Histological activity and basal plasmacytosis are non-predictive markers for subsequent relapse in ulcerative colitis patients with mucosal healing

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Abstract

Introduction: The assessment of histological remission started to become a more accurate and favorable therapeutic endpoint in ulcerative colitis (UC). This study aimed to investigate the rate of clinical relapse in UC patients after achieving mucosal healing and to evaluate the predictive role of basal plasmacytosis and microscopic inflammation on disease relapse.

Patients and methods: This was a prospective observational study conducted in UC patients with endoscopic remission defined by endoscopic Mayo (eMayo) subscore 0 or 1. All patients underwent colonoscopy and biopsy samples were taken from the uninflamed colonic mucosa. Follow-up appointments were months 6, and 12. Microscopic inflammation was defined as a Geboes score ≥3.1.

Results: Sixty-nine adult UC patients were enrolled in the study. Histology revealed basal plasmacytosis in 81.2% (focal plasmacytosis in 63.8%, diffuse plasmacytosis in 17.4% of the cases) and microscopic inflammatory activity in 37.7% of patients with mucosal healing. At 6 and 12 months, clinical relapse occurred in 16.2%, and in 14.5% of the patients. Geboes score ≥3.1 and plasmacytosis detected in the biopsy samples at baseline were present in 9.1 and 72.7% of the patients’ samples relapsed at month 6, in 40 and 80% of the patients’ samples relapsed at months 12. Neither the presence of basal plasmacytosis, nor Geboes score ≥3.1 was shown to be predictive of disease relapse.

Conclusion: The role of histological inflammation with mucosal healing requires more extensive research. Our results suggest that maintaining therapy after achieving endoscopic remission may influence the association between basal plasmacytosis and clinical relapse.

Keywords: Ulcerative colitis; Mucosal healing; Microscopic inflammation; Basal plasmacytosis; Relapse

Introduction

Mucosal healing has now been accepted as an essential target both in clinical trials and practice as well. Although many data support that mucosal healing is associated with prolonged clinical remission, lower rates of hospitalization and colectomy, recent studies came up with reverse data showing that mucosal healing does not predict sustained clinical remission in patients stopping biological therapy [1, 2]. Since microscopic inflammation can even be detected in patients with mucosal healing, the assessment of histological remission started to become a more accurate and favorable therapeutic endpoint [3].

Geboes score including five features (architectural change, lamina propria neutrophils and eosinophils, neutrophils in epithelium, crypt destruction, and erosion or ulceration), is one of the best validated and most widely used index for the assessment of histological healing that was shown to predict relapse in ulcerative colitis (UC) patients achieving clinical and endoscopic remission [4, 5]. Moreover, Bitton et al. revealed that basal plasmacytosis, defined as the presence of plasma cells between the base of the crypts and the muscularis mucosae, was a significant predictor of relapse [6]. Since none of the histological scoring systems includes the assessment of basal plasmacytosis and limited data are available about the value of basal plasmacytosis and microscopic inflammation in quiescent UC, we aimed to investigate the rate of clinical relapse in UC patients after achieving mucosal healing and to evaluate the predictive role of basal plasmacytosis and microscopic inflammation on disease relapse.

Patient and Method

Patient population

This was a prospective observational study conducted in UC patients with endoscopic remission defined by endoscopic Mayo (eMayo) subscore 0 or 1 [7]. All patients underwent colonoscopy, and biopsy samples were taken from the uninflamed colonic mucosa. All colonic biopsies were separately evaluated by two
expert pathologists for histologic activity (Geboes score) and the presence of basal plasmacytosis with focal or diffuse pattern. Basal plasmacytosis was defined as dense infiltrate of plasma cells around the deep part of the lamina propria or at the base of the crypts. C-reactive protein (CRP), partial Mayo (pMayo) scores and the used medications were documented at the time of the endoscopy, and the follow-up appointments: at months 6, and 12. Microscopic inflammation was defined as a Geboes score ≥3.1 Disease relapse was defined as a partial Mayo (pMayo) score ≥3. Alteration in CRP levels was compared to the baseline CRP values.

**Statistical analyses**

Multinominal logistic regression and linear mixed models were used to assess the predictive value of basal plasmacytosis and microscopic inflammation on disease relapse with evaluating the alteration of CRP and pMayo scores during the follow-up appointments. P-values < 0.05 were considered significant for the analysis.

