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STUDY ON HISTOPATHOLOGICAL FEATURES AND IMMUNOPHENOTYPE OF GASTROINTESTINAL LYMPHOMA

SUMMARY OF MEDICAL PHD DISSERTATION

MAJOR: BIOMEDICAL SCIENCE
CODE: 9720101
ACADEMIC SUPERVISOR:
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HUE – 2025

This dissertation was completed at
UNIVERSITY OF MEDICINE AND PHARMACY, HUE UNIVERSITY
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The dissertation was defended at 8 o'clock, on 19/11/2026.
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INTRODUCTION

1. THE URGENCY OF THE TOPIC

Gastrointestinal lymphoma is a complex group of diseases, accounting for 10–15% of non-Hodgkin lymphomas and representing the most common form of extranodal lymphoma, comprising 30–40% of such cases. Among these, gastrointestinal lymphomas are being increasingly diagnosed, largely due to the significant advancements in endoscopic techniques. In 2019, the World Health Organization released the fifth edition of the Classification of Tumors of the Digestive System, in which gastrointestinal lymphomas were categorized into a separate classification, primarily focusing on lymphomas of the stomach and intestines. This classification includes updates and a reorganization of several subtypes.

Does the combination of histopathological and immunohistochemical techniques meet the diagnostic and classification criteria for gastrointestinal lymphomas according to the 2019 World Health Organization (WHO) classification? In-depth studies on the histopathology and immunohistochemistry of gastrointestinal lymphomas, such as those conducted by Nguyen Van Chu in 2005 and Tran Huong Giang in 2011, were based on the 2001 and 2008 WHO classifications and were limited by relatively small sample sizes. Therefore, we conducted the study entitled ***'Histopathological and Immunophenotypic Characteristics of Gastrointestinal Lymphomas'*** with the aim of identifying, establishing, and proposing characteristic immunophenotypic profiles for the common histological subtypes of gastrointestinal lymphomas.

2. RESEARCH OBJECTIVES

1. To characterize the histopathological and immunohistochemical features of gastrointestinal non-Hodgkin lymphoma according to the 2019 World Health Organization classification.

2. To investigate the immunophenotypes of various histopathological subtypes and evaluate the correlation between these subtypes and specific endoscopic characteristics.

3. NOVEL CONTRIBUTIONS OF THE DISSERTATION

This study provides data on the distribution of gastrointestinal lymphoma subtypes according to the 2019 World Health Organization (WHO) classification, along with detailed descriptions of the histopathological and immunophenotypic characteristics of the most common subtypes found in Vietnam.

The research identifies correlations between immunophenotypic profiles and certain clinical features, endoscopic lesion patterns, and histopathological characteristics of gastrointestinal lymphomas.

A diagnostic algorithm for gastrointestinal lymphomas is proposed, suggesting appropriate panels of immunohistochemical markers tailored to specific histopathological groups. This facilitates more accurate subtype identification based on histopathology and immunohistochemistry.

4. THESIS LAYOUT

The dissertation consists of 119 pages and is divided into the following sections: Introduction: 3 pages, Literature Review: 38 pages, Subjects and Research Methods: 23 pages, Research

Results: 18 pages, Discussion: 25 pages, Conclusion: 2 pages, Recommendations: 1 page.

The dissertation includes: 34 tables, 29 figures, 3 diagrams, and 148 references. Among the references, 14 are in Vietnamese and 134 are in English.

CHAPTER 1. LITERATURE OVERVIEW

1.1. OVERVIEW GASTROINTESTINAL LYMPHOMA

1.1.1. Definition of Gastrointestinal Lymphoma

Gastrointestinal lymphoma can present either as a primary tumor localized in the stomach or intestines, or as a secondary manifestation within the context of systemic lymphoma lympho.

1.1.2. Pathogenesis of Gastrointestinal Lymphoma

Mucosa-associated lymphoid tissue (MALT) interacts with the mucosal surface through immune responses, helping to maintain immune homeostasis in the gut. Therefore, it is not surprising that gastrointestinal MALT lymphoma is the most common site of extranodal MALT lymphoma. The established causes of non-Hodgkin gastrointestinal lymphoma generally fall into two main categories: immune system disorders and infections.

1.1.3. Diagnosis and Classification

The diagnosis and classification of lymphoma are based on macroscopic and microscopic features, immunophenotypic and molecular characteristics, within a specific clinical context.

