

Colitis

Terminology for the diagnosis of colitis

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Are indeterminate colitis and microscopic colitis useful terms?

During the past few years, there has been a “proliferation” of terms used for the diagnosis of colitis. This reflects the fact that colitis is a complex condition, but the different terminologies are often a source of disagreement between pathologists and clinicians and, at times, can result in misdiagnosis. “Microscopic colitis”, “indeterminate colitis”, and “non-specific colitis” are terms frequently used but not always clear to the clinician. Therefore, it is reasonable for the clinician to abide by the dictum “when I receive a diagnosis of non-specific colitis, I prescribe a non-specific treatment”. However, the clinician may also have insufficient knowledge. The major problem is a vague definition or lack of definition. Non-specific colitis is an acceptable diagnosis when clinical information is lacking. The microscopic picture is characterised by an increase in inflammatory cells beyond what would be expected physiologically in the corresponding anatomical sites. The cellular infiltrate is predominantly chronic, with the absence of architectural distortion and multiple basal lymphoid aggregates or plasma cells immediately above the muscularis mucosae. Crypts may show an increase in mitoses and slight irregularity in shape. Lack of sufficient clinical data or distinctive pathological features precludes further classification into specific aetiological types of colitis.¹ Such a pattern can be seen in resolving infections, complicated diverticular disease, drug induced colitis, and bile salt malabsorption, but may also be seen in Crohn’s disease (CD). However, it is impossible to make a positive diagnosis of CD in these circumstances, although in a patient with known CD the lesions may represent local involvement.²

However, a more precise diagnosis by the pathologist is often possible when clinical information is available. In such a situation, the clinician should decide on the final diagnosis or provide the clinical data.

The term “microscopic colitis” was introduced to describe lesions found in patients with chronic watery diarrhoea of unknown origin.³ Later, microscopic colitis was proposed as an umbrella

term for two conditions (lymphocytic colitis (LC) and collagenous colitis (CC)) and defined as a condition in which there was histological but no endoscopic or radiological abnormality.^{4, 5}

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Yet, there are several diseases with normal endoscopy and abnormal histology (intestinal spirochetosis, quiescent ulcerative colitis, infectious colitis, diverticular disease, and non-steroidal anti-inflammatory drug induced colitis). Although these conditions could be covered by the definition, they are not usually considered as microscopic colitis. Today, the term microscopic colitis is used for two entities—CC and LC—the first mainly characterised by an increase of the subepithelial collagen layer over 10–15 µm and the second by an increase in the surface epithelium of T cells over 30/100 epithelial cells. Several variants of these two conditions have been reported but these are probably not specific entities. LC, CC, and the variant forms are clinically characterised by chronic watery diarrhoea.^{6, 7} The correct differential diagnosis between the two conditions and between LC and CC and the other forms of colitis is very important for the patient because treatment may differ. Terms such as non-specific chronic inflammation or signs of chronic inflammatory bowel disease but non-diagnostic should be avoided. Nevertheless, the conclusion in a pathology report is not always clear. One of the reasons may be lack of sufficient clinical data and another may be the absence of diagnostic features. In such cases, it is better to indicate that alterations are minor and may not explain the complaints. Minor features of inflammation may indicate resolving colitis—it has been shown that mononuclear cells can persist for a long time after an infection.⁸

When the pathologist proposes a diagnosis of either LC or CC, further investigation is required. This problem is illustrated by a review of eight cases of LC and 31 cases of CC (V Villanacci,

unpublished data, 2004). In LC, the range of patients’ (five women, three men) ages was 36–69 years for women and 35–61 years for men, whereas in CC (17 women, 14 men) the range was 51–82 for women and 35–79 for men. In the LC group, five cases were present in patients with coeliac disease, one case in slow transit constipation (not an autoimmune colitis), one in diverticulitis, and one in a patient with non-steroidal anti-inflammatory drug abuse. Chronic watery diarrhoea was present in all patients in the CC group. Three cases were present in patients with coeliac disease, and in another three patients there was a history of ticlopidine treatment. These findings reveal that similar morphological patterns can have different aetiologies, including idiopathic cases and infections. Although both CC and LC respond dramatically to anti-inflammatory treatment, other options must be considered in drug related cases. The association between LC or CC and coeliac disease deserves special attention. Colon biopsies showed changes characteristic of LC in 25% of patients with coeliac disease.⁹ Microscopic abnormalities of the colon are common in patients with coeliac disease after experimental exposure to wheat or gliadin enemas, suggesting that the entire intestinal tract may be susceptible to gluten induced injury. Because of the large variety of possible diseases, the term microscopic colitis has little clinical value. We propose to drop this “umbrella” term, because a large variety of conditions can present with diarrhoea without macroscopic lesions and because collagenous and lymphocytic colitis can be associated with endoscopic abnormalities. We propose to use only the precise terms of CC and LC for patients presenting with a history of chronic watery diarrhoea, normal endoscopy, and normal radiology, being aware of the fact that several aetiological possibilities must be considered.

“It is important to define the terminology as clearly as possible and to use the terminology consistently to avoid confusion”

There is also a similar situation in the field of inflammatory bowel disease with the category of indeterminate colitis (IC). This term, in its original definition, was used mainly in cases of fulminant colitis and only on surgical specimens.¹⁰ Over the years, the meaning of the term has changed and IC has been used also for endoscopic biopsies.¹¹ More recently, Guindi and Riddel¹² wrote: “It is preferable to reserve the term IC for colectomy specimens. When

faced with difficulties in classifying inflammatory bowel disease into CD or ulcerative colitis in biopsies, the term IC should not be used. We prefer to use the term 'inflammatory bowel disease not yet classified'. However, it may not be so simple. IC is a term that is often used by clinicians for patients with an uncertain diagnosis. In such patients, serology for antineutrophil cytoplasmic antibodies and anti-*Saccharomyces cerevisiae* antibodies may also not be useful, in contrast to other cases where positive serology may help to reach a definite diagnosis. In difficult cases, biopsies from the stomach and the duodenum, imaging of the small intestine (ultrasound, x ray, videocapsule, and enteroscopy), and control biopsies may help to solve the diagnostic problem. For the remaining cases, a proper terminology is required, which needs a proper definition. IC should be used only for surgical cases where the diagnosis is equivocal, because pathologists have certain features and guidelines for the analysis of these cases, or for cases where the overall

diagnosis (clinical, serological, etc.) is uncertain, or better still, not used at all.

In conclusion, it is important to define the terminology as clearly as possible and to use the terminology consistently to avoid confusion. Changes in terminology should only be considered when scientific progress can provide a better understanding of these entities.

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