter pylori* infection in adults is 82% [11] but cases of gastric lymphoma remain exceptional. This low rate could be explained by the fact that gastric lymphoma is under-diagnosed in Madagascar due to the difficult access to anatomopathological examination of the majority of patients. Diagnostic difficulties exist. They arise from the fact that biopsy samples are often small and of low quantity. They sometimes contain only undifferentiated areas [12]. A study by Andriamampionona and al on a case of gastric lymphoma showed that the analysis of biopsy fragments showed incomplete dystrophic glandular structures developing on a lymphocytic background and concluded to a gastric adenocarcinoma. A 2/3 gastrectomy with trans-mesocolic gastro-jejunal anastomosis was performed. Histological examination of the surgical specimen revealed a diffuse lymphoid proliferation of large cells, centroblastic and immunoblastic type, associated with some lympho-epithelial lesions, which led to the conclusion of a diffuse large B cell lymphoma [13].

As for small bowel lymphoma, the involvement of Epstein-Barr virus (EBV) has been described in primary lymphomas of the digestive tract as well as in Burkitt's lymphoma, often of intestinal or mesenteric location [14]. In our case, the search for EBV in the ileum could not be performed because the technical platform for its realization is not available in Madagascar.

Some predisposing factors have been incriminated in the development of digestive lymphoma including extensive follicular hyperplasia of the small intestine, immune deficiencies and *Helicobacter pylori* infection for gastric lymphoma. Radiation therapy, chemotherapy as well as immunosuppressive drugs that are used in inflammatory bowel disease and organ transplantation also play a role [15] [16]. In our series, none of these predisposing factors were documented.

Regarding the histological type of gastrointestinal tract lymphoma, diffuse large B cell lymphoma (**Figure 3**) was the main type encountered in our study and that of Juarez-Salcedo LM and al [17]. The majority of authors have found it [18]. The tumor is composed of large B cells of centroblastic type. This proliferation results either from a probable transformation of a marginal zone lymphoma of the MALT or from a large B-cell lymphoma developed in novo in the digestive tract. The distinction between these two forms does not seem to have any therapeutic or prognostic value [14].

The diagnosis of digestive lymphomas is based on histology from biopsy samples taken during digestive endoscopy or from surgical samples taken during a complication. In our series, biopsy samples were taken in 50% of cases, while ileal resection was performed in 42.86% and ileo-colectomy in 7.14%. The frequency of surgical resection could be explained by the fact that digestive lymphoma was mainly discovered as a complication.

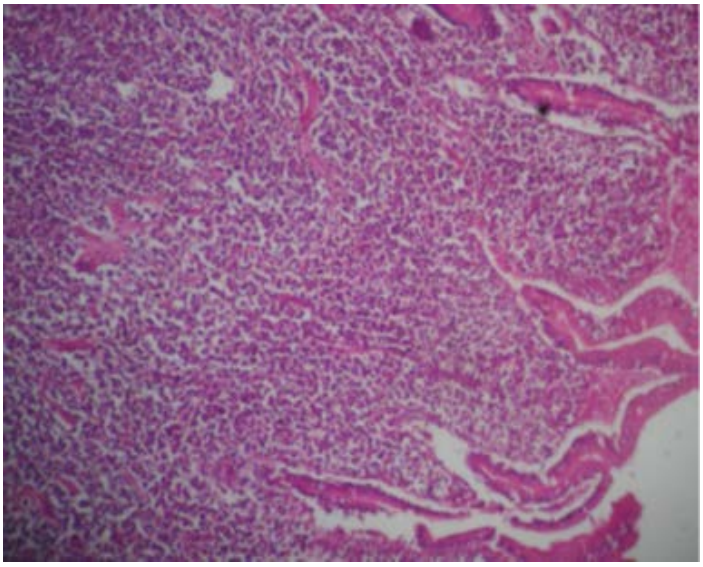

Figure 3. Small intestine: diffuse large cells lymphoid proliferation. HE, Gx100. Source: Department of Pathology of Soavinandriana Center Hospital.

Regarding to the limitations of our study, our series is not representative of the Malagasy population. Only three of our patients had an immunohistochemical examination due to lack of funds. And Long-term follow-up (evaluation of remission, setback, potential metastasis and mortality) of patients can't be done in the Madagascar context. Due to lack of resources, only a minority of patients can access appropriate treatment.

5. Conclusion

Primary lymphomas of the gastrointestinal tract include several anatomic entities with different presentation and prognosis. Clinical symptoms and imaging are not specific. Pathological examination is essential for diagnosis. Immunohistochemical examination is a valuable aid for immunophenotyping despite its difficult access in Madagascar. A multidisciplinary collaboration is necessary for an optimal management of these rare lymphomas.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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