

## Clinical data

| Patient No | Age/sex | Duration of EMS* before cyclosporin A use (months) | Duration of cyclosporin A use (months) | Significant side effects of cyclosporin A         | Reason for discontinuing cyclosporin A |
|------------|---------|--|--|---|--|
| 1          | 44/F    | 13   | 3                                      | 'Stiffness'                                       | Patient's request                      |
| 2          | 61/F    | 20   | 4                                      | Abdominal pain, diarrhoea                         | Patient's request                      |
| 3          | 35/F    | 7  | 19                                     | Renal insufficiency, hypertension, hirsutism      | Renal insufficiency                    |
| 4          | 41/F    | 11   | 8                                      | Renal insufficiency, hypertension                 | Renal insufficiency                    |
| 5          | 56/F    | 15   | 8                                      | Renal insufficiency, rhabdomyolysis, hypertension | Lack of efficacy                       |
| 6          | 33/M    | 6  | 16                                     |   | Renal insufficiency                    |
| 7          | 38/F    | 18   | 6                                      | Worsening myalgias                                | Lack of efficacy                       |
| 8          | 52/F    | 12   | 1                                      |   | Myalgias                               |

\*EMS=eosinophilia myalgia syndrome.

were included in this study; this group might have derived a substantial benefit from corticosteroid treatment that cyclosporin A would do little to augment. Alternatively, the manifestations unresponsive to cyclosporin A might have been either irreversible or too slow to reverse to be detected in a small, short term trial.

Our data show limited usefulness of cyclosporin when used relatively early in this disease. Given what is now known about EMS, one would expect that the efficacy of any regimen aimed at reduction of inflammation would diminish further as the syndrome progressed, and that any advances in treatment are unlikely to be found among the immunomodulatory drugs.

DANIEL J CLAUW  
JEFF A ALLOWAY  
PAUL KATZ

Division of Rheumatology, Immunology and Allergy  
Department of Medicine  
Georgetown University Medical Center  
3800 Reservoir Road NW  
Washington DC 20007-2197  
USA

- Swygert L A, Maes E F, Sewell L E, *et al.* Eosinophilia myalgia syndrome: results of national surveillance. *JAMA* 1990; 264: 1698-703.
- Read C A, Clauw D J, Weir C, DaSilva A T, Katz P. Dyspnea and pulmonary function in the L-tryptophan induced eosinophilia myalgia syndrome (EMS). *Chest* 1992; 101: 1282-6.
- James T N, Kamb M L, Sandberg G A, Silver R M, Kilbourne E M. Postmortem studies of the heart in three fatal cases of the eosinophilia-myalgia syndrome. *Ann Intern Med* 1991; 115: 102-10.
- Smith B E, Dyck P J. Peripheral neuropathy in the eosinophilia-myalgia syndrome associated with L-tryptophan ingestion. *Neurology* 1990; 40: 1035-40.
- Belongia E A, Hedberg C W, Gleich G J, *et al.* An investigation of the cause of the eosinophilia-myalgia syndrome associated with tryptophan use. *N Engl J Med* 1990; 323: 357-65.
- Toyooka T, Yamazaki T, Tanimoto T, *et al.* Characterization of contaminants in EMS-associated L-tryptophan samples by high performance liquid chromatography. *Chem Pharm Bull (Tokyo)* 1991; 39: 820-2.

## Postural variation in von Willebrand factor antigen

Sir: von Willebrand factor antigen (vWFAg) is the antigenic component of von Willebrand factor and is synthesised by endothelial cells and megakaryocytes. Raised concentrations of vWFAg have been reported in a variety of connective tissue diseases, including vasculitis, systemic lupus erythematosus, and systemic sclerosis.<sup>1</sup> Although it is an acute phase reactant,<sup>2</sup> raised levels in some of these diseases may reflect damage to the endothelial

cell.<sup>3</sup> As most inpatients lie quietly on a bed, and most outpatients are subject to movement during their clinic visits we sought to determine whether differences in vWFAg between these groups might be due to posture and activity.

We tested the effect of different postures on circulating levels of vWFAg in healthy hospital and laboratory staff. In the first study blood was taken into an EDTA tube from a group of five men and five women (mean age 29 (SD 5) years) immediately after normal kinetic laboratory activity. After resting quietly in the sitting position for 15 minutes, blood was taken from the opposite arm. Plasma was obtained after centrifugation at 3000 rpm for 10 minutes and vWFAg estimated by enzyme linked immunosorbent assay (ELISA).<sup>4</sup> Mean (SD) concentrations of vWFAg immediately after activity were 1160 IU/l (150), but after the rest period they had fallen to 1040 (220) ( $p < 0.05$ ), Wilcoxon rank sum test applied).

