Gastric dysplasia: update and practical approach

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Abstract

Gastric epithelial dysplasia (GED), which is universally accepted as an epithelial neoplastic process confined to the basement membrane, has been the subject of numerous studies especially because of the significant differences in the prevalence, nomenclature, and diagnostic criteria across the continents. This review concisely summarizes current controversies, and discusses the updated guidelines and newly recognized subtypes of gastric dysplasia as they relate to the diagnosis and patient management. Establishing the correct diagnosis of GED is not only important for predicting the risk of malignant transformation in the biopsied lesion but is also critical in determining the risk of metachronous gastric cancer.

Keywords adenomatous; dysplasia; foveolar; gastric; preneoplastic; pyloric adenoma

Introduction

The topic of gastric epithelial dysplasia (GED) has long been a source of controversy, with challenges regarding its nomenclature and classifying schemes which in part are secondary to differences between the east and west in prevalence, screening protocols, and rate of progression.[1]

From a pathogenetic standpoint, GED is considered a neoplastic lesion and a direct precursor of gastric cancer.[2,3] Conventional GED represents the penultimate stage of Correa's pathogenetic sequence preceding intestinal type gastric adenocarcinoma. It is characterized by nuclear and/or cytoarchitectural features reflective of neoplastic growth, while still confined to the basement membranes.

The objective of this review is to provide a concise review of the subject for practicing pathologists, to summarize the current most accepted classification schemes, and to discuss the updated guidelines and new entities as they relate to the diagnosis and management of GED.

Clinical and demographic features

The prevalence of gastric dysplasia mirrors the prevalence of gastric cancer and is high in East Asian countries (Korea, China) and low in North America, India, and Australia.[4] Pre-neoplastic lesions such as intestinal metaplasia and atrophy also show a similar trend.[5] The mean age of individuals with GED is about a decade younger than with gastric cancer (61.35 years for GED vs. 70 years for gastric carcinoma).[4] Male predominance is seen similar to cancer (M/F = 1.9/1).[4,6]

Risk factors

GED shares the pathogenetic risk factors of gastric cancer and is included in the multi-step gastric carcinogenesis: inflammation—atrophic gastritis—intestinal metaplasia—dysplasia—carcinoma. GED is strongly associated with *Helicobacter pylori* infection. In one study, the presence of antibodies to *H. pylori* was associated with an increased risk of progression to dysplasia [or gastric cancer] (odds ratio [OR] = 1.8; 95% confidence interval [CI] = 1.2—2.6). The risk of developing GED increases with cigarette smoking as well.[7,8] Other reported risk factors include family history positive for gastric cancer, Menetrier disease, gastric stump, and alcohol consumption.[9] Although rare, GED may also be seen in gastric polyposis syndromes including Familial adenomatous polyposis, Peutz—Jeghers polyps, Juvenile polyposis syndrome, Familial gastric polyposis, and Gastric adenocarcinoma and proximal polyposis syndrome.[10]

Morphologic indicators of an individual at high risk for GED include biopsy evidence of chronic atrophic gastritis or intestinal metaplasia. Classification schemes for chronic gastritis and preneoplastic staging of gastritis have been developed, including the updated Sydney System, OLGA (operative link for gastritis assessment), and OLGIM (operative link on gastric intestinal metaplasia) assessment. However, the clinical applicability of these systems is limited because of the considerable inter- and intra-observer variation.[11,12]

Overview of gastric dysplasia classification systems

Five classification systems are most commonly quoted in the literature: the "Japanese group" classification, the conventional western classification, the "Padova system," the "Vienna classification," and "the WHO classification" (See Table 1).

