

Lymphoproliferative Diseases of the Gut

A Survival Guide for the General Pathologist



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KEYWORDS

• Gastrointestinal • Lymphoma • Lymphoproliferative • B cell • T cell

Key points

- Although uncommon in comparison with epithelial neoplasms, lymphomas in the gastrointestinal tract are seen on a regular basis by pathologists examining gastrointestinal tissues.
- B-cell lymphomas are far more common than T-cell lymphomas in the gastrointestinal tract, but there are a few T-cell neoplasms that have characteristic presentations and/or associations.
- The most common lymphoma throughout the gastrointestinal tract is diffuse large B-cell lymphoma.
- A pragmatic approach to lymphoma diagnosis as outlined in this article will allow the pathologist to approach most cases encountered on a regular basis.

ABSTRACT

The gastrointestinal tract is the most common extranodal site of involvement by lymphoma, with B-cell tumors outnumbering T-cell tumors by a wide margin. Diffuse large B-cell lymphoma is the most common lymphoid neoplasm involving the gastrointestinal tract; but a variety of other B- and T-cell neoplasms occur in the gastrointestinal organs, often with characteristic associations and/or manifestations. Although the diagnosis of gastrointestinal lymphomas can sometimes seem daunting to general pathologists, a knowledge of the most commonly encountered entities, in combination with a reasoned and pragmatic approach to the diagnostic workup, makes it possible to approach most cases with confidence.

OVERVIEW

Although the gastrointestinal (GI) tract gives rise to many different types of neoplasia, perhaps nothing

strikes fear into the heart of the pathologist the way that an atypical lymphoid infiltrate can. The specter of multiple immunohistochemical stains, correlation with gene rearrangement studies, and decisions regarding the need for additional tissue to send for flow cytometry makes it tempting to package up the entire case and send it to a hematolymphoid specialist. Although lymphomas are uncommon compared with epithelial neoplasms of the GI tract, this organ system is the most common extranodal site of involvement by lymphoma; up to 20% of all lymphomas occur in the GI tract, and they often present with characteristic findings.¹ Despite inherent complexities in lymphoma classification, any pathologist who reviews GI specimens can make a confident diagnosis or at least begin the process, using a rational and pragmatic approach. This article begins with a review of normal and reactive GI tract lymphoid populations followed by specific examples of GI lymphomas. The emphasis is on lymphomas of mature B- and T-cell phenotypes, as these entities are most commonly encountered.

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GASTROINTESTINAL LYMPHOID TISSUE

The normal and acquired lymphoid populations of the GI tract vary in a site-specific fashion depending on the nature of stimuli. The terminal ileum, for example, normally contains a large population of organized lymphoid tissue that is most prominent in children and young adults. These Peyer patches consist of lymphoid follicles/germinal centers surrounded by B-cell containing mantle zones and marginal zones with T lymphocytes in the interfollicular areas. The architecture recapitulates that of a lymph node and represents one type of native mucosa-associated lymphoid tissue (MALT).² Peyer patches may appear as an endoscopically

visible mucosal nodularity or even appear as small polyps that prompt endoscopic biopsy. The lymphoid population in Peyer patches may push aside the normal crypts, flatten the overlying villi (**Fig. 1**), and interdigitate with fibers of the muscularis mucosae (**Fig. 2**); these features should not be overinterpreted as atypical. Similar aggregates are scattered throughout the GI tract.

Acquired MALT refers to lymphoid infiltrates that develop in response to a stimulus, such as chronic gastritis associated with *Helicobacter pylori*.² Infection with *H pylori* elicits a dense, bandlike infiltrate of plasma cells and lymphocytes in the superficial (foveolar or pit) compartment of the gastric mucosa (**Fig. 3A**). Organized lymphoid

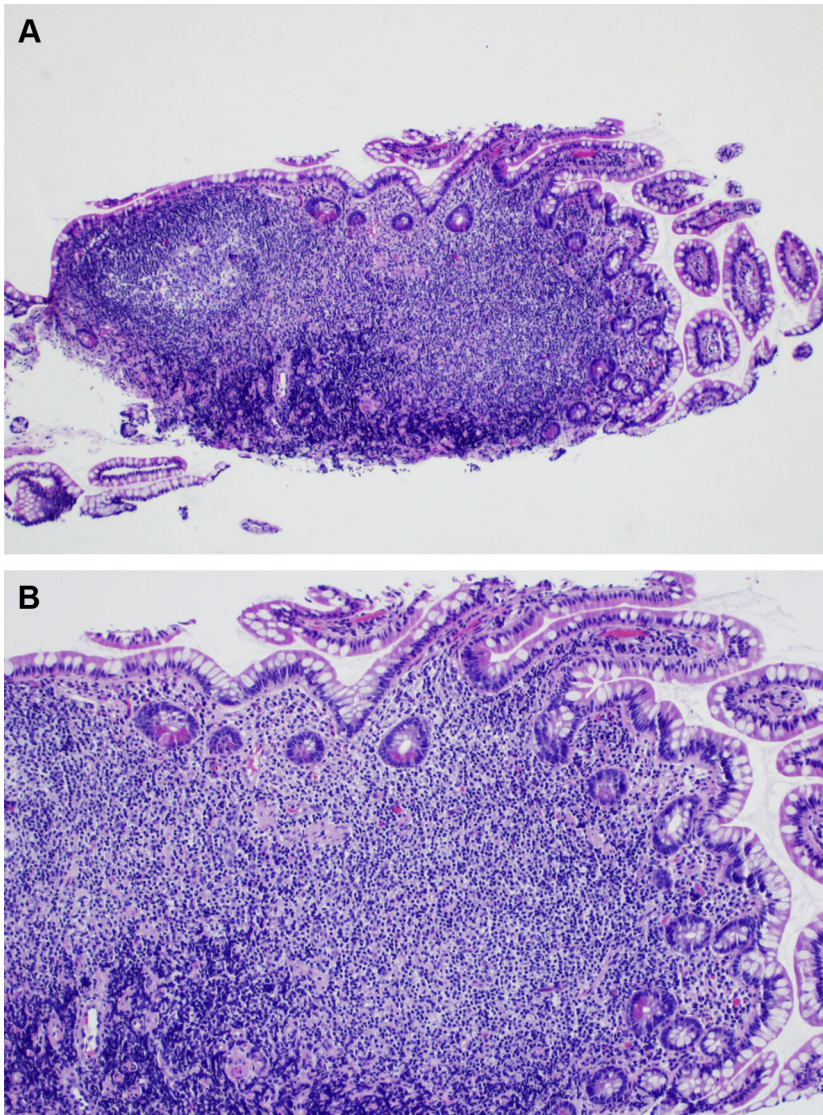


Fig. 1. A typical Peyer patch is seen in a biopsy from the terminal ileum. (A) Note the flattened area of mucosa toward the left of the lymphoid aggregate (H&E, original magnification $\times 40$). (B) At higher magnification, the benign lymphoid infiltrate can be seen among the intestinal crypts, which are otherwise intact (H&E, original magnification $\times 100$).

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