Laboratory Diagnosis of Degenerative Joint Disease

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ABSTRACT

Degenerative joint disease (DJD) is characterized by pain on use. X-rays show cartilage narrowing and osteophytes. Synovial effusions are non-inflammatory, i.e. clear with good viscosity and less than 2000 WBC per mm.³ Cartilage fragments may be seen in the joint fluid. Important systemic diseases that can cause degenerative joint disease include ochronosis, hemochromatosis, hyperparathyroidism, acromegaly, Ehlers-Danlos syndrome, diabetes and syphilis with their neuropathic joints, Wilson's disease and hypothyroidism. The late results of other diseases such as rheumatoid arthritis and aseptic necrosis may resemble DJD.

Introduction

On medical services any suggestion of degenerative joint disease or osteoarthritis often seems to be a signal for a search for a way to avoid the problem rather than for techniques to pursue it. This is partly because techniques for treatment are tedious and provide only partial relief. Even orthopedic surgical measures have not been dramatically successful except for the total hip replacement. In addition, very little research is being done into degenerative joint disease so that faculty rarely abounds with ideas about how to evaluate these patients. This report describes techniques used to distinguish degenerative joint disease (DJD) from other types of arthritis and reviews methods of searching for a variety of important systemic diseases that can initially present as DJD.

Diagnosis of Degenerative Joint Disease

DJD clinically is suggested by pain that increases on use or motion. Swelling may be present but heat, redness and erythema are not prominent. Bony crepitus is often detectable. X-rays obtained for other reasons often provide the first report of DJD. Typical findings include para-articular sclerosis, joint space narrowing (loss of articular cartilage), osteophyte formation and subchondral cysts (figure 1). Especially in the spine, considerable X-ray changes can be present without symptoms.

Laboratory evaluation in practice often begins with blood tests to exclude the systemic inflammatory diseases. A normal erythrocyte sedimentation rate, rheumatoid factor and antinuclear factor provide some reassurance to the casual evaluator. Unfortunately, all these studies have a greater incidence of abnormality even without clinical disease in older patients who also

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DEGENERATIVE JOINT DISEASE

243

serum concentrations of calcium, phosphorus and alkaline phosphatase remain within the normal ranges of values.

Of far greater value in diagnosis is arthrocentesis and study of the synovial fluid. Fluid can be aspirated from any swollen joint. The knee is most frequently aspirated because of the ease of entering the joint medially into the retropatellar space. The site of aspiration is washed and painted with iodine. A 20 gauge needle is satisfactory for most aspirations. Sterile technique keeping fingers off the needle and the aspiration site makes this an extremely safe procedure with less than one infection per 14,000 aspirations reported by Hollander.

Ethyl chloride spray on the skin at the site of entry can be used as a mild local anesthetic. Fluid should be placed promptly into a tube containing ethylene diamine tetraacetic acid anticoagulant for the studies described.

Uncomplicated DJD (osteoarthritis) can be distinguished from all the inflammatory joint diseases as shown in table I by its "non-inflammatory" joint effusion. It must be emphasized that leucocyte counts (WBC) on synovial fluid can be done using a standard WBC counting pipet and chamber, but the usual WBC counting fluid must be replaced with 0.3 percent saline. The acetic acid nor-

have the greatest incidence of DJD. Rheumatoid factor has been reported in up to 42 percent of persons over age 60. Westergren sedimentation rates were over 20mm Hg in 75 percent of women over age 65. Of course, rheumatoid factor tests are also negative in about 30 percent of patients with classical rheumatoid arthritis. Sedimentation rates can occasionally be within normal limits in a variety of inflammatory diseases including systemic lupus. In persons suffering from degenerative joint disease, the

TABLE I
Classification of Synovial Effusions

<table>
<thead>
<tr>
<th>Group</th>
<th>Normal</th>
<th>Non-Inflammatory</th>
<th>Inflammatory</th>
<th>Septic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (cc) (Knee)</td>
<td>&lt;3.5</td>
<td>&gt;3.5</td>
<td>&gt;3.5</td>
<td>&gt;3.5</td>
</tr>
<tr>
<td>Viscosity</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td>Variable</td>
</tr>
<tr>
<td>Color</td>
<td>Clear</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Opaque</td>
</tr>
<tr>
<td>Clarity</td>
<td>Transparent</td>
<td>Transparent</td>
<td>Translucent</td>
<td>Opaque</td>
</tr>
<tr>
<td>WBC (mm³)</td>
<td>&lt;200</td>
<td>200 - 2,000</td>
<td>2,000 - 100,000</td>
<td>100,000*</td>
</tr>
<tr>
<td>Polys (%)</td>
<td>&lt;25</td>
<td>&gt;25</td>
<td>&gt;25</td>
<td>&gt;75*</td>
</tr>
<tr>
<td>Culture</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Often positive</td>
</tr>
<tr>
<td>Mucin clot</td>
<td>Firm</td>
<td>Firm</td>
<td>Pliable</td>
<td>Pliable</td>
</tr>
<tr>
<td>Glucose (mg per 100 ml)</td>
<td>Nearly equal</td>
<td>Nearly equal</td>
<td>&lt;25 lower</td>
<td>&gt;25 lower</td>
</tr>
<tr>
<td>AM fasting</td>
<td>to blood</td>
<td>to blood</td>
<td>than blood</td>
<td>than blood</td>
</tr>
</tbody>
</table>

