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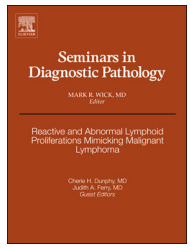

Barrett esophagus: Diagnostic challenges

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ABSTRACT

The incidence of esophageal adenocarcinoma and associated mortality has risen dramatically over the past several decades, and, thus, it is increasingly important to understand its pathogenesis and risk factors. Barrett esophagus is the established precursor to esophageal adenocarcinoma that progresses through a metaplasia–dysplasia-carcinoma sequence. Its risk of transforming to carcinoma is not as high as previously reported and there appears to be a biological heterogeneity among patients with this disease. The overall prevalence of Barrett esophagus in the United States ranges from 1% to 25% and is closer to 5% in patients with gastroesophageal reflux disease. Because of the frequency of Barrett esophagus and associated implications, it is important for the practicing pathologist to have a thorough understanding of this disease and its diagnostic pitfalls. In this review, we will discuss issues associated with the diagnosis of Barrett esophagus, including the definition of Barrett esophagus and its distinction from carditis with intestinal metaplasia. We will also discuss challenges in the grading of dysplasia and new variants of dysplasia, including crypt dysplasia and foveolar-type dysplasia. Finally, we will touch upon the evaluation of dysplasia in endoscopic mucosal resection specimens.

Introduction

The incidence of esophageal adenocarcinoma and associated mortality has risen dramatically over the past several decades, increasing approximately 6% per year, which is far more than most other cancers in the United States.[1] Consequently, it is increasingly important to understand the pathogenesis and risk factors for esophageal adenocarcinoma. Barrett esophagus is the established precursor lesion to esophageal adenocarcinoma, although its cancer risk is not as high as previously reported. The annual incidence of cancer among patients with Barrett esophagus is approximately 0.5% per year, and it is much lower (0.12%) in populations that are not plagued by obesity and other risk factors.[2,3] The risk of developing dysplasia is also limited. The annual incidence of low-grade dysplasia is 4.3% and that of high-grade dysplasia is 0.9%.[4] The risk of cancer development varies with extent of disease. Patients with long-segment Barrett esophagus, as defined by the presence of metaplastic glandular mucosa affecting an esophageal segment spanning at least 3 cm, comprise the minority of Barrett esophagus patients and are at higher risk for cancer development than those with less extensive disease.

The definition of Barrett esophageal mucosa varies among different geographic regions. In North America, Barrett esophagus is defined as replacement of squamous mucosa in the distal esophagus with columnar metaplasia that contains goblet cells. However, this definition is not followed

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worldwide. A diagnosis of Barrett esophagus in the United Kingdom requires the presence of endoscopic features of Barrett esophagus, but not detection of goblet cells in the affected segment. Failure to detect goblet cells when there is an endoscopic evidence of disease can simply reflect inadequate sampling. However, some evidence suggests that nongoblet columnar cells in the esophagus may be biologically intestinalized and at risk for cancer development, even in the absence of goblet cells. The Japanese do not require the presence of intestinal epithelium either, but do require the presence of endoscopically evident palisading vessels in an apparent area of Barrett esophagus. The prevalence of Barrett esophagus depends on the population studied and presence of associated risk factors. Estimates in the United States range from 1% to 25% of the general population to 5% among patients with gastroesophageal reflux disease.[5,6] Gastroesophageal reflux disease is a well-known risk factor for Barrett esophagus and is extremely common.[7–9] Other well-recognized risk factors for Barrett esophagus include male sex, Caucasian race, advanced age, and increased body mass index. Cigarette smoking is a minor risk factor with a relative risk of 2, although smoking in conjunction with other risk factors is implicated in only 25–40% of cases.[10–12]

Definition of Barrett esophagus

Three types of columnar epithelium can be recognized in the setting of endoscopically suspected Barrett esophagus: gastric–fundic type, cardiac type, and intestinal type, although the former usually reflects the presence of a small hiatal hernia and warrants no further discussion (Fig. 1).[13] The 2011 American Gastroenterological Association (AGA) guidelines define Barrett esophagus as specialized metaplastic columnar epithelium (i.e., intestinal type) that replaces the squamous epithelium of the distal esophagus and predisposes to cancer development.[14] This definition is based on the long held opinion that intestinal-type epithelium with goblet cells is the only type of metaplastic columnar epithelium predisposed to malignancy, and, thus, the presence of goblet cells is required for a diagnosis of Barrett esophagus in the United States.[2,14–16]

