Prolonged remission in established rheumatoid arthritis (RA) is extremely rare. During a six year follow up of 458 patients Wolfe and Hawley observed two prolonged remissions of more than 48 months, and concluded that ‘once established, RA tends to remain, interrupted briefly in a small minority of patients by remission of disease.’ However prolonged remissions or cures have been described as secondary to Cushing’s disease and human immunodeficiency virus infection.6 We have observed a case of cure of RA accompanied by, and possibly secondary to, the development of γ heavy chain disease in the context of secondary Sjögren’s syndrome.7 RA was diagnosed in January 1986, in a 53 year old woman. Retrospective examination of her chart shows the presence of six of seven 1987 American Rheumatism Association revised criteria for the diagnosis of RA. Her treatment included intramuscular gold, non-steroid anti-inflammatory drugs, and several intra-articular injections of corticosteroids. Considerable improvement was noted at the end of 1988 and has persisted since. Gold injections (cumulative dose 2.4 g) were discontinued in March 1989 after discovery of proteinuria. There was decreased γ globulinaemia (4.8 g/l, normal value = 6 to 16 g/l) with free monoclonal γ heavy chains representing 75% of total IgG and an additional faint IgG representing 25%. The idiotypic γ band suggestive of a second monoclonal paraprotein. Flow cytometry of blood and bone marrow confirmed the presence of two B cell clones. The eyelid enlargement recurred quickly. Subsequent irradiation relieved the visual fields obstruction and was later successfully extended to the swollen submandibular regions. Sixteen months after diagnosis, the patient’s condition is stable.

The immunologically active polyclonal γ globulin concentration was 1 g/l (reference value 5.4 to 14.8 g/l), which is lower than in other leukaemias/lymphomas. The levels of IgA (0.38 g/l, reference value 0.65 to 1.48 g/l) and IgM (0.28 g/l, reference value 0.45 to 2.6 g/l) were also low. Lymphocyte count was 1120/µl with 54% of T cells and most of the B cells part of the clonal processes. Fifteen months later the paraprotein levels were stable, the polyclonal IgG have increased to 3 g/l, IgA to 0.55 g/l, IgM to 0.35 and lymphopenia worsened at 800.

We think that the following chain of events occurred in this case: immune disorder, autoimmune disease (RA and secondary Sjögren’s syndrome), malignant B cell neoplasm, secondary immunodeficiency with cure of the RA. The first three steps are well known, the fourth is probably exceptional but this case and others1 suggest that secondary immunodeficiency should be considered during spontaneous cures of well established RA.

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Does lymphoma ‘cure’ rheumatoid arthritis?


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LETTERS TO THE EDITOR

Insufficiency fracture of the sacrum revealing a pregnancy associated osteoporosis. First case report

Osteoporosis of pregnancy, usually responsible for spinal or femoral fracture, is rare as is insufficiency fracture of the sacrum, usually occurring in the elderly.7 Magnetic resonance imaging (MRI) permitted during pregnancy, led us to diagnose an insufficiency fracture of the sacrum revealing a pregnancy associated osteoporosis, never previously reported to the best of our knowledge. Rheumatologists need to be aware of this new cause of pelvic pain during pregnancy.

A 29 year old pregnant (seventh month) woman presented with a spontaneous acute claudication in conjunction with a left hyperalgesic buttck pain. Her past medical history showed: low back pain, since the second month of her pregnancy, relieved by rest and paracetamol; smoking (10 packet years) stopped at the sixth month of pregnancy; one spontaneous miscarriage at six months responsible for an isocouagulagen harpin treatment (Calciparine 10000 IU daily) at the fourth month, without any other abnormality in her menstrual history. She did not take part in athletic activities and had no history of pelvic trauma or osteoporosis family history. Physical examination showed an exquisite painful point on the left sacroiliac articulation. Pelvic MRI was performed, showing on the left part of the sacrum a ‘no signal intensity’ line surrounded by a low signal on T1 weighted sequences and high signal intensity on T2 weighted sequences with an oedematous area, revealing a longitudinal insufficiency fracture (fig 1). Biological markers, summarised in table 1, were within the normal range except a 25 OH vitamin D deficiency and a moderate increase in alkaline phosphatase activity. There was no evidence for any other disease (for example, excess alcohol, systemic lupus erythematous, malignancy, etc). The pain disappeared with bed rest. Standard pelvic MRI performed after delivery showed the fracture of the sacrum, without marked osteopenia; dual energy x ray absorptiometry examination showed: lumbar spine T score: −1.21, femoral neck Tscore: −2.02.

