Gastrointestinal Lymphoma
Radiologic–Pathologic Correlation

Maria A. Manning, MD[a,b,*], Alexander S. Somwaru, MD[b], Anupamjit K. Mehrotra, MD[c], Marc S. Levine, MD[d]

KEYWORDS

• Extranodal • Lymphoma • Gastrointestinal tract • Diagnosis • Imaging • Pathology

KEY POINTS

- Extranodal non-Hodgkin lymphoma is most commonly found in the gastrointestinal tract.
- The most common subtype of extranodal lymphoma found within the gastrointestinal tract is diffuse large B-cell lymphoma.
- The absence of an associated desmoplastic reaction allows these malignant lymphoid cells to expand and penetrate the wall of the gastrointestinal tract, producing characteristic radiographic findings.
- Radiologic imaging is crucial for diagnosis, staging, management, response assessment, surveillance for recurrence, and assessment of complications.

INTRODUCTION

Normal Anatomy and Histology

The gastrointestinal (GI) tract is an important component of the immune system; there are as many lymphocytes in intestinal lymphoid tissue as in the rest of the body.[1] Normal lymphoid tissue exists in varying quantities and types throughout the GI tract. Although the esophagus and stomach have minimal native mucosal lymphoid tissue, the intestines contain abundant lymphoid tissue, predominantly in the mucosa and submucosa, also known as mucosa-associated lymphoid tissue (MALT). This lymphoid tissue has an important role protecting the freely permeable intestinal mucosa against environmental antigens. Chronic antigenic stimulation or inflammation of the GI tract can lead to monoclonal proliferation in typical sites such as the distal ileum or in atypical sites such as the stomach as a response to chronic *Helicobacter pylori* gastritis. Over time, this lymphoproliferation can lead to the development of various forms of GI lymphoma.

Clinical Features

The GI tract is the most common site of extranodal lymphoma.[2–4] Although the stomach contains minimal native lymphoid tissue, it is paradoxically the most common location for extranodal lymphoma in the GI tract, followed by the small intestine (most commonly the distal ileum), colon, and

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[a] American Institute for Radiologic Pathology, 1010 Wayne Avenue, Suite 320, Silver Spring, MD 20910, USA; [b] Division of Abdominal Imaging, Department of Radiology, MedStar Georgetown University Hospital, 3800 Reservoir Road Northwest, Washington, DC 20007, USA; [c] The Joint Pathology Center, 606 Stephen Sitter Avenue, Silver Spring, MD 20910, USA; [d] Department of Radiology, Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104, USA

* Corresponding author. American Institute for Radiologic Pathology, 1010 Wayne Avenue, Suite 320, Silver Spring, MD 20910.

E-mail address: mmanning@acr.org

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rectum.[3,5] GI lymphoma most commonly occurs in patients with generalized lymphoma secondarily involving the GI tract, but some patients can have primary GI lymphoma in the absence of disseminated disease. The definition of primary GI lymphoma varies among authors, but lymphomas that predominantly involve the GI tract and cause (GI) symptoms at the time of presentation are considered primary GI lymphomas, regardless of the presence or absence of lymph node involvement.[6]

There is a slight male predominance for all subtypes of lymphoma, with the exception of follicular cell lymphoma. Other than Burkitt lymphoma, which tends to affect a younger population (median age, 41 years), the majority of patients with primary GI lymphoma (>75%) present after 55 years of age (the average age at diagnosis is approximately 64 years).[3,4,7,8] When patients are symptomatic, they most commonly complain of nonspecific dysphagia or dyspepsia, vague abdominal pain, nausea and vomiting, anorexia, weight loss, and diarrhea, depending on the site of involvement.[9] Patients with more aggressive tumors may present with severe abdominal pain, a palpable mass, or acute GI perforation.[10]

Pathologic Features

Although it would be easy to consider lymphoma as a single disease with a spectrum of histologic grades, lymphomas are actually a heterogeneous group of distinct pathologic entities associated with a wide spectrum of clinical findings. These pathologic and clinical features often enable diagnosis of a specific lymphoma subtype.[11] GI lymphomas are broadly characterized by the World Health Organization as B cell or T cell, with subcategorization as precursor cell or mature cell origins.[12] Non-Hodgkin B-cell lymphomas constitute the majority of primary GI lymphomas in the Western hemisphere. However, there is considerable geographic variation in subtype prevalence; primary GI lymphomas most commonly are diffuse large B cell or extranodal marginal zone B cell of MALT subtype in North America (**Table 1**).[3,4,7]

It is important to understand the underlying pathology and characteristic imaging appearances of the most common types of GI lymphoma, because the evaluation, diagnosis, treatment, and prognosis of these lesions are generally different from those of other, more common cancers of the GI tract.

B-CELL LYMPHOMA

Diffuse Large B-Cell Lymphoma

Diffuse large B-cell lymphoma (DLBCL), the most common form of primary GI lymphoma in adults, most commonly arises in the stomach, although it can be found throughout the GI tract.[3,4,7] DLBCL is an aggressive form of lymphoma that can arise de novo in the GI tract or from progression or transformation of indolent or low-grade small B-cell lymphoma. When DLBCL develops in the stomach, it is commonly associated with chronic *H pylori* infection, and up to 50% of patients have coexisting extranodal marginal zone lymphoma (ENMZL).[13,14] Major risk factors include immunodeficiency states and Epstein–Barr virus (EBV). Prognosis and survival depend on the age of the patient and the stage of the disease at the time of presentation. Progression is rapid, and, if untreated, the prognosis is poor. Nevertheless, excellent responses have been obtained using aggressive combination chemoimmunotherapy with or without concomitant radiation therapy. For a subset of patients with limited stage *H pylori*–related gastric DLBCL, with or without

Table 1
Gastrointestinal extranodal lymphoma by type, frequency and clinical behavior

Lymphoma Type	Frequency (%)	Clinical Behavior
Diffuse large B-cell lymphoma	47	Aggressive; curable (40%)
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue	24	Localized; curable
Follicular lymphoma	8	Indolent- moderately aggressive; incurable
Mantle cell lymphoma	5	Moderately aggressive, bulky disease; incurable
Burkitt lymphoma	5	Aggressive; curable (90%)
Enteropathy associated T-cell lymphoma	3	Poor prognosis owing to abdominal complications