

## Part 4

# Common Clinical Challenges: Beyond the Text Book

## 34

### Functional problems

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#### LEARNING POINTS

##### Functional problems

- Evidence accumulates for low-grade mucosal and muscularis inflammation in irritable bowel syndrome (IBS)
- Inflammation in inflammatory bowel disease (IBD) may disrupt intestinal motor and sensory systems and alter gut function
- Patients with IBS and IBD may, at times, share similar symptoms
- Confusion between IBS and IBD is most likely to occur when IBD is “subclinical” or in apparent remission
- Upper gastrointestinal symptoms in the IBD patient are more likely to be caused by reflux or functional dyspepsia than IBD

#### Introduction

In the past, inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS) were regarded as such distinct and separate entities that they were never even considered in the same context. We now recognize, not only that they may coexist and that IBD patients may have a predilection to IBS-type symptoms, but that mucosal inflammation may be an important phenomenon in IBS. How things have changed!

#### Theory

Recent interest in a putative role for inflammation in IBS, coupled with experimental evidence for important interactions between inflammation and gut muscle and nerve,

have rekindled an examination of relationships between IBS and IBD. Few would propose that these disorders represent one and the same disease process; what we know of their respective natural histories, genetics, immunology, pathophysiology, and pathology renders such a proposal a non-starter. However, recent information suggests that lessons derived from research and clinical experience in one disorder may cast light on enigmas and clinical challenges in the other. Interactions with the “internal” or luminal environment appear important in both; it is now not unreasonable to suggest that IBD and IBS represent dysfunctional responses to luminal antigens, whether presented by the indigenous or an aberrant flora. In IBD, in particular, there is abundant evidence to indicate a central role for the gut flora in the initiation and perpetuation of the inflammatory process.

Evidence to support a role for luminal factors in IBS can be garnered from three main sources: the role of prior infection in the initiation of IBS; the suggestion that chronic, low-grade inflammation is common in IBS; and, finally, and most contentious, reports of alterations in the gut flora in IBS. The concept of post-infectious IBS (P-I IBS), long-recognized by clinicians, is now well established and supported by several prospective and retrospective studies [1]. There is also compelling evidence for a role for low-grade inflammation in IBS [2]. In one study of 77 IBS patients, 31 demonstrated microscopic inflammation and eight fulfilled criteria for lymphocytic colitis [3]. Among the group with “normal” histology, immunohistology revealed evidence of immune activation in all. That IBS patients may be predisposed to an – albeit contained – inflammatory response to luminal triggers is also supported by findings of a reduced frequency of the high-producer

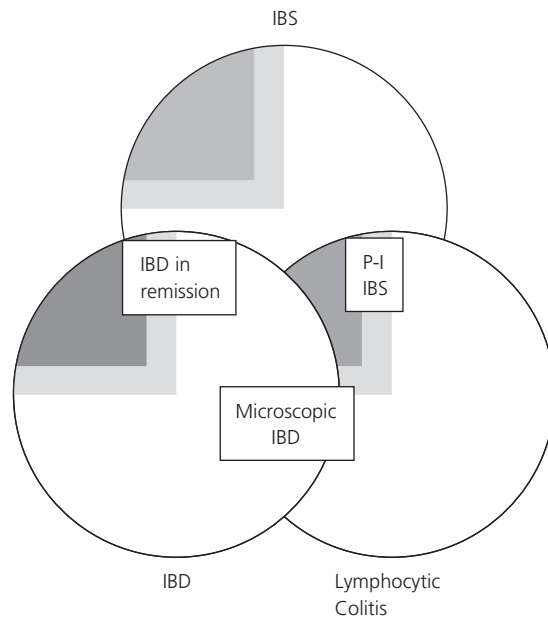
phenotype for the anti-inflammatory cytokine interleukin-10 (IL-10) [4] and by the documentation of a reversal of the normal ratio between IL-10 and the pro-inflammatory cytokine IL-12 [5]. The finding, in one study, of low-grade infiltration of lymphocytes in the myenteric plexus in 9/10 patients with severe IBS provides evidence for the extension of the inflammatory process beyond the confines of the mucosal compartment [6].

