8. Endoscopy in inflammatory bowel diseases

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Synopsis

The widespread availability of gastrointestinal endoscopy has changed the management of inflammatory bowel diseases (IBD) to an important extent. The need for an unpleasant bowel preparation, the high cost, and the discomfort sometimes caused by endoscopic procedures should nonetheless force the clinician to optimize the indications. In this section we will describe the most characteristic lesions of Crohn's disease and ulcerative colitis, the value of endoscopy in the initial assessment and monitoring of IBD and therapeutic endoscopic interventions. Discussion of surveillance in IBD is discussed elsewhere.

Characteristic endoscopic findings in inflammatory bowel disease

The nature and distribution of the mucosal abnormalities will often allow an experienced endoscopist to diagnose IBD with a good level of confidence. In some instances, though, the endoscopic picture may have features of both Crohn's disease and ulcerative colitis and then the term ‘indeterminate colitis’ is more appropriate. Biopsies will confirm the suspected endoscopic diagnosis in the majority of cases, with signs of nonspecific idiopathic inflammation and chronicity. Only in a minority of cases is the diagnosis of Crohn's disease ascertained by the presence of granulomas.

Crohn's disease

Distribution

Crohn's disease can affect any part of the gastrointestinal tract, including the oropharynx and the anorectum. Once the disease has settled in, the extent and location tends to stay the same in most patients, although exceptions do occur, especially following surgical resections [1]. The commonest involvement is ileocecal, observed in 41% to 55% of the patients with Crohn's disease. Colonic Crohn's disease without small bowel involvement is less common (5–25%). Crohn's disease is confined to the small bowel alone in approximately 30% of cases [2,3].

Aphthous ulcer

The aphthous ulcer is the earliest and most characteristic endoscopic finding in Crohn's disease. (Fig 1). It can be found throughout the gastrointestinal tract. An aphthous ulcer represents a small (max. 5 mm) superficial ulcer surrounded by a characteristic tiny rim of erythema (Fig. 2). Aphthous ulcers can appear in a single segment or be spread throughout the colon [3–7]. They are often seen in groups, tend to enlarge concentrically, and give rise to larger and deeper ulcerations. Larger and deeper ulcers are also commonly observed [8]. They have clear margins and are often surrounded by normal colonic mucosa with very little reactive change (Fig. 3).

The ulcers can be of various sizes and shapes including deep, punched out ulcerations, stellate ulcers, longitudinal, tortuous, or serpiginous ulcerations.
Ulcers and cobblestoning

The mucosa lying between long linear ulcerations can be normal or very edematous, reddish and hyperplastic, almost polyp like. This is referred to as the *cobblestone appearance* (Fig. 3) [7]. Different areas of the colon can be involved within a specific patient and larger areas can be completely spared from disease (i.e. *patchiness*). An example of this is the typical ‘rectal sparing’, which has been reported in up to half of the cases. If the whole rectum is involved (5–10% of colonic Crohn's disease), however, the inflammatory activity in this area is not indicative of the severity higher up [9].

In the prospective European Cooperative Crohn's Disease Study (ECCDS) fissure or cleft-like ulcerations and aphthous lesions were the most common abnormalities followed by pseudopolyps, cobblestone lesions, and stenosis. A segmental pattern was the most common form of ulceration, whereas only 14% of patients had a continuous pattern of ulcerations [10].

Strictures and fistulae

Where the inflammation is deep and extensive luminal narrowing or strictures can occur (Fig. 4) [6,7]. *Strictures* virtually always arise in areas of severe ulceration. Both length and width of the strictures can vary considerably, ranging from less than 3 to more than 10 cm in length and to less than 5 mm in width [2,9]. Features that suggest possible malignancy within a stricture include rigidity, nodularity at the margins, and an eccentric lumen [12]. The inflammation and ulcerations in Crohn's disease are often transmural and can lead to perforation, inflammatory mass, and/or fistula formation, reported in up to 8% of patients with Crohn's colitis. Fistulas are most often seen proximal to strictures and are frequently surrounded by extensive inflammatory changes [3].

Vascular pattern

When the active disease becomes quiescent signs of chronic inflammation often remain visible, with a diminished or disturbed vascular pattern (Fig. 5). In patients with more extensive disease healing may be more irregular and hypertrophic zones may alternate with areas of atrophy. This gives rise to the so called *pseudopolyps*.

