

What is the natural history of a patient with “non-specific” colitis on large bowel histology?

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From the histologic point of view ‘colitis’ is microscopic inflammation of the colon. Colitis may be acute or chronic, diffuse or focal based on the etiological factor(s) and the type and distribution of the inflammatory infiltrate that prevails in the colon. Very often the pathologist encounters acute inflammation superimposed on chronic inflammation; this may be indicative of an acute exacerbation of chronic colitis, as is the case in a recent flare of chronic ulcerative colitis.

Although ‘changes of non-specific colitis’ is a very common concluding remark in histology reports on colonic biopsies, I was unable to trace the term ‘non-specific’ colitis’ as a unique clinical entity. Strictly speaking this is a misnomer which refers essentially to the histologic interpretation of an underlying colonic inflammation that has no characteristic qualitative and/or quantitative features to be properly classified as a specific form of acute or, usually, chronic colitis. Essentially, either the pathologist has not found a specific cellular infiltrate or any characteristic changes in the gland architecture or epithelial cells that can be helpful in classifying the inflammation he/she sees, or alternatively, despite adequate information the pathologist is unable to identify a specific form of colitis.

Why is that?

Basically, there are several reasons potentially related both to the gastroenterologist and the pathologist.

One scenario is that the gastroenterologist has *actually* found endoscopic features of colitis but has failed to

obtain proper biopsies that would otherwise have given clues to the histological diagnosis. Timing of biopsies in relation to the natural history of certain forms of colitis may also be important. For instance, the histology underlying acute self-limiting colitis may change during the course of disease.¹ Another scenario is that the endoscopist sees a normal colon in a patient with colitic symptoms but underestimates or ignores the need to obtain biopsies from the entire colon. For instance biopsies restricted to the rectal area may be inadequate for the diagnosis of microscopic colitis and the pathologist may interpret colonic histology erroneously as non-specific.² Finally, since gastroenterologist-pathologist feedback is an integral part of the diagnostic workup of the patient, failing to report on key-issues of the patient’s present and past medical history which are related to the current illness may misguide the pathologist.

Technical failures, such as improper or inadequate processing, orientation, cutting, and staining of the histology specimens, usually pose serious obstacles to the pathologist in assessing the true histological features of colitis. Furthermore, it is of utmost importance that the pathologist has a particular interest and expertise in interpreting colonic biopsies.

However, assuming that none of the aforementioned scenarios actually occur and indeed the pathologist truly cannot reach a firm conclusion regarding the specificity of histological features, what does this mean to the patient?

Well! I am afraid that this cannot be answered in a quiz-like style. The prognosis of ‘non-specific’ colitis cannot be based solely on histological features. One needs to be aware of the patient’s medical history and certain demographic, clinical, and laboratory parameters. Information regarding recent treatments, co-morbidities, reactions to medicines, prior surgical procedures, etc is all

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too important. A history of irritable bowel syndrome-like symptoms, allergies, asthma, chronic laxative or NSAIDs intake, autoimmune diseases, congestive heart failure, chronic liver disease, alcohol abuse, smoking, etc may be very relevant to the interpretation of 'non specific' colonic histology. A family cluster of gastrointestinal diseases such as inflammatory bowel disease or coeliac disease may also be invaluable. Additional tests tailored to patient's medical history may be needed to establish a proper diagnosis and predict the long-term outcome.

What are the medical conditions or diseases that may be potentially associated with 'non-specific' colonic histology?

Irritable bowel syndrome (IBS) is probably by far the commonest cause of non-specific colonic inflammation. Being aware that IBS is actually an inflamed colon compared to the colon of healthy people would prevent the pathologist from labeling IBS as a non-specific colitis. Unless complicated by another colonic disease, such as diverticulosis, histologic features of IBS are highly unlikely to change overtime.

Inflammation of the mucosa intervening neighboring diverticuli may be seen on colonoscopy. Although this form of colitis may share in common some histologic features with solitary rectal ulcer, ischemic colitis, or Crohn's disease, histology is often non-specific and, therefore, difficult to classify.^{3,4} Worsening of colitis, diarrhea and rectal bleeding may be seen with progression of diverticular disease. On the contrary, mesalazine may relieve symptoms and colonic inflammation.

Although microscopic (or lymphocytic) colitis (MC, CC) was initially termed as 'minimal changes colitis' intensive research has characterized specific histologic features both in the colonic epithelium and the lamina propria.^{5,6} As mentioned earlier, failure to identify these specific histological features of MC may be the consequence of inadequate yielding or interpretation of colonic biopsies. Some investigators claim that MC and CC are the far ends in the spectrum of a single disease and, therefore, treatment may turn a CC into MC. On the other hand, MC if left untreated may end up to full-blown Crohn's disease.

Untreated coeliac disease produces colonic inflammation with histologic features similar to MC.² However, CD may be associated occasionally with non-specific colonic histology. Symptoms are not generally related to colonic involvement but gluten-free diet is expected to restore a normal colonic histology. The colon may also be microscopically and non-specifically involved in the

course of other autoimmune diseases, usually extra-intestinal. This may be related to disease or its treatment, and usually does not have any long-term clinical implications.²

Infective colitis has specific features which are easily detected by an expert GI pathologist. However, if random biopsies are taken during the late restorative phase of the disease histologic features may not be specific for the diagnosis.¹ Rectal biopsies in patients with mild diarrhoea after a recent use of antibiotics may show non-specific inflammation.⁷ However, obtaining more widespread colonic biopsies compensates for the non-specific rectal histology. This colitis usually resolves spontaneously.

In conclusion, there is no clinical condition defined as 'non-specific colitis'. When applied, this term implies a positive diagnosis and creates anxiety both to the patient and the physician regarding its long-term outcome and prognosis. Therefore, the pathologist who has all the background clinical information and proper biopsies should not report this term in the concluding remark. However, if features of chronic colitis are seen and these cannot be interpreted in view of the medical history of the patient, it is much more preferable to describe the histology as '*not characteristic for a particular disease*' rather than labeling it a 'non-disease'. In general, non-specific histological features are often encountered in patients with functional or benign organic colonic disorders and occasionally in the context of colonic involvement in the natural history of an extra-colonic disease. Therefore, the long-term prognosis is that of the underlying functional or organic disease and usually resolves with proper treatment or, at least, is not aggravated in most cases.

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