Techniques in Gastrointestinal Endoscopy 15 (2013) 113–120

Contents lists available at SciVerse ScienceDirect

Techniques in Gastrointestinal Endoscopy

journal homepage: www.elsevier.com/locate/tgie

Techniques in GASTROINTESTINAL ENDOSCOPY

www.techgiendoscopy.com

Polypoid lesions in inflammatory bowel disease ☆

Kyle L. Viani, MD[a], Leona A. Doyle, MD[a], Francis A. Farraye, MD,MSc[b], Robert D. Odze, MD[a,*]

[a] Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, 75 Francis St, Boston 02115, Massachusetts
[b] Section of Gastroenterology, Boston Medical Center, Boston University School of Medicine, Boston, Massachusetts

ARTICLE INFO

Keywords:
Dysplasia-associated lesion or mass (DALM)
Ulcerative colitis
Crohn disease
Dysplasia
Polypectomy

ABSTRACT

Patients with inflammatory bowel disease (IBD) may develop a variety of neoplastic and nonneoplastic polyps. This review covers the pathology, pathogenesis, natural history, and treatment of polyps in IBD with special emphasis on dysplastic lesions. Elevated or polypoid dysplastic lesions in IBD patients are referred to by the acronym DALM (dyspasia-associated lesion or mass). DALMs are further categorized as adenoma-like (endoscopically resectable polypoid dysplasia) or non–adenoma-like (non–endoscopically resectable polypoid dysplasia) based on their endoscopic appearance. Colectomy is recommended for patients with a non–adenoma-like DALM because of the high risk of synchronous or metachronous adenocarcinoma. In contrast, adenoma-like DALMs can be safely treated by polypectomy and continued surveillance provided that the lesion is removed in total, with negative margins, and no flat dysplasia is identified in the colon adjacent to and distant from the polyp.

1. Introduction and risk of cancer

Colorectal carcinoma as a complication of inflammatory bowel disease (IBD) was first reported in ulcerative colitis (UC) in 1925 [1] and subsequently described in a patient with Crohn's disease (CD) in 1948 [2]. Since these initial reports, substantial progress has been made in our understanding of the pathogenesis of neoplasia in IBD and its treatment. Nevertheless, colorectal carcinoma continues to cause significant morbidity and mortality in patients with IBD.

In a recent meta-analysis [3], the risk of developing adenocarcinoma is estimated at 2% after 10 years of UC, 8% at 20 years, and 18% after 30 years of disease. More recent studies have documented a substantially lower risk [4]. Several studies have demonstrated a similar risk in patients with CD [5-10]. The risk of developing carcinoma is highest in patients with longer duration of disease, greater anatomical extent of disease, greater severity of histologic inflammation, a family history of sporadic colorectal carcinoma, and in patients with UC and primary sclerosing cholangitis [5,11,12]. Recent studies have suggested that male gender may be a risk factor for IBD-related neoplasia [13,14]. IBD-related carcinomas tend to be diagnosed at a younger age and are more evenly distributed throughout the colorectum, compared with sporadic carcinomas [15,16]. In addition, a greater proportion of IBD-related carcinomas are high grade, multifocal, and have signet ring or mucinous morphology [15,17,18]. However, 5-year survival rates are similar for IBD-related and sporadic tumors [15].

2. Pathogenesis of neoplasia in IBD

The pathogenesis of carcinoma in IBD is thought to be secondary to the effects of long-standing inflammation on the colonic epithelium. Our understanding of the mechanism by which mediators of both the innate and adaptive immune system promote tumorigenesis is evolving [19-21]. Oxidative stress resulting from the inflammatory response is thought to play a critical role in this process, by directly damaging DNA and altering signaling pathways [22]. The net effect of sustained inflammation is a stepwise accumulation of mutations in colonic epithelial cells.

Many of the molecular pathways involved in the development of sporadic colorectal cancer are also dysregulated in IBD-related tumors. IBD-related adenocarcinomas exhibit a similar frequency of chromosomal instability (85%) and microsatellite instability (15%) as sporadic tumors [23]. Similar to sporadic colorectal carcinoma, mutations in *KRAS*, *p53*, and *APC* are involved in the pathogenesis of IBD-related carcinoma. However, the prevalence and sequence of mutations differ in IBD-related carcinogenesis. For instance, although *APC* mutations are an early event in the sporadic adenoma-carcinoma sequence, they are less frequent, and often late, events in the development of IBD-related carcinoma [24,25]. In contrast, *p53* is frequently mutated early in the

☆ The author reports no direct financial interests that might pose a conflict of interest in connection with the submitted manuscript.

* *Corresponding author.*
E-mail address: rodze@partners.org (R.D. Odze).

0049-0172/$ - see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.tgie.2013.02.002

development of IBD-related neoplasia but represents a late event in the pathogenesis of sporadic colorectal carcinoma [26,27].

The progressive accumulation of mutations in intestinal epithelial cells manifests morphologically by the development of dysplasia. Similar to the adenoma-carcinoma sequence in sporadic carcinogenesis described by Fearon and Vogelstein [28], a stepwise chronic inflammation-dysplasia-carcinoma sequence underlies the progression of IBD-related neoplasia. Although many IBD-related carcinomas evolve from lesions that have progressed from low- to high-grade dysplasia, some carcinomas may also develop directly from low-grade dysplastic lesions. For instance, an unusually well-differentiated form of carcinoma, termed low-grade tubuloglandular adenocarcinoma, has been shown to derive directly from low-grade dysplasia in patients with IBD [29].