1.1.4.1. Clinical Manifestations of Gastrointestinal Lymphoma

The clinical symptoms of gastrointestinal lymphoma are often vague and nonspecific, depending on the tumor's location and varying significantly between individuals. Patients may

present with systemic manifestations and signs of tumor progression, commonly referred to as B symptoms.

1.1.4.2. Role of gastrointestinal endoscopy

The endoscopic appearance of gastric lymphoma can be classified into three main types: (1)Polypoid mass protruding into the gastric lumen, (2) Infiltrative ulcerative lesions, and (3)Tumor-like enlarged gastric folds with mucosal hypertrophy.

1.1.4.3. Role of Radiological imaging

Diagnostic imaging serves as an essential tool for evaluating the extent of disease and staging prior to treatment initiation.

1.1.4.4. Histopathological Subtype Classification

The 2019 revision of the WHO classification of gastrointestinal lymphomas has clarified and resolved several limitations of earlier histopathological classification systems.

1.1.4.5. Stage classification

Lugano classification and widely used for stage evaluation

1.1.4. Prognosis, Treatment, and Follow-up

The prognosis of lymphoma depends primarily on two factors: the histopathological subtype and the stage of the disease. The treatment of gastrointestinal lymphoma ranges from watchful waiting to stem cell transplantation. Recurrence can occur across all subtypes, making regular follow-up essential.

1.2. HISTOPATHOLOGICAL CHARACTERISTICS OF GASTROENTERIC LYMPHOMA

Mucosa-Associated Lymphoid Tissue (MALT) Lymphoma with histological feature is the presence of lymphoepithelial lesions. Duodenal follicular lymphoma and

conventional follicular lymphoma, these follicles are predominantly composed of small, mature lymphocytes (centrocytes), with rare to occasional centroblasts. Mantle cell lymphoma is characterized by a monomorphic proliferation of small to medium-sized lymphocytes with scant cytoplasm and irregular nuclei, dispersed chromatin, and inconspicuous nucleoli. Diffuse Large B-Cell Lymphoma is predominant cells resemble centroblasts or immunoblasts. The tumor cells are medium to large in size, with round to oval or slightly irregular nuclear contours, vesicular chromatin, prominent nucleoli, and basophilic cytoplasm. Burkitt lymphoma is characterized by a population of medium-sized lymphoid cells with abundant mitochondria, frequent apoptotic bodies, and numerous macrophages, resulting in the characteristic 'starry-sky' appearance observed under the microscope

1.2.6. Gastrointestinal T/NK-Cell Lymphomas

Enteropathy-associated T-cell lymphoma (EATL): Characterized by medium to large lymphoid cells interspersed with inflammatory infiltrates, including eosinophils. Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL): Similar to EATL, neoplastic lymphoid cells diffusely infiltrate the intestinal mucosal epithelium. Extranodal NK/T-cell lymphoma: lymphoid cells exhibit angiocentric infiltration and vascular destruction. Intestinal T-cell lymphoma, not otherwise specified (NOS): a category for T-cell lymphomas of the gastrointestinal tract that do not fit into other defined subtypes

1.3. IMMUNOHISTOCHEMICAL CHARACTERISTICS OF GASTROINTESTINAL LYMPHOMAS

1.3.1. Characteristics of Receptors and Immunohistochemical Markers Used in the Diagnosis of Gastrointestinal Lymphomas

Immunohistochemistry plays a crucial role in the diagnosis, classification, and prediction of treatment response in hematopoietic and lymphoid tissue disorders, including gastrointestinal lymphomas.

1.3.2. Immunophenotypic Characteristics of Gastrointestinal Lymphomas

MALT lymphoma lacks specific immunophenotypic markers. In contrast, mantle cell lymphoma exhibits a characteristic immunophenotype, showing strong positivity for CD5, Cyclin D1, and SOX11. The immunophenotype of duodenal follicular lymphoma is similar to that of nodal follicular lymphoma. Diffuse large B-cell lymphoma (DLBCL) typically displays variable immunophenotypic profiles. Burkitt lymphoma is usually positive for B-cell markers and germinal center markers, and is notably characterized by a high Ki-67 proliferation index (90–100%). T-cell lymphomas include enteropathy-associated T-cell lymphoma (EATL), monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL)—formerly known as type II EATL—and indolent T-cell lymphoproliferative disorders.

