Review Article

A review of recent advances in the diagnosis of gastrointestinal lymphoma

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Abstract

A broad category of malignancies that develop in the digestive system, gastrointestinal lymphomas include a variety of histological subtypes and clinical manifestations. Significant advancements have been achieved in the knowledge, diagnosis, and treatment of various lymphomas in recent years. This review article offers an overview of the most recent discoveries in the study of gastrointestinal lymphoma, with a particular focus on advancements in diagnostic plans. The article examines developments in histopathology and molecular classification, emphasizing their influence on the diagnosis and prognosis of diseases. It also looks at how endoscopic and imaging techniques are advancing in their use for proper staging and early diagnosis of gastrointestinal lymphomas. This article provides a thorough update on the state-of-the-art in identifying and treating gastrointestinal lymphoma through the synthesis of recent literature and research findings, highlighting the possibility for better patient outcomes and increased quality of life.

Key words

Gastrointestinal lymphoma, Helicobacter pylori, Diagnosis, Treatment, Recent advancement.

Introduction

Over the past two to three decades, there has been an increase in the incidence of lymphoma. It has been shown that extra nodal forms have increased [1, 2]. The most frequent extra nodal region where lymphoma occurs, accounting for 5%–20% of all cases, is the digestive tract [3]. But about 1% to 4% of gastrointestinal malignancies are primary gastrointestinal lymphomas (PGL), making them extremely uncommon. The common nodal illnesses usually come second to gastrointestinal lymphoma [4]. Although practically any part of the gastrointestinal system can develop lymphoma, the stomach, small intestine, and ileocecal region are the areas most frequently affected in terms of its occurrence [5, 6].

Patients over the age of 50 are more prone to develop PGL, while patients in their second decade of life may also be impacted [7, 8]. Males have a 2–3 times greater chance than females of developing PGL [9, 10]. According to histopathology, only a small percentage of Hodgkin lymphoma and T-cell lymphomas and PGL are of the B-cell lineage. Due to the lack of diagnostic techniques and the symptoms' resemblance to those of other gastrointestinal illnesses, diagnosing gastrointestinal lymphoma has historically been difficult. The diagnosis procedure has been revolutionized by the development of improved imaging techniques, endoscopic advancements, and molecular markers, which has allowed for early detection, precise staging, and wise treatment choices. The development of customized therapy approaches that take into consideration the distinctive characteristics of each patient's disease has been made possible by this shift towards more accurate diagnostics.

There have been notable advancements in the therapeutic options for gastrointestinal lymphomas as well. While traditional chemotherapy is still a key component of therapy, targeted treatments, immunomodulatory drugs, and combination regimens have emerged in recent years that exhibit promise efficacy with minimal side effects. These cutting-edge therapeutic approaches could lead to better patient outcomes, especially in cases of recurrent or resistant disease. This review seeks to synthesize and offer a thorough overview of the most recent discoveries in the diagnosis and treatment of gastrointestinal lymphoma in light of these paradigm-shifting advancements. This article aims to contribute to a deeper understanding of the current state-of-the-art and shed light on the future directions that hold promise for further improving the management of this complex group of malignancies by analyzing the key developments, difficulties, and prospects in the field.

Epidemiology

Based on specific clinical and genetic characteristics, the WHO broadly divides lymphoid neoplasms into four categories: mature B-cell, mature T-cell, and natural killer cell neoplasms, as well as Hodgkin's lymphomas [11]. Hodgkin's lymphoma that has spread outside of its nodes is extremely uncommon. Extranodal GI B-cell lymphomas are more prevalent than T-cell lymphomas (80% of the total), more chemosensitive, and have a better prognosis [12]. A pathological diagnosis of lymphomas is aided by the majority of them exhibiting fairly regular architectural characteristics and certain chromosomal abnormalities.