*WBC and percent polys will be less if organism is less virulent or partially treated
mally used to lyse erythrocytes for leucocyte counts clots the synovial hyaluronic acid and yields unreliable counts. This clotting of synovial fluid on addition of acetic acid is also the basis for the mucin clot test.\textsuperscript{2}

Further support for the presence of DJD or at least cartilage degeneration can be obtained by the identification of cartilage fragments (figure 2A). These are easily visualized on examination of wet drop preparations of fluid but chondrocytes must be seen to be certain that this is not other debris such as fragments from a plastic syringe (figure 2B). Fibrils (figure 2C) may be due to collagen from cartilage but fibrils from fibrin clotting can be confused by light microscopy.\textsuperscript{7}

Other processes can be superimposed on DJD. Chondrocalcinosis commonly develops in elderly patients with DJD and attacks of pseudogout inflammation owing to the calcium pyrophosphate crystals may complicate what began as DJD. Degenerative arthritis can exist in one joint with another disease, including even septic arthritis, in another joint.

Search for Causes of Degenerative Joint Disease

Careful examination of synovial fluid may provide clues to underlying diseases that can cause DJD. Dark fragments seen on wet drop examination\textsuperscript{9} or floating in the fluid\textsuperscript{6} should suggest ochronosis (figure 3). With Wright’s stain and higher magnification, the ochronotic fragments appear brown or golden.

Hemochromatosis should be considered if phagocytic synovial fluid cells stain positively for iron on Prussian blue stain. Weak positive birefringent crystals of calcium pyrophosphate with or without any inflammatory reaction suggest several metabolic diseases associated with both DJD and chondrocalcinosis. These include hemochromatosis, ochronosis, acromegaly, Wilson’s disease, hypothyroidism and hyperparathyroidism. Examination for calcium pyrophosphate crystals requires experience with use of compensated polarized light as described by Phelps et al\textsuperscript{8} since these crystals may be only very faintly birefringent and difficult to detect.

Non-inflammatory joint effusions can also be seen in diseases beside DJD. Amyloidosis can be diagnosed by centrifuging the fluid to obtain a button that can then be embedded
in paraffin and stained with Congo red. Sickle cell effusions may be suspected by seeing sickled cells in the fluid. Acute trauma produces non-inflammatory effusions, usually with some erythrocytes and often with less viscosity than in DJD, presumably because of the acute transudation of fluid into the joint before additional hyaluronate can be synthesized. Other mechanical problems not strictly DJD include osteochondromas, Charcot joints, osteochondritis dissecans and meniscus injuries. Ehlers-Danlos syndrome with its unstable joints predisposes to both traumatic effusions and DJD. Hypertrophic pulmonary osteoarthropathy causes non-inflammatory knee, ankle, wrist and elbow effusions and is extremely important to exclude because it is often a clue to bronchogenic carcinoma or other important systemic disease. Clubbing and periosteal elevation are usually present. The fluid often clots spontaneously in contrast to other non-inflammatory effusions. Both gout and pseudogout can have
non-inflammatory effusions between attacks. Systemic lupus, rheumatic fever and scleroderma often have only borderline synovial fluid leucocyte counts around 2000 cells per mm.\textsuperscript{9}

Synovial biopsies, whether obtained by needle\textsuperscript{13} or surgical exploration, may also aide in diagnosis of underlying diseases. In hemochromatosis,\textsuperscript{10} iron is largely limited to the synovial lining cells (figure 4) in contrast to the deep perivascular macrophages where most iron deposits appear after hemarthrosis. In ochronosis, pigmented shards can be seen embedded in synovium (figure 5). Wilson's disease so far has not been shown to have a distinctive biopsy appearance.

There is also no diagnostic histologic appearance of synovium in primary osteoarthritis. Cartilage fragments can be seen embedded in the tissue but extreme numbers of fragments should favor consideration of the more destructive Charcot joints. Varying degrees of congestion, fibrosis and edema are seen. Fibrin and polymorphonuclear leucocytes are usually lacking but a moderate number of lymphocytes are often seen around small vessels.

Wilson's disease can be suggested by the clinical picture including Kayser-Fleisher rings and then by demonstration of low serum ceruloplasmin and high levels of hepatic copper.\textsuperscript{3} Serum iron is elevated with a high percentage of saturation of total iron binding capacity in hemochromatosis. In acromegalic arthritis,\textsuperscript{1} cartilage overgrowth often initially produces widening of joint spaces on x-ray with only later DJD presumably due to joint incongruity. Biopsy of an osteochondral junction can show persistent endochondral bone formation in the adult with acromegaly.\textsuperscript{14} Determination of plasma growth hormone provides definitive diagnosis.

Ochronosis is confirmed in the laboratory by elevation of homogentisic acid in the urine. Homogentisic acid is not increased in synovial fluid. Hyperparathyroidism is suspected by showing elevation of serum calcium, low phosphate and decreased tubular
resorption of phosphate. Hypothyroidism is diagnosed by low thyroxine levels in blood. Synovial fluid viscosity is often greatly increased in hypothyroidism.

References