1.4. DOMESTIC AND INTERNATIONAL STUDIES ON HISTOPATHOLOGY AND IMMUNOHISTOCHEMISTRY OF GASTROINTESTINAL LYMPHOMAS

1.4.1. Studies Abroad

In 2003, Shotaro Nakamura conducted a study on 455 patients with gastrointestinal lymphoma. According to Dana

Hashim (2009), the application of immunohistochemistry brought significant changes to the classification of gastrointestinal lymphomas during the 1990s and 2000s. In 2011, Neeraj Arora studied 361 cases of gastrointestinal lymphoma using an immunohistochemical panel based on histomorphological features. Wenshuang Ding (2016) analyzed 1,010 cases of gastrointestinal lymphoma in southeastern China, applying the Hans algorithm to classify diffuse large B-cell lymphoma (DLBCL) into germinal center B-cell-like (GCB) and non-GCB subtypes. In 2018, F.M. Ona-Ortiz conducted research on mantle cell lymphoma patients. In 2020, Marco Pizzi proposed a diagnostic approach for gastrointestinal lymphomas.

1.4.2. Studies in Viet Nam

A subsequent study by Nguyen Van Chu (2006), which combined histopathological and immunohistochemical analysis, successfully classified various gastrointestinal lymphoma entities according to the WHO 2001 classification. In 2011, Tran Huong Giang and Hua Thi Ngoc Ha proposed several immunophenotypic profiles for gastrointestinal lymphomas. More recently, a study by Vu Thanh Huyen et al (2022) focused on the clinical and paraclinical characteristics of gastrointestinal presentations of non-Hodgkin lymphoma. In 2023, Tran Thang reported on treatment responses and survival outcomes across different histopathological subtypes.

CHAPTER 2. RESEARCH SUBJECTS AND METHODS

2.1. RESEARCH SUBJECTS

A study was conducted on 159 patients with gastrointestinal lymphoma who presented for diagnosis and

treatment at Hue University of Medicine and Pharmacy Hospital, Hue Central Hospital, and K Hospital (Hanoi) from June 2021 to June 2024.

2.1.1. Inclusion Criteria

- Histopathological diagnosis from endoscopic biopsy or surgical specimen confirming lymphoma or suspected gastrointestinal lymphoma.
- Availability of tissue samples with sufficient quality and a minimum size of ≥ 3 mm for immunohistochemical analysis.
- Confirmed diagnosis of gastrointestinal non-Hodgkin lymphoma based on immunohistochemical (IHC) staining results.
- Availability of complete clinical data, as well as endoscopic and macroscopic findings, in accordance with the study parameters.

2.1.2. Exclusion Criteria

Patients who had previously been treated for gastrointestinal lymphoma or gastric/intestinal cancer. Patients whose diagnosis was not gastrointestinal lymphoma after immunohistochemical staining, or whose tissue samples were inadequate for immunohistochemical diagnosis..

2.1.3. Study Location and Duration

Department of Pathology – Hue University of Medicine and Pharmacy Hospital, from June 2021 to June 2024.

2.2. RESEARCH METHODS

2.2.1. Study Design

- A cross-sectional descriptive study, incorporating both retrospective and prospective data collection.

- Sampling Method: Convenience sampling; all patients who meet the inclusion criteria during the study period will be included in the study.

2.2.2. Research Procedures

Routine histopathological examination using hematoxylin and eosin (H&E) staining, along with immunohistochemical testing using relevant antibody panels. Lymphoma types and subtypes were classified according to the 2019 World Health Organization (WHO) classification of gastrointestinal lymphomas. General characteristics, clinical features, endoscopic findings, and gross pathology were collected from patient medical records.

2.2.3. Research Techniques

Histopathological diagnostic technique using Hematoxylin and Eosin (HE) staining and evaluation method

Immunohistochemical staining and evaluation method

Administrative, clinical, and gastrointestinal endoscopy information was collected from medical records.