Upper GI involvement

When Crohn's disease involves the upper gastrointestinal tract it is almost invariably accompanied by small bowel or colonic disease [13]. The prevalence of upper GI tract involvement is much higher in prospective studies of both symptomatic and asymptomatic patients (17–75% for upper endoscopy) than in retrospective series (0.5–13%) [14]. In retrospective series oral lesions were more frequent (6–9%) than gastroduodenal (1.8–4.5%) and esophageal (1.8%) involvement.

Esophageal involvement is usually seen in seriously ill patients presenting with dysphagia, odynophagia, heartburn, and chest pain. Characteristic endoscopic features in the esophagus include hyperemia, granularity, friable mucosa, erosions or aphthoid lesions, ulcers, nodular thickening, cobblestones, and stenosis [15]. It is unclear what the true incidence of gross gastroduodenal involvement by Crohn's disease is. Reported incidence ranges from 2 to 49% of patients with Crohn's ileocolitis [16–19]. Many patients, however, do not have endoscopic detectable lesions in the stomach and duodenum, but examination of biopsies does reveal histopathologic changes suggestive of Crohn's disease [19–23]. Gastroduodenal involvement often leads to symptoms similar to peptic ulcer disease or non-ulcer dyspepsia such as epigastric pain, anorexia, and sometimes signs of gastric outlet obstruction. In isolated duodenal disease any part of the duodenum can be involved but the second part is most
frequently affected, with typical mucosal defects on top of the Kerckring's folds, called ‘notching’. In the duodenum stricturing may also occur (Fig. 6).

**Ulcerative colitis ▲▼**

**Distribution ▲▼**

In ulcerative colitis the inflammation extends typically from the anal verge up to a variable distance, which can change during the course of the disease. Since the rectum is virtually always involved in this disease, a rigid proctoscopy is often sufficient for evaluation during follow-up. In patients whose disease is limited to the left colon, a flexible sigmoidsopy may suffice for evaluation. However, when topical treatment is being used the rectum may appear relatively normal in spite of the fact that more proximal segments remain inflamed. In patients with more extensive involvement a full colonoscopy with ileoscopy is advised to help differentiate from Crohn's colitis [24]. It is generally accepted that one should be cautious about performing endoscopic examinations in patients with fulminant colitis, given the increased risk for perforation and toxic megacolon.

Ulcerative colitis may involve the rectum (proctitis, approximately 30%), the rectosigmoid area (proctosigmoiditis or distal ulcerative colitis), the left colon (left-sided colitis in 30–40%), or the entire colon (total colitis, approximately 30%) [25]. During follow-up, a large Scandinavian cohort-study showed that up to 40% of the patients had extension of their disease. Patients with initial extensive colitis showed regression over time in 44% [26].

**Endoscopic appearances ▲▼**

The endoscopic appearance of ulcerative colitis is quite characteristic (Fig. 7 and 8). Unlike in Crohn's disease, the inflammation is continuous and circumferential from the anal verge up. The mucosa shows erythema, friability, and often frank superficial bleeding (Fig. 9). Slight edema usually causes a shiny appearance. Additionally, there may be granularity with a typical greyish discharge. In moderate UC, one can appreciate erosions and microulcerations, and in more severe attacks shallow ulcerations may develop (Figs 10 and 11). Only rarely do deeper ulcerations and luminal narrowing occur. ‘Cecal patch’ inflammation represents a limited zone of colitis surrounding the appendiceal orifice in patients with left-sided colitis [27].

In patients with longstanding moderate to severe colitis the colonic mucosa will show signs of chronic inflammation and healing. The colon may contain pseudopolyps and even mucosal bridging and an attenuated or loss of vascular pattern. Once stricture formation is encountered a high level of suspicion is warranted as this may be a sign of malignancy. In reality it may be difficult to detect dysplastic lesions especially in a scarred colon with many pseudopolyps. Therefore colonoscopies performed for prevention of colorectal cancer in patients with longstanding pancolitis should always include multiple biopsies from all different segments.