Insufficiency fracture of the sacrum is a recently described, rarely reported disorder, occurring usually in the elderly.7 The main aetiological circumstances include post-menopausal osteoporosis, pelvic irradiation,4 corticosteroid induced osteoporosis, and primary biliary cirrhosis.7

Pregnancy related osteoporosis is rare and its pathogenesis is unknown. It is responsible for painful acute events during pregnancy, in conjunction with spontaneous fractures, usually affecting the spine8 and sometimes femoral neck,9 wrist or clavicle.1

Table 1 Biological markers

<table>
<thead>
<tr>
<th>Biological markers</th>
<th>Patient</th>
<th>Normal range for our laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum calcemia</td>
<td>2.46 mmol/l</td>
<td>2.2-2.6</td>
</tr>
<tr>
<td>Serum phosphorus</td>
<td>1.07 mmol/l</td>
<td>0.98-1.3</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>140 U/l</td>
<td>36-120</td>
</tr>
<tr>
<td>Protdemia</td>
<td>70 g/l</td>
<td>65-75</td>
</tr>
<tr>
<td>Creatinemia</td>
<td>91 µmol/l</td>
<td>45-90</td>
</tr>
<tr>
<td>25 OH vitamin D</td>
<td>4 ng/ml</td>
<td>10-35</td>
</tr>
<tr>
<td>Parathyroid hormone</td>
<td>27 ng/l</td>
<td>10-65</td>
</tr>
<tr>
<td>gla-protein</td>
<td>5.70 ng/ml</td>
<td>4-9</td>
</tr>
<tr>
<td>Antiphospholipid antibody</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>Blood count</td>
<td>normal</td>
<td></td>
</tr>
<tr>
<td>CRP</td>
<td>5 mg/l</td>
<td>0-10</td>
</tr>
<tr>
<td>ESR</td>
<td>21 mm/1st h</td>
<td>5-15</td>
</tr>
<tr>
<td>Thyroid hormone</td>
<td>normal</td>
<td></td>
</tr>
</tbody>
</table>

CRP=C reactive protein, ESR=erythrocyte sedimentation rate.
Our case is original because both the localisation and the aetiology of the fracture are unusual. To the best of our knowledge, no spontaneous fracture of the sacrum during pregnancy had previously been reported in the medical literature. Calcium disorders may occur pregnancy; this patient’s previous bone status was unknown. The increase in alkaline phosphatase activity could be attributed both to a physiological process of remodelling and to vitamin D deficiency. In this case the fracture might have occurred in relation with the vitamin D deficiency (possibly in relation with seasonal variation in winter time and bed rest), a mechanical mechanism (fetus weight, as the fracture occurred during the last trimester), and a metabolic mechanism, related to a long term heparin therapy (> 4 months). Heparin may have been a relevant risk factor, because any other risk factor (malignancy, excess alcohol, systemic lupus erythematosus), would have been detected. The heparin osteopenic effect, probably related to a direct effect on osteoclast development and activity, has been demonstrated during pregnancy with dose related calcium homeostasis disorders induced by heparin, although fractures may occur during low dose, short-term prophylaxis.

Saccrum fracture during pregnancy may be an underestimated occurrence, because of the lack of specificity of the symptoms and because x ray imaging is not possible. Magnetic resonance imaging should be considered instead of radiographs during pregnancy when clinical features suggest sacrum fracture.

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No endotoxin detected in plasma of patients with ankylosing spondylitis

Endotoxin has long been known to be an important virulence factor for Gram negative bacteria. It is chemically classified as lipopolysaccharide (LPS) and it is one of the major constituents of the outer membrane of Gram negative bacteria. This molecule is also known to be responsible for many injurious effects of Gram negative bacterial infections and thus is clinically important.

The pathogenesis of ankylosing spondylitis (AS) is still unknown. A microbial aetiology has been suggested such as an increased faecal carriage of Klebsiella spp, as well as increased antibody values, particularly against the LPS part of K pneumoniae have been reported in AS patients. Furthermore, Wagener et al.1 have reported that the plasma endotoxin concentrations were increased in approximately 30% of the AS patients and that a significant correlation was found between the increased endotoxin values and increased C reactive protein (CRP) concentrations. Therefore, it seems that LPS plays an important part in the pathogenesis of AS.

In this study we have examined the plasma of 28 hospital AS patients (eight females, 20 males; mean age 43 years (range 26-62)); mean erythrocyte sedimentation rate 22 mm/1st h (range 5-64) and the mean CRP value 12 mg/l (range 0-37) from the Rheumatism Foundation Hospital, Heinola, Finland for the presence of endotoxin. The mean (SD) duration of the disease was 14.5 (9.0) years: less than five years for three patients, 5-10 years for nine patients, and more than 10 years for 16 patients.

Blood samples were taken from the Vacutainer blood collection system (Becton & Dickinson Diagnostic Instrument System, Tewson, MD, USA) into Vacutainer tubes containing sodium citrate and kept in melting ice until separation of plasma. The samples were centrifuged immediately at 400 g for 10 minutes at +4°C, and plasma carefully removed and stored at −70°C until assayed.

All equipment was autoclaved endotoxin.

