Correspondence

Joint scintigraphy and erosions

Sirs. Isotope studies have been widely used in rheumatology for about 20 years. The study by Desaulniers and coworkers indicated that skeletal scintigraphy was a more sensitive method for the detection of inflammatory joint disease than radiography. It appeared to be more sensitive than clinical evaluation in the diagnosis of joint inflammation of wrists, hands, ankles, and feet. We read with interest the study of Pitt, Berry, Clarke, and coworkers, in which x rays and joint scans with ⁹⁹ᵐTc methylene diphosphonate (⁹⁹ᵐTc MDP) were compared. They found no association between the uptake of isotope in the hands and the development of new erosions.

They studied 10 patients with RA whose hands were x rayed at 0 and 12 months, whereas ⁹⁹ᵐTc MDP scanning was performed only at the beginning of the study. Five patients had 30 eroded joints, 57% of which were scintigraphically active. The high proportion of scintigraphically negative erosions at the start of the study is not surprising since patients with early RA were not included. The duration of disease was 11 years on average (range 2-47) and obviously many joints with erosions would have been clinically inactive for years. Data on clinical activity of the joints were not presented. Demonstration of an old erosion by scintigraphy is not important as erosions can be seen in x ray pictures.

The interesting question is how valuable joint scanning is in predicting the joints to be eroded. The x rays done after 12 months' follow up showed 28 new erosions, of which 46% were in scintigraphically active joints. Development of a new erosion in a joint which was negative on scanning 12 months earlier does not argue against the predictive value of scanning because arthritis may exacerbate during the period of observation. The inflammation in a joint may decrease, remain unchanged, increase, or start in a previously inactive joint during the follow up period of one year.

We have followed up 16 newly diagnosed patients with RA (average duration 10 months) for 18 months with careful serial clinical assessment (Ritchie index and joint effusion) and with ⁹⁹ᵐTc MDP scintigraphy of peripheral joints (n=477) at 0, 6, and 12 months. ⁹⁹ᵐTc MDP with an activity of 370 MBq/m² was injected, and pictures were taken after three hours. The collection 128×128 word matrix was used. Visual measurement (normal, slight, or clear contrasts) of metacarpophalangeal, proximal interphalangeal, metatarsophalangeal II-IV, and interphalangeal of the first toe joints was performed by comparing the gray scale with the pictures of uninflamed control joints. The uptake of isotope in the joints was scored from 0 to 2 points at each assessment, and the total scintigraphical activity of the joint was determined by adding the scores at 0, 6, and 12 months. X rays of the hands and feet were taken at each assessment and at 18 months. The radiological destruction of the joint was estimated according to the method of Larsen, Dale, and Eek.

Five eroded joints in four patients with RA were found initially, and they were all scintigraphically active. All 72 joints in which new erosions developed during the follow up were also active by scanning. There were 85 scintigraphically highly active joints, 45 of which eroded during the follow up (Table 1). When isotope activity remained normal in serial scannings new erosions were not discovered in the joints. Eleven joints with new erosions were initially scintigraphically inactive, but the activity increased during the follow up.

The clinical assessment could not predict erosiveness in 27 joints, while ⁹⁹ᵐTc MDP scanning missed only four. The calculated sensitivity and specificity of the methods in predicting erosions were 94.4% and 77.3% by ⁹⁹ᵐTc MDP scanning and 62.5% and 85.7% by clinical assessment. Our patients suffered from active RA and the scanning was performed three times during 18 months. This could account for the difference between the results of Pitt et al and our study. The gammacamera used by Pitt and others was interfaced to a computer system, and the average count density in the joint was compared with background counts per unit area. In our study the measurement was performed visually, which is known to have a good correlation with the method of region of interest.

We conclude that serial joint scans correlate with clinical activity but are more sensitive than clinical assessment. Erosions are most likely to develop in the joints of intense radionuclide uptake, provided that the high activity persists. In a few cases erosions may develop in joints which scintigraphically are initially inactive or slightly active but highly active later at 6 and 12 months.

The radiation dose of three ⁹⁹ᵐTc MDP isotope studies did not exceed the dose of lumbar sacral radiography.

