Synovium

Abstracts

Histochemical localisation of hyaluronan in healthy and diseased cartilage of knee joints
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Hyaluronan was identified and localised in biopsies from human articular cartilage of normal and osteoarthritic knee joints by use of a hyaluronan binding protein and the biotin-avidin peroxidase staining method. Fixation and decalcification of tissue samples were performed using a microwave oven technique.

Hyaluronan was localised predominantly in the superficial layers of the fibrocartilaginous articular cartilage. Free hyaluronan was scattered throughout the deeper zones of the cartilage. In cartilage from patients with osteoarthritis, superficial spurs of regenerating cartilage were devoid of hyaluronan staining, but in the underlying bone tissue, weak hyaluronan staining was present.

Hyaluronan synthesis in joint cavitation
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A band of tissue matrix rich in hyaluronan, as recognised by a histochemical probe for hyaluronan has been observed before cavity formation in joints in the developing chick limb. Uridine diphosphoglucose dehydrogenase (UDPGD) activity is an enzyme involved in the formation of one of the monosaccharides of hyaluronan. The relationship between the cellular enzymatic activity of UDPGD and the distribution of hyaluronan, assessed histochemically, has been investigated.

Chick and mouse limb buds were removed at stages close to the time of cavity formation in the knee, ankle, and foot joints. Chick tissue was chosen for convenience and comparison with previous findings, and mouse tissue to ensure findings were comparable in mammalian joints. Tissues were snap frozen and cryostat sections cut at 10 μm thickness. Unfixed sections were assayed for UDPGD activity by a modified cytochemical method, and for hyaluronan distribution using a biotinylated probe derived from the aggrecan hyaluronan binding region. As previously observed, an area rich in stainable hyaluronan was found at the joint line before cavity formation. A band of cells of relatively high UDPGD activity was seen bordering the same site. As cavitation developed, this band was seen to correspond to the surface layer of chondrocytes of the separating articular surfaces. The band also continued into the area of the developing synovial tissue to form a more or less complete border to the developing cavity. Within the deeper cartilage, UDPGD activity was generally lower but showed variation relating to zonal changes in chondrocyte morphology and orientation.

Synovial fluid flow

Synovial fluid flow

Intravenous Gd-DTPA enhancement of joint fluid on magnetic resonance imaging: a measurement of trans-synovial flow
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Joint fluid has been shown to enhance on magnetic resonance images after intravenous (IV) injection of gadolinium-diesthyretril amino pentacetic acid (Gd-DTPA). We investigated the relationship between joint inflammation and the rate of joint fluid enhancement in an antigen induced arthritis (AIA) rabbit model.

The knees of 13 New Zealand White rabbits were imaged before and 7 and 14 days after induction of AIA. Knee diameters were measured at each imaging session. Seven rabbits (treatment group) received 0.5 mg/kg methylprenisolone IV twice daily on days 10 to 14. Precontrast T1-weighted (T1W) and T2-weighted images were obtained. Repeat T1W images were performed 1, 15, 30, 45, and 60 minutes after 0.1 mmol/kg Gd-DTPA. Enhancement of peripheral joint fluid at each time point was expressed as the percent of maximal enhancement.

All knees with AIA demonstrated swelling on day 7 (p < 0.001). The knees of the untreated group remained swollen on day 14, while those of the treatment group showed a reduction in swelling (p < 0.001). On day 14, the untreated group showed more rapid fluid enhancement, reaching 78% of maximal at one minute and 96% at 15 minutes compared with 55% and 74%, respectively, for the untreated group before induction (p < 0.01). The treated group had less rapid enhancement at one minute (53%) than the untreated group (p = 0.07).

The rate of joint fluid enhancement following Gd-DTPA correlated with the degree of joint inflammation and was sensitive to pharmacological modulation. The method may prove useful for measurement of trans-synovial flow.

Measurement of synovial volume and rates of synovial enhancement with Gd-DTPA enhanced magnetic resonance imaging

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We aimed to devise a method to quantify synovial volume by magnetic resonance imaging. As part of the study, the pattern of synovial enhancement by intravenously administered gadolinium-diesthyretril amino pentacetic acid (Gd-DTPA) was studied in patients with knee synovitis.

T1-weighted sagittal knee images were acquired in nine patients with synovitis using magnetisation prepared rapid acquisition gradient echo (MP-RAGE) (repetition, echo and inversion times = 110, 4, and 300 ms, respectively; flip = 40°) before and after injection of 0.2 mmol/kg Gd-DTPA. Subtraction of non-enhanced from enhanced images allowed the calculation of synovial volume from pixel count and the known voxel volume. Data sets were processed on a Sun Sparc workstation using Analyze (BIR, Mayo). Additionally, a dynamic T1-weighted sequence was used during enhancement (2D fast low angle shot, every 15 seconds for five minutes then every five minutes for 60 minutes) and the ratio of post- to pre-enhancement synovial signal for each patient calculated at times up to one hour after injection.

Synovial enhancement was detected in all patients. Range of synovial volume (calculated in nine patients) was 93–271 ml. Fifty percent of synovial volume was found to vary. The time to maximal signal intensity in seven of eight patients varied, but occurred within 500 seconds of Gd-DTPA injection, except for the patient with polyartritis nodosa, in whom maximal signal was not detected until 60 minutes after Gd-DTPA injection. The pattern of reduction in signal intensity in seven of eight patients suggested Gd-DTPA elimination consistent with its clearance from the extracellular compartment. No significant synovial fluid enhancement was detected.

A simple method of measuring synovial volumes has been presented. Variations in the rate of synovial enhancement with Gd-DTPA occur and may reflect differences in synovial perfusion and vascularity.

Glycosaminoglycan concentration in rabbit synovium and its relation to pressure induced increased permeability
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The low hydraulic conductance of normal synovial interstitium helps to retain synovial fluid in the joint cavity. The conductance increases at pathological intra-articular pressures, and as this is only partly explained by stretching, we investigated if changes in matrix concentration also occur. One knee of a rabbit was anesthetised and the joint infused with saline to 25 cm H₂O over three hours, increasing the conductance of the lining 5:23 (SEM 1:5) times. The opposite unperfused knee served as control (n=8). Synovium was then microdissected (1 mm x 1 mm x 1 mm per joint). Digested tissue was analysed for chondroitin 4 and 6 sulphate disaccharides (C4Sd, C6Sd) by capillary zone electrophoresis; heparin sulphate (HS) by capillary electrophoresis, uronic acid, DNA, and RNA by spectrophotometry. Concentrations

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plasmic latex particles. No pannus formation or cartilage erosion and damage was noted. Latex particles were not observed in chondrocytes. Rare synovial effusion cells laden with latex particles were seen only at three (0-04) and seven days.

The phagocytosis of the inert latex particles by cells in and deep to the synovial membrane in the rat knee joint was not associated with inflammatory changes. Pannus formation and cartilage erosion were not observed. There was a striking retention of particles in the subsynovial cells; this may have implications for the local treatment of chronic arthritis in man.

Synovial joints are immune to metastasis
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Stephen Paget (1889) predicted that tumour cell populations that are incontrollable metastatic can colonise only certain sites. The synovial membrane appears immune, and evidence of synovial metastasis has been reported in the literature on only 33 occasions. In 26 of these case reports, the evidence suggests that the synovia could have been invaded from para-articular bone or other tissues. Consequently, there are only seven documented cases in which blood borne synovial metastasis can be accepted as proven. To examine the significance of this surprising evidence, six blocks were taken from the right knee joints of each of 29 patients dying in hospital with metastatic carcinomatosis, lymphoma, or other malignant tumour. The blocks represented adipose, areolar, and fibrous synovium. Sections stained with haematoxylin and eosin and with anti-creatinine kinase, CAM 5-2, EMA and S100 antisera were examined by two observers and contrasted with control material from 69 non-cancer patients and with positive and negative immunostained samples. No malignant cells were identified.

In a preliminary attempt to identify factor(s) synthesised by synovial cells that might inhibit tumour cell growth, tests with synovial fibroblasts grown in monolayer culture showed that conditioned medium from the cultures did not significantly inhibit the growth of lymphoma (Raji), carcinoma (MCF-7), or two fibrosarcoma cell lines (208F and RH0ST1). It is concluded, first, that metastatic tumour cells very rarely colonise synovial tissue and second, that the differential permeability of synovial blood vessels is more likely to account for this immunity than the influence of molecules exported by synovial cells.

Multinucleate cells in pigmented villonodular synovitis express osteoclast markers
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Pigmented villonodular synovitis (PVNS) and the related lesion, giant cell tumour of tendon sheath (GCTTS) are idiopathic proliferations of multinucleate cells. Mononuclear cells (MNC) exhibit markers suggestive of derivation from a monocyte lineage. The derivation of the multinucleate cells and their relationship to osteoclasts is not known; to define their phenotype, tissue sections from seven patients with PVNS and two patients with GCTTS were examined for osteoclast markers. Multinucleate cells in both lesions were strongly positive for vimentin receptor, as were some MNC surrounding the multinucleate cells. Tissues from seven of the nine patients contained intensely tartrate resistant acid phosphatase (TRAP) positive multinucleate cells; fewer than 5% of the MNC were TRAP positive. These TRAP positive MNC also tended to surround multinucleate cells. To demonstrate the presence of calcitonin receptor, a definitive marker for osteoclasts, snap frozen sections from eight patients (six PVNS, two GCTTS) were incubated with 125I-labelled salmon calcitonin and examined by emulsion autoradiography. Multinucleate cells in four of six PVNS and two of two GCTTS samples demonstrated specific calcitonin binding that was competed by unlabelled calcitonin; no definite calcitonin binding was detected in the MNC. Calcitonin receptor expression was confirmed by polymerase chain reaction using calcitonin receptor specific primers on cDNA synthesised from PVNS total RNA (two samples), and RNA from tissue sections (seven PVNS, two GCTTS). All samples were positive for calcitonin receptor transcript.

The multinucleate--multinucleate cells could provide the cellular mechanism for the osteolysis that characterises PVNS/GCTTS. These lesions may provide a useful model for defining factors involved in osteoclast differentiation.