

Figure 1 (A) Orbital computed tomography scan showing fusiform enlargement of the right internal rectus muscle. (B) Complete regression of the myositis after cyclosporin treatment.

its origin remains unclear, immunological mechanisms have been postulated. Seldom has orbital myositis been reported in association with autoimmune diseases, such as systemic lupus erythematosus,<sup>4</sup> Wegener's granulomatosis,<sup>5</sup> or viral syndrome.<sup>6</sup> The cardinal feature of this disease is an acute, afebrile, unilateral onset with bulbar pain intensified by ocular movement. Alternatively, there may be ophthalmoplegia, chemosis, proptosis, blepharoptosis, and conjunctival infection.<sup>2-7</sup> Differentiating from other orbital pseudotumors (especially from thyroid ophthalmopathy, carotid-cavernous fistulae, orbital cellulitis, and tumours of the orbit) has been simplified by the advent of CT and nuclear magnetic resonance imaging.<sup>7-8</sup> A fusiform enlargement of the affected muscle is usually detected in a CT scan: extension of this process to the zone of insertion into the ocular globe (tendon sign),<sup>9</sup> although not consistently found, is specific for idiopathic orbital myositis and is not seen in dysthyroid myopathy. In contrast with the latter disorder, idiopathic orbital myositis is usually unilateral and only one muscle is affected (generally the internal rectus).<sup>8-9</sup> Idiopathic orbital myositis responds rapidly to steroid treatment with no residual sequelae.<sup>7-8</sup> Nevertheless, some patients have a chronic and recurrent course with fibrotic muscle transformation and permanent loss of ocular motility.<sup>3</sup> Clinical and radiological features in our patient were absolutely characteristic of idiopathic orbital myositis. However, the multiple relapses which occurred upon attempting to cut back the steroids, even when associated with azathioprine, made us look for an alternative treatment. The use of cyclosporin in ophthalmic Graves' disease is well documented,<sup>10</sup> but no references have been made to its use in idiopathic orbital myositis. Reported favourable results obtained in patients with polymyositis,<sup>11</sup> and our own experience, led us to use it successfully in our patient. We consider cyclosporin to be a valuable alternative for patients who develop dependency on steroids or who cannot tolerate or are resistant to such treatment.

J SÁNCHEZ-ROMÁN  
J M VARELA-AGUILAR  
J BRAVO-FERRER  
Collagenosis Unit  
Department of Medicine  
Virgen del Rocío University Hospital,  
Sevilla, Spain

E SEQUEIROS MADUENO  
Department of Ophthalmology  
Virgen del Rocío University Hospital,  
Sevilla, Spain

M FERNÁNDEZ DE BOBADILLA  
Department of Radiology  
Virgen del Rocío University Hospital,  
Sevilla, Spain

Correspondence to:  
Dr Julio Sánchez Román,  
Plaza San Martín nº 3, F-2,  
41003 Sevilla, Spain.

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## Non-Hodgkin's lymphoma: initial manifestation

Sir: Skeletal involvement frequently occurs in malignant lymphoma,<sup>1</sup> but monoarthritis and polyarthritis are uncommon and are usually considered to be synovial reactions secondary to adjacent bone disease.<sup>2-4</sup> We report the case of an elderly woman who presented with seronegative symmetrical synovitis and pitting oedema, resembling the 'RS3PE' syndrome described by McCarty *et al*,<sup>5</sup> in whom non-Hodgkin's lymphoma became apparent subsequently.

A 63 year old woman presented in November 1989 with sudden onset of swelling of her metacarpophalangeal joints, knees, and feet; morning stiffness of hands of more than one hour; and oral ulcerations. Examination showed tenderness or swelling, or both, of all hand joints, flexor digitorum tendons, wrists, carpal joints, knees, and tarsal joints. Pitting oedema of the dorsum of hands and feet was seen bilaterally. There was no evidence of lymphadenopathy or hepatosplenomegaly. Roentgenograms of the hands and feet showed soft tissue swelling but no erosions or joint space narrowing. Results of routine laboratory studies were normal. Rheumatoid factor, antinuclear antibodies, and precipitin tests for antibodies to Sm, nRNP, Ro, and La antigens

were absent. C3, C4, and lactate dehydrogenase were normal.

