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Lack of a difference in increased capillary blood cell velocity in the skin over proximal interphalangeal joints between rheumatoid arthritis and osteoarthritis

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Abstract

Early detection of synovitis in rheumatoid arthritis (RA) and distinction from osteoarthritis (OA) are important to establish the most appropriate treatment. Increased perfusion over affected joints observed by laser Doppler perfusion imaging was supposed to arise from the underlying joint, because it was detected only by a near-infrared laser and not by a less penetrating red laser source. Using laser Doppler anemometry, this study addressed two questions: (1) whether capillary blood cell velocity (CBV) is increased in the skin over finger joints affected by RA or OA; (2) whether there is a difference between RA and OA in CBV above affected proximal interphalangeal (PIP) joints. Levels of soluble adhesion molecules were measured, because they indicate rheumatoid vasculitis raising flow resistance. Thirty-one patients with RA and 20 with OA were investigated. Compared to 18 controls, CBV (mean ± SEM) was elevated above PIP joints clinically affected by RA (0.35 ± 0.06 mm/s vs. 0.21 ± 0.02 mm/s; $P < 0.05$) and over PIP (0.27 ± 0.02 mm/s vs. 0.21 ± 0.02 mm/s; $P < 0.05$) and distal interphalangeal joints (0.27 ± 0.02 mm/s vs. 0.17 ± 0.01 mm/s; $P < 0.001$) affected by OA. Levels of soluble adhesion molecules were not correlated with CBV over PIP joints in RA. These observations demonstrated that elevated blood cell velocity is detectable by laser Doppler anemometry in skin capillaries over interphalangeal joints affected by RA or OA and contradict the previous assumption that there is hyperemia only in the affected joint. The lack of a significant difference in CBV over PIP joints between RA and OA patients might be due to some inflammation also occurring in OA rather than to vasculitic processes in RA associated with elevated levels of soluble adhesion molecules.

Keywords: Laser Doppler anemometry; Laser Doppler perfusion imaging; Rheumatoid arthritis; Osteoarthritis; Capillary blood cell velocity; sICAM-1; sVCAM-1; sE-selectin; sP-selectin; Rheumatoid vasculitis; Interphalangeal joints

Introduction

Pain and tenderness of the proximal interphalangeal (PIP) joints are common symptoms in patients with rheumatoid arthritis (RA) and osteoarthritis (OA). Clinical assessment, laboratory investigations, ultrasonography, radiography, and scintigraphic imaging help to discriminate between RA, OA, and arthralgia of other origin, but they sometimes fail to detect inflammation. Magnetic resonance imaging has proved to be much more sensitive for depiction of soft-tissue changes (Ostergaard et al., 1998), particularly in the early stages of RA (Sugimoto et al., 1996, 2000), but it has substantial resource implications.

Laser Doppler perfusion imaging (LDPI), a non-invasive technique for assessment of spatial distribution of blood flow in the skin (Wårdell et al., 1993), can detect areas of increased perfusion associated with inflamed finger joints in RA (Ferrell et al., 1996, 2001) and in OA (Ng and How, 2003). It was supposed that the hyperaemic areas detected by LDPI arose mainly from the underlying joint, as

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scanning the fingers of RA patients with a red laser (λ = 633 nm) showed little increase in perfusion, whereas using the more penetrating near-infrared laser diodes (λ = 780 or 850 nm) revealed areas of hyperemia (Ferrell et al., 1996). Likewise in patients with OA, the red laser source failed to detect any hyperaemic areas associated with joint inflammation except for deformed joints (Ng et al., 2003). Since the skin over the PIP joints is relatively thin and the dorsum of the joint is relatively unobscured by the extensor tendon, the distance from the skin surface to the hyperaemic synovium may be as little as 2–3 mm. The near-infrared laser can penetrate skin to a depth of approximately 1300 μm before the incident optical energy density diminishes to one-third of its original value (Anderson and Parrish, 1981). Because only a small fraction of backscattered photons is necessary to yield the flux signal, measurements can be obtained from vascular beds deeper than 1300 μm. The fact that the areas of increased perfusion do not correspond to the pattern of subcutaneous superficial veins, and that they correlate loosely to the Ritchie articular index suggests that the blood flow of the hypervascularized pannus which invades cartilage and bone in RA is at least partly being detected with LDPI (Ferrell et al., 1996). Beside angiogenesis in the pannus, recruitment of non-perfused capillaries is another explanation for a higher functional capillary density, i.e., the density of synovial capillaries perfused by red blood cells, in the rheumatoid synovium (Veihelmann et al., 1999).