**Results**

Sixty-nine adult UC patients over 18 years of age with an endoscopically inactive disease and at least a 12-month follow-up were enrolled in the study. The mean age at diagnosis was 31.4 years. The mean value of pMayo score at the time of the endoscopy was 0.65. Maintenance therapies at enrollment consisted of corticosteroids in 11.6%, immunomodulators in 52.2% and biologicals in 18.8% of the patients. Demographic data are summarized in Table 1. Histology revealed basal plasmacytosis in 81.2% (focal plasmacytosis in 63.8%, diffuse plasmacytosis in 17.4% of the cases) and microscopic inflammatory activity with a Geboes score ≥3.1 in 37.7% of patients with mucosal healing. The mean time of follow-up was 1 year. At 6 and 12 months, clinical relapse occurred in 16.2%, and in 14.5% of the patients.

Geboes score ≥3.1 and plasmacytosis were detected in the biopsy samples at baseline histological examination in 9.1 and 72.7% of the patients who relapsed at month 6 and in 40 and 80% of the patients who relapsed at months 12. In nonrelapsers, microscopic inflammation and basal plasmacytosis were detected at the baseline in 43.1 and 82.8% of the patients’ samples at month 6, and in 44.2 and 82.7% at month 12.

Neither the presence of basal plasmacytosis, nor Geboes score ≥3.1 was shown to be predictive of disease relapse nor alteration in CRP levels at 6, and 12 months. No difference was observed if the data were analyzed separately in subgroups of eMayo score of 0 or 1. Presence of basal plasmacytosis and microscopic inflammation in relapers and nonrelapers are shown in Figure 1 and Figure 2. Figure 3 contain the alterations of the medications during the examined period.

**Discussion**

Our results did not confirm the previous hypothesis that the presence of basal plasmacytosis and microscopic inflammation predicts UC clinical relapse in patients with mucosal healing at
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The presence of basal plasmacytosis in colonic endoscopic biopsies was a strong histological feature of IBD and helped in the differentiation from non IBD colitis. Basal plasmacytosis was always present in the ileum, cecum, and ascending colon, and variably present (17–60%) in the other segments in CD, whereas in UC patients it was always present in the transverse and descending colon, and consistently present (77–87%) in the other segments. The study by Bessissow et al. consisted of 75 UC patients confirmed that basal plasmacytosis, whether present in a focal or diffuse pattern, is an independent predictor of clinical relapse in UC patients with mucosal healing with a sensitivity, specificity, and accuracy of 47, 85, and 77%, respectively. Inflammatory activity with a Geboes score ≥3.1 was shown in 40% and basal plasmacytosis in 21% of the patients with endoscopic remission. At 12 months, clinical relapse occurred in 20% of the patients. The study also revealed a strong trend toward a protective effect of biological therapy [5]. Comparing Bessissow’s data with ours, the most remarkable difference is the higher rate of basal plasmacytosis in our cohort. Notably, focal plasmacytosis consisted almost two-thirds of our cases that may influence the statistical analysis in these works. In our study relapse rates also differed markedly, in the Bitton’s study 36%, in the Bessissow’s study 20% of the patients relapsed. In our study the relapse rates were lower than in the above mentioned works despite of the high rate of basal plasmacytosis. Moreover, although maintenance therapy did not prove to be associated with the presence of basal plasmacytosis or microscopic inflammation in our relapsers, the type and the distribution of the medications differed in the two studies (etc. using steroids), therefore the role of concomitant therapy cannot be irrelevant when analyzing the results.

Although our results did not show that the presence of basal plasmacytosis and microscopic inflammation predicts UC clinical relapse in patients with mucosal healing despite having a normal mucosa endoscopically, the role of histological inflammation with mucosal healing requires more extensive research. Our results suggest that maintaining therapy after achieving endoscopic remission may influence the association between basal plasmacytosis and clinical relapse.

Take home messages

Markers predictive to disease relapse in UC patients achieving mucosal healing are becoming more and more important. Our study did not confirm the predictive role of basal plasmacytosis and microscopic inflammation in clinical relapse in UC patients with endoscopic remission; however, maintenance therapy was suggested to influence the association between basal plasmacytosis and clinical relapse.

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