Pigmented villonodular synovitis

I write with regard to the paper by Zuber and colleagues that purports to demonstrate a case of pigmented villonodular synovitis (PVNS).

The patient under discussion—who presented with progressive, bilateral ulnar deviation at the MCPs—most probably had rheumatoid arthritis. Although I do not agree that rheumatoid arthritis has to be considered as a differential diagnosis, the described patient did not fulfil the 1987 revised criteria for the classification of rheumatoid arthritis. The patient did not suffer from morning stiffness in and around joints. She did have swellings of the MCP joints that were asymmetrical—that is, far more prominent on her left side; no signs of arthritis in these joints were present, however. The symptoms were not symmetrical. The patient did not have subcutaneous nodules, no rheumatoid factor was present in her serum, x rays of hands and feet did not show any erosions.

The patient was presented in the department of traumatology, hand and reconstructive surgery with a fixed flexion deformity of her left MCP joints, which caused inability to open her hand properly. She did not present with typical symptoms of rheumatoid arthritis such as morning stiffness, tenderness or pain. Synovectomy of the second to fifth MCP joints and reconstruction of the extensor hood of the left hand was performed. The right hand showed discrete thickening of the MCP joints. No need for surgery was discovered there. After surgery the patient was referred to rheumatology. Here there was a discrepancy between the lack of typical symptoms and signs of rheumatoid arthritis and the severe and asymmetric ulnar deviation, both of which was very unusual, was noted. Because of this discrepancy it was decided to ask for the routinely performed histological evaluation of the operation specimen, which clearly stated that PVNS was present.

I would like to offer some comments on the paper by O’Dell. We would like to offer some comments on the paper by O’Dell. We read with great interest the paper by Zuber and colleagues that purports to demonstrate a case of pigmented villonodular synovitis (PVNS). The patient under discussion—who presented with progressive, bilateral ulnar deviation at the MCPs—most probably had rheumatoid arthritis.

In addition, the authors suggest that in their patient PVNS was found to affect the second to fifth MCP joints. However, the diffuse form of PVNS is nearly always monarticular; documented cases of polyarticular (usually biarticular) involvement by PVNS are exceptionally rare, and probably other than PVNS. It is the histiocyte that renders the pathology of PVNS unique and characteristic for the pathology of the PVNS. Lipid filled histiocytes, also called foam cells, are depicted in figure 2 of the paper. With giant cells and scattered lymphocytes. The third issue Dr Docken raises is the fact that diffuse PVNS tends to occur monarticular. The knee is the most frequent joint involved, followed by the hip and ankle. Infrequently, the diffuse form will present in the hand, shoulder, wrist, and vertebral. Bilateral forms do occur occasionally and polyarticular forms are rare.

Recently an unusual case of multiple site involvement of PVNS in a child has been reported. The case presented in our paper belongs to the rare polyarticular forms of diffuse PVNS.

Dr Docken expresses the opinion that the patient under discussion did not suffer from pigmented villonodular synovitis (PVNS) but from rheumatoid arthritis. Although I do agree that rheumatoid arthritis has to be considered as a differential diagnosis, the described patient did not fulfil the 1987 revised criteria for the classification of rheumatoid arthritis.

Some studies have used full doses of single drugs or of various drugs in combination for long periods of time. Some negative results, at least, could have resulted from low doses or the results with single drug therapy could have been improved by using full doses of the drugs.

As clearly hypothesised by O’Dell, by using full doses of the available drugs, the results should be even better either in terms of time lapse before the appearance of the response or in the degree of the response. Whether or not a clear distinction among the patients, those who improve in a clinically meaningful manner (50% or more) and those who survive while receiving treatment without such a significant clinical benefit for example, in our own experience with MTX, only 37% of 159 patients with active, erosive RA, followed up for three years, had a clinically important response, even though 83% were still receiving the drug.
Tissue crosslinks concentrations in normal joints and chronic articular diseases

We read with interest the recent paper by Takahashi et al concerning joint tissue concentrations of collagen crosslinks (Pyr, Dpyr) in patients with osteoarthritis (OA) and rheumatoid arthritis (RA). The main discovery of this study was the presence of Dpyr also in extra-osseous tissues, namely cartilage and synovium in patients with joint disorders and in the synovium of nonarthritic controls. These data suggest that extra-skeletal sources may contribute to the increased urinary excretion of the two crosslinks in joint disorders, as several observers have reported in recent years. 1–6

We recently performed a similar study on samples of subchondral bone, cartilage, and synovium of six patients with OA (mean (SD) age 58.1 (10.7)) and six patients with RA (age 61.1 (18.1)) who underwent total hip arthroplasty. In contrast with the study by Takahashi, as a control group we studied joints from six young patients (aged 37.5 (13.5)) who underwent surgical amputation of the highest content of Pyr (table 1).

