Multimodality Treatment of Gastric Lymphoma

Naruhiko Ikoma, MD[a], Brian D. Badgwell, MD, MS[a], Paul F. Mansfield, MD[b,*]

KEYWORDS

• Primary gastric lymphoma • Chemotherapy • Radiation therapy
• *Helicobacter pylori* infection • Surgery

KEY POINTS

- Primary gastric lymphoma is rare.
- Appropriate use of multimodality therapy guided by tumor stage, histology subtypes, status of *Helicobacter pylori* infection, and status of t(11;18) translocation, can result in excellent outcomes in gastric lymphoma.
- Surgical resection has limited value in the treatment of gastric lymphoma.

INTRODUCTION

Non-Hodgkin lymphoma (NHL), which is more common than Hodgkin lymphoma, can be classified as nodal or extranodal. The gastrointestinal tract is the predominant site of extranodal NHL, accounting for 4% to 20% of all NHL cases and 30% to 45% of all extranodal cases.[1–4] The stomach is the most commonly affected site along the gastrointestinal tract (60%–75%) and can be a primary or secondary site.[5,6] Nevertheless, gastric NHL only accounts for 3% of gastric neoplasms and 10% of lymphomas.[7]

Primary gastric NHL has not been defined consistently. Dawson and colleagues[8] originally defined it as a case in which the tumor predominantly involves the stomach and lymphadenopathy is limited to the lymphatic drainage of the stomach, whereas the Danish Lymphoma Study Group defined it as a case in which the stomach or gastrointestinal tract represented 75% or more of the total tumor volume on clinical and radiological assessment.[1] Primary gastric lymphoma arises from the mucosa or submucosal layer, originating from lymphoid tissue in the lamina propria.

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[a] Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Unit 1484, 1515 Holcombe Boulevard, Houston, TX 77030, USA; [b] Acute Care Services, The University of Texas MD Anderson Cancer Center, Unit 1485, 1515 Holcombe Boulevard, Houston, TX 77030, USA
* Corresponding author. Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, 1400 Pressler, FCT 18.6032, Houston, TX 77030.
E-mail address: pmansfie@mdanderson.org

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This article briefly summarizes diagnosis, staging, and subtypes of primary gastric NHL, and discusses multimodality treatment of primary gastric NHL by reviewing important evidences that guide current standard treatment strategy.

PRESENTATION AND DIAGNOSIS

The most common presentation of gastric lymphoma is epigastric pain (78%), followed by appetite loss (47%), unintentional weight loss (25%), bleeding (19%), and vomiting (18%).[6] B symptoms (fever and night sweats) are not common in gastric lymphoma (12%).[6] Often, no signs of disease are found on physical examination; however, palpable masses or lymphadenopathy may be found in patients with advanced disease.

The diagnosis of gastric lymphoma is based on histologic characteristics found on tissue biopsy during upper gastrointestinal endoscopy. A histologic diagnosis is crucial to guiding the treatment strategy. Endoscopic findings of gastric lymphoma include mucosal erythema, polypoid lesions (with or without ulceration), nodularity, ulceration, and mucosal thickening.[9,10] Multiple large and deep biopsies, possibly with endoscopic mucosal resection from both abnormal-appearing and normal-appearing mucosa should be obtained to improve diagnostic accuracy because the tumor can be multifocal or can infiltrate the submucosal layer under normal-appearing mucosa.[11,12]

A staging work-up is necessary to guide the treatment strategy for gastric lymphoma. Chest radiographs and computed tomography scans are the most commonly used imaging techniques for evaluating distant disease. Further evaluation with endoscopic ultrasound[13,14] and positron emission tomography may be beneficial.[15–17] Peripheral blood smear and bone marrow aspiration are fundamental to excluding metastatic disease. Patients with gastric lymphoma should be tested for *Helicobacter pylori* infection due to its importance in treatment. The t(11;18) translocation, which is detectable in one-third of gastric mucosa-associated lymphoid tissue (MALT) lymphoma cases, has demonstrated resistance to various treatments, especially *H pylori* eradication therapies.[18–20] Evaluating t(11;18) using polymerase chain reaction (PCR) or fluorescence in situ hybridization (FISH) is recommended in gastric MALT lymphoma patients.[21] Patients being considered for treatment with rituximab need to be tested for hepatitis B virus infection because rituximab can cause reactivation of the virus.

STAGING

TNM staging is ineffective for lymphoma in general and the Ann Arbor classification, or a modification by Musshoff[22] (**Table 1**), has been applied to gastrointestinal tract lymphoma.[5,6,22–25] The Lugano staging system for gastrointestinal lymphomas, which was a modification of the original Ann Arbor staging system, was introduced to incorporate measures of distant nodal involvement.[26] It has been widely used over the last 2 decades.[27] However, the lack of a uniform staging system has made some historical interstudy comparisons difficult. In brief, a stage I tumor is confined to the stomach and a stage II tumor extends outside of the primary organ but is limited to regional lymph nodes. Stages III and IV represent distant spread disease (the Lugano system has no stage III). Ruskone-Fourmestraux and colleagues[28] introduced the Paris staging system, which describes the depth of gastric wall involvement more accurately.

Disease stage is the most important prognostic factor in gastric lymphoma[6,25]; therefore, accurate staging using a combination of clinical and radiological assessment is essential to providing appropriate treatment.