Sulphasalazine treatment in rheumatoid arthritis

Sir: We read with great interest the article by Englert and colleagues on their experiences with sulphasalazine treatment in rheumatoid arthritis (RA).\(^1\) They noted the disappearance of rheumatoid nodules in four patients with RA in eight to twelve weeks after the start of treatment, parallel with a decrease in disease activity.

We also have used sulphasalazine regularly for the treatment of RA since 1983,\(^2\) but we have not found any favourable effect on the extra-articular manifestations of the disease. After reading Englert’s article, therefore, we decided to carry out a trial of sulphasalazine treatment in RA.

During a 24 week prospective trial we followed up seven patients with RA, who had subcutaneous rheumatoid nodules. They received 2 g/day sulphasalazine. Nine patients with RA and rheumatoid nodules treated with gold (sodium aurothiomalate) and six receiving various types of non-steroidal anti-inflammatory drugs (NSAIDs) alone served as controls.

Patients were randomly allocated to receive sulphasalazine, gold, or only NSAID. Intrarticular corticosteroids were not allowed during the course of the study, but some patients continued to receive oral prednisolone 7.5 mg daily or less, which had been started previously. All doses remained constant throughout the trial. There was no statistically significant difference in the characteristics of the patients at the start of the study among the three groups (p>0.05, Mann-Whitney U test).

All patients had active classical or definite RA according to American Rheumatism Association criteria and all were seropositive for rheumatoid factor. The size of the rheumatoid nodules varied between 7 and 28 mm, their localisation was typical (over olecranon, extensor surface of the forearm, proximal interphalangeal joints, patella, Achilles tendon). To assess the disease activity we used the following indices: Ritchie articular index, visual analogue pain scale, duration of early morning stiffness, hand grip strength, and erythrocyte sedimentation rate. Disease activity was considered to be decreased when at least four of the five variables improved by 50% or more.

At the end of the 24 week observation period no difference in the rate of regression of rheumatoid nodules could be detected between the patients taking sulphasalazine and those in the other two groups.

In the group taking sulphasalazine the size of the subcutaneous nodules had decreased in one patient only, but at the same time improvement in disease activity was seen in five patients. In the control group treated with gold we noticed a diminution of nodules in two patients and a decrease of inflammatory activity in six. In the group taking an NSAID alone the nodule size had decreased in three patients and the disease activity had diminished in four. The use of oral corticosteroids had no influence on the regression of the rheumatoid nodules. The table shows the results of our study.

Complete disappearance of nodules could not be found in any of the 22 patients. It is noteworthy that, like other investigators,\(^1\) we found no relation between the regression of nodules and the reduction of disease activity. Thus our results failed to confirm the experiences of Englert et al. In our opinion the total disappearance of rheumatoid nodules during sulphasalazine treatment may be explained by spontaneous regression. This phenomenon, though rare, is well known in everyday clinical practice and in rheumatological reports.\(^3\)\(^,\)\(^4\)

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Characteristics of patients and results of treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Disease duration (years)</th>
<th>Localisation of rheumatoid nodule</th>
<th>Reduction of disease activity</th>
<th>Decrease in nodule size</th>
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<tr>
<td>Sulphasalazine</td>
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<tr>
<td></td>
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NSAID = non-steroidal anti-inflammatory drug; PIP = proximal interphalangeal joint.

Methotrexate treatment of Felty's syndrome

Sir: We report the response to low dose oral methotrexate treatment in a patient with Felty’s syndrome.

A 65 year old white man developed Felty’s syndrome in 1987 with polyarthitis, rheumatoid nodules, and splenomegaly. He was found to have neutropenia (white cell count 2.8 x 10\(^9\) \text{/L}; neutrophils 11% and thrombocytopenia (platelets 123 x 10\(^9\) \text{/L}). Other laboratory indices included a high IgG, erythrocyte sedimentation rate 109 mm/h, rheumatoid factor 1 in 10 240. He also developed severe intermittent claudication. Angiography showed severe "atherosclerotic" changes in the iliac arteries. Angioplasty was deferred in view of his blood picture. He developed a rash on treatment with penicillamine and treatment was started with prednisolone 7.5 mg daily. There was no improvement in his clinical or haematological status and he was referred to St Thomas’s Hospital. In July 1988 treatment was started with methotrexate in an oral dose of 7.5 mg a week, while continuing the prednisolone at 7.5 mg a day. Prednisolone was eventually tapered to 2.5 mg/day.

He showed rapid clinical improvement. At three months his arthritis had subsided and after nine months of treatment the spleen was no longer palpable. The intermittent claudication had completely disappeared, and the neutrophil and platelet counts had increased: white cell count 5.4 x 10\(^9\) \text{/L} (neutrophils 46%), platelets 150 x 10\(^9\) \text{/L}. Erythrocyte sedimentation rate was 10 mm/h and rheumatoid factor 1 in 2560. The rheumatoid nodules remained. He has had no side effects to date, one year after starting methotrexate.

This report confirms earlier reports of a response of the neutrophilia of Felty’s syndrome to methotrexate.\(^2\) It was also interesting to note the fall in rheumatoid factor titre and marked improvement in intermittent claudication in this patient, in addition to the response of his rheumatoid arthritis.

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Giant cell arteritis presenting as a supraclavicular nodule

Sir: Giant cell arteritis is a systemic vasculitis that usually affects cranial arteries. Many manifestations secondary to involvement of other territories have also been described, however.\(^1\) We have recently seen an atypical case of giant cell arteritis clasped in subcutaneous tissue. A supraclavicular nodule simulating a lymphadenopathy was the main clinical expression of this disease.