Table 1 Mean (SEM) concentrations of collagen crosslinks (nmol/g of fresh tissue) in articular tissue of healthy controls and in patients with osteoarthritis (OA) and rheumatoid arthritis (RA)

<table>
<thead>
<tr>
<th>Crosslink</th>
<th>OA</th>
<th>RA</th>
<th>OA/RA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyr</td>
<td>1313 (366)</td>
<td>1166 (342)</td>
<td>1.09</td>
</tr>
<tr>
<td>Dpyr</td>
<td>221 (92)</td>
<td>2150 (241)</td>
<td>0.61</td>
</tr>
<tr>
<td>Pyr/Dpyr</td>
<td>6.0 (2.0)</td>
<td>6.0 (2.0)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Table 1: Mean (SEM) concentrations of collagen crosslinks (nmol/g of fresh tissue) in articular tissue of healthy controls and in patients with osteoarthritis (OA) and rheumatoid arthritis (RA)

Figure 1 Mean concentrations (SEM) of PYR and DPYR in subchondral bone and cartilage in patients with osteoarthritis, rheumatoid arthritis, and in healthy controls.
between controls and patients, which has been reported also by Takahashi et al. makes unlikely the contributory role of synovial membrane to urinary excretion of crosslinks in chronic joint diseases, which seems to be related to subchondral bone and articular cartilage increased turnover. This hypothesis is consistent with data from our previous study demonstrating that crosslinks concentrations in synovial fluid are similar in two conditions with a highly different metabolic turnover of synovial membrane such as OA and RA.

**Authors’ reply**

As stated by Sinigaglia et al both pyridinoline (Pyr) and deoxypyridinoline (Dpyr) have been recently found in more various tissues than previously expected. I would like to offer the following comments.

Firstly, the usefulness of a biochemical marker does not need to be related to change of the concentrations of materials for marker in tissues. For instance both of the above crosslinks in urine have been established as bone resorption markers. The urinary crosslinks considerably increase in metabolic bone disorders, however they do not increase in bone, but an increase in the bone resorption (bone turnover) leads to an increase of crosslinks in urine. For a biochemical marker reflecting tissue turnover, if the content of a marker material does not change in disease, change in urinary excretion of the marker reflects the net turnover of its distributed tissue. Therefore, the authors conclusion that no change in turnover of its distributed tissue. Therefore, their reduction is expected to be responsible for the degeneration of collagen and also the fragility of extracellular matrix. Our paper did not concentrate on this issue, so does not give the solution because of the absence of normal control in the study for bone and cartilage. Our previous study showed that Pyr did not change in cartilage in OA and RA compared with that in osteoporosis where a significant degeneration of cartilage is not involved.

There are two problems in methodology in the comments made by Sinigaglia et al. One is that the concentrations of crosslinks were expressed per gram of fresh weight. The authors maintain that crosslinks tissue levels per weight is more representative of the true collagen content, which however implies that content of collagen changes but not crosslinks in collagen. The other is that the control group is considerably younger than the OA and RA groups. I do not claim, however, that the crosslinks are constant among OA, RA, and normal groups. A reduction of crosslinks in cartilage in OA and RA seen by Sinigaglia et al may explain the degenerative change of cartilage in those diseases. However, the concentrations of Pyr and Dpyr in bone were considerably lower in OA and RA compared with the control group. In contrast, but in agreement with what I have previously mentioned, as Pyr and Dpyr are physiological crosslinks, the considerable change of these crosslinks induces diseases such as lathyresis. Therefore, the extreme reduction of crosslinks in bone is unlikely.

The ideal way to solve this problem is to study the degenerated lesion and intact lesion of tissues mostly in cartilage in the same subjects, although I understand that it is difficult to critically distinguish those two lesions.

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