2.3. VARIABLES IN THE STUDY

2.3.1. General Characteristics, Clinical Features, Endoscopic and Macroscopic Characteristics

Age, Gender

Main symptoms: abdominal pain, obstruction, bloody stool, diarrhea, other symptoms

Presence of one or more “B symptoms”

Complications: no complications, gastrointestinal bleeding, intestinal obstruction, hollow organ perforation

Stage variable: based on the Lugano classification

Lesion location: determined by endoscopy or surgical

specimens, including the following sites: stomach, duodenum, jejunum–ileum, ileocecal region, colon, rectum

Lesion type: classified according to the proposal by T. Kanno, consisting of 6 categories

H. pylori test: based on rapid urease test (CLO test) during endoscopy: negative or positive.

2.3.2. Histopathological Characteristics Variables

Histological pattern: two variables — Diffuse; Nodular/Follicular

Tumor cell size: Small, Mixed small and medium, Medium, Mixed medium and large, Large

Cellular morphological features:

Presence of lymphoepithelial lesions: Present or Absent

Histopathological diagnosis: the final diagnosis based on routine Hematoxylin and Eosin (HE) staining.

2.3.3. Immunohistochemical Characteristics

Evaluation of positivity or negativity for each immunohistochemical marker: CD3, CD5, CD10, CD20, CD23, CD79a, Bcl-2, Bcl-6, Cyclin D1, CD4, CD8, and MUM1. For the Ki-67 marker, the expression level is assessed using a percentage index, estimated as the percentage of tumor cells showing positive staining among the total tumor cells on the slide.

Conclusion: The histopathological subtype diagnosis is determined based on both histopathological and immunohistochemical characteristics.

2.4. DATA PROCESSING AND ANALYSIS

The cleaned data were entered using Microsoft Excel 2016. Statistical calculations and hypothesis testing were performed using RStudio 2024 (version 4.2.1).

2.5. ETHICS IN BIOMEDICAL RESEARCH

The study was conducted in accordance with Decision No. 2130/QĐ-ĐHYD, dated August 20, 2021, issued by the Rector of Hue University of Medicine and Pharmacy, Hue University, and with the approval document H2022/016 from the Ethics Committee in Biomedical Research, Hue University of Medicine and Pharmacy. All participant information was kept strictly confidential. Identities were protected and used solely for research purposes.

CHAPTER 3. RESULTS

3.1. GENERAL CHARACTERISTICS OF THE STUDY SUBJECTS, CLINICAL AND ENDOSCOPIC – MACROSCOPIC FEATURES

3.1.1. General Characteristics of the Study Subjects

The study sample had a mean age of 56.1 ± 15.1 years, ranging from 11 to 99 years, and did not follow a normal distribution ($p < 0.05$). The age group from 50 to 70 years was predominant, accounting for 59.1%. The male-to-female ratio was approximately 3:2.

3.1.2. Clinical Characteristics of Gastrointestinal Lymphoma

Abdominal pain was the most common symptom (75.5%), while a smaller proportion of patients presented with hematochezia, diarrhea, obstruction, or other symptoms. B symptoms were observed in 11.3% of all patients. Reported complications included gastrointestinal obstruction (12.6%), gastrointestinal bleeding (6.9%), and hollow organ perforation (1.9%). Regarding disease staging, the majority of cases were diagnosed at stages I, II1, and II2 (71.7%), while stages IIE and IV accounted for

28.3%.

3.1.3. Macroscopic and Endoscopic Characteristics

3.1.3.1. Characteristics of biopsy specimens

Endoscopic biopsy fragments predominated in the study sample (60.4%).

3.1.3.2. Location of gastrointestinal lymphoma lesions

Lymphoma lesions were most commonly detected in the stomach (60.4%), followed by the small intestine (11.9%), colon (10.1%), ileocecal region (7.5%), rectum (6.9%), and finally the duodenum (3.2%).

3.1.3.3. Endoscopic findings of lesions

Surface lesions were the most common, accounting for more than half of the cases. The remaining types included protruding masses (20.1%), ulcerative masses (14.5%), ulcers on protruding masses (9.4%), mucosal fold hypertrophy (3.8%), and diffuse nodules (1.9%).

3.2. CLASSIFICATION OF IMMUNOHISTOCHEMICAL PATTERNS AND HISTOPATHOLOGICAL CHARACTERISTICS

3.2.1. Classification of immunohistochemical patterns of Gastrointestinal Lymphoma

Histopathological characteristics of gastrointestinal lymphoma: B-cell lymphomas accounted for 96.2%, while a small proportion originated from T lymphocytes (3.8%). The most common type was diffuse large B-cell lymphoma (DLBCL), with 99 cases. Among these, the activated B-cell (ABC) subtype accounted for 56%, and the germinal center B-cell-like (GCB) subtype accounted for 44%. The second most common was

mucosa-associated lymphoid tissue (MALT) lymphoma, with 33 cases. Mantle cell lymphoma was identified in 15 cases.

