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Diagnosing inflammatory bowel disease and differentiating it from potential mimics

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ABSTRACT

The initial diagnosis of inflammatory bowel disease (IBD) requires multiple diagnostic modalities; however, endoscopic evaluation as a diagnostic test is considered the gold standard. Endoscopic evaluation includes colonoscopy with ileoscopy, esophagogastroduodenoscopy, enteroscopy, and capsule endoscopy. IBD encompasses Crohn's disease, ulcerative colitis, and IBD unclassified. Colonoscopy with ileoscopy along with biopsy collection is essential in most IBD cases for diagnosis and to rule out alternative findings that may mimic IBD including ischemia, diverticulitis, segmental colitis associated with diverticulosis, neoplasia, radiation enteritis, and drug-induced colitis. Esophagogastroduodenoscopy, enteroscopy, and capsule endoscopy are used in the initial workup of specific groups of patients with IBD. The role of endoluminal diagnostic studies in the initial diagnosis of IBD is discussed in detail in this article.

Inflammatory bowel diseases (IBD) are generally classified into Crohn's disease (CD), ulcerative colitis (UC), and IBD unclassified (IBDU). Although IBD may be evaluated with multiple methods of testing, only endoscopic evaluation allows direct visualization of the gastrointestinal mucosa. In addition, most endoscopic tests permit histologic assessment using biopsy collection, with the exception of capsule endoscopy (CE), which allows for visual assessment only. Procedures including colonoscopy with ileoscopy (ileocolonoscopy), esophagogastroduodenoscopy (EGD), enteroscopy, and CE enable assessment of distinct regions of the digestive tract, and although ileocolonoscopy is the gold standard for diagnosis of IBD in most patients, EGD, enteroscopy, and CE may be helpful for the initial diagnosis of IBD in select populations. We review the use of the aforementioned endoscopic procedures to make the initial diagnosis of IBD and to differentiate other diseases that may mimic IBD on initial evaluation. Additional evaluation with clinical assessment and history, laboratory testing, and imaging studies is also important in the initial diagnosis of IBD; however, these are not discussed in this article.

Ileocolonoscopy

Role in IBD diagnosis

Ileocolonoscopy with biopsies is considered the gold standard for making the diagnosis of IBD in most patients [1-3]. Ileocolonoscopy enables the assessment of terminal ileal, colonic, and rectal mucosa through direct endoscopic visualization, allowing evaluation of disease severity, extent, and histologic assessment [4]. Identifying the disease location and severity, including the disease involving the terminal ileum, is important for accurate initial IBD diagnosis; intubation of the terminal ileum should always be attempted and is possible in 95% of patients with UC and 75% of patients with CD [2,5,6]. For most patients presenting for evaluation of IBD, ileocolonoscopy is essential in the initial diagnosis and helpful in differentiating CD, UC, and other pathology that can present with similar clinical findings. In a few of the cases of patients being evaluated for IBD, ileocolonoscopy may not be of significant use, for example, if the patient's disease location does not involve the colon or terminal ileum or when surgical intervention is imminent and endoscopic results would not change patient management.

Biopsy collection during ileocolonoscopy

Ileocolonoscopy with multiple biopsies is the gold standard for diagnosis of IBD; thus, biopsy collection is an integral part of the initial diagnosis [2,3,7]. Guidelines suggest that ideal biopsy collection includes at least 2 biopsy specimen collected from 5 sites throughout the bowel, including the rectum and ileum [8,9]. Biopsies during the initial ileocolonoscopy should always be obtained from the terminal ileum and throughout the colon even if the mucosa appears normal, because although there may be no evidence of macroscopic disease, histologic inflammation may be present in areas that appear normal endoscopically [8,10-12]. Biopsies should be collected from inflamed as well as normal-appearing mucosa, particularly from the terminal ileum to evaluate for small bowel disease [5,13]. Sampling from the

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entire colon provides more accurate pathologic diagnosis than limited-biopsy collection; researchers describe that expert pathologists correctly diagnose 64% of CD cases when provided with a full series of biopsies as compared with 24% when analysis is limited to only a rectal biopsy [14]. Histologic evaluation may help to differentiate UC from CD, for example, macroscopic or microscopic evidence of skip areas may be more suggestive of CD [8]. Biopsy results may also assist in ruling out other etiologies that mimic IBD. Furthermore, histology may reveal evidence of chronic or active inflammation, which can aid in prognosis, direct medical therapy, and predicting risk for dysplasia [8].

Contraindications and complications

Potential complications of ileocolonoscopy include perforation; bleeding; infection; and rarely, postpolypectomy syndrome, which is uncommon in patients with IBD. Complications related to sedation and bowel preparation are also possible. Perforation is the most serious complication, with a high morbidity, and in most cases, it would require urgent surgery and colostomy [2].