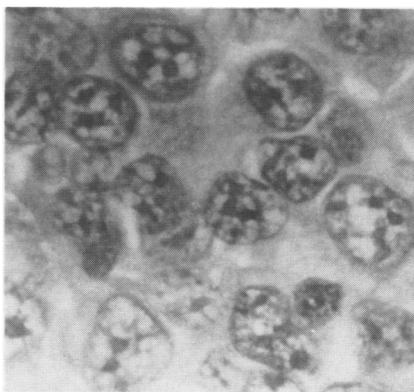
She was treated with hydroxychloroquine 200 mg twice a day, salicylates in anti-inflammatory doses and, later, with prednisone 5 mg daily, without symptomatic improvement.

In March 1990 several cervical, axillary and inguinal lymph nodes became enlarged, her temperature rose to 38.3-39.2°C, and she lost weight progressively. Results of laboratory tests were negative or normal, except for lactate dehydrogenase: 250 U/ml (normal range 83-157 U/ml) and erythrocyte sedimentation rate: 89 mm/hour. A biopsy specimen of a laterocervical lymph node showed diffuse large cell lymphoma (figure) and synovial biopsy of a metacarpophalangeal joint disclosed non-specific synovitis without lymphomatous cell infiltration. A computed tomographic scan of the abdomen and chest showed several anterior mediastinal, pre-tracheal, coeliac, portal, mesenteric, para-aortic, hepatic hilar, renal hilar, and retroperitoneal lymph nodes greater than 1.5-2 cm and hepatosplenomegaly. Results of a technetium-99m bone scan were normal. Bilateral iliac crest bone marrow biopsy specimens did not show malignant infiltration.

The patient was treated with six series chemotherapy according to the IMVP-16 regimen (ifosfamide 1 g/m<sup>2</sup> for five days, methotrexate 30 mg/m<sup>2</sup> for two days, and etoposide 100 mg/m<sup>2</sup> for three days over a period of 21 days). The oedema and synovitis resolved after two cycles of this protocol. Two years after treatment was stopped she remains in complete haematological remission and has no signs or symptoms of rheumatic disease.

Although uncommon, polyarthritis is well recognised in lymphoma. The interest of this case lies in the associated pitting oedema and tentative diagnosis of 'RS3PE' syndrome. In 1985 McCarty *et al* described eight elderly men and two elderly women who presented with symmetrical polysynovitis of acute onset, affecting most of their appendicular joints and flexor digitorum tendons with pitting oedema of the dorsum of both hands and both feet.<sup>5</sup> Rheumatoid factors were absent from serum samples in all, and no radiologically evident erosions developed. They believed that this disease represented a distinct subset of 'seronegative rheumatoid arthritis', with a predictable course to complete remission.

In our patient the first signs and symptoms of non-Hodgkin's lymphoma resembled this syndrome. Little symptomatic improvement



Histological section of a cervical lymph node biopsy specimen, showing large lymphoid cells with vesicular nuclei that have two to four small to medium sized nucleoli, often adjacent to the nuclear membrane. The cytoplasmic borders are not clearly outlined. (Haematoxylin-eosin stain.)

was noted with low doses of prednisone, however, in contrast with the dramatic improvement obtained in the original papers.<sup>5 6</sup>

On the other hand, synovial biopsy in our case did not show malignant infiltration. Thus it is reasonable to suggest that the rheumatic manifestations belong to a paraneoplastic syndrome, as has been previously reported with other neoplasms.<sup>7</sup>

To our knowledge this is the first description of peripheral synovitis and pitting oedema as an initial manifestation of non-Hodgkin's lymphoma. We would like to emphasise the need to consider the possibility of an underlying malignancy in a patient with these clinical characteristics who is unresponsive to the usual medical treatment.

M R ROLDAN  
F MARTINEZ  
Department of Rheumatology  
'Reina Sofia' Hospital  
Cordoba  
Spain

J ROMAN  
A TORRES  
Department of Hematology  
'Reina Sofia' Hospital  
Cordoba  
Spain

Correspondence to: M<sup>a</sup> Rosa Roldan Molina, c/Sanchez de Feria 3, 1<sup>o</sup> 3, 14003 Cordoba, Spain.

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## Arthritis and carcinoma

Sir: We read with interest the paper by Chakravarty and Webley describing two cases of asymptomatic renal cell carcinoma causing an acute monoarthritis, previously unreported.<sup>1</sup> They suggested that this occurrence is both rare and underreported. In our experience this is not necessarily the case. We have recently seen two patients whose cases illustrate some interesting similarities.