3.2.2. Histopathological characteristics of Gastrointestinal Lymphoma

3.2.2.1. General Histopathological Characteristics of Gastrointestinal Lymphoma

The most common histological pattern was the diffuse form (90.6%). Regarding cell size, large cells were most frequently observed (48.5%), followed by mixed small and medium-sized cells (17.6%), and mixed medium and large-sized cells (13.8%). Lymphoepithelial lesions were found in 13.8% of gastrointestinal lymphoma cases. In the histopathological diagnosis of gastrointestinal lymphoma patients, the majority were diagnosed with non-Hodgkin lymphoma (69.2%)

3.2.2.2. Histopathological characteristics of diffuse large B-cell lymphoma

All cases of DLBCL exhibited a diffuse growth pattern (100%). Most tumor cells were large in size (77.8%). The predominant cellular morphology was a mixture of centroblasts and immunoblasts (72.7%), followed by pure centroblasts (17.2%) and pure immunoblasts (10.1%). No cases showed anaplastic morphology.

3.2.2.3. Histopathological characteristics of mucosa-associated lymphoid tissue lymphoma

All cases exhibited a diffuse growth pattern (100%), with a mixture of small and medium-sized cells in 59.4% of cases. The predominant morphological subtypes included monocytoid cells (43.7%), centrocyte-like cells (25%), plasmacytoid cells (18.7%),

and small lymphocytes (12.6%). Lymphoepithelial lesions were observed in 62.5% of cases.

3.2.2.4. Histopathological Characteristics of Mantle Cell Lymphoma

Most mantle cell lymphomas in the gastrointestinal tract exhibited a nodular histological pattern (73.3%). In the majority of cases, the tumor cells were of mixed small and medium size (53.3%). No cases showed evidence of lymphoepithelial lesions.

3.2.2.5. Histopathological Characteristics of Small Lymphocytic Lymphoma

Small lymphocytic lymphomas in the gastrointestinal tract exhibited a diffuse growth pattern (2 out of 2 cases). No cases showed evidence of lymphoepithelial lesions or plasmacytic differentiation

3.2.2.6. Histopathological Characteristics of Follicular Lymphoma and Duodenal-Type Follicular Lymphoma

Follicular lymphomas in the gastrointestinal tract (including duodenal-type follicular lymphoma) exhibited a follicular growth pattern in all cases (4/4). All tumors consisted of medium-sized cells (4/4 cases) and were classified as histological grade 1 (4/4 cases). No cases showed evidence of lymphoepithelial lesions or plasmacytic differentiation.

3.2.2.7. T-cell–origin gastrointestinal lymphoma

T-cell lymphomas in the gastrointestinal tract exhibited a diffuse growth pattern in all cases (6/6). Tumor cells were small in 2 out of 6 cases and medium-sized in 4 out of 6 cases. No cases showed evidence of lymphoepithelial lesions or plasmacytic differentiation.

3.2.2.8. Correlation between histopathological classification

orientation and immunohistochemical results

Histopathology can provide orientation toward certain lymphoma subtypes such as DLBCL, MALT, and MCL. Their specificity ranges from 97% to 99%. The positive predictive value (PPV) for DLBCL reaches up to 93%, while for MALT it is 67%. MCL has no positive predictive value, but its negative predictive value (NPV) is as high as 90%.

3.3. THE RELATIONSHIP BETWEEN PATHOLOGY TYPE AND ENDOSCOPIC FEATURES OF GASTROINTESTINAL LYMPHOMA

3.3.1. The Relationship Between Lesion Location and pathology type

The most common site for DLBCL (69 out of 99 cases) and MALT (23 out of 33 cases) was the stomach. MCL (Mantle Cell Lymphoma) was found at nearly all investigated sites, with a relatively even distribution. TCL (T-cell Lymphoma) was not found in the rectum or duodenum. There was a statistically significant association between lesion location and immunophenotype ($p < 0.001$).