The GI tract is the most frequent site for extranodal lymphoma, with GI lymphomas accounting for 1%–4% of all GI malignancies, 10%–15% of all non-Hodgkin's lymphomas (NHL), and 30%–40% of all extranodal NHLs [13]. The stomach, small bowel, and colorectum

are the three anatomical locations where cancers are most frequently found; oesophageal lymphoma is quite uncommon [14, 15]. The anatomical distribution in one significant research of primary GI NHLs was as follows: gastric—74.8%; small bowel—8.6%; and ileocaecal—7.0%. 6.5% of the time, multiple places were identified [17].

GI lymphomas often manifest in the sixth decade of life and are slightly more frequent in men [18]. The difficulty for the clinical gastroenterologist is that these tumors might present in a wide range of symptoms, from non-specific ones like dyspepsia or bloating to those that are particular like abdominal pain, nausea, emesis, GI bleeding, diarrhoea, weight loss, or stool blockage. Endoscopic evaluation using biopsies that is properly guided may be able to produce a conclusive diagnosis and enable the patient to receive final treatment. Biopsies can be subjected to routine histology, immunohistochemistry, flow cytometry, in situ hybridization, and fluorescence in situ hybridization in order to provide the comprehensive data required for the best possible treatment.

Imaging characteristics of gastrointestinal lymphomas

Oropharngeal lymphoma

Extra-nodal lymphoma occurs most frequently in the head and neck area, where it accounts for 10% to 15% of all malignancies. Adenoids, palatine tonsils, the base of the tongue, and the oropharyngeal walls make up most of the Waldeyer's ring, which is where 2.5% of malignant lymphomas first appear. Following the nasopharynx and the base of the tongue as the most often affected sites (> 50% each), are the tonsils [19]. Oropharyngeal lymphoma risk is influenced by a number of variables, including EBV infection. These lymphomas typically afflict people over 50, with males being more likely to develop them. Airway blockage, ear ache, a localized increase in size without any pain, dysphagia, and the perception of a foreign body in the throat are typical clinical manifestations. In more than half of patients with tonsillar lymphoma, there is cervical lymphadenopathy [20].

Diffuse large B-cell lymphoma (DLBCL), the most prevalent subtype of non-Hodgkin lymphoma (NHL), accounts for more than 80%–90% of oropharyngeal lymphomas [21]. Histologically, DLBCL is identified by intermediate-large cells that express pan-B-cell antigens. Occasionally, a translocation between the BCL-2 and IgH genes is visible [22]. The marginal zone MALT lymphomas, peripheral T-cell lymphomas, follicular lymphomas, and mantle cell lymphomas (MCLs) are other lymphomas in the Waldeyer's ring. Rare cases of Hodgkin lymphoma (HL) in the oropharynx often have a specific immunophenotype of Reed-Sternberg cells and are lymphocyte-predominant or nodular sclerosis in nature [23].

Oropharyngeal lymphoma frequently presents radiographically as a lobular mass close to the root of the tongue, with nodular mucosa overlaying it in barium tests. It can be difficult to tell them apart from pharyngeal carcinomas. Imaging methods like CT or PET with FDG and CT (PET/CT) are essential for illness diagnosis, staging, and determining how effectively treatments are working. A short clinical history, a sizable homogeneous mass that displaces rather than invades nearby tissues, and sizable homogeneous non-necrotic cervical nodes are some imaging characteristics that may suggest NHL [24].

Esophageal lymphoma

Less than 1% of all gastrointestinal lymphomas involve the oesophagus, making it a rare site for lymphoma involvement. The majority of instances of esophageal lymphoma are caused by extension from gastric lymphoma or metastases from cervical or mediastinal lymph nodes. Less than 30 cases of primary esophageal lymphoma have been documented in the literature, making it extremely uncommon [25-27]. DLBCL (diffuse

large B-cell lymphoma) is the subtype of primary esophageal lymphoma that predominates. Other lymphoma forms, such as MALT lymphoma, mantle cell lymphoma (MCL), T-cell lymphoma, and Hodgkin lymphoma (HL), have been associated with the oesophagus in a small number of cases [27-30].

