swollen and painful knees during physical examination and effusion of the joint; duration of the disease was 4-28 years. The second group contained 14 patients with JIA; 5 girls, 9 boys; 8-17 years old; six of them had polyarticular and eight oligoarticular onset JIA; duration of the disease was 1-11 years. At the time of sampling eight patients were in very active and six in subacute periods of the disease according to Mallya and Mace (5). Our reference group was composed of 20 patients with injured anterior ligament or meniscus medialis/lateralis (6 female, 14 male; 15-21 years old).

Arthrocentesis of the knee joint of RA and JIA patients was performed because of prolonged edema or intracapsular injection of steroids. Samples of the SF of patients with traumatized knees were obtained during routine diagnostic arthroscopy. The activity of HEX in the SF was determined as described by Zwierz et al. (6). The activity of cathepsin D in the SF was performed as described by Greczaniuk et al. (7). Statistical analysis was conducted with a Stata software program by Statistica 6, and the Levine test was applied to the data. This revealed significant differences among the studied groups. We used non-hoc analysis calculated by test N, which indicated the least significant difference. Results were expressed as mean and SD. P-values of less than 0.05 were considered significant. The study design was approved by the Ethical Committee of the Medical University of Białystok, Poland. In the SF of patients with RA and JIA, HEX activity was calculated as 105.9±4.30, 128.3±4.28, 85.13±2.87, 80.45±2.19 nmol/ml/min, respectively, and in RA patients was significantly elevated (p = 0.000003) in comparison to traumatized patients.

Sohar et al. (9) recently reported a 1.28 fold increase in HEX, and 1.49 fold increase in cathepsin D activity in the leukocytes of RA patients. It is worthy of note that HEX activity in the SF of our RA and JIA patients was 8.3 and 6.6 but cathepsin D was only 2.8 and 2 times higher than that in the SF of the control group. Our results suggest that in the knee joint cavitites of RA and JIA patients, increased degradation of glycosaminoglycans (hyaluronic acid, chondroitin and keratan sulfates) and glycoproteins with HEX is greater than degradation of proteins by cathepsin D. Our results are in agreement with data reported by Orütay et al. (2) which suggest that exoglycosidases, which are present in the SF of RA patients, may contribute to the depletion of GAGs from cartilage. The conclusion is that some possible interplay between proteases and glycosidases in the SF of RA patients can take place. Analysis of the above enzyme system may be an important complement to molecular and genetic studies in the effort to fully understand the mechanism of RA. Our data indicate HEX as an important complement of the joint damage diagnostic system and inhibition of HEX as a potential target of RA therapy.

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References

Atypical axial osteomalacia: Report of a HLA-B27 negative elderly female patient without features of sacroiliitis

Sirs,

Atypical axial osteomalacia (AAO) is a very rare bone disorder characterized by dense coarseness of the trabecular bone on radiographs located in the axial but not appendicular skeleton, and osteomalacia on bone biopsy of affected areas. Since the first case was described in 1961/62 (1) not more than 18 AAO-patients have been reported (2-9). All of them, except one (report of an affected mother and son) (5) were middle-aged or elderly Caucasian men. The cause of AAO is still unknown and some authors suggest that AAO could be a genetic bone cell abnormality. Sacroiliitis (3/5) and positive HLA-B27 antigen (2/4) is the most described concomitant disease. Axial increased and peripheral decreased bone mineral density (7, 9), moderate phosphate diabetes (8) and associations with polycystic kidney (5) and liver disease (5) have been reported. A 83-years-old Caucasian female patient was admitted to our unit for dorsal and lumbar back pain. The patient was in normal general health, with no living relatives and no relevant medical or surgical history. X-rays of the lumbar spine and pelvis showed a marked osteocclerosis without changes in size. There were no signs of sacroiliitis, which was confirmed by CAT, MR and scintigraphic examinations, whereby X-rays and MR are usually sufficient to make diag-

Table I. The activity of N-acetyl-β- D-hexosaminidase and cathepsin D in synovial fluid of patients with rheumatoid arthritis (RA), idiopathic juvenile arthritis (JIA) and traumatized knees (p value means that the difference between the experimental and control groups was statistically significant.