3.3.4. The Relationship Between Endoscopic Features and Pathology type

MALT and DLBCL lymphomas primarily exhibited superficial lesion types on endoscopy, with 19 out of 33 cases and 53 out of 99 cases, respectively. There was a statistically significant association between endoscopic lesion characteristics and immunophenotype ($p = 0.002$).

3.3.5. The Relationship Between Endoscopic Features and Pathology type Group

There was a statistically significant association between endoscopic lesion characteristics and the immunophenotypic groups of aggressive and indolent lymphomas ($p < 0.05$).

CHAPTER 4. DISCUSSION

4.1. General, clinical, and endoscopic characteristics

4.1.1. General Characteristics of the Study Sample

A study by Vu Thanh Huyen conducted from 2019 to 2022 at K Hospital showed that the most common age range for gastrointestinal non-Hodgkin lymphoma was 50–70 years (59.8%), with a mean age of 54.62 ± 12.69 years. The male-to-female ratio in the study sample was approximately 3:2, and the gender difference was statistically significant ($p = 0.034$).

4.1.2. Clinical characteristics

The most common symptom is abdominal pain. The majority of cases are detected at a localized stage, with 71.7% in stages I and II, and 28.3% in advanced stages IIE and IV. The rates of complications and B symptoms are 21.4% and 11.3%, respectively. In Wei Wang's study, 27.88% of cases were in early stages (I, II1,2), while 72.12% were in advanced stages (IIE/IV). Most histopathological samples were obtained through endoscopic biopsy (60.4%). The distribution of gastrointestinal lymphoma is consistent with the findings of Nguyen Van Chu.

4.1.3. Endoscopic Characteristics

Previous studies have proposed various classifications to analyze the endoscopic features of the disease. In both groups, the predominant endoscopic appearances were superficial lesions and protruding masses without ulceration.

4.2. HISTOPATHOLOGICAL AND

IMMUNOHISTOCHEMICAL CHARACTERISTICS OF GASTROINTESTINAL LYMPHOMA

4.2.1. Histopathological Characteristics of Gastrointestinal Lymphomas

4.2.1.1. Histopathological Characteristics of Diffuse Large B-Cell Lymphoma

According to the literature and previous studies, DLBCL in the gastrointestinal tract shares similar histopathological features with nodal DLBCL, characterized by large tumor cells and a diffuse infiltrative growth pattern.

4.2.1.2. Histopathological Characteristics of Mucosa-Associated Lymphoma

In our study, lymphoepithelial lesions were observed in 62.5% of cases of mucosa-associated lymphoma in the gastrointestinal tract.

4.2.1.3. Histopathological Characteristics of Mantle Cell Lymphoma

In our study, most mantle cell lymphomas in the gastrointestinal tract exhibited a nodular histological pattern (73.3%). There was a mixture of small and medium-sized cells (53.3%), and no cases showed lymphoepithelial lesions.

4.2.1.4. Histopathological Characteristics of Small Lymphocytic Lymphoma

There were two cases, both showing diffuse proliferation of small-sized lymphocytes.

4.2.1.5. Histopathological Characteristics of Follicular Lymphoma and Duodenal-Type Follicular Lymphoma

In our study, there were four cases of follicular

lymphoma in the gastrointestinal tract, including two cases of duodenal-type follicular lymphoma. The tumor cells were uniform, forming atypical follicular structures with a high density of follicles, poorly defined mantle zones, and absence of tangible-body macrophages.

4.2.1.6. Histopathological Characteristics of T-cell Lymphoma

All cases showed a diffuse pattern of tumor cells. The size of the tumor cells varied: two cases had small-sized cells, and four cases had medium-sized cells. According to the literature and previous studies, the histopathology of T-cell lymphoma in general, and in the gastrointestinal tract in particular, is relatively diverse.

4.2.2. Immunohistochemical Characteristics of Gastrointestinal Lymphomas

B-cell lymphomas accounted for the majority, representing 97.4% of cases, while T-cell lymphomas made up 2.6%. The proportion of T-cell lymphomas in our study is comparable to that reported by Nguyen Van Chu (2006), but lower than the findings of Tran Huong Giang (2011).