Esophageal lymphoma's precise cause is still unknown, and it's unclear how much EBV contributed to the disease's emergence. In immunocompromized people, esophageal lymphoma is more frequent, and HIV infection is a possible risk factor. Common symptoms include dysphagia, odynophagia, weight loss, chest pain, and complications include bleeding, blockage, or perforation with the development of a tracheoesophageal fistula. The age of presentation varies. Typical absences of constitutional B symptoms including fever and nocturnal sweats. The majority of primary esophageal lymphomas are DLBCLs that have immunofluorescent staining for immunoglobulin G and light chain in the positive range. Unlike in the stomach, the oesophagus' MALT lymphoma is not connected to H. pylori infection. The oesophagus is frequently involved in a multifocal presentation of follicular lymphoma in the gastrointestinal system, and HL of the oesophagus is a very uncommon condition.

Esophageal lymphoma's nonspecific radiological and endoscopic features make it difficult to distinguish it from other benign and malignant diseases. Stricture, ulcerated masses, submucosal nodules, varicoid patterns, achalasia-like patterns, aneurysmal dilatation, and the development of tracheoesophageal fistulas are only a few radiographic patterns. Endoscopic features might be ulcerated and stenotic to nodular and polypoidal. EUS is a useful tool for determining the depth of invasion and structural abnormalities. CT scans play a crucial role in staging, treatment planning, monitoring outcomes, and relapse detection by assessing extraluminal extension, mediastinal involvement, and lymph node status [31]. Despite variations in FDG uptake caused by tumour features and other factors, PET/CT has become crucial for staging and follow-up, particularly for extranodal involvement of Hodgkin's and non-Hodgkin's lymphoma. Diffuse large B-cell non-Hodgkin lymphoma of the oesophagus is characterized by circumferential wall thickening and enhanced FDG uptake on PET/CT imaging [32].

Gastric lymphoma

60%–75% of cases of gastrointestinal involvement occur in the stomach, with the small bowel, the ileocecal area, and the rectum following [33]. Between 3% and 5% of all malignant stomach tumors are gastric lymphomas [34]. It's interesting to note that while the prevalence of stomach cancer has dropped, that of primary gastric lymphoma has increased [35]. The majority of MALT lymphomas are thought to be caused by H. pylori infection, while the exact mechanism is still unclear [36]. Through the multiplication of B cells sparked by tumor-infiltrating T cells, chronic inflammation brought on by H. pylori may facilitate malignant transformation. H. pylori may also be a factor in the emergence of DLBCL, and some trials have demonstrated complete recovery with eradication therapy alone. Notably, people who test positive for HBsAg have a higher chance of developing NHL, particularly B-cell NHL [37]. In contrast, primary gastric lymphomas with a T-cell phenotype are rather rare, making up just 7% of primary gastric lymphomas in endemic areas with HTLV-1 infection. Adult T-cell leukaemia frequently affects the stomach secondarily. There have been isolated reports of primary gastric T-cell lymphomas without HTLV-1 infection [38]. Patients with gastric lymphoma are often older than 50 and more likely to be men. Gastric lymphoma's non-specific clinical signs can coexist with both benign and malignant disorders. Weight loss, nausea, vomiting, and occasionally a discernible abdominal mass are among the common complaints. Epigastric pain is another. Constitutional B symptoms are uncommon, and lymphadenopathy is uncommon,

in contrast to nodal lymphoma. These situations rarely involve perforation, hemorrhage, or blockage.

While necessary for the initial diagnosis, follow-up care, and collection of biopsy samples in cases with gastric lymphoma, endoscopy does not provide a clear differentiation between gastric lymphoma and the more frequent stomach carcinoma [39]. Endoscopy distinguishes between three main patterns: polypoid bulk, diffuse infiltration, and ulceration. These patterns, however, are not very specific. Despite its drawbacks, endoscopy is still a useful diagnostic technique. An important technique for determining the size of the lesion and the degree of invasion is endoscopic ultrasonography (EUS) [40]. On EUS, lesions typically show up as hypoechoic, while some examples of hyperechoic lesions have been documented. Infiltrative cancer frequently grows vertically into the stomach wall, whereas lymphoma frequently extends horizontally and involves more perigastric lymph nodes. The detection of perigastric lymph nodes and the depth of lymphomatous infiltration are two things that EUS is very good at identifying [41]. By making it easier to distinguish between lymphoma and carcinoma in both their early and advanced phases, this new knowledge supports therapy planning.