<table>
<thead>
<tr>
<th>Lyosomal enzymes</th>
<th>Enzymatic activity (mean) in the synovial fluid of patients with</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>RA</td>
</tr>
<tr>
<td></td>
<td>n = 11</td>
</tr>
<tr>
<td>Hexosaminidase nM/ml/min</td>
<td>105.9 ± 4.30</td>
</tr>
<tr>
<td>p = 0.00003</td>
<td>p = 0.0005</td>
</tr>
<tr>
<td>Cathepsin D nM/ml</td>
<td>146.6 ± 31.85</td>
</tr>
<tr>
<td>p = 0.000001</td>
<td>p = 0.00002</td>
</tr>
</tbody>
</table>

Letters to the Editor
nosis of a sacroiliitis. The skull, cervical and thoracal spine, upper and lower limbs showed normal bones and moderate osteoarthritic changes. Looser’s zones have not been identified. Measurements of bone mineral density (DEXA) revealed a T-score of the lumbar spine (L2-L4) of +3.9 and of the femoral neck of -2.2. Routine laboratory parameters and biochemical markers of bone metabolism, including serum calcium, inorganic phosphate, total alkaline phosphatase, bone specific alkaline phosphatase, 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D, osteocalcin, intact PTH, creatinine and phosphate clearance were within normal limits. Testing for HLA-B27 was negative. Only one time (due to bone biopsy) there was a slight increase of total alkaline phosphatase. Histological examination of an iliac crest bone biopsy showed thickening of the cortices, increased trabecular bone with broad seams of unmineralized osteoid due to osteomalacia. The radiologic, densitometric, laboratory and histologic findings in the patient presented herein are compatible with AAO and histologic findings in the patient presented herein are compatible with AAO.

References

Letters to the Editor

Haemorrhagic gastritis and bleeding following rofecoxib administration

Sir,

Selective inhibitors of cyclooxygenase-2 (COX-2) have been clinically developed to achieve therapeutic effects comparable to those of conventional non-steroidal anti-inflammatory drugs (NSAIDs), without causing damage to the digestive mucosa (1). Here we describe a case of gastrointestinal bleeding which occurred after treatment with the selective COX-2 inhibitor rofecoxib, reported to us by Pharmasearch, an Italian network of general practitioners for the spontaneous reporting of adverse drug reactions.

A 76-year-old woman referred to her family physician for the onset of severe epigastric pain, associated with the emission of dark stools and one episode of coffee-ground emesis. She was affected by bilateral gonarthrosis, diffuse osteoarthritides, and low back pain. Rofecoxib 25 mg/day had been prescribed by her physician to treat a flare of osteoarthritic pain. The patient assumed rofecoxib for 20 days without complaining of digestive symptoms and then, once the pain was relieved, the treatment was suspended. A few days after rofecoxib withdrawal, the patient developed epigastric pain accompanied by the emission of dark stools and one episode of coffee-ground emesis. After neglecting such disturbances for about one month, the patient referred her symptoms to the physician during a visit scheduled to review the results of routine laboratory examinations (all values being normal). The physician prescribed lansoprazole 60 mg/day, and requested an upper digestive endoscopy. The endoscopic examination revealed haemorrhagic-erosive gastritis, with the body and antrum mucosa being extensively affected by both flat and protruding erosions, and with broad intervening areas of intramucoal bleeding. The patient reported no tobacco or alcohol consumption, but referred previous digestive disturbances in concomitance with NSAID use. The patient’s medical history did not indicate documented episodes of peptic ulcer or dyspepsia. The patient had been having treatment with the antiepileptic drug carbamazepine 400 mg/day, for 12 years, following the surgical removal of a meningioma. Lansoprazole treatment for two months fully relieved the patient’s digestive symptoms. The application of Naranjo algorithm (2) to the present case allowed to rank as ‘probable’ the causal link between rofecoxib administration and the occurrence of adverse digestive events. A putative interaction with carbamazepine was taken also into account to explain the above symptoms, but there is no evidence in literature to support such a hypothesis.

Based on pharmacoepidemiological data, this patient can be considered at increased risk for NSAID-induced digestive toxicity, due to sex, age and history of NSAID-induced digestive toxicity (3,4), and therefore she is likely to have experienced an episode of upper digestive bleeding following treatment with a COX-2 inhibitor. Although COX-2-inhibitors appear to be safer than conventional NSAIDs in controlled trials (5), treatments with the former drugs have been associated with upper gastrointestinal complications in post-marketing studies (6). There is also recent evidence of selective prescription of COX-2 inhibitors.

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