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Intra-articular and circulating levels of type I and III collagen markers in inflammatory and degenerative joint disease

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In a chronic inflammatory disease as rheumatoid arthritis, the local processes in the affected tissues lead to destruction of the joint. When estimating the inflammatory activity in rheumatic joint diseases, a major problem is the rather unspecific and indirect character of the biochemical and the crude character of the clinical measures used.

As more specific markers of the local pathological processes, metabolites from the collagen turnover have been introduced (Risteli 1990, Hørslev-Petersen, 1988).

The object of our study was to investigate the relation between circulating and local levels of type I and III metabolites, and whether the local concentrations reflect the local processes in the knee joint.

Materials

The aminoterminal propeptide of type III procollagen

(PIIINP) as a marker of type III collagen formation, the carboxyterminal propeptide of type I procollagen (PICP) as a marker of type I collagen formation and the crosslinked carboxyterminal telopeptide of type I collagen (ICTP) as a marker of type I collagen degradation were measured in eleven patients (6 females and 5 males) with chronic knee synovitis (13 knees) who underwent chemical synovectomy by intraarticular osmic acid (osmium tetroxide). Collagen markers were analysed by commercially available radioimmuno assays. (Orion Diagnostica, SF-90460, Oulunsalo, Finland). Standard radiograph of the affected knee was taken prior to treatment. Conventional clinical and biochemical evaluations were performed.

Results (Table)

The circulating levels of PIIINP and ICTP were sig-

Table. Values given as median with interquartile range in ng/ml

	PIIINP		ICTP		PICP	
	serum	synovial fluid	serum	synovial fluid	serum	synovial fluid
<i>All patients n = 13</i>						
Before osmic acid	4.0 (2.9–4.7)	854 (600–1380)	5.4 (3.4–7.8)	17 (13–22)	172 (105–225)	1030 (790–1660)
After osmic acid (t30)	3.9 (2.6–4.9)	1118 (1030–3160)	4.9 (3.5–8.4)	20 (12–55)	155 (106–222)	1375 (1170–2270)
<i>Remission group n = 7</i>						
Before osmic acid	3.7 (2.6–4.4)	850.6 (587–929)	4.6 (3.3–7.6)	15 (13–22)	172 (105–185)	1030 (740–1660)
After osmic acid (t30)	3.1 (2.1–4.4)	–	4.0 (3.4–7.8)	–	145 (93–225)	–
<i>Relapse group n = 6</i>						
Before osmic acid	4.5 (3.3–5.2)	1254 (600–2580)	7.6 (5.4–8.0)	18 (12–40)	168 (96–248)	1235 (870–2470)
After osmic acid (t30)	4.8 (3.9–5.1)	1118 (1030–3160)	7.5 (4.9–8.8)	20 (12–55)	187 (114–222)	1375 (1170–2270)

nificantly elevated compared to healthy controls and correlated to biochemical but not to clinical markers of disease activity. However, serum PIIINP was correlated to the inflamed synovial mass involved using a joint index score ($r = 0.55$; $p < 0.05$) and to the state of destructive changes ($r = 0.64$; $p < 0.05$). Serum PICP did neither differ from controls nor correlate to other markers of disease activity, but was related to duration of disease ($r = 0.84$; $p < 0.01$).

The serum/synovial fluid -ratio was for PIIINP 1:200, for PICP 1:6 and for ICTP 1:3. The synovial concentration of ICTP was correlated to degree of joint damage and to the circulating levels of ICTP.

Six patients have had recurrent synovitis within the first month. However, fluctuations in the collagen markers in serum or intraarticularly, did not differ between groups neither in pre-treatment values nor after 30 days.

Conclusion

The very high local concentrations of PIIINP may reflect a significant type III collagen formation in the synovial membrane. This is supported by the relation between the circulating levels and the synovial mass involved. The value of ICTP as a marker of bone degradation is supported by the correlation between the degree of destructive changes of the joint and the local concentrations of ICTP.

Circulating markers of collagen type I degradation and type III formation reflect the inflammatory state of joint disease.

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An examination of some molecular markers in blood and urine for discriminating patients with osteoarthritis from healthy individuals

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The identification of molecular markers (MM) in blood or urine, which reflect disease changes in osteoarthritis (OA), would greatly facilitate clinical studies (Lohmander et al. 1992). One application for molecular marker measurements is for diagnostic purposes. Thus one criterion for a good molecular marker is that it should discriminate between OA patients and normal individuals. A number of candidate molecular markers have been recently identified (Poole et al. 1994). The purpose of this study was to examine the ability of those markers to discriminate OA patients and normal individuals.

Methods

Sera and 24 hr urines were collected from 398 patients with a diagnosis of idiopathic OA with radiological grade 1–3 and symptoms. All patients had involvement of at least one large joint (knee, $n=32$, or

hip, $n=6$). Each patient was removed from prior NSAID therapy for one week prior to the baseline visit. A cohort of 20 healthy individuals without joint pain were sampled twice at a one month interval. Samples were stored at -72°C until assayed.

Keratan sulfate (KS) was measured using antibody AN9P1 in a competitive ELISA (Poole et al. 1989). C-propeptide of type II collagen (CP-II) was measured by RIA (Månsson et al. 1995); bone sialoprotein (BSP) was measured by ELISA (Saxne et al. 1995); cartilage oligomeric matrix protein (COMP) was measured using rabbit polyclonal antibody (Saxne and Heinegård 1992); the chondroitin sulfate epitope 846 of aggrecan was measured as described (Poole et al. 1994). Commercial ELISAs were used to measure C-reactive protein (CRP), Hemagen CRP Kit, Hemagen Diagnostics, Inc., 34 Bear Hill Road, Waltham, MA 02154; TNF-receptor type I