An 81 year old woman was admitted to our hospital for evaluation of a right supraclavicular nodule. Her personal history was unremarkable. One month before admission she had noted a slightly tender nodule in the right supraclavicular fossa. She also complained of malaise, anorexia, and loss of 10 kg in

Letters to the editor

weight during the past three months. Physical examination disclosed a moderately ill woman. Skin and mucosae were pale. A 2-5 cm, indurated, slightly tender, not erythematous nodule was palpable in the right supraclavicular region. Temporal arteries were not swollen, but the right one beat weakly. The rest of the physical examination was normal. Laboratory data showed a mild normochromic, normocytic anaemia and an erythrocyte sedimentation rate of 92 mm/h. Biopsy of the nodule was then performed. Its histological examination disclosed an abundant fibroblastic tissue with foci of blood vessels showing inflammatory changes consisting of giant cell granulomatous vasculitis. Biopsy of the right temporal artery was also performed and a segmentary inflammatory infiltrate by aggregates of giant cells was seen. Treatment with prednisolone (60 mg/day) was started. Two days later the patient showed general improvement. Six months later, she is symptom free, with low dose steroid treatment.

Several dermatological manifestations of giant cell arteritis have been described. Most are either inflammatory changes, such as oedema, erythema, and tender nodules overlying inflamed superficial arteries, or ischaemic lesions, such as vesicles, bullae, ulcers, and gangrene due to occlusion of these vessels. These abnormalities are usually located at the scalp. Other uncommon reported cutaneous manifestations include urticaria, hyperpigmentation, purpura, and ecchymoses. 2, 3 Recently, Goldberg et al described tender nodules in lower extremities simulating erythema nodosum, 4 and Stephenson and Underwood reported mammary masses. 5 In both cases a histological examination of the nodules showed typical giant cell vasculitic lesions within the subcutaneous fat. These lesions were similar to those seen in our case. Our patient had both non-specific symptoms and laboratory findings which were suggestive of any of these clinical entity. Thus the main clinical manifestation was the presence of a supraclavicular nodule simulating a lymph node, its biopsy being consistent with giant cell arteritis. In addition, temporal artery biopsy was also consistent with this diagnosis and the response to steroids was dramatic.

We concluded that giant cell arteritis could cause vasculitis in the subcutaneous tissue, presenting clinically as a palpable mass. Furthermore, this mass may show the typical histological features of this disease.


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Oculous vascular disease and antiphospholipid antibodies
Sir: We read with interest the report by Asherson et al, which concluded that 8% of patients with systemic lupus erythematosus (SLE) and raised levels of antiphospholipid antibodies develop occlusive ocular vascular disease. 6 One of our recent patients reported had the primary antiphospholipid syndrome, which includes one or more of recurrent fetal loss, venous and arterial thrombosis, and thrombocytopenia together with raised levels of antiphospholipid antibodies or lupus anticoagulant, or both and no other well defined autoimmune disease, such as SLE. 7

There have been a few reports linking occlusive ocular vascular disease and antiphospholipid antibodies, most of them in SLE. 8-10 Another recent report found no raised levels of antiphospholipid antibodies in any of the 40 patients with retinal vascular occlusion in the absence of autoimmune disease, suggesting that antiphospholipid antibodies are important only in the presence of SLE.

We studied 26 patients with the primary antiphospholipid syndrome and found three with vascular retinopathy—that is, prevalence of 12%, which is slightly higher than that found by Asherson et al. 1 The table records the main clinical and serological features of our patients. We observed that in patients 1 and 2 was made because they had complained of loss of vision. Both were found to have inferotemporal branch vein occlusions. Patient 1 was also moderately hypertensive (blood pressure 170/90 mmHg). We then made a prospective oculal examination of our other patients with primary antiphospholipid syndrome and found a third case who showed peripheral ischaemic retinopathy. This patient had not complained of visual disturbance at any time. All the patients had normal intracerebral pressure.

Oculous vascular disease and primary antiphospholipid syndrome

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age (years)</th>
<th>ACA*†</th>
<th>LA*</th>
<th>ANA*</th>
<th>Manifestations of PAPS</th>
<th>Occlusal lesions</th>
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<tbody>
<tr>
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<td>M</td>
<td>30</td>
<td>Medium</td>
<td>-</td>
<td>+</td>
<td></td>
<td>Deep vein thrombosis, thrombocytopenia, aortic valve lesion, thrombotic renal microangiopathy</td>
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<tr>
<td>2</td>
<td>M</td>
<td>43</td>
<td>Low</td>
<td>-</td>
<td>+</td>
<td></td>
<td>Aortic valve lesion</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>49</td>
<td>Medium</td>
<td>+</td>
<td>1/320</td>
<td>Multi-infarct dementia, thrombocytopenia, livedo reticularis, aortic valve lesion, thrombotic renal microangiopathy</td>
<td></td>
</tr>
</tbody>
</table>

*ACA=antiphospholipid antibodies; LA=lupus anticoagulant; ANA=antinuclear antibody titre; PAPS=primary antiphospholipid syndrome

†ACA=high ≥ 80 GPL units; medium = 15–80 GPL units; low = 5–15 GPL units

‡IgA: high = ≥ 50 MPL units; medium = 6–50 MPL units; low = < 6 MPL units

The higher prevalence of occlusive vascular retinopathy in patients with raised antiphospholipid antibody levels and SLE 1 and the prevalence found in our 26 cases with clinical manifestations related solely to raised antiphospholipid antibody levels suggest that the presence of these antibodies, with or without any associated disease, may increase the risk of developing occlusive ocular vascular disease.

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