Double-contrast upper gastrointestinal (UGI) examinations have revealed radiographic patterns of gastric lymphoma that include ulcers, polypoid masses, thickened folds, mucosal nodularities, and infiltrating lesions. Although these patterns are suggestive, it is difficult to distinguish lymphoma from other benign and malignant diseases. Even with significant gastric fold thickening, the preservation of stomach distensibility and pliability is more indicative of lymphoma. In low-grade lymphoma, abdominal lymphadenopathy is less frequent and stomach wall thickening is typically less severe on CT scans than in high-grade lymphoma. Although it is not specific, preservation of the fat plane without invasion of neighbouring structures may indicate lymphoma. The presence of large lymph nodes and transpyloric spread, as well as lymphadenopathy that extends below the renal hilum, are signs that are more suggestive of lymphoma rather than carcinoma [42, 43]. Mesenteric masses, submucosal infiltration irregularities, annular constricting lesions, exophytic tumour growth, and mesenteric/retroperitoneal lymphadenopathy are all MRI findings. On T1-weighted images, tumours frequently have intermediate signal intensities, but on T2-weighted images, they have heterogeneously elevated signal intensities. Enhancement is typically mild to moderate following gadolinium dimeglumine IV injection [44]. Due to physiological FDG activity in the stomach and varying absorption across several histologic subtypes, the use of 18F-FDG PET/CT for the diagnosis of gastric lymphoma is complicated. According to the research, aggressive gastric lymphoma typically displays stronger uptake than low-grade MALT lymphoma [45].

Small intestinal lymphoma

Small intestinal primary malignant tumors make up fewer than 2% of all gastrointestinal malignancies, making them extremely uncommon. Among these, lymphoma makes up 20%–30% of all primary gastrointestinal lymphomas and 15%–20% of all small intestine neoplasms. The jejunum (20%–25%), the duodenum (6%–8%), and other sites (8%–9%) are the next most often afflicted sites after the ileum (60%–65%) [46].Depending on the lymphoma's histological subtype, the age of manifestation varies. Small intestinal lymphoma does not have any distinct clinical symptoms. Colicky stomach pain, nausea, vomiting, weight loss, and, while infrequently, acute obstructive symptoms such intussusceptions, perforation, or diarrhoea are common in patients [47].

With the development of push-and-pull enteroscopy and capsule endoscopy (CE), the evaluation of small intestinal lymphoma has

undergone a fundamental change. These developments have made biopsies and interventions possible and have lessened the need for complicated surgical operations. However, because lymphoma might present on CE as a tumour, polyp, or ulcer, CE observations and discoveries using these techniques cannot clearly distinguish small intestinal lymphoma from other lesions [48]. Small intestine lymphoma is difficult to distinguish from other benign and malignant illnesses due to the lack of specificity in its radiological features. The polypoid shape, many nodules, infiltrative form, endoexoenteric form with excavation and fistulization, and mesenteric invasive form with an extraluminal mass are common characteristics found on barium studies and CT scans. The pathological subtypes of lymphoma rarely directly correlate with these radiological features. However, several salient characteristics merit attention. Though it is uncommon, multiple lymphomatouspolyposis can be seen in MCL, follicular lymphoma, and MALT lymphoma. Burkitt lymphoma frequently manifests as a large mass in the lower right quadrant. The proximal small intestine is frequently affected by IPSID, which manifests as mucosal fold thickness, irregularity, and speculation [49].

