学 位 論 文 の 要 旨

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学 位 論 文 名　Capabilities of Fecal Calprotectin and Blood Biomarkers as Surrogate Endoscopic Markers according to Ulcerative Colitis Disease Type

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論 文 内 容 の 要 旨

INTRODUCTION

Ulcerative colitis (UC) is an immune-mediated disorder characterized by chronic mucosal inflammation in the colon. In recent years, management of UC has substantially changed in accordance with development of novel effective drugs, while evaluations of mucosal inflammation and healing have emerged as essential management procedures for considering the necessity of therapeutic intervention. In general, though an endoscopic examination is the gold standard for accurate assessment of disease activity associated with UC, it is relatively invasive and difficult to frequently perform in clinical practice. On the other hand, while blood biomarkers are noninvasive, they are insufficient to precisely reflect endoscopic findings. Recent studies have indicated that the level of fecal calprotectin (FC) is well correlated with disease severity as well as extent of affected mucosa in UC patients. Thus, measurement of FC level as a surrogate marker that reflects colonic inflammation associated with UC is recommended as a part of clinical examinations performed for affected patients. However, the association of that level with various UC disease types has not been fully elucidated. In the present study, we investigated the utility of FC level according to disease type as compared to conventional noninvasive blood biomarkers for predicting endoscopic findings.

MATERIALS AND METHODS

UC patients who underwent colonoscopy examinations were enrolled. FC as well as blood biomarkers, including C-reactive protein (CRP), white blood cell count (WBC), erythrocyte sedimentation rate (ESR), hemoglobin (Hb), platelets, and serum albumin (Alb), were measured within the 3-day period prior to the colonoscopy. Disease type was divided into proctitis (E1), left-sided colitis (E2), and extensive colitis (E3), according to the Montreal classification. Correlations of FC, clinical disease activity shown by partial Mayo score (stool frequency, rectal bleeding, physician's global assessment) or blood biomarker levels with Mayo endoscopic subscore (MES) were analyzed by Spearman's rank correlation coefficient. A total of 186 colonoscopy examinations were performed in 124 patients with UC. The study protocol was approved by the Ethics Committee of Shimane University and written informed consent was obtained from all subjects.

RESULTS AND DISCUSSION

Of the 186 colonoscopy examinations, 93 (50.0%) showed extensive colitis (E3), 54 (29.0%) left-sided colitis (E2), and 39 (21.0%) proctitis (E1). FC level had a significant correlation with MES regardless of disease type (E1, $r=0.54$, $p<0.01$; E2, $r=0.75$, $p<0.01$; E3, $r=0.78$, $p<0.01$). Notably, FC value was able to clearly discriminate inactive (MES 0) from active (MES 1-3) stages. On the other hand, none of the examined blood biomarkers showed a correlation with MES in the E1 group, while there were weak correlations of several markers (CRP, WBC, ESR, PLT, Alb) with MES found in the E2 and E3 cases. Moreover, regardless of disease type, clinical disease activity determined by partial Mayo score was significantly correlated with MES (E1, $r=0.74$, $p<0.01$; E2, $r=0.68$, $p<0.01$; E3, $r=0.73$, $p<0.01$) as well as FC level (E1, $r=0.62$, $p<0.01$; E2, $r=0.50$, $p<0.01$; E3, $r=0.71$, $p<0.01$).

Previous studies have found that FC is a reliable noninvasive marker that reflects endoscopic findings. However, whether its level is associated with endoscopic activity according to UC disease type has not been clearly elucidated. In this regard, this is the first report to show a differential capability of FC as compared to conventional blood biomarkers according to UC disease type in a clinical setting.

In addition, our results indicate that FC has a significant correlation with MES regardless of UC disease type. The most important finding of this study is the ability of FC to clearly discriminate inactive (MES 0) from a mildly active stage (MES 1) regardless of disease type, whereas CRP was not found useful for assessment of low-grade mucosal inflammation. Moreover, blood biomarkers were shown useful to predict endoscopic findings only in UC patients with left-sided or extensive colitis, while FC assessment was more sensitive and suitable for UC patients with proctitis. In addition, clinical disease activity was also well correlated with both MES and FC. Taken together, a scheduled assessment of UC patients using FC level as well as partial Mayo score would be helpful for predicting endoscopic findings showing proctitis without the need for invasive testing, and the results useful for deciding a suitable maintenance

strategy in clinical settings.

CONCLUSION

The present results revealed that FC level is significantly correlated with endoscopic findings regardless of UC disease type. On the other hand, none of the examined blood biomarkers showed correlations with endoscopic findings in UC patients with proctitis. We concluded that the utility of FC for predicting endoscopic activity in UC is superior to that of blood biomarkers regardless of disease type.