Consent for our study was granted by the ethics committee of the Central Hospital of Jyväskylä.

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Table 1 Comparison of scintigraphic activity with the development of erosions

<table>
<thead>
<tr>
<th>Scintigraphic activity score</th>
<th>Number of joints</th>
<th>Number of joints with new erosions</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-6</td>
<td>85</td>
<td>45</td>
</tr>
<tr>
<td>3-4</td>
<td>75</td>
<td>23</td>
</tr>
<tr>
<td>1-2</td>
<td>141</td>
<td>4</td>
</tr>
<tr>
<td>0</td>
<td>176</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>477</td>
<td>72</td>
</tr>
</tbody>
</table>
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SIR. We read with interest the above letter.

We have investigated 17 patients with two diphosphonate scans of their hands one year apart as we were also concerned with the value of a single isotope scan. We have calculated the scintigraphical activity of each joint, maximum score 4, using a similar scoring system and visual assessment (Table 1).

The results support our original report, showing no apparent association between the uptake of isotope and the development of erosions. Even when nine patients with early disease (mean 20 months) were examined a similar pattern of isotope uptake was found.

It is possible that the high proportion of joints reported by the above authors, showing increased uptake, reflects increased disease activity. We note that 47% of these highly active joints on isotope scanning have not developed erosions during the study.

We believe our original observation that increased uptake of isotope may be associated with some, but not all erosions, still stands and that isotope uptake probably reflects other processes of acute inflammation unassociated with the development of an erosion.

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Table 1 Scintigraphical activity score of rheumatoid joints with new, healed, and unchanged erosions

<table>
<thead>
<tr>
<th>Scintigraphical activity score</th>
<th>No of joints</th>
<th>No of joints with new erosions</th>
<th>No of joints with healed erosions</th>
<th>No of joints with unchanged erosions</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>25</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>66</td>
<td>10</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>128</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>117</td>
<td>3</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>340</td>
<td>21</td>
<td>4</td>
<td>13</td>
</tr>
</tbody>
</table>

Sulphasalazine hepatotoxicity: lack of a hypersensitivity response

SIR, Dr Farr and colleagues report two cases of suspected sulphasalazine hepatotoxicity in rheumatoid patients.1 The absence of hepatic histology and drug rechallenge, and the failure to exclude other possible explanations (for example extrahepatic biliary obstruction in case 1) make these presumptive diagnoses based solely on the temporal relation of the biochemical abnormalities to the sulphasalazine administration. The authors fail to clarify the exact timing of these abnormalities in relation to drug administration. Also, in case 2 there was only a twofold rise in an already abnormal alkaline phosphatase level, which had still not returned to its pretreatment level three weeks after the drug was stopped. The case for a drug related phenomenon remains uncertain.

If the hepatic enzyme rises are accepted as probably drug induced, however, there is a more important aspect to note, namely the lack of a clinical hypersensitivity reaction. All but one2 of the 17 cases in the literature of sulphasalazine hepatotoxicity in inflammatory bowel disease showed such a reaction, comprising fever, lymphadenopathy, and peripheral eosinophilia. We wish to draw your readers' attention to another rheumatoid patient who developed sulphasalazine hepatotoxicity, in whom this hypersensitivity reaction was also notably absent.

Case history

A 50 year old woman with rheumatoid arthritis developed anorexia, nausea, and upper abdominal pain after 11 weeks of sulphasalazine therapy at a dose of 3 g/day. She was anicteric and had no fever, lymphadenopathy, skin rash, or any stigmata of liver disease. Hepatic transaminases, which had been normal immediately before treatment, were now markedly raised (see Table). There was no history of jaundice, hepatitis contact, or blood transfusion, she had not travelled abroad, and her only other medication was ketoprofen, which she had been receiving for 18 months. Screening for hepatitis A and B, cytomegalovirus, Epstein-Barr, and herpes simplex viruses was negative. Upper abdominal ultrasound was normal, and antibodies to smooth muscle and mitochondria were not detected. A liver biopsy showed a severe acute hepatitis with focal

References

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T Möttönen, P Hannonen, A Rekonen and M Oka

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