Conclusion

In conclusion, significant developments in gastrointestinal lymphoma detection and treatment have revolutionized the treatment of this wide range of cancers in recent years. By combining genetic and histological classifications, disease has been more accurately characterized, allowing for individualized treatment plans and precise prognostication. Early detection and accurate staging have been made possible by non-invasive diagnostic methods like endoscopy and sophisticated imaging techniques, which have also facilitated prompt therapies. With significant responses seen in clinical studies, the development of targeted treatments and Immunomodulatory drugs has given patients with refractory or relapsed illness fresh hope. With continuing research attempting to identify new therapeutic targets, improve treatment protocols, and improve patient outcomes, the management of gastrointestinal lymphoma appears to have a bright future. The need for standardized guidelines, larger prospective studies, and long-term follow-up data to evaluate the efficacy and safety of developing therapeutic modalities are obstacles that still need to be overcome. In order to successfully navigate the difficulties of gastrointestinal lymphoma care, multidisciplinary teams made up of oncologists, hematologists, radiologists, pathologists, and gastroenterologists will be essential.

References

1. Groves F, Linet M, Travis L, Devesa S. Cancer surveillance series: non-Hodgkin's lymphoma incidence by histologic subtype in the united states from 1978 through 1995. J Natl Cancer Inst., 2000; 92(15): 1240-1251.
2. Chiu B, Weisenburger D. An update of the epidemiology of nonHodgkin's lymphoma. Clin Lymphoma, 2003; 4(3): 161-168.
3. Freeman C, Berg JW, Cutler SJ. Occurrence and prognosis of extranodal lymphomas. Cancer, 1972; 29: 252–260.
4. Al-AkwaaAM, Siddiqui N, Al-Mofleh IA. Primary gastric lymphoma. World J Gastroenterol., 2004; 10(1): 5-11.
5. Herrmann R, Panahon AM, Barcos MP, Walsh D, Stutzman L. Gastrointestinal involvement in non-Hodgkin's lymphoma. Cancer, 1980; 46: 215–222.
6. Herrmann R, Panahon AM, Barcos MP, et al. Gastrointestinal involvement in non-Hodgkin's lymphoma. Cancer, 1980; 46(1): 215-222.
7. Kyriacou C, Loewen RD, Gibbon K, et al. Pathology and clinical features of gastrointestinal lymphoma in Saudi Arabia. Scott Med J., 1991; 36(3): 68-74.
8. Kitamura K, Yamaguchi T, Okamoto K, et al. Early gastric lymphoma: a clinicopathologic study of ten patients,

literature review, and comparison with early gastric adenocarcinoma. Cancer, 1996; 77(5): 850-857.

9. Shimm DS, Dosoretz DE, Anderson T, Linggood RM, Harris NL, Wang CC. Primary gastric lymphoma. An analysis with emphasis on prognostic factors and radiation therapy. Cancer, 1983; 52(11): 2044-2048
10. Cogliatti S, Schmid U, Schumacher U, et al. Primary B-cell gastric lymphoma: a clinicopathological study of 145 patients. Gastroenterology, 1991; 101(5): 1159-1170.
11. Swerdlow SH. WHO classification of tumours of haematopoietic and lymphoid tissues. 4th edition revised, Lyon, France: International Agency on Research on Cancer (IARC) Press, 2017.
12. Groves FD, Linet MS, Travis LB, et al. Cancer surveillance series: non-Hodgkin's lymphoma incidence by histologic subtype in the United States from 1978 through 1995. J Natl Cancer Inst., 2000; 92: 1240–51.doi:10.1093/jnci/92.15.
13. Bautista-Quach MA, Ake CD, Chen M, et al. Gastrointestinal lymphomas: morphology, immunophenotype and molecular features. J Gastrointest Oncol., 2012; 3: 209–25. doi:10.3978/j.issn.2078-6891.2012.
14. Morton JE, Leyland MJ, Vaughan Hudson G, et al. Primary gastrointestinal non-Hodgkin's lymphoma: a review of 175 British National lymphoma investigation cases. Br J Cancer, 1993; 67: 776–82. doi:10.1038/bjc.1993.141
15. Peng JC, Zhong L, Ran ZH. Primary lymphomas in the gastrointestinal tract. J Dig Dis, 2015; 16: 169–76. doi:10.1111/1751-2980.12234
16. Koch P, del Valle F, Berdel WE, et al. Primary Gastrointestinal Non-Hodgkin's Lymphoma: I. Anatomic and Histologic Distribution, Clinical Features, and Survival Data of 371 Patients Registered in the German Multicenter Study GIT NHL 01/92. J Clin Oncol, 2001; 19: 3861–73. doi:10.1200/JCO.2001.19.18.3861Abstract/FREE Full Text
17. Cardona DM, Layne A, Lagoo AS. Lymphomas of the gastro-intestinal tract - pathophysiology, pathology, and differential diagnosis. Indian J Pathol Microbiol, 2012; 55: 1–16.
18. Yuen A, Jacobs C. Lymphomas of the head and neck. Semin Oncol., 1999; 26: 338–345.
19. Kemp S, Gallagher G, Kabani S, Noonan V, O'Hara C. Oral non-Hodgkin's lymphoma: review of the literature and World Health Organization classification with reference to 40 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod., 2008; 105: 194–201.
20. Solomides CC, Miller AS, Christman RA, Talwar J, Simpkins H. Lymphomas of the oral cavity: histology, immunologic type, and incidence of Epstein-Barr virus infection. Hum Pathol., 2002; 33: 153–157.
21. López-Guillermo A, Colomo L, Jiménez M, Bosch F, Villamor N, Arenillas L, Muntañola A, Montoto S, Giné E, Colomer D, et al. Diffuse large B-cell lymphoma: clinical and biological characterization and outcome according to the nodal or extranodal primary origin. J Clin Oncol., 2005; 23: 2797–2804.
22. Quiñones-Avila Mdel P, Gonzalez-Longoria AA, Admirand JH, Medeiros LJ. Hodgkin lymphoma involving Waldeyer ring: a clinicopathologic study of 22 cases. Am J Clin Pathol., 2005; 123: 651–656.
23. Elstrom RL, Leonard JP, Coleman M, Brown RK. Combined PET and low-dose, non-contrast CT scanning obviates the need for additional diagnostic contrast-enhanced CT scans in patients undergoing staging or restaging for

