FUNCTIONS OF POLYMORPHONUCLEAR LEUKOCYTES IN EARLY RHEUMATOID ARTHRITIS

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Abstract—We carried out a prospective study on clinical variables and functions of polymorphonuclear leukocytes (PMNs) of 20 patients with early rheumatoid arthritis (RA) and compared the results with the presence of erosions before treatment and at a one-year follow-up. Migration of PMNs determined by agarose and filter assays and respiratory burst of PMNs determined by luminol-enhanced chemiluminescence (CL) test were studied both before starting RA-modifying treatment and 6–12 (mean 7.3) months later. PMNs of the patients without erosions at one year, as compared to the patients with erosions, showed significantly depressed migration into filter and significantly depressed CL responses to N-formyl-methionyl-leucyl-phenylalanine, both before starting the treatment and at 7.3 months. Although causality remains uncertain, the results suggest that depressed functional capacity of PMNs is associated with low risk of joint destruction in early RA.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease with varying clinical activity, characterized by development of cartilage and bone erosions. Joint destruction usually begins early, often during the first two to three years of the disease (1, 2). Various clinical features of early RA have been associated with poor prognosis. These include high age, male sex, insidious start, symmetric polyarticular onset, seropositivity, high erythrocyte sedimentation rate (ESR),
and early detection of erosions in radiographs of hands and feet (3–5). The many pretreatment laboratory and clinical variables, however, fail to predict subsequent progression in erosions (6, 7).

In the inflamed joint, large numbers of polymorphonuclear leukocytes (PMNs) are found in the synovial fluid of the patients with RA, whereas in the synovial tissues the major cells are macrophages and lymphocytes (8). However, PMNs also are found in the synovium, particularly at an early stage of RA (9, 10). Chemotactic mediators are considered to attract PMNs from peripheral blood into the joints (11), where activated PMNs can account for joint destruction by generating oxygen-derived free radicals and by releasing proteolytic enzymes (12).

Compared with healthy subjects, chemotaxis of peripheral blood PMNs of RA patients has been reported to be depressed (13–17), normal (18, 19, reviewed in reference 20), or increased (21), and oxygen radical production normal (22, 23) or enhanced (24). The possibility that aberrant PMN function is present in early untreated RA or that differences in PMN function would be associated with presence or absence of joint destruction has not been investigated thoroughly. We therefore carried out a prospective study on clinical variables and on chemotaxis and chemiluminescence (CL) responses of peripheral blood PMNs of patients with early diagnosed RA both before starting antirheumatic treatment and 6–12 months later.

MATERIALS AND METHODS

Subjects. The present series included 20 patients (16 women, 4 men, mean age 40.1 years, range 22–63) attending Kivelä Hospital or the Outpatient Department of Helsinki University Central Hospital. The patients had early active, definite or classical RA according to the 1958 criteria of the American Rheumatism Association (25). The duration of joint symptoms was ≤ 12 months (mean 7.3 months, range 2–12). None of the patients had received disease-modifying antirheumatic drug (DMARD) treatment previously. Thirteen patients (65%) were seropositive (Waaler-Rose ≥ 1:64). Sodium aurothiomalate was started in 14 patients (70%) and sulfasalazine in six patients (30%). During a one-year follow-up, the DMARD was changed individually according to adverse effects and drug efficacy.

Twenty sex-matched controls (mean age 42 years, range 25–57), one control for each patient, were recruited from the hospital and laboratory staff.

Study Design. Clinical variables of disease activity were determined by the same rheumatologist (L.P.) at months 0, 6 (or at the time of second blood sample collected for neutrophil function studies; see below), and 12 of the study. Clinical disease activity was evaluated using the Ritchie articular index (26), duration of morning stiffness, and severity of pain on a visual analog scale (27). Simultaneously with the clinical examination, inflammatory activity was assessed by measuring the erythrocyte sedimentation rate (ESR) and C-reactive protein level. White blood cell counts and hemoglobin levels were also recorded.

Blood samples for the neutrophil function tests from a patient and a control were always studied concurrently. At the time of bleeding, the subjects had no clinical signs of infection.