**Differentiation between Crohn's disease, ulcerative colitis, and indeterminate colitis (Fig. 12) ▲▼**

In the majority of patients with chronic idiopathic colitis the differential diagnosis between Crohn's disease and ulcerative colitis will be quite clear. Pera et al. [28] prospectively examined 357 patients with 606 colonoscopies in order to determine the accuracy and ‘weight’ of various endoscopic signs. Complete colonoscopy allowed a correct differentiation between Crohn's disease, ulcerative colitis, and
‘indeterminate colitis’ in 89% of cases, with 4% errors and 7% indeterminate diagnoses. Errors were more frequent in the presence of severe colonic inflammation. The most distinctive endoscopic features in the differential diagnosis were discontinuous involvement, anal lesions, and cobblestoning of the mucosa for Crohn's disease and erosions, microulcers, and granularity for ulcerative colitis. Five to 10 per cent of patients showed abnormalities that were suggestive of both conditions. Most of the patients had an UC-like endoscopy with one or more features possibly suggesting Crohn's disease. These so-called ‘indeterminate features’ included anal abnormalities (such as skin tags, an unusual fissure or an abscess), rectal sparing, skip areas, and deeper ulcerations. In these patients, the term ‘indeterminate colitis’ should be used as a reminder that the differential diagnosis is not completely clear.

**Endoscopic assessment of extent and severity of inflammatory bowel disease**

The knowledge of the location of the intestinal inflammation affects management decisions, since certain medications can be used topically. The extent of the inflammation tends to be underestimated in both ulcerative colitis and Crohn's disease. The severity of the inflammatory lesions also has some prognostic value in a number of situations: in ulcerative colitis, for example, deep ulcers are an indicator of a poor response to medical therapy. In Crohn's disease the severity of endoscopic lesions in the neoterminal ileum after an ileocolonic resection is an indicator of the ensuing clinical disease behavior [30].

The French ‘GETAID’ (Groupe d'Etudes Thérapeutiques sur les Affections Inflammatoires Digestives) developed and validated a ‘Crohn’s disease endoscopic index of severity’ (CDEIS). The four mucosal lesions which were found to be of significant importance to establish a final formula for CDEIS calculation were deep ulcerations, superficial ulcerations, non-ulcerated and ulcerated stenosis. The presence of the lesions is scored in each of 5 ileocolonic segments. For every segment, the proportion of surface which is ulcerated or affected by any other lesions is also scored. With this score interobserver agreement was excellent ($P < 0.001$) [31].

The same group then studied 142 patients with active colonic or ileocolonic Crohn's disease who all underwent a colonoscopy prior to treatment with prednisolone 1 mg/kg/day. Treatment was continued until clinical remission for a maximum of 7 weeks. Surprisingly, a significant correlation between clinical disease activity (CDAI), biochemical markers, and CDEIS could not be established [8].

In ulcerative colitis, to the contrary, the endoscopic lesions represent an important parameter of disease activity and correlate better with the clinical course of the disease. Although the endoscopic appearance does not give an exact estimate of the histologic changes in the colonic mucosa, endoscopic criteria are included in most clinical trials. Several endoscopic scoring systems have been developed. All scores distinguish 3 or 4 stages of mucosal alterations based on the disturbance or disappearance of the vascular pattern, presence of friability and/or bleeding of the mucosa, and presence of several types of ulcers and/or mucopus. An overview of several scores is given in Fig. 10[32–35]. The extent of inflammation in UC often changes during the course of the disease. Niv et al. [36] reported change of extent in 77% of the patients during a mean follow-up period of 17 months.

**Endoscopic monitoring of therapeutic efficacy and its value in clinical trials**

As mentioned above, the correlation between endoscopic severity and clinical activity is often poor in
Crohn's disease but NOT in ulcerative colitis. The GETAID demonstrated that only about a quarter of patients in clinical remission under corticosteroid treatment also had endoscopic healing of their ulcerations. Persistence of lesions was not predictive of early relapse and adjustment of steroid treatment duration based on endoscopic findings proved to be without benefit. It was concluded that endoscopic monitoring of ‘healing’ is a waste of time and money \[8,37,38\], but it needs to be emphasized that this statement may only be applicable to treatment with corticosteroids. In general, the pattern of healing of endoscopic lesions under glucocorticoid therapy depends on the location of the lesions: esophageal lesions almost completely and rapidly disappear, whereas gastric lesions hardly show any change, even with symptomatic relief. Ileal lesions have the same tendency to persist whereas colonic lesions can heal slowly after tapering of the steroids \[39\].