The increased number of blood vessels per joint due to tissue hypertrophy in the rheumatoid synovium results in an elevation of joint temperature. In the overlying skin, the local temperature elevation causes vasodilatation partly due to relaxation of sympathetic tone. According to the aforementioned observations, it was considered unlikely that areas of elevated perfusion detected by LDPI were due to hyperemia of the skin that overlies the inflamed joint, since scans with a less penetrating red laser failed to show increased perfusion over these joints. However, regarding vasodilatation in response to local temperature elevation at sites of inflammation and the fact that red blood cell velocity was found to be decreased at the nailfold in RA (Grassi et al., 1989), it remains uncertain as to what extent cutaneous perfusion is increased above inflamed joints. Therefore, this study addressed two questions: (1) whether blood cell velocity is increased in cutaneous capillaries over joints affected with RA and OA; (2) whether there is a difference in capillary blood cell velocity above affected PIP joints between patients with RA and OA, which would help to distinguish between both diseases. To answer these questions, laser Doppler anemometry was used because with a sample depth of less than 100 μm, this technique detects blood cell velocity only in skin capillaries and not in the underlying synovium. Because increased levels of soluble adhesion molecules were found in RA patients with vasculitis (Aoki et al., 1993; Kuryliszyn-Moskal et al., 1996; Voskuyl et al., 1995), which might influence microvascular flow dynamics, soluble forms of intercellular adhesion molecule-1 (sICAM-1), vascular cell adhesion molecule-1 (sVCAM-1), E-selectin, and P-selectin were measured in the present study.

Subjects and methods

Subjects

Thirty-one consecutive patients aged from 27 to 76 years with known RA, on the basis of American Rheumatism Association criteria (Arnett et al., 1988), were recruited for the study from the clinic of rheumatology “Rheumazentrum Ruhrgebiet”. Clinical characteristics are presented in Table 1. Inclusion criteria were involvement of the hand with pain and swelling of proximal interphalangeal joints. Disease duration varied from 8 months to 26 years (mean 7.2 ± 1.4 years). Rheumatoid factor was positive in 15 patients. The erythrocyte sedimentation rates (ESR) of these patients ranged from 2 to 51 mm/first hour with a mean (± SEM) of 23.1 ± 2.9 mm/first hour. C reactive protein levels (normal < 1.0 mg/dl) ranged from 0.0 to 4.7 mg/dl with a mean of 1.1 ± 0.3 mg/dl. Mean duration of morning stiffness was 2.4 ± 1.1 h. Twenty-four RA patients had evidence for extra-articular manifestations including Sjoegren’s syndrome (22.6%), Raynaud’s phenomenon (22.6%), rheumatoid nodules (16.1%), and neuropathy (51.6%). Twenty-four patients currently received disease modifying antirheumatic drugs (DMARDs): methotrexate (17), sulfasalazine (6), (hydroxy-) chloroquine (3), leflunomide (4), and etanercept (2). Sixteen patients were on 1 DMARD and 8 on 2 DMARDs. Twenty-six patients were treated with oral corticosteroids equivalent to a mean dosage of 6.2 ± 0.8 mg prednisolone. Twenty-three received non-steroidal anti-inflammatory drugs (NSAID) when required.

A further group comprised 20 patients aged from 51 to 72 years with OA in proximal or distal interphalangeal joints (Table 1). Fourteen of these were treated with

Table 1
Clinical characteristics

	Rheumatoid arthritis (n = 31)	Osteoarthritis (n = 20)	Control subjects (n = 18)
Sex: male/female (n)	8/23	4/16	5/13
Age (years)	59.9 ± 2.2	59.7 ± 1.5	51.8 ± 2.8
BMI (kg/m^2)	27.9 ± 0.8	27.9 ± 1.0	26.4 ± 0.8
Systolic blood pressure (mm Hg)	124.5 ± 2.5	118.3 ± 3.2	120.0 ± 3.8
Diastolic blood pressure (mm Hg)	76.5 ± 1.4	76.5 ± 1.7	77.2 ± 2.8
Essential hypertension (n)	13	5	4
Smokers (n)	9	4	8
Hyperlipoproteinaemia (n)	9	8	1
Skin temperature (°C)	29.4 ± 0.5	29.3 ± 0.6	30.7 ± 0.4

Results expressed as number (n) or mean ± SEM.