In a separate study six men and five women (aged 22-38) were rested lying down, face up, for 25 minutes, after which blood was taken. They then sat upright in a chair for a further 25 minutes and blood was taken a second time. After 25 minutes lying down plasma vWFAg concentrations were 950 (270) IU/l, but after 25 minutes sitting up levels increased to 1070 (200) IU/l ( $p < 0.05$ ).

This small study identified changes in vWFAg concentrations depending upon variations in posture and activity. As vWFAg has been shown to rise after exercise<sup>5</sup> this finding is not surprising. It points, however, to a possible artefact in vWFAg determination in patients. This may become important in the case of patients with, for example, rheumatoid arthritis, who are often admitted to hospital for bed rest. Reductions in vWFAg in these patients may reflect their posture and not necessarily reduced activation/injury of the endothelium. To avoid the possible problem in outpatient clinics we suggest that patients rest sitting for a minimum of 15 minutes before venepuncture.

A BLANN  
M I V JAYSON  
Rheumatic Diseases Centre  
University of Manchester  
Hope Hospital  
Salford M6 8HD  
United Kingdom

M H POPE  
A M KAIGLE  
D WILDER  
Orthopaedic and Rehabilitation  
University of Vermont  
Burlington VT05404, USA

J N WEINSTEIN  
University of Iowa  
Hospitals and Clinics  
Iowa 52202, USA

Correspondence to: Professor Jayson.

- Belch J F F, Zoma A, Richards I M, McLaughlin K, Forbes C D, Sturrock R D. Vascular damage and factor VIII related antigen in the rheumatic diseases. *Rheumatol Int* 1987; 7: 107-11.
- Pottinger B E, Read R C, Paleolog E M, Higgins P G, Pearson J D. von Willebrand factor is an acute phase reactant in man. *Thromb Res* 1989; 53: 387-94.
- Kahaleh M B. The role of vascular endothelium in the pathogenesis of connective tissue disease: endothelial injury, activation, participation and response. *Clin Exp Rheumatol* 1990; 8: 595-601.
- Short P E, Williams I C E, Picken A M, Hill F H G. Factor VIII related antigen: an improved immunoassay. *Med Lab Sci* 1982; 39: 351-5.
- Prowse C V, Farrugia A, Boulton F E, *et al.* A comparative study using immunological and biological assays of the haemostatic responses to DDAVP infusion, venous occlusion and exercise in normal men. *Thromb Haemost* 1984; 51: 110-4.

## Hypertrophic osteoarthropathy and AIDS

Sir: Rheumatic manifestations of human immunodeficiency virus (HIV) are diverse. Some conditions appear to be unique to HIV infected patients, whereas others, such as Reiter's syndrome, may be more widespread. Reports of patients with coexistent acquired immune deficiency syndrome (AIDS) and diseases of unknown cause are often interesting as they may help to clarify their pathogenesis. One of these syndromes is hypertrophic osteoarthropathy, an entity occasionally associated with chronic bacterial infections and other conditions, especially bronchogenic carcinoma. Despite the high prevalence of opportunistic infections in patients with AIDS, associated hypertrophic osteoarthropathy has rarely been reported. We present a patient with AIDS who developed severe rapidly progressive hypertrophic osteoarthropathy concurrently with anaerobic necrotising pneumonitis.

A 29 year old man, an intravenous drug and alcohol abuser, known to be HIV positive, was admitted owing to development of severe pain and oedema in his arms and legs two months previously. He also complained of a persistent cough, with foul smelling sputum, occasionally haemoptoic, fever, and pleuritic chest pain. He had lost 10 kg of weight.

On admission, the patient appeared cachectic, was unable to walk, and had a temperature of 38.5°C. His mouth showed oropharyngeal candidiasis. Inspiratory rates were heard in the superior field of the right hemithorax. Heart sounds were normal, except for rhythmic tachycardia. The liver was felt 5 cm under the costal margin. There was no splenomegaly and diseased lymph nodes were not palpable. Both forearms, hands, legs, and feet showed prominent oedema, local warmth, perspiration, and tenderness to pressure. Osteoarticular examination disclosed prominent clubbing of the fingers and toes, as well as synovitis, with moderate effusion of the knees, ankles, elbows, wrists, and proximal interphalangeal joints of the hands.

Blood studies showed haemoglobin 90 g/l, leucocytes  $7.3 \times 10^9/l$  (lymphocytes  $1.965 \times 10^9/l$  CD4+  $0.55 \times 10^9/l$ , CD4+/CD8+ ratio 0.5), platelets  $367 \times 10^9/l$ , erythrocyte sedimentation rate 105 mm/h. Serum alkaline phosphatase was 425 U/l (normal <279). Results of other routine tests were normal, including calcium, phosphorus, creatinine, glucose, aspartate transaminase, alanine transaminase, and lactate dehydrogenase. Urine analysis results were also normal.