4.2.2.1. Immunohistochemical Characteristics of Diffuse Large B-Cell Lymphoma

CD20 expression was positive in 100% of cases, and CD79a positivity ranged from 64% to 73%. Diffuse large B-cell lymphoma is classified into two subtypes: the germinal center B-cell-like (GCB) subtype and the activated B-cell-like (ABC) subtype. Hans et al. proposed a classification algorithm using three markers—CD10, BCL6, and MUM1—with a positivity threshold of ≥30% of tumor cells for each marker. Other classification algorithms used for DLBCL subtyping include

those by Muris, Choi, and Tally.

4.2.2.2. Immunohistochemical Characteristics of Mucosa-Associated Lymphoid Tissue Lymphoma

Tumor cells showed strong positivity for B-cell markers, with CD20 expressed in 100% of cases and CD79a in 75%. A smaller proportion of tumor cells were positive for Bcl2 (33%) and MUM1 (22%).

4.2.2.3. Immunohistochemical Characteristics of Mantle Cell Lymphoma

Mantle cell lymphoma is characterized by proliferating lymphoid cells that are positive for CD20, CD5, and Cyclin D1. The role of SOX11 in diagnosing mantle cell lymphoma involving both lymph nodes and the gastrointestinal tract is considered complementary to Cyclin D1.

4.2.2.4. Immunohistochemical Characteristics of Rare Gastrointestinal Lymphoma Subtypes

There were two cases of small lymphocytic lymphoma (SLL), in which tumor cells were completely positive for CD20, CD79a, CD23, and CD5. Six cases of T-cell lymphoma were identified: four were positive for the CD3 marker, while two CD3-negative cases were stained for CD4 and showed positive results; two cases stained for CD8 were negative.

4.2.3. Correlation Between Histopathological Classification and Immunohistochemical Results

The sensitivity of identifying gastrointestinal lymphoma subtypes based on histopathological orientation alone was relatively low (0–28%), while the specificity was high (97%). This finding is consistent with previous studies and literature,

which indicate that it is very difficult to distinguish these cells from other lymphoid cell types within the lymphoid population.

4.3. ASSOCIATION BETWEEN ENDOSCOPIC FEATURES AND PATHOLOGY TYPE OF GASTROINTESTINAL LYMPHOMAS

4.3.1. Association Between Lesion Location and Pathological type Classification

The most common site of involvement for both DLBCL (70%) and MALT (68.8%) was the stomach. There was a statistically significant difference in the distribution of immunophenotypic types at the gastric site ($p < 0.001$).

4.3.2. Association Between Endoscopic Lesion Patterns and Pathological type

MALT and DLBCL lymphomas predominantly presented with superficial-type lesions on endoscopy, accounting for 59.4% and 53.8% of cases, respectively. There was a statistically significant association between endoscopic lesion characteristics and immunophenotypes ($p = 0.012$). This difference was particularly evident in the superficial lesion type ($p < 0.001$).

4.3.3. Association Between Endoscopic Lesion Patterns and Pathological type Groups

There is a statistically significant association between the endoscopic lesion characteristics and the two groups of lymphomas—indolent and aggressive types ($p < 0.05$).

DO LIMITATIONS OF THE STUDY

Due to research constraints, we were unable to classify gastric T-cell lymphomas into specific subtypes according to the World

Health Organization (WHO) classification. Additionally, some histological subtypes have a low prevalence, making it difficult to identify all corresponding immunophenotypes and their associations with other clinical and pathological features.

CONCLUSION

1. Histopathological and Immunohistochemical Characteristics of Gastrointestinal Lymphomas

Diffuse large B-cell lymphoma (DLBCL) accounted for 62.3%, mucosa-associated lymphoid tissue (MALT) lymphoma for 20.7%, mantle cell lymphoma (MCL) for 9.4%, T-cell lymphoma (TCL) for 3.8%, and follicular lymphoma (FL), duodenal-type follicular lymphoma (D-FL), and small lymphocytic lymphoma (SLL) each accounted for 1.3%. 100% of DLBCL cases exhibited a diffuse growth pattern; 77.8% had large tumor cells, and 72.7% showed a mixed morphology of centroblasts and immunoblasts. 100% of MALT cases also had a diffuse pattern, with small to medium-sized tumor cells in 59.4% of cases. Monocytoid cell morphology was observed in 43.7%, and lymphoepithelial lesions were present in 62.5% of cases. MCL cases predominantly showed a nodular histological pattern (73.3%), with tumor cells of mixed small and medium size in 53.3% of cases..