Dysmotility and visceral hypersensitivity are widely believed to be foremost in the pathogenesis of symptoms in IBS [7]; both also occur in IBD. IBD provides considerable evidence for a role for inflammation in motor dysfunction; there is, indeed, a suggestion that some of the motor abnormalities associated with IBD [8] may persist following apparent resolution of inflammation, thus providing one potential explanation for why some IBD patients' disease could evolve into an IBS-type syndrome during periods of remission. This intriguing suggestion is supported by studies associating IBS-type symptoms with impaired quality of life among IBD patients in remission [9,10]. Another example of a potential interaction between IBS and IBD was recently presented by Shen *et al.* [11]. Among 61 patients who developed symptoms suggestive of pouchitis following ileal pouch-anal anastomoses for UC, 26 failed to achieve diagnostic criteria for pouchitis and were described as suffering from the irritable pouch syndrome (IPS). Observations from experimental studies indicate that chronic inflammation may lead to changes in the phenotype of both smooth muscle and enteric neurons, to the extent that they can assume immunologic functions, leading to a self-perpetuating cycle of interactions between inflammatory cells and the enteric neuromuscular apparatus, *per se*. These changes have been noted in the context of inflammation limited to the mucosa, even at sites remote from the inflammation [12].

It has been suggested that visceral hypersensitivity is highly specific for IBS [7]. While visceral sensation has received little attention in IBD, in general, the potential role of sensory dysfunction is amply exemplified by acute proctitis where rectal compliance is reduced and the rectum is hypersensitive, factors that contribute to the symptoms of urgency and tenesmus which are the hallmarks of this disorder [13].

### Clinical dilemmas

The interactions between IBS and IBD may impinge on



**FIG 34.1** Potential relationships between irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD). PI-IBS, post-infective IBS.

clinical practice and present significant diagnostic and therapeutic challenges, both at initial presentation and during follow-up (Fig. 34.1).

At the time of initial evaluation, the following clinical presentations may present a diagnostic challenge.

### Chronic abdominal pain and constipation-predominant IBS

Here, IBD and IBS may both be considered in the differential diagnosis. It must be emphasized, however, that chronic abdominal pain, *in the absence of* any alteration of bowel habit or of any evidence of systemic upset is an exceptionally rare manifestation of IBD and cannot, by definition, be regarded as IBS [14]. Other causes, or in the absence of any evidence of an “organic” cause, functional abdominal pain should be considered. In the absence of evidence of episodes of acute or subacute obstruction, the diagnosis of chronic intestinal pseudo-obstruction should, in general, not be considered.

Similarly, it must also be stressed that the likelihood of missing IBD in a young female with the typical symptoms of constipation-predominant IBS, *in the absence of* diarrhea, systemic upset, or any of the physical or laboratory

findings characteristic of Crohn's disease, is rare. For these reasons, the yield of small bowel X-rays and colonoscopy in these populations is as close to zero as makes no clinical difference [14].

My personal view is that colonoscopy is *not* indicated in either of these scenarios and could well be regarded as inappropriately invasive.

### Chronic diarrhea or diarrhea-predominant IBS

This clinical context is completely different from those described above and the threshold for investigation much lower. Diagnoses such as IBD, celiac disease, and disaccharide intolerance should always be considered in a patient who truly presents with chronic persistent diarrhea.

As ever in clinical medicine, attention to the patient's history and an awareness of the clinical context are of critical importance in the approach to the patient at initial presentation. The attentive and aware clinician should be able to avoid performing unnecessary, invasive, and distressful procedures.

### Established IBD

There is, to my mind, more potential for diagnostic confusion in the follow-up of patients with established IBD. The following scenarios may present special challenges.

#### Altered bowel habit

*The recurrence, or persistence of, altered bowel habit, associated with abdominal discomfort, in the patient with IBD who has been in apparent remission.*

In Crohn's disease, in particular, there are many potential causes, other than active disease, for diarrhea (see Chapter 46) and associated abdominal cramps. Once these have been eliminated, and clinical and laboratory evaluations provide no evidence of disease activity, IBS may be considered. It is of interest that systemic markers of inflammation have been shown to be elevated to a similar extent in IBD in remission, and in diarrhea-predominant IBS [15]. It should be remembered, especially in areas of high prevalence, that coincidental celiac disease may generate similar symptoms.

### Development of upper gastrointestinal symptoms

#### Esophageal symptoms

In this context it must be remembered that gastroesophageal reflux disease (GORD) is a much more likely

explanation for heartburn, chest pain, or regurgitation in a patient with IBD than esophageal Crohn's disease. If empiric treatment does not resolve the issue, endoscopy will.

#### Dyspeptic symptoms

Symptoms suggestive of delayed gastric emptying may arise in IBD for a number of reasons. Clearly, antroduodenal Crohn's may actually obstruct the gastric outlet. Furthermore, gastric emptying delay has also been documented in patients with active IBD, and especially Crohn's disease, in the absence of actual involvement of the foregut [8]. Finally, there is no reason why patients with IBD should be regarded as immune from the development of functional or non-ulcer dyspepsia. In each of these instances, attention to clinical details, basic laboratory assessment and, where doubt persists, endoscopy should resolve the dilemma.

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