Data on mucosal healing with anti-inflammatory agents other than glucocorticosteroids are scarce. Azathioprine was shown to induce significant healing in Crohn's ileocolitis, colitis, and severe postoperative recurrent ileitis \[40,41\]. Variable degrees of ileal and colonic healing have also been reported with methotrexate \[42\].

The most impressive and rapid healing of Crohn's disease lesions was observed after treatment with the monoclonal anti-TNF antibody infliximab \[43\]. A group of European investigators demonstrated significant healing of colonic lesions only four weeks after intravenous administration of a single dose of this drug. All parts of the colon improved to the same extent. A significant correlation between clinical improvement (DCDAI) and endoscopic changes (DCDEIS) was demonstrated \[44\]. A few patients in this study developed fibrous strictures which were dilated endoscopically. It remains to be studied if clinical remission with accompanying endoscopic healing should become a treatment objective in the future.

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**Perioperative endoscopy in Crohn's disease**

Up to 70% of the patients with Crohn's disease will undergo at least one surgical resection of inflamed bowel segments, usually in order to treat complications of the disease. Usually the surgeon aims to be curative, i.e. to resect all macroscopic disease, although sometimes resections are limited to segments which are responsible for the symptoms, leaving active disease behind (segmental resection). More and more patients are treated with strictureplasties whereas bypass operations are no longer performed.

After surgery most patients will suffer recurrence of their disease. Risk factors for early symptomatic recurrence are perforating indications for surgery (abscess or fistula), ileocolonic anastomosis, and smoking. Ileocolonoscopy is a key method for planning treatment strategies in the preoperative as well as postoperative period.

In order to optimize the outcome of surgery it is critical to study the anatomic distribution of Crohn's involvement prior to surgery. This has become even more imperative with the broader use of the laparoscopic surgical approach, since reliable evaluation of disease extent based on serosal inspection may sometimes be difficult. If the colon is spared at endoscopy the surgeon performs an ileal resection with ileocecral or ileoascending anastomosis. If right colonic disease is visualized the surgeon should extend the colonic resection guided by colonoscopic findings and suture the neoterminal ileum to uninvolved colon.

Systematic endoscopic studies following curative resection in Crohn's disease have allowed study of the natural history of the evolution of Crohn's disease from the earliest lesions to full blown Crohn's disease. Within weeks to months after resection with ileocolonic anastomosis ‘new’ lesions can already be visualized in the neoterminal ileum \[5\]. Ileocolonoscopic studies after surgery also allow prediction
of the clinical outcome of Crohn's disease after resection. The severity of recurrent lesions as visualized at endoscopy predicts the clinical evolution in the years following surgery [30].

The severity of recurrent lesions early after resection are assessed using an endoscopic scoring system (Fig. 13).

Patients displaying no or only mild lesions (score i0, i1) do well over time and carry a low risk of rapid symptomatic relapse whereas patients presenting with diffuse severe endoscopic recurrence (score i3, i4) are at risk of progressive clinical disease. Patients with endoscopic lesions of intermediate severity also have an intermediate risk. This score has also been valuable for studies of drug prophylaxis of postoperative recurrence [45,46].

Patients with an ileostomy can also develop recurrent inflammation in the most distal ileal segments, but the risk is much lower than after an ileocolonic reanastomosis. Endoscopic examination of the bowel proximal to the stoma allows easy and precise evaluation of the abnormalities and collection of biopsies.

**Endoscopic features of the ileoanal pouch and pouchitis**

Restorative coloproctectomy with ileal pouch–anal anastomosis (IPAA) has become an established surgical option for patients with severe ulcerative colitis [47]. The most common long-term complication besides intestinal obstruction is inflammation of the pouch, known as pouchitis. Approximately 50% of patients with an IPAA can be expected to develop an episode of pouchitis [48]. This inflammation becomes chronic in as little as 5% of patients.

Although the inflammation remains limited to the pouch reservoir in the majority of patients, extension into the prepouch ileum can occur. The endoscopic features of pouchitis resemble those of ulcerative colitis: in an early stage erythema, fading of the vascular pattern, granularity, and friability appear. Later, punctiform mucosal hemorrhages, mucus secretion, adherent purulent material, and superficial ulcerations develop. Less frequently large isolated ulcers with normal surrounding mucosa can be found like in Crohn's disease. Undiagnosed Crohn's disease is a rare but important differential diagnosis particularly if large ulcers or fistulas (e.g. pouch–vaginal fistulas) are present. Seldom pseudomembranous lesions may be observed, which mandates stool sampling to exclude *C. difficile* infection.