Patient No 1, a 63 year old man presented to our hospital with a five week history of a painful, swollen knee joint and was unable to bear weight. Clinical examination confirmed an acute monoarthritis of the knee joint, with a tense effusion, warmth, and tenderness. He had been previously treated for a large cell solid temporo-orbital tumour by radiotherapy because the lesion was considered inoperable. The knee joint effusion was aspirated to rule

out sepsis. Bacteriology was negative, no crystals were found, but adenocarcinoma cells were seen in abundance. He made an excellent functional recovery after palliative irradiation to the knee.

Patient No 2, a 63 year old woman, was referred to the radiotherapy department of the same hospital with metastatic disease for which no primary tumour had been located despite extensive investigation. She had initially presented with a painful knee of one year's duration. Clinical examination showed an acute monoarthritis with a moderate effusion. Isotope bone scan disclosed a hot spot in the upper tibia. She had a synovial biopsy and cytological examination of the synovial fluid. The synovial biopsy sample showed evidence of infiltration with adenocarcinomatous cells as did the synovial fluid.

While we agree with the authors that in cases where there is doubt about the cause of a joint effusion, early examination of synovial fluid is important, and may prevent the need for an open or closed bone biopsy, we are of the opinion that the occurrence of malignant joint effusions is not rare but more likely to be underreported.

CIARAN DUNNE  
TIM ILLIDGE  
Poole Hospital  
Longfleet Road  
Poole  
Dorset BH15 2JB  
United Kingdom

- 1 Chakravarty K K, Webley M. Monoarthritis: an unusual presentation of renal cell carcinoma. *Ann Rheum Dis* 1992; 51: 681-2.

## Angiotensin converting enzyme in rheumatoid arthritis

Sir: Being interested in vascular endothelial cell transdifferentiation,<sup>1</sup> I read with interest the instructive articles by Veale *et al*<sup>2</sup> and Goto *et al*<sup>3</sup> about the angiotensin converting enzyme production in rheumatoid arthritis. Although there is no doubt that vascular endothelial cells participate in this process, the role of macrophages remains questionable because the antibodies used for their identification (antigen CD14) are not macrophage specific and cross react with vascular endothelial cells.<sup>4 5</sup> Moreover, undifferentiated vascular endothelial cells can transdifferentiate into macrophage-like cells and migrate into the extravascular space.<sup>6</sup>

It may be useful to re-evaluate the role of macrophages in rheumatoid arthritis in the light of the new knowledge about the transdifferentiation of vascular endothelium.<sup>6</sup> For example, the mesenchymoid transformation cells responsible for joint destruction differentiate into fibroblasts in due course<sup>7</sup> and are not, therefore, inflammatory cells. McCachren considers, however, any collagenase producing cells immunoreactive with Leu-M3 or HAM56 to be macrophages.<sup>8</sup> Again, these antibodies are not macrophage specific and cross react with vascular endothelium.<sup>9 10</sup> Mesenchymoid transformation cells remind me of undifferentiated vascular endothelial cells<sup>1</sup> by their character and aggressiveness.<sup>7</sup> The facts that antiangiogenesis suppresses arthritis<sup>11</sup> and

that angiotensin II is an angiogenic factor<sup>12</sup> are in excellent keeping with that proposition.

JIRI T BERANEK  
Division of Cardiology  
Department of Medicine  
UMC—School of Medicine  
Columbia, Missouri  
USA

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## Endothelium damage and von Willebrand factor antigen

Sir: We read with great interest the recent paper by Blann *et al* on damage to the endothelium in Sjögren's syndrome.<sup>1</sup> The authors examined the relation of the auto-antibodies SSA and SSB to endothelium damage using serum levels of von Willebrand factor antigen (vWFAG) as an index of damage to the endothelium.

Damage of the endothelium may be present in Sjögren's syndrome, but there is no real evidence whether such damage results in high or low levels of vWFAG. The extent of the production of vWFAG in megakaryocytes in Sjögren's syndrome and other diseases is unknown; mainly because the plasma levels of the factor do not follow changes in the numbers of thrombocytes in peripheral blood and so this production site is no longer a part of the scenerium. Further, in our opinion, endothelium damage cannot explain why increased concentrations of vWFAG are present in such varied diseases as proliferative glomerulonephritis, diabetes mellitus, systemic sclerosis, Sjögren's syndrome, and arteritis temporalis, as endothelial damage in these diseases is not a common denominator.

We have recently studied the immunohistochemistry in arteritis temporalis, in which