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ARTICULAR LYMPHOSCINTIGRAPHY IN HUMAN KNEES USING RADIOLABELED DEXTRAN

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ABSTRACT

Whereas joint lymphatics are inaccessible to conventional (oil-contrast) lymphography, articular lymphatic dysfunction can be assessed by lymphoscintigraphy (isotope lymphography). Using 99mTc-labeled dextran (molecular weight~70,000 daltons), we performed dynamic lymphoscintigraphy in 38 patients with degenerative osteoarthropathy of the knee. Comparison with the normal (contralateral knee) in 25 patients demonstrated that tracer disappeared at 24 hours more slowly from the abnormal side (86.5±3.3% retention in the abnormal joint compared with 77.1±4.6%; $p<0.01$), but accumulated more intensely in regional lymph nodes on the pathologic side (3.8±2.4% vs 1.9±0.3%; $p<0.01$). The findings suggest deranged macromolecular transport and lymphatic dysfunction in degenerative knee joint disease.

A paucity of information exists as to the functional role of lymphatic drainage in joint diseases (1,2). Since 1984, we have been using, as described by Henze et al (3), 99mTc-labeled dextran to explore lymphatic articular drainage in chronic arthropathies (4). After an investigational period in experimental animals, we have used articular lymphoscintigraphy over the last 5 years to study lymphatic vascular alterations in patients with degenerative knee joint disease and this experience forms the basis of this report.

MATERIALS AND METHODS

99mTc-labeled dextran was prepared according to the method of Henze et al (5). Labeling was tested by chromatography using several solvents and its efficiency was uniformly greater than 95%. Non-labeled dextran with an average molecular weight of 70,000 has been widely used clinically without undue risk. Scintigraphic images were obtained with a gamma camera (Maxi Camera GE II, 400 T) and frames displayed on a computer (Data General Dasher D II). The time of radiotracer migration to the regional inguinal lymph nodes as well as the visualization time to the liver and kidney were recorded. Radioactivity in the thyroid, stomach, and bone marrow was also imaged.

The study group included 25 normal and 51 pathologic knees (38 male patients) with degenerative arthropathy. The diagnosis of joint disease was made clinically, radiographically, and verified by notable cartilage damage at time of arthrotomy. The range in age was from 16-59 years (mean 33 years).

2mCi of 99mTc-labeled dextran dissolved in 10cc of physiological saline was injected in both knees using a fine needle. After 3-6 hours, scintigrams of the injected joints and the regional inguinal lymph nodes (corresponding to the nodal lymphatic drainage zones from the knee) were obtained. These images were obtained using a gamma camera after counts accumulated between 200,000-

500,000 and time frames imaged on a computer. The frames were recorded for 60 seconds for each knee and 300 seconds for the inguinal nodal region. Data analysis allowed quantification of detected tracer activity at several intervals in selected areas of interest. We used 7 different intervals (15, 30, 60, 180, 360, 1080, and 1440 minutes) and discrete rectangular areas of interest. For the normal (contralateral) and pathologic knee, two types of values were followed.

Disappearing joint radioactivity

From an area of interest incorporating the entire knee joint, we examined tracer activity or disappearance as a function of time. This value represented the percentage of radioactivity which remained in the knee as a function of the amount initially injected or residual counts/initial counts x100.

Regional nodal uptake

Using an area of interest overlying the draining inguinal nodes, we determined the level of radioactivity as a function of time. The tracer activity represented the percentage of activity accumulated in the nodes in relation to the tracer activity after first injected in the knee or uptake counts/initial counts x100.

During the period between imaging and counting, the patients were allowed to walk around.

Statistical analysis was performed using the Mann-Whitney U Test.

RESULTS

Morphologic findings

The radiopharmaceutical injected in the knee joint *(Fig. 1)* was transported via lymphatics *(Fig. 2)* to regional nodes *(Fig. 3)* (6), thereby providing an image of the injected joint (regional lymphatics) and draining lymph nodes.

Tracer activity appeared in the liver, kidney, and bladder within 60-180 minutes. No radioactivity was detected in the thyroid or stomach.

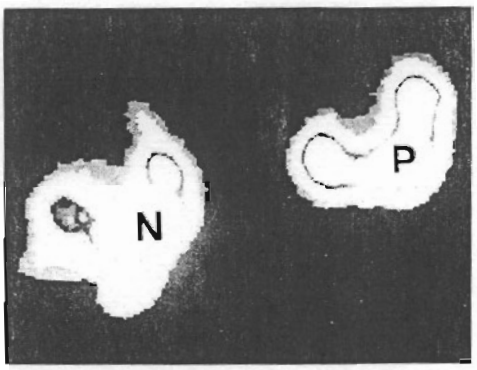

Fig. 1. Articular lymphoscintigraphy (99mTc-labeled dextran) demonstrating images at 6 hours after tracer injection into the knee joint in a patient with degenerative arthropathy (P) and joint stiffness compared with the contralateral normal knee (N).

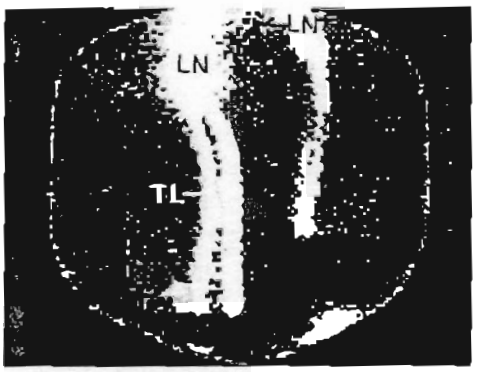

Fig. 2. Articular lymphoscintigraphy (99mTc-labeled dextran) demonstrating lymphatic drainage channels at 6 hours in a patient with bilateral osteoarthropathy more severe on the right side. LN = lymph nodes; TL = lymphatic channels.

Functional findings

In contrast to the normal knee, the radiopharmaceutical disappeared more slowly from the pathologic joint (tracer retention 86.5±3.3% in the pathologic knee vs 77.1±4.6%; $p<0.01$). The tracer also accumulated more in the regional nodes draining the pathologic knee as compared to the normal side (3.8±2.4% vs 1.9±0.3% after 30 minutes; $p<0.01$).

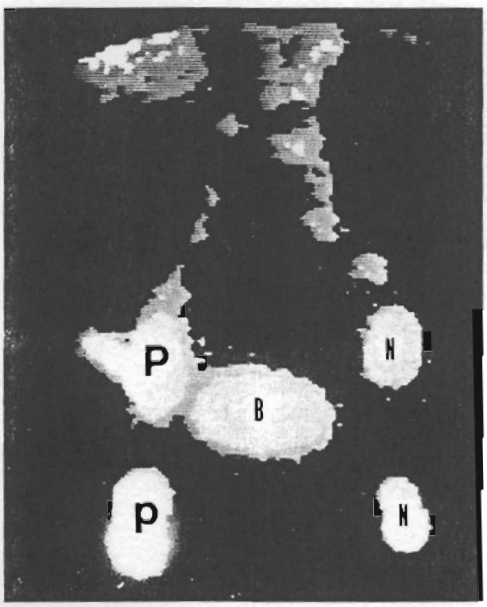

Fig. 3. Articular lymphoscintigraphy (99mTc-labeled dextran) imaged at 6 hours after knee joint injection with 2mCi in a patient with unilateral degenerative osteoarthropathy. On the pathologic side (P), more intense accumulation in inguinal and lumbar paraaortic lymph nodes is seen compared to the normal (N) side. B = bladder.

DISCUSSION

Joints like other tissue spaces have an extracellular circulation of water, proteins, and other nutrients (8), although synovium has its own specialized characteristics (9,10). The absence of a basal membrane facilitates exchange of nutrients in articular cartilage where blood vessels are lacking (11). Of note, there are two distinct interfaces--the synovial membrane/joint itself with active and direct nutrient exchange and joint/articular cartilage with much more sluggish but nonetheless equally biologically important extracellular fluid turnover. Between these exchange areas is hyaluronic acid which acts as a biologic semiconductor to regulate diffusion and permeability (12).

From this concept, it is suggested that the lymphatic system helps regulate chondrosynovial tissue pressure and joint fluid volume. Because joint lymphatic resorption is less efficient than in other organ systems (e.g., skin), use of radiolabeled dextran with a molecular weight of 70,000 daltons is probably optimal for articular lymphoscintigraphy. Larger particles are likely to remain sequestered in the joint and smaller ones are probably readily absorbed directly into the bloodstream (13).

From these preliminary studies in patients with degenerative knee joint disease, it appears that macromolecules are more slowly absorbed from the pathologic joint and accumulate more intensely in regional draining lymph nodes. The findings are in keeping with other studies showing lymphatic dysfunction in joint disease (14).

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