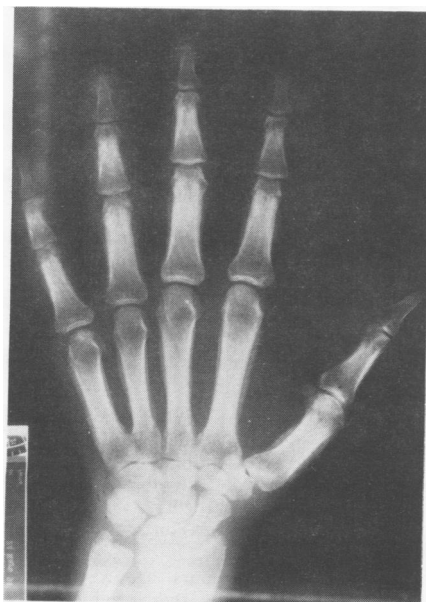
A protein profile disclosed no abnormalities except for mild hypoalbuminaemia (30 g/l). Antibodies against hepatitis B surface antigens and hepatitis B core antigens were positive. A test for hepatitis surface B antigen was negative. Complement C3 and C4 were normal. Immunoglobulin A was 5 g/l (normal <3.75). Tests for IgG and IgM, rheumatoid factor, antinuclear antibodies, the Venereal Disease Research Laboratory test, tests for thyroid hormones and somatotropin were all normal or negative, as were HLA-B27 and serological assays for *Brucella*, *Salmonella*, *Yersinia enterocolitica*, and *Chlamydia* spp.

Roentgenograms of the chest showed images of consolidation and multiple cavitations in the superior lobe of the right lung, compatible with necrotising pneumonitis. Intradermoreaction with tuberculin 2U was positive. Microbiological examination of samples of sputum showed Gram positive cocci. Sputum and blood cultures were negative, and repeated searches found no mycobacteria in the sputum. Thereafter, percutaneous needle aspiration of the lung was performed. Cultures of the samples in anaerobic media were positive for microaerophilic Gram positive cocci and *Bacteroides melaninogenicus*.

Cultures of stools were positive for *Candida albicans*. Upper gastrointestinal fibre endoscopy confirmed the presence of intense candida oesophagitis and hiatal hernia.

Radiographs of the hands, feet, forearms, and legs showed typical signs of hypertrophic osteoarthropathy (figure). Synovial fluid from one knee was mildly inflammatory, it contained  $3.5 \times 10^9$  cells/l, with more than 90% lymphocytes. The glucose concentration was 3.9 mmol/l, C3 was 500 mg/l, C4 80 mg/l. A search for microorganisms and crystals was negative.

The patient was diagnosed as having AIDS, anaerobic necrotising pneumonitis, and secondary hypertrophic osteoarthropathy. He was treated with clindamycin, indomethacin, and zidovudine (AZT) and both his general condition and lung lesions improved rapidly. Five months later he was asymptomatic in his joints, and bone radiographic changes had almost disappeared.



Radiograph of the left hand of the patient, showing diffuse oedema, clubbing, and periostitis of long bones. The other hand, forearms, and legs, as well as the feet were similarly affected.

To the best of our knowledge the case of only one patient with hypertrophic osteoarthropathy and AIDS has been published, being a young male abuser of parenteral drugs with *Pneumocystis carinii* pneumonitis.<sup>1</sup> The severe osteoarthropathic manifestations of the patient that we report reinforce both the possibility of this association and the typical painful character common to many of the rheumatic syndromes that have been described in HIV infected patients.<sup>2</sup>

The excellent response of our patient to antibiotics suggests that hypertrophic osteoarthropathy was due to lung infection. As the patient had severe manifestations we do not exclude a possible role for HIV or its effects on immunity as modulator or amplifier of the mechanisms that led to hypertrophic osteoarthropathy. Some authors have proposed immune mechanisms in the pathogenesis of hypertrophic osteoarthropathy.<sup>3</sup> Further studies are needed before this possibility can be confirmed.

LOURDES GIL-GARCIA  
J MANUEL MARTIN-SANTOS  
MANUEL BLANCO-CABERO  
J ANGEL TAPIAS DEL POZO  
FELICISIMO MARTINEZ-BARRERO  
Department of Internal Medicine  
Hospital Del Rio Hortega,  
Valladolid, Spain

Correspondence to: Dr J M Martin-Santos, Unit of Rheumatology, Hospital 'Del Rio Hortega', C/Cardenal Torquemada s/n, 47010 Valladolid, Spain.

- 1 Bhat S, Heurich A E, Vaguer R A, *et al*. Hypertrophic osteoarthropathy associated with *Pneumocystis carinii* pneumonia in AIDS. *Chest* 1989; **96**: 1208-9.
- 2 Rynes R I. Painful rheumatic syndromes associated with human immunodeficiency virus infection. *Rheum Dis Clin North Am* 1991; **17**: 79-87.
- 3 Schumacher H R. Articular manifestations of hypertrophic osteoarthropathy in bronchogenic carcinoma: a clinical and pathologic study. *Arthritis Rheum* 1976; **19**: 629-36.