The Japanese Society for Research on Gastric Cancer (JSRGC) classification consists of five groups. Although the system does not use "low and high grade dysplasia," neoplastic low grade noninvasive lesions correspond to the borderline lesions of group III. High grade lesions are qualified as non-invasive intramucosal carcinoma (Group IV).[13]

In many Western countries, and particularly in North America, the practically used diagnostic scheme for GED is also a five-tier system: Negative for dysplasia, indefinite for dysplasia, low-grade adenoma/dysplasia, high-grade adenoma/dysplasia, and suspicious for invasive carcinoma. The two-tiered classification of low- and high-grade dysplasia was adopted because it enhances diagnostic reproducibility and is of therapeutic relevance.[14] Of note, some authors have suggested identifying and documenting polypoid dysplasia, i.e., adenomas, as a distinct form of dysplasia, based on the circumscription of lesion and presence of inflammation in the background mucosa.[15,16]

A series of international meetings gathering Japanese and Western pathologists emphasized the lack of diagnostic consensus between the two groups, with failure to recognize non-invasive carcinoma and mucosal carcinoma without

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Comparison between the different classifications of Gastric Epithelial Dysplasia (GED) proposed over the years

Japanese (1998)	Western (1998)	Padova (1998)		Vienna Classification (1998)			WHO Classification (2000 and 2010)
Group I: Normal or benign.	Negative for dysplasia	**Category 1:** Negative for dysplasia		**Category 1:** Negative for dysplasia			No intraepithelial neoplasia/dysplasia
Group II: Benign with atypia	Indefinite for dysplasia	**Category 2:** Indefinite for dysplasia		**Category 2:** Indefinite for dysplasia			Indefinite for intraepithelial neoplasia/dysplasia
Group III: Borderline	Low grade adenoma	**Category 3.1:** Non-invasive low grade neoplasia (low grade adenoma / dysplasia)		**Category 3:** Non-invasive low grade neoplasia (low grade adenoma / dysplasia)			Low grade intraepithelial neoplasia/dysplasia (low grade adenoma; low grade dysplasia)
	Low grade dysplasia						
Group IV: Strongly suspicious for Invasive carcinoma	High grade adenoma	**Category 3.2:** Non-invasive high grade neoplasia (high grade adenoma / dysplasia)		**Category 4:** Non-invasive high grade neoplasia			High grade intraepithelial neoplasia/dysplasia (high grade adenoma; high grade dysplasia) Non invasive intramucosal carcinoma
	High grade dysplasia	**Category 3.2.1:** Suspicious for carcinoma (without lamina propria invasion)	**Category 3.2.2:** Non invasive carcinoma (CIS)	**Category 4.1:** High grade adenoma/dysplasia	**Category 4.2:** Non-invasive mucosal carcinoma	**Category 4.3:** Suspicious for invasive carcinoma	
Group V: Definitive for invasive carcinoma	Invasive carcinoma	**Category 4.:** Suspicious for Invasive carcinoma (with lamina propria invasion).		**Category 5:** Invasive neoplasia			Intramucosal invasive neoplasia (Intramucosal invasive carcinoma)
		Category 5.: Invasive neoplasia (Intramucosal/ Submucosal carcinoma or beyond)		**Category 5.1:** Intramucosal carcinoma	**Category 5.2:** Submucosal carcinoma or beyond		Invasive neoplasia

Table 1

submucosal invasion in the West, and the lack of the terms dysplasia and adenoma in Japanese practice.[17]

This led to the conception of the Padova, Vienna, and finally WHO classification schemes with a purpose of providing a universally accepted classification structure for GED. These systems allowed the use of adenoma and dysplasia by Western pathologists and non-invasive carcinoma by Japanese pathologists. In addition, these newly developed schemes were assigned risk categories for developing gastric cancer and helped establish clinical management guidelines.

Both the Padova international classification and the "Vienna classification" have five categories that parallel the Japanese system. The sub-categorization of category 3.2 (non-invasive high grade dysplasia) of the Padova classification was recognized as a separate category 4 in the Vienna system due to potential treatment differences between non-invasive low and high grade dysplasia/neoplasia. However, the histologic subcategorization of high grade dysplasia/neoplasia of the Padova classification into "suspicious for non-invasive carcinoma" and "non-invasive carcinoma/CIS" was determined as irreproducible. Additionally, the treatment recommendations are similar in these subcategories. These diagnoses were clustered into one category, category 4, termed "noninvasive high-grade neoplasia." The revised Vienna classification (2000) added another category of intramucosal carcinoma (Category 5).[18]