Letters to the Editor

Rheumatology 2007;46:1858–1859
doi:10.1093/rheumatology/kem254
Advance Access publication 25 September 2007

Cartilage oligomeric matrix protein in systemic sclerosis

Sir, Few biomarkers of systemic sclerosis (SSc) are useful, so physicians must largely depend on physical findings. However, we found that cartilage oligomeric matrix protein (COMP) appears clinically informative in patients with SSc. Here, we describe the relationship between COMP and SSc.

COMP is an extracellular glycoprotein belonging to the thrombospondin gene family that forms a disulfide-linked pentamer and is predominantly found in cartilage, tendons, ligaments and bone growth plates. COMP binds to type II collagen fibres and stabilizes the collagen fibre network [1, 2], and is carried to the bloodstream when cartilage is damaged in arthritis. COMP is thus considered a marker of some types of arthritis, such as osteoarthritis and rheumatoid arthritis [3, 4]. However, a relationship has recently been identified between COMP and some types of fibrosis, such as chronic pancreatitis and renal fibrosis [5, 6]. We, therefore, measured the concentrations of serum COMP in SSc and analysed COMP expression in SSc and healthy skin specimens.

We analysed skin samples from 48 patients (6 men, 42 women; mean age 55.8 yrs; range 27–80 yrs) with SSc who attended Sapporo Medical University Hospital and 20 healthy volunteers (3 men, 17 women; mean age 53.9 yrs; range 29–78 yrs). SSc patients fulfilled the classification of the American College of Rheumatology [7]. No SSc patients displayed any other rheumatic diseases. Radiography excluded arthritis as a cause of joint damage in the knees of patients. Clinical symptoms, complications and serological characteristics including autoantibodies were investigated. We initially measured serum levels of COMP in patients with and without arthralgia, interstitial pneumonia and auto-antibodies using enzyme-linked immunosorbent assay (ELISA). We then immunohistologically evaluated punch biopsies from SSc skin lesions and normal skin by anti-COMP antibody staining. We obtained written consent from all subjects according to the Declaration of Helsinki, and the local ethics committee reviewed the study and raised no objections.

SSc was diffuse cutaneous type in 19 patients and limited cutaneous type in 29 patients. Arthralgia due to SSc was seen in 19 patients, while interstitial pneumonia was present in 14 patients. Serological findings revealed anti-topoisomerase I antibodies in five patients, anti-centromere antibodies in 16 and anti-RNA polymerase III antibody and anti-Ku antibody in one patient each.

Serological analyses showed that serum COMP concentrations were higher in SSc patients than in healthy controls (Fig. 1). Mean serum COMP level was 13.5 U/ml (range, 0.0–33.4 U/ml), higher than the mean levels we previously identified in patients with rheumatoid arthritis (10.9 U/ml, n = 20) or Sjögren’s syndrome (8.6 U/ml, n = 13) [4]. Mean serum levels of COMP were 16.8 U/ml in diffuse cutaneous SSc and 11.3 U/ml in limited cutaneous SSc (P < 0.005). Serum concentrations of COMP did not differ significantly between SSc patients with and without arthralgia (12.0 vs 14.5 U/ml, respectively; P = 0.18). Mean serum levels of COMP were also similar between groups with and without interstitial pneumonia (P = 0.85). Values also did not differ significantly with respect to the presence or absence of auto-antibodies. Immunohistological findings were surprising, with COMP expressed in coarse and hypertrophic dermis only from SSc patients.

COMP was originally described in 1992 as a non-collagenous protein located mainly in cartilage [3], and has since been considered as a biomarker of joint disorders. However, COMP might in fact be involved in various pathogenic mechanisms, since the protein is up-regulated in degenerating acinar cells of chronic pancreatitis [5] and vascular lesions of atherosclerosis [8]. COMP might accumulate in abnormal sites associated with some types of fibrosis.

Human dermal fibroblasts can produce COMP in vitro [9]. A study by Tan et al. [10] using DNA-microarrays showed that the COMP gene is expressed more frequently in cultured dermal fibroblasts from SSc patients than in those from healthy controls. COMP protein also accumulates in SSc, but not in normal skin. We have further confirmed abnormal COMP protein expression in SSc skin samples by immunochemistry. COMP overexpression can stimulate excess matrix deposition.

The present study showed that serum COMP levels are significantly elevated in patients with SSc. This is the first report to describe a relationship between SSc and serum COMP, revealing that serum COMP levels are higher in diffuse cutaneous type than in limited cutaneous type. Serum COMP concentrations may reflect the degree of skin sclerosis. However, serum concentrations of COMP were not associated with SSc symptoms and complications, suggesting a derivation from abnormal sclerotic skin rather than from joints or organs. We are presently investigating correlations between serum COMP and skin thickness, and evaluating the feasibility of COMP as a novel biomarker of SSc.

Fig. 1. Concentration of serum COMP. Serological analyses revealed that serum COMP levels were significantly higher in SSc patients than in healthy controls.

Disclosure Statement: The authors have declared no conflicts of interest.

M. YAMAMOTO1, H. TAKAHASHI1, C. SUZUKI1, Y. NAISHIRO1, H. YAMAMOTO1, K. IMAI2, Y. SHINOMURA1

1First Department of Internal Medicine, Sapporo Medical University School of Medicine, 2Sapporo Medical University, Japan

Accepted 17 August 2007
Adherence to immunosuppressants in patients with connective tissue diseases

Sir, We read with interest the Editorial by Chambers et al. [1] regarding treatment adherence in systemic lupus erythematosus (SLE). It has been estimated that up to 50% of patients who suffer from chronic diseases do not adhere to treatment recommendations [2]. We have recently reviewed our experience of compliance with immunosuppressive treatment amongst patients with connective tissue diseases (CTDs) at The Royal London Hospital. We used a physician-designed questionnaire, which was distributed to consecutive patients attending the CTD clinic. The questionnaires were filled anonymously. Data collected included age, sex, ethnicity, immunosuppressant prescribed, clinic attendance and reasons for non-adherence. Our catchment area in East London has a large ethnic-minority group from the Asian subcontinent.

One hundred questionnaires were given. All were filled but 10 were subsequently discarded as eight patients were on no immunosuppressants and two had a diagnosis of rheumatoid arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remainder had other CTDs including arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remainder had other CTDs including arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remainder had other CTDs including arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remainder had other CTDs including arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remainder had other CTDs including arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remainder had other CTDs including arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remainder had other CTDs including arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remainder had other CTDs including arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remainder had other CTDs including arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remainder had other CTDs including arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remainder had other CTDs including arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remainder had other CTDs including arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remainder had other CTDs including arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remainder had other CTDs including arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remainder had other CTDs including arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remainder had other CTDs including arthritis. Ninety questionnaires were analysed. Seventy per cent of patients had SLE. The remain...