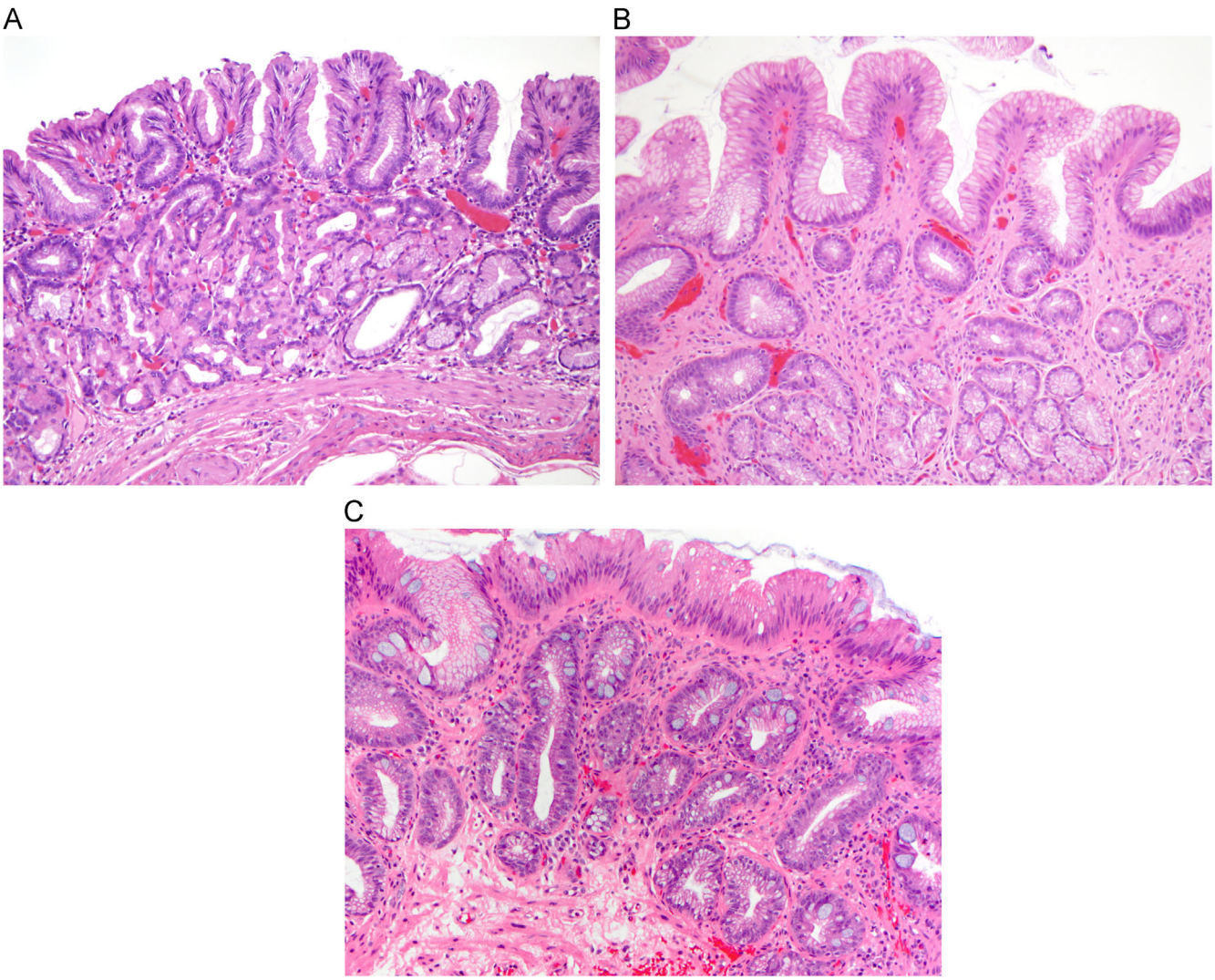

Fig. 1 – Three types of columnar epithelium can be identified in endoscopically determined Barrett esophagus: gastric–fundic type (A), cardiac type (B), and intestinal type (C).