This hypothesis remains to be tested. The changes in the raised blood pressure after six months of leflunomide treatment will be clarified after the final report of all extended studies.

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Adhesion molecule expression in the synovial membrane of psoriatic arthritis

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Endothelium may play a part in the pathogenesis of long-standing psoriatic arthritis (PsA),[1] whereas a higher vascularisation and a less intense adhesion molecule expression have been found in PsA synovial membrane compared with rheumatoid arthritis.[2] Some proinflammatory molecules, such as tumour necrosis factors (TNFs), can induce synovial endothelial cells and fibroblast-like synoviocytes to express adhesion molecules.[3 4]

PATIENTS AND METHODS

In two groups of patients with PsA—eight patients with synovitis of <1 year and six patients with synovitis >1 year—we studied the expression and pattern of the synovial distribution of endothelial leucocyte adhesion molecule-1 (ELAM-1 or E-selectin) (CD62E), intercellular adhesion molecule-1 (ICAM-1) (CD54), vascular cell adhesion molecule-1 (VCAM-1) (CD106) (Immunotech, Marseille, France), and of TNFα and TNFβ cytokines (Chemicon International, Temecula, CA, USA) using a standard three stage immunoperoxidase labelling technique (LAB VISION, Fremont, CA, USA).[5] The lining layer, the infiltrating elements, and the endothelial cells were evaluated for the number of positive cells per high power field (×40).[6]

RESULTS

Table 1 summarises the main clinical and laboratory data of the two groups; no significant clinical or laboratory differences were seen.

E-selectin was present more often at endothelial, cellular infiltrate, and lining layer levels in 7/8 (88%) patients with a disease duration <1 year, where only 3/6 patients (50%) with disease duration >1 year were positive. ICAM-1 was

Table 1 Main clinical and demographic features of 14 patients with PsA with a disease duration of less (group 1) or more (group 2) than one year

Patient number	Sex	Age (years)	Duration of arthritis (years)	Duration of psoriasis (years)	PASI	Ritchie index	Subgroup	CRP (mg/l)	ESR (mm/1st h)	Treatment
Group 1										
1	F	60	<1	1	3.2	17	Polyarthritis	5	14	NSAIDs
2	F	28	<1	1	4.5	11	Polyarthritis	4	28	NSAIDs
3	F	48	<1	<1	0.3	3	Oligoarthritis	35	52	Steroids
4	M	37	<1	4	0.9	18	Polyarthritis	6	8	NSAIDs
5	M	31	<1	2	0.3	9	Polyarthritis	12	24	None
6	F	35	<1	1	9.0	20	Polyarthritis	24	66	NSAIDs
7	F	25	<1	19	2.1	5	Oligoarthritis	6	16	HCQ/NSAIDs
8	F	35	<1	18	0.9	15	Polyarthritis	6	23	HCQ/NSAIDs
Group 2										
1	M	35	2	10	3.1	9	Polyarthritis	21	38	NSAIDs
2	M	36	5	13	6.6	10	Polyarthritis	80	86	MTX/steroids
3	M	53	3	37	8.9	21	Polyarthritis	6	3	NSAIDs
4	M	39	3	2	1.2	9	Polyarthritis	25	11	SSZ
5	M	43	5	30	4.2	6	Oligoarthritis	6	8	NSAIDs
6	M	50	10	25	9.0	15	Polyarthritis	6	10	NSAIDs

PASI, Psoriasis Areas Severity Index; CRP, C reactive protein; ESR, erythrocyte sedimentation rate (Westergren); NSAIDs, non-steroidal anti-inflammatory drugs; HCQ, hydroxychloroquine; MTX, methotrexate; SSZ, sulfasalazine.

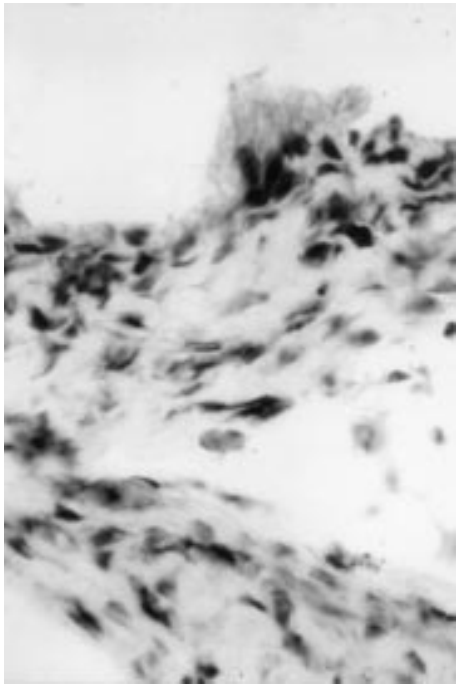

Figure 1 Representative specimen from the synovial membrane of a patient with psoriatic arthritis of <1 year; staining with ICAM-1 using monoclonal antibody CD54. Antigen positive cells are present throughout the entire specimen (original magnification ×250).

overexpressed in the lining layer of the early synovitic specimens compared with the longstanding samples (100% *v* 33%; $p<0.001$) (fig 1). On the contrary, VCAM-1 positivity was more commonly found in patients with longstanding PsA (5/5 (100%) *v* 4/7 (57%)). Cells containing TNFα and TNFβ were consistently found in the synovial lining layer, in the infiltrates, and in the blood vessels, with no appreciable difference between the two groups.

DISCUSSION

Our results show that longstanding psoriatic synovitis may reduce the E-selectin expression, as already found in different forms of synovitis,[7] and confirms the presence of ICAM-1 and VCAM-1 positivity in PsA, as already described.[2] As ICAM-1 was present in vessel walls in all tissue samples, this supports the view that this adhesion molecule is not only constitutively expressed on endothelial cells but is also increased during activation and is the most important adhesion molecule for cell binding to endothelium in inflamed tissue.[7] VCAM-1 expression, generally absent on normal synovium, is found on activated endothelium and its up regulation has been recently implicated in various pathological conditions.[8]

The different expression of these adhesion molecules seems to be connected to the disease duration. A more frequent positivity for E-selectin, and partly for ICAM-1, in earlier synovitis compared with longstanding disease, where VCAM-1 expression was constantly found, shows for the first time how these molecules may separately participate in the synovitic process in the different phases of PsA, with a changing involvement as the disease evolves.

The presence of TNFα and TNFβ, together with E-selectin, ICAM-1, and VCAM-1 positivity in the same samples, confirms the ability of TNFs to induce the expression of such adhesion molecules.[3] Their localisation on the endothelial cells also suggests that these cells can produce TNFs, indicating the involvement of TNFs in the regulation of cell adhesion before migration into diseased joints. Our findings gain more importance in view of a recent immunohistochemical study, which showed a convincing effect of anti-TNF treatment on synovium in spondyloarthropathy, suggesting immunomodulatory mechanisms involving adhesion molecule expression.[9]

In conclusion, the variations in the presence of some adhesion molecules and TNFs shown in our study, partly related to disease duration, indicate their relative importance in mediating the succeeding mechanisms of psoriatic synovitis. This should be taken into account in the assessment of disease progression and in developing possible new therapeutic approaches.

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