lymphoma. Ann Oncol., 2008; 19: 1770–1773.

24. King AD, Lei KI, Ahuja AT. MRI of primary non-Hodgkin's lymphoma of the palatine tonsil. Br J Radiol., 2001; 74: 226–229.
25. Weeratunge CN, Bolivar HH, Anstead GM, Lu DH. Primary esophageal lymphoma: a diagnostic challenge in acquired immunodeficiency syndrome--two case reports and review. South Med J., 2004; 97: 383–387.
26. Carnovale RL, Goldstein HM, Zornoza J, Dodd GD. Radiologic manifestations of esophageal lymphoma. AJR Am J Roentgenol., 1977; 128: 751–754.
27. Coppens E, El Nakadi I, Nagy N, Zalcman M. Primary Hodgkin's lymphoma of the esophagus. AJR Am J Roentgenol., 2003; 180: 1335–1337.
28. Levine MS, Sunshine AG, Reynolds JC, Saul SH. Diffuse nodularity in esophageal lymphoma. AJR Am J Roentgenol., 1985; 145: 1218–1220.
29. Zhu Q, Xu B, Xu K, Li J, Jin XL. Primary non-Hodgkin's lymphoma in the esophagus. J Dig Dis., 2008; 9: 241–244.
30. Kalogeropoulos IV, Chalazonitis AN, Tsolaki S, Laspas F, Ptohis N, Neofytou I, Rontogianni D. A case of primary isolated non-Hodgkin's lymphoma of the esophagus in an immunocompetent patient. World J Gastroenterol., 2009; 15: 1901–1903.
31. Ghimire P, Wu GY, Zhu L. Primary esophageal lymphoma in immunocompetent patients: Two case reports and literature review. World J Radiol., 2010; 2: 334–338.
32. Paes FM, Kalkanis DG, Sideras PA, Serafini AN. FDG PET/CT of extranodal involvement in non-Hodgkin lymphoma and Hodgkin disease. Radiographics, 2010; 30: 269–291.
33. Papaxoinis G, Papageorgiou S, Rontogianni D, Kaloutsi V, Fountzilas G, Pavlidis N, Dimopoulos M, Tsatalas C, Xiros N, Economopoulos T. Primary gastrointestinal non-Hodgkin's lymphoma: a clinicopathologic study of 128 cases in Greece. A Hellenic Cooperative Oncology Group study (HeCOG) Leuk Lymphoma, 2006; 47: 2140–2146
34. Ferrucci PF, Zucca E. Primary gastric lymphoma pathogenesis and treatment: what has changed over the past 10 years? Br J Haematol., 2007; 136: 521–538.
35. Cogliatti SB, Schmid U, Schumacher U, Eckert F, Hansmann ML, Hedderich J, Takahashi H, Lennert K. Primary B-cell gastric lymphoma: a clinicopathological study of 145 patients. Gastroenterology, 1991; 101: 1159–1170.
36. Hussell T, Isaacson PG, Crabtree JE, Spencer J. Helicobacter pylori-specific tumour-infiltrating T cells provide contact dependent help for the growth of malignant B cells in low-grade gastric lymphoma of mucosa-associated lymphoid tissue. J Pathol., 1996; 178: 122–127.
37. Engels EA, Cho ER, Jee SH. Hepatitis B virus infection and risk of non-Hodgkin lymphoma in South Korea: a cohort study. Lancet Oncol., 2010; 11: 827–834.
38. Wang F, Xu RH, Han B, Shi YX, Luo HY, Jiang WQ, Lin TY, Huang HQ, Xia ZJ, Guan ZZ. High incidence of hepatitis B virus infection in B-cell subtype non-Hodgkin lymphoma compared with other cancers. Cancer, 2007; 109: 1360–1364.
39. Sugita S, Iijima T, Furuya S, Kano J, Yanaka A, Ohta K, Kojima H, Noguchi M. Gastric T-cell lymphoma with cytotoxic phenotype. Pathol Int., 2007; 57: 108–114.
40. Taal BG, Burgers JM. Primary non-Hodgkin's lymphoma of the stomach: endoscopic diagnosis and the role of