3. Classification of dysplasia in IBD

3.1. Gross or endoscopic features

Dysplastic lesions in IBD are classified based on their endoscopic (gross) and histologic appearances. Endoscopically, they are broadly divided into flat and elevated lesions. Historically, flat dysplasia is defined as a lesion that is invisible on endoscopy, and thus detected only via random sampling of colonic mucosa. However, this definition is currently in transition because some lesions that are "flat" or "plaquelike" may be identified endoscopically with high-definition endoscopes, and special techniques, such as chromoendoscopy.

All elevated or polypoid dysplastic lesions in IBD are referred as dysplasia-associated lesions or masses (DALMs). DALMs are further categorized as "adenoma-like" or "non–adenoma-like" based on their endoscopic features [30]. Adenoma-like DALMs have a similar gross appearance to sporadic adenomas. They are well circumscribed, smooth, sessile or pedunculated, and lack ulceration and necrosis (Figure 1). These lesions are typically amenable to endoscopic removal. In contrast, non–adenoma-like DALMs cannot be completely removed by endoscopic methods and include poorly circumscribed or stricturing lesions, mucosal patches, or broad-based plaques. Ulceration, necrosis, and hemorrhage are frequently present in these lesions (Figure 2). There is variability among gastroenterologists regarding the use of this classification system of DALMs as adenoma-like or non–adenoma-like [31]. Thus, some have suggested that a more objective classification is to classify lesions as to whether they can be completely removed endoscopically or not [32,33]. Using this classification, adenoma-like DALMs are considered endoscopically resectable and non–adenoma-like DALMs are non–endoscopically resectable.

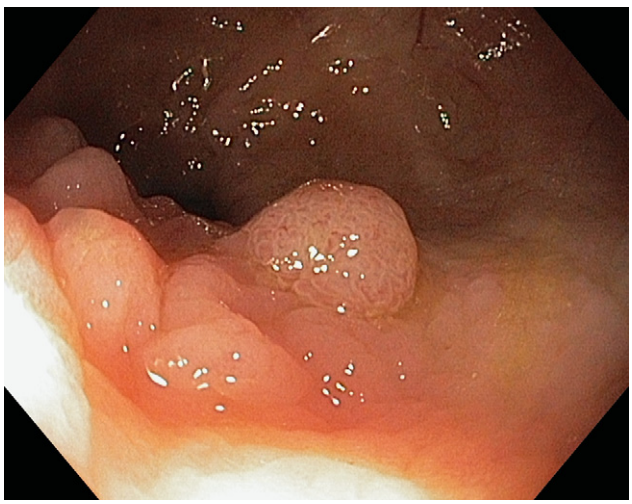

Fig. 1. Adenoma-like DALM. (Color version of the figure is available online.)

Recent retrospective studies have demonstrated that, in fact, most dysplastic lesions in IBD may be DALMs rather than flat dysplasia [33,34]. For instance, in a large retrospective review of 2204 surveillance colonoscopies in patients with UC, of the 104 dysplastic lesions identified, 80 (77%) were DALMs and 24 (23%) were flat dysplasia [33]. In a similar retrospective review of 1339 surveillance endoscopies in patients with UC that identified 65 dysplastic lesions and 10 carcinomas, 58.5% of dysplastic lesions were endoscopically visible [34]. Of the visible lesions, 57% were described as "polyps" or "masses" and 40% as "irregular mucosa."

4. Grading of dysplasia in IBD

The histologic scheme for grading dysplasia in UC is used regardless of the endoscopic appearance of the lesion. The classification system that was initially developed in 1983 by a group of gastrointestinal pathologists, referred to as the IBD Dysplasia Morphology Study Group, is the one used most often in the United States [35]. Three diagnostic categories are defined: negative for dysplasia, indefinite for dysplasia, and positive for dysplasia (low or high grade or both). An alternative system, the "Vienna classification," [36] is less frequently used by pathologists in the United States, but is commonly applied in Japan and Europe. This system was developed in an attempt to minimize differences in interpretation of carcinoma and dysplasia between Japanese and Western pathologists. Five diagnostic categories are defined: negative, indefinite, noninvasive low grade, noninvasive high grade and invasive neoplasia. The noninvasive neoplasia category corresponds to low- and high-grade dysplasia of the IBD Dysplasia Morphology Study Group classification system. Dysplasia is defined as neoplastic epithelium that is confined by the basement membrane. Dysplastic epithelium is characterized by cells with hyperchromatic, enlarged, stratified nuclei, mitoses, and lack of surface maturation. High-grade dysplasia is distinguished from low-grade dysplasia by showing a greater degree of cytologic and architectural atypia, such as loss of cell polarity, with nuclear stratification involving the apical half of cells, increased nuclear or cytoplasmic ratio, and budding, branching, and back-to-back gland formation (Figs 3 and 4).

Histologically, adenoma-like DALMs, non–adenoma-like DALMs, and sporadic adenomas have similar morphologic features [37-40]. All represent polypoid lesions composed of dysplastic epithelium with a tubular or villous growth pattern.

5. Adenoma-like DALM vs sporadic adenoma

Several studies have examined histologic, molecular, and immunophenotypic characteristics of DALMs in an effort to separate lesions into those that represent polypoid dysplasia related to chronic colitis from sporadic adenomas. It is generally accepted that adenoma-like DALMs that develop outside areas of colitis (prior or current), in fact, represent sporadic adenomas because there is no data to suggest that IBD-related neoplasia develops in previously noninflamed mucosa. The etiology of adenoma-like DALMs arising within regions of colitis is less clear. These lesions represent a heterogeneous group of both colitis-related polypoid dysplasia and sporadic adenomas that have coincidentally developed within an area of chronic inflammation.