In stable patients with IBD, the rates of endoscopy-related complications are similar to those of the general population, and they most commonly include bleeding and perforation. A 2013 study evaluating 685 patients with IBD suggests that the overall rate of endoscopy-related complications is 1.17% compared with 0.96% in the general population, and the lifetime risk of complication in patients with IBD undergoing screening colonoscopy is 12.7% compared with 2.0% in patients with non-IBD [15]. In the general population undergoing diagnostic colonoscopy, the incidence of hemorrhage is 0.02%, and the overall rate of perforation is 0.045% [2,16]. The incidence of hemorrhage in the setting of polypectomy is 1.61%. In IBD population groups, a study reports no episodes of bleeding, perforation, post-polypectomy fever, or mortality in a series of 151 colonoscopies and 70 polypectomies in patients with IBD [2,16]. The incidence of complications has decreased over time, presumably because of advancements in colonoscopy technology as well as improvement in training of endoscopists [2].

In hospitalized patients with IBD, the risk of endoscopy-related complication is also similar to that in patients with non-IBD. A retrospective study reports colonoscopy perforation rates for hospitalized patients with IBD as 1% compared with 0.6% in patients with non-IBD [17]. Certain IBD population groups, including those with severe, fulminant colitis or those with stricture formation, are at increased risk of complications [2]. Risk factors associated with perforation in severe colitis include female sex, older age, and performing endoscopic dilation [17,18]. Minimizing air insufflation and avoiding advancing the scope in a tortuous colon can help reduce risk of complications [18]. Although the risk of complication may be higher in these populations, colonoscopy may still be performed safely, and endoscopic evaluation may provide essential information that would affect both surgical and medical management, especially in the acutely hospitalized patient who often requires surgical intervention urgently. This information includes ensuring that the causative etiology of the patient's symptoms is indeed IBD and not an alternative one that can mimic the clinical symptoms of IBD. However, in emergency settings where surgery is indicated urgently, endoscopy often plays a limited role as it would not affect the immediate management of this group of patients who most likely would require urgent surgery. This scenario is uncommon in the initial presentation and diagnosis of IBD [2].

In general, endoscopic evaluation can be performed safely and plays a pivotal role in the diagnosis and ongoing management in most patients with IBD. Endoscopic evaluation in specific scenarios, such as complete obstruction from stricture or toxic colitis, has higher risks and is unlikely to change patient management as urgent surgical intervention is often warranted. In these patients, careful consideration should be taken before performing ileocolonoscopy, and the study should be performed only if the procedure is likely to change patient management [19].

Mucosal appearance and disease distribution

Crohn's disease

Although the typical endoscopic appearance of CD is described as patchy ulceration affecting any part of the gastrointestinal tract, endoscopic findings in CD vary greatly depending on the disease activity and duration [5,18]. Classically, CD presents as regions of inflamed mucosa separated by areas of normal tissue (skip areas) [5]. The inflamed mucosa can have variable appearance including endoscopically normal-appearing mucosa, aphthous erosions, deep ulcerations, or a more diffuse circumferential contiguous ulceration similar to UC [19] (Fig. 2).

The inflammation in CD may present on the antimesenteric side of the colon and does not generally extend circumferentially [5]. In early, mild disease, lesions present as small, punched-out ulcers surrounded by healthy mucosa. In moderate CD, stellate ulcers form as small aphthous lesions coalesce to create larger ulcers. Submucosal edema and tissue damage can cause mucosal cobblestoning, which occurs when overlapping linear and transverse ulcers are superimposed on relatively normal mucosa [5]. In severe CD, deep serpiginous ulcers and large linear ulcers (bear claw) may be appreciated. The continuous pattern of inflammation in severe CD may be difficult or impossible to differentiate from UC, where inflammatory changes are also continuous [5]. In up to 50% of patients with colonic CD, the rectum is spared [18,20]. Inflammatory pseudopolyps may be seen in CD, a finding consistent with UC [5,21]. Although the aforementioned mucosal findings are typical in patients with CD, they are all nonspecific and can be found in other disease states including having indistinguishable appearance from typical UC findings. Additionally, patients with CD may have other mucosal findings not described earlier [19].

Ulcerative colitis

Early in the course of UC, the endoscopic evaluation may reveal very subtle findings such as loss of normal vascular markings in the colon, which is followed by mucosal hyperemia due to increased blood flow to the affected area [5]. As the disease progresses, mucosal edema presents with a fine, granular appearance that may be referred to as *wet sandpaper*, and the mucosa may be friable and may bleed easily with contact. Next, discrete ulcers surrounded by inflamed mucosa may form. In severe UC, discrete ulcers may coalesce and form large continuous ulcers. Pseudopolyps may form in areas with longstanding active inflammation, and disease extent is generally limited to the colon. Generally, the typical inflammatory pattern on presentation with UC should initiate in the rectum and continue proximally in a contiguous, circumferential manner without skip lesions; however, in severe disease, UC is difficult to differentiate from CD [5] (Fig. 1). For example, severe CD may also present with contiguous, circumferential inflammation and may be difficult to differentiate from severe UC in this setting [19]. These are typical findings in UC, but again, they are all nonspecific and not definitive of UC presentation.

Esophagogastroduodenoscopy

Role in IBD diagnosis

IBD may affect any portion of the gastrointestinal tract from mouth to anus. Although the most commonly affected areas are