Dysplasia in Barrett’s Esophagus—An Update on Grading
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Barrett’s esophagus (BE) is a condition that defines a change at the gastroesophageal junctional mucosa in which the squamous epithelium is replaced by intestinalized (columnar) epithelium. BE is recognized by its pink color on endoscopy, and it can be confirmed histologically by the presence of intestinal columnar epithelium with goblet cells. One of the most common reasons pathologists evaluate biopsies of the esophagus is to rule out Barrett’s esophagus either with or without dysplasia. Close coordination between clinicians and pathologists is critical in the diagnosis of BE because morphological evaluation alone cannot differentiate whether the columnar mucosa arises from the distal esophagus or proximal stomach. Recognition of BE and any associated dysplasia is very important for the effective management of the patient either by surveillance or immediate intervention. A significant issue in BE’s accurate diagnosis includes intraobserver and interobserver variation in grading dysplasia, which is categorized histologically as follows:

1. **Negative for dysplasia**
   This category describes a finding that no architecture distortion of the intestinalized epithelium has occurred, and the nuclei remain basally located with no variation in size or shape.

2. **Indefinite for dysplasia**
   This grading term is reserved for those cases having changes too marked to be negative but insufficient for dysplasia. It applies to esophageal biopsies with mild architectural distortion and subtle nuclear changes. Some medical experts also suggest this term in difficult cases where marked cytologic atypia is related to acute inflammation and ulceration, and dysplasia-appearing changes are present in the bases of the crypts, with evidence of surface maturation. In any event, rebiopsy is recommended for reassessment of the nature of epithelial changes after antiacid therapy when acute inflammation subsides.

3. **Low-grade dysplasia**
   This diagnosis describes changes that include minimal architecture distortion; hyperchromatic, elongated, and crowded nuclei; mucin depletion; and decreased number of goblet cells.

4. **High-grade dysplasia**
   This grade of dysplasia describes changes that include increased architectural complexity and cytological atypia, loss of nuclear polarity with full thickness nuclear stratification, and decreased or absent goblet cells. The distinction between high-grade glandular dysplasia and superficial carcinoma can be challenging. Montgomery further defined the criteria for high
grade by separating ordinary high grade from high grade with features suspicious for adenocarcinoma. In the 7th edition American Joint Committee on Cancer (AJCC) cancer staging system, high-grade dysplasia is staged as in situ carcinoma pTis.

5. Superficial Adenocarcinoma
This grade of dysplasia, as well as the term intramucosal carcinoma, is used to describe an invasion of the lamina propria or muscularis mucosa; it is considered as pT1 adenocarcinoma and is sometimes difficult to diagnose on superficial esophageal biopsies.

Barrett's esophagus can be associated with the development of esophageal adenocarcinoma. In patients with BE, the risk of progressing to high-grade dysplasia and adenocarcinoma depends on certain factors, including the presence of low-grade dysplasia, duration of BE, and length of BE (more common in long-segment BE) involving the esophagus. Patients with 17p (p53) LOH are at increased risk for developing high-grade dysplasia and adenocarcinoma. Surveillance of patients diagnosed with BE should include endoscopy every three years; and in patients with confirmed diagnosis of high-grade dysplasia, this endoscopic interval should increase to every three months.

By knowing the natural history, screening, surveillance, and treatment of Barrett's esophagus, pathologists can contribute to the prevention and early detection of dysplasia and significantly reduce patient morbidity and mortality.

References: