INTRODUCTION: With the current use of biologics in rheumatoid arthritis (RA), it is necessary to monitor ongoing structural joint damage due to the dissociation of articular cartilage damage from disease activity of RA (1). In this study, levels of serum cartilage biomarkers were longitudinally analyzed during 54 weeks of infliximab therapy, and the feasibility of biomarkers for monitoring structural joint damage was evaluated.

METHODS: The study was approved by the institutional review board at Saitama Medical Center. All the participants were informed about the study and written consent was obtained. Subjects comprised 26 patients with early RA (mean age, 47.8 years) and 26 patients with established RA (mean age, 62.8 years). Mean baseline characteristics were disease duration of 5.6 months and DAS28-CRP 5.22 for early RA, and disease duration of 323 months and DAS28-CRP 4.72 for established RA. All patients received 3 mg/kg of infliximab and methotrexate for 54 weeks. Levels of serum cartilage marker were measured at baseline and at weeks 14, 22, and 54, including hyaluronan (HA), cartilage oligometric matrix protein (COMP), type II collagen (CII)-related neoepitope (C2C), type II procollagen carboxy-propeptide (CPII), and keratin sulfate (KS). Time courses for each biomarker were assessed, and relationships between these biomarkers and clinical or radiographic parameters generally used for RA were investigated.

RESULTS: Satisfactory results were achieved after 54-week infliximab therapy, according to CRP, MMP-3, DAS28-CRP, EULAR response criteria, and annual progression of total sharp score (TSS). Although these parameters were improved to similar degrees in both groups, serum levels of HA and C2C/CPII at week 54 were significantly improved compared to baseline in the early RA group (p<0.001)(Fig.1A), but not in the established RA group (Fig.1B). Strikingly, serum C2C/CPII levels universally improved in early RA, regardless of EULAR response grade and ∆TSS (Fig.2A). In contrast, C2C/CPII levels universally worsened in established RA, even though patients achieved good response (Fig.2B). While ∆HA correlated only with the standard inflammatory indices of ∆CRP and ∆MMP3, ∆C2C/CPII demonstrated significant correlations with ∆NS (r=0.48, p=0.031) and ∆HAQ (r=-0.64, p=0.008), suggesting that CII turnover is closely related to radiographic joint narrowing and patient function.

DISCUSSION: This study suggested that anti-TNF therapy should be started in the early phase from the perspective of CII turnover, while the regenerative capacity of articular cartilage is maintained. As a marker reflecting therapeutic efficacy of anti-TNF therapy, ∆C2C/CPII appears particularly useful for determining the degree of ongoing structural joint deterioration, which is dissociated from clinical assessment of disease activity in RA.

SIGNIFICANCE: As cartilage metabolism dramatically changes during anti-TNF therapy, cartilage biomarkers are applicable for clinical use particularly in monitoring efficacy of this therapy in RA. Type II collagen markers particularly reflect structural joint damage which cannot be detected by CRP and MMP-3 due to the dissociation of articular cartilage damage from systemic inflammation in RA.

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REFERENCE