Several scores to assess the severity of pouchitis have been developed, the first of which was proposed by Moskowtiz et al. [49] applying very strict clinical and endoscopic criteria. Sandborn and colleagues introduced the Pouchitis Disease Activity Index (PDAI) combining clinical, endoscopic, and histological findings [50], which is now most often used in clinical studies. This score evaluates the presence of edema, granularity, friability, faded vascular pattern, mucous exudate, and ulceration. Equal weight is attributed to all these parameters. A similar score, the pouchitis activity score (PAS), was proposed by the Heidelberg group and utilizes the same endoscopic criteria but differentiates between mild and severe lesions [51]. The treatment of pouchitis should not only aim at symptomatic improvement, but at complete healing and restoration of the pouch mucosa, as well.

Pouchitis generally involves most of the pouch reservoir and should be differentiated from ‘cuffitis’. This entity represents a recurrence of ulcerative colitis in the short cuff of the rectoanal transitional zone that has been preserved in case of a double-stapled pouch anastomosis. It usually extends over a distance of 1 cm. The endoscopic feature is that of a distal ulcerative proctitis with a clear demarcation
to ileal pouch mucosa. It is important to know that mucosal dysplasia can occur in this transitional zone, although the risk is very low [52].

**Endoscopic treatment of Crohn's disease complications**

Fibrotic strictures are commonly observed in Crohn's disease, even in quiescent disease or in bowel segments ‘healed’ with immunomodulatory or biologic therapy. Strictures causing obstructive symptoms can occur anywhere in the gastrointestinal tract, but there is a clear predilection for the ileocecal valve, the ileocolonic anastomosis, the duodenum, the sigmoid colon, and the anal canal. Anal and distal colonic strictures can be treated with Savary dilators over a guidewire but for stenoses more proximal in the colon endoscopic balloon dilation is the sole option. The efficacy and safety of through-the-scope (TTS) balloon dilatation for Crohn's disease strictures has been reported in a number of studies [53–58]. Success rates in our series (defined as easy passage of a 13.6-mm colonoscope through the stenosis after dilatation) was achieved in 90% of patients. Sixty-two per cent of patients avoided a surgical resection in the long term. A minority of patients needs repeated dilatations. Complications of TTS dilatation include perforation and bleeding. On average a 10% complication rate has been reported in the literature. For this reason, patients should be carefully selected on the basis of X-ray studies. Anastomoses situated in a sharp angle from the colon, long stenoses, multiple stenoses, and stenoses more proximal in the terminal ileum usually do not qualify for endoscopic dilation procedures.

Anal or supra-anal dilation is usually performed with a thin endoscope and additional Savary dilation. The procedure can be reinforced by home autodilation of the stenosis. It is our opinion that balloon dilatation of the anus is not recommended because of the potential risk of sphincter damage.

**Conclusion: the role of endoscopy in IBD (Fig. 14)**

The endoscopic evaluation of patients with IBD is extremely valuable and has changed the management of these diseases. Ileocolonoscopy has replaced contrast enemas in the first evaluation of patients with suspected IBD. Nonetheless, these procedures are only justified when they are likely to influence therapeutic decisions. Ileocolonoscopy can be necessary to establish an exact (‘tissue’) diagnosis, to determine the severity and extent of inflammatory activity, in the preoperative setting to ‘guide’ the surgeon, and to examine the bowel proximal to stomas. Early endoscopic examination of the ileocolonic anastomosis after resection of the terminal ileum and part of the colon enables evaluation of the severity of recurrence of Crohn's disease, predicting clinical outcome.

Endoscopic examination of the upper gastrointestinal tract should be performed whenever upper GI symptoms develop. It is important for the treatment to differentiate between intrinsic Crohn's lesions, peptic disease or drug-associated lesions in the esophagus, stomach, or duodenum.

Endoscopic observations certainly have therapeutic consequences in pouchitis, in patients with Crohn's disease following surgical resection and in severe attacks of ulcerative colitis. Complete mucosal healing should be a therapeutic goal in all patients with ulcerative colitis. Whether it should be a therapeutic goal in Crohn's disease as well remains to be established.

**References**

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