surgery. Scand J Gastroenterol Suppl., 1991; 188: 33–37.

41. Püspök A, Raderer M, Chott A, Dragosics B, Gangl A, Schöfl R. Endoscopic ultrasound in the follow up and response assessment of patients with primary gastric lymphoma. Gut., 2002; 51: 691–694.
42. Al-AkwaaAM, Siddiqui N, Al-Mofleh IA. Primary gastric lymphoma. World J Gastroenterol., 2004; 10: 5–11.
43. Ghai S, Pattison J, Ghai S, O'Malley ME, Khalili K, Stephens M. Primary gastrointestinal lymphoma: spectrum of imaging findings with pathologic correlation. Radiographics, 2007; 27: 1371–1388.
44. Lupescu IG, Grasu M, Goldis G, Popa G, Gheorghe C, Vasilescu C, Moicean A, Herlea V, Georgescu SA. Computer tomographic evaluation of digestive tract non-Hodgkin lymphomas. J Gastrointestin Liver Dis., 2007; 16: 315–319.
45. Chou CK, Chen LT, Sheu RS, Yang CW, Wang ML, Jaw TS, Liu GC. MRI manifestations of gastrointestinal lymphoma. Abdom Imaging., 1994; 19: 495–500.
46. Schottenfeld D, Beebe-Dimmer JL, Vigneau FD. The epidemiology and pathogenesis of neoplasia in the small intestine. Ann Epidemiol., 2009; 19: 58–69.
47. Li B, Shi YK, He XH, Zou SM, Zhou SY, Dong M, Yang JL, Liu P, Xue LY. Primary non-Hodgkin lymphomas in the small and large intestine: clinicopathological characteristics and management of 40 patients. Int J Hematol., 2008; 87: 375–381.
48. Pennazio M. Small-intestinal pathology on capsule endoscopy: spectrum of vascular lesions. Endoscopy, 2005; 37: 864–869.
49. Chung HH, Kim YH, Kim JH, Cha SH, Kim BH, Kim TK, Kim AR, Cho SJ. Imaging findings of mantle cell lymphoma involving gastrointestinal tract. Yonsei Med J., 2003; 44: 49–57.