2. Immunohistochemical Phenotypes of Gastrointestinal Lymphomas and Relationship between Endoscopic features and Pathological type

Among DLBCL-ABC subtype (56%), two immunophenotypes were identified:

CD20/CD79a+, CD3−, CD10−, Bcl6− (45%)

CD20/CD79a+, CD3−, CD10−, Bcl6+, MUM1+ (55%)

Among DLBCL-GCB subtype (44%), two immunophenotypes were identified:

CD20/CD79a+, CD3−, CD10+ (86%)

CD20/CD79a+, CD3−, CD10−, Bcl6+, MUM1− (14%)

MCL: CD20/CD79a+, CD3−, Cyclin D1+, SOX11+/− (100%)

MALT: two immunophenotypes were identified:

CD20/CD79a+, CD3−, Cyclin D1−, CD10/Bcl6−, CD5− (79%)

CD20/CD79a+, CD3−, Cyclin D1−, CD10/Bcl6−, CD5+, CD23− (21%)

Aggressive lymphomas were more frequently detected at stage IV compared to indolent lymphomas.

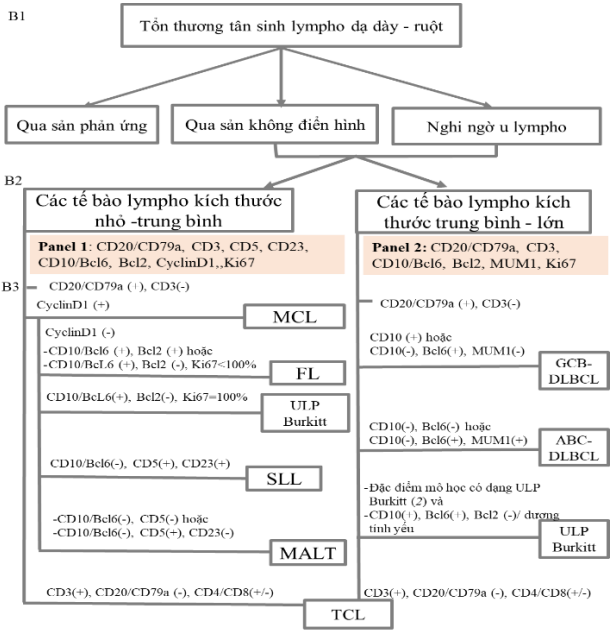
Lesion locations were most commonly found in the stomach (60.4%), followed by the jejunum (11.9%) and colon (10.1%) ($p < 0.001$).

Superficial lesions were the predominant endoscopic feature in MALT lymphomas (59.4%) and DLBCL (53.6%) ($p < 0.001$).

Endoscopic lesion characteristics were significantly associated with immunophenotypic groups ($p < 0.05$).

RECOMMENDATION

We propose a summarized diagnostic and histological classification approach for common types of gastrointestinal lymphomas, based on histopathology and immunohistochemistry, consisting of the following four steps:



B4: Chẩn đoán xác định dựa trên sự tương thích với mô bệnh học

ABC: activated-B-cell**; GCB:** germinal-center B-cell**; MALT**: mucosa-associated lymphoid tissue; **MCL**: mantle cell U LYMPHO ; **SLL**: small lymphocytic lymphoma; **DLBCL**: diffuse large B-cell; **FL**: follicular lymphoma; **TCL**: T-cell lymphoma.

LIST OF PUBLICATIONS BY THE DOCTORAL CANDIDATE

1. Dang Cong Thuan, **Nguyen Duy Thinh**, Nguyen Tran Bao Song, Nguyen Van Mao, Phan Trung Nam, Ngo Quy Tran, Tran Thi Nam Phuong, Nguyen Thanh Tung, Le Thi Tam, Le Vi, Tran Thi Hoang Lien (2023). "First approach on gastrointestinal lymphoma classification based on histopathology and immunohistochemistry". *Journal of Medicine and Pharmacy*, Hue University of Medicine and Pharmacy, Vol. 13(01), pp. 90–97.

2. **Nguyen Duy Thinh**, Dang Cong Thuan, Nguyen Tran Bao Song, Ngo Quy Tran, Tran Thi Nam Phuong (2021). "The Role of Immunohistochemistry in the Diagnosis and Classification of Gastrointestinal Lymphomas". *Journal of Medicine and Pharmacy*, Hue University of Medicine and Pharmacy, Vol. 11(06), pp. 7–14.

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