The concentration of endotoxin in plasma was determined by a chromogenic Limulus assay using Coatest kit (Chromogenix AB, Stockholm, Sweden) with a microtitre modification. The detection limit was 5 pg/ml; among normal controls, endotoxin levels do not exceed this concentration.

Some of the AS patients had plasma endotoxin concentrations exceeding the level of 5 pg/ml. This is surprising, as increased gut permeability has been found in AS patients and consequently gut microbes might easily pass through the mucosa to enter the circulation. The increased serum antibody concentrations against LPS of certain enterobacteria in AS patients.

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In a recent overview of current and potential future drug treatments for osteoporosis, the therapies for osteoporosis in men were discussed briefly. Osteoporosis in men is a heterogeneous disease of which 50% of the cases are classified as idiopathic osteoporosis (IOP). Long term data on treatment of men with IOP are not yet available.

In an uncontrolled open study of 22 white men with IOP, we have studied prospectively, the effect of a two year treatment with cyclic etidronate (400 mg/d during two weeks every three months) and calcium (500 mg/d during 10 weeks every three months). All patients were extensively screened to exclude any causes of secondary osteoporosis, such as hypogonadism and hypercalcuria, or any other risk factors. Liver function tests were normal in all patients and there was no excessive alcohol consumption either. Bone mineral density (BMD) measurements were performed every six months in the lumbar spine (L2-L4) and in the femoral neck, using dual energy x ray absorptiometry. Precision was <1% in the spine and <2% in the femoral neck. Results were expressed as mean (SEM). Per cent changes from baseline were analysed by a paired t test. Patients with vertebral fractures or a T score of < −2 in the lumbar spine, or both were included (a T score of 1 being the number of standard deviations from the mean bone density of young healthy controls). Mean (SD) age of the patients was 56 (2) years. Seventeen patients showed fractures of vertebrae (one fracture in seven patients and ≥ two in 10 patients) and 11 patients of the appendicular skeleton (one fracture in eight patients and ≥ two in three patients).

Mean T score was −3.2 (0.3) (range −5.4 to −0.6) in the spine and −2.8 (0.2) (range −5.0 to −0.5) in the femoral neck. After two years of treatment with cyclic etidronate, intention to treat analysis indicated an increase in BMD of +7.3 (1.1)% in the spine (p<0.001) and of +2.4 (1.2)% in the hip (p<0.05) (fig 1). The increase of BMD in the spine was similar if patients with spinal fractures (n=8) were excluded (+7.9 (2.0), p<0.01).

The significant increase of BMD in the spine during cyclic etidronate therapy is comparable to the treatment effect in postmenopausal osteoporosis. This is the first study to indicate that cyclic etidronate can significantly increase BMD in the hip of men with IOP and substantial bone loss. This study suggests that cyclic etidronate may be valuable in men with IOP, although double blind controlled prospective studies, with long term follow up are necessary to adequately assess this. In addition, whether cyclic etidronate will beneficially influence fracture rates in men will probably remain unknown, as large groups of patients are required to study this effect and as osteoporosis is less frequent in men than in women.

Authors’ reply

We thank Dr Ehrlich for his interest in our case report of a patient with a posterior interosseous nerve lesion, secondary to rheumatoid arthritis with synovitis of the elbow joint. We were not aware of his paper describing antecubital cysts in rheumatoid arthritis but, as our case was mainly an illustration of an unusual compressive neuropathy rather than a description of synovial cysts of the elbow joint, we would not have included the topic of his paper in our literature search. We agree that there is a similarity between the arthrogroms in Dr Ehrlich’s paper and that illustrated in our paper. Our case reinforces the conclusions of Dr Ehrlich’s paper 23 years ago that antecubital cysts are relatively common, are frequently overlooked, and should be actively sought when a patient with rheumatoid arthritis presents with symptoms suggestive of a compressive neuropathy in the forearm. We hope that our case report and Dr Ehrlich’s letter will remind rheumatologists to consider this potentially treatable cause of upper limb disability in patients with rheumatoid arthritis.

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Finger drop in a patient with rheumatoid arthritis

I wish to comment on the case report by McDonald and Smith. Although the authors report that a tomographic arthrogram showed no cystic extension of the joint capsule, the two figures are almost identical with those previously seen in antecubital cysts in rheumatoid arthritis. These ‘cysts’ are corollaries to the popliteal cysts and are generally missed in physical examinations because the bulge they produce often disappears into the fleshy part of the forearm. Clearly, they represent an escape for the effusion in a joint distended by severe synovitis and its products. The proximity of major nerves puts them at risk, as the paper by McDonald and Smith shows.

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Treatment with etidronate for men with idiopathic osteoporosis

PIET GEUSENS, JOHAN VANHOOF, JEF RAUS, JAN DEQUEKER, JOS NIJS and JO JOLY

Ann Rheum Dis 1997 56: 280
doi: 10.1136/ard.56.4.280a

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