## Disseminated gonococcal infection in an elderly patient

Sir: We present the case of an elderly patient with disseminated gonococcal infection and congenital C2 deficiency.

A 72 year old married woman was admitted to our hospital because of arthritis of her right wrist and knee. She had been well until 10 days before admission, when she developed chills with painful swelling of the wrist and knee. She denied any rash, diarrhoea, vaginal discharge, recent sexual contacts, ocular or genitourinary symptoms. Her husband also denied sexual activity.

On examination she had a fever (38°C) and painful swelling of the right wrist and knee. No cutaneous lesions or tenosynovitis were seen.

A diagnostic arthrocentesis of the right knee showed 20 ml of purulent synovial fluid containing  $80 \times 10^9$  cells/l. Gram staining showed no microorganism, but *Neisseria gonorrhoeae* was cultured. Blood cultures remained sterile. The erythrocyte sedimentation rate was 75 mm/h, results of a routine biochemistry test and urine analysis were normal and serological tests for syphilis and brucella were negative. The hands, knees, and pelvis radiographs were normal. Total haemolytic complement (CH50) was 0 U/ml. No

complement C2 was detected in two consecutive determinations.

She was treated with intravenous benzylpenicillin 1.2 g four times a day for seven days, followed by oral amoxicillin 1.5 g daily for 10 days. She required closed drainage for three consecutive days.

Patients with deficiencies in the terminal components of the complement system may develop episodes of disseminated infection with *N gonorrhoeae* and *N meningitidis*.<sup>1</sup> C2 deficiency is the most common complement deficiency, often associated with immune complex disease and recurrent sepsis.<sup>2</sup> To our knowledge, only one case of disseminated gonococcal infection associated with C2 deficiency has been reported.<sup>3</sup> Our patient had not had any previous neisserial or recurrent infections.

Disseminated gonococcal infection has been infrequently reported in the elderly<sup>5, 6</sup>; patients with disseminated gonococcal infection are usually younger than 40.<sup>4, 7-9</sup> The importance of suspecting this diagnosis, even in elderly patients without an appropriate history, is that the organism may be missed unless correct cultures are taken.<sup>10</sup> *N gonorrhoeae* is recovered from less than 50% of purulent effusions, and positive blood cultures may occur in only 30% of patients; therefore, in suspected cases, cervical, urethral, rectal, and pharyngeal cultures should be obtained.

This report highlights the need to consider a broad range of microorganisms in elderly patients with septic arthritis.

IÑIGO RÚA FIGUEROA  
EDUARDO LOZA CORTINA  
SENEN GONZÁLEZ SUÁREZ  
CELIA ERAUSQUIN ARRUABARRENA  
JOSE L PEÑA SAGREDO  
Rheumatology Division,  
Hospital Universitario  
Marqués de Valdecilla,  
Santander, Spain

Correspondence to: Dr Rúa-Figueroa, Hospital Universitario Marqués de Valdecilla, Rheumatology Division, Avda de Valdecilla s/n, 3908 Santander (Cantabria), Spain.

- 1 Petersen B H, Lee T J, Snyderman R, Brooks G F. *Neisseria meningitidis* and *Neisseria gonorrhoeae* bacteremia associated with C6, C7 and C8 deficiencies. *Ann Intern Med* 1979; **90**: 917-20.
- 2 Kelly W N, Harris E D, Ruddy S, Sledge C B. *Textbook of rheumatology*, 3rd ed, Philadelphia: Saunders, 1989.
- 3 McWhinney P H M, Langhorne P, Love W C, Whaley K. Disseminated gonococcal infection associated with deficiency of the second component of complement. *Postgrad Med J* 1991; **67**: 297-8.
- 4 O'Brien J P, Goldenberg D L, Rice P A. Disseminated gonococcal infection: a prospective analysis of 49 patients and review of pathophysiology and immune mechanism. *Medicine (Baltimore)* 1983; **62**: 395-406.
- 5 Geelhoed-Duyvestijn P H L M, van der Meer J W M, Lichtendahl-Bernards A T, Mulder Ch J, Meyers K A E, Poolman J T. Disseminated gonococcal infection in elderly patients. *Arch Intern Med* 1986; **146**: 1739-40.
- 6 Fernández Guerrero M L, Macarrón P, Barros C, Azofra J, Aguado J M. Disseminated gonococcal infection. *Arch Intern Med* 1989; **149**: 227.
- 7 Holmes K K, Counts B W, Beaty H N. Disseminated gonococcal infection. *Ann Intern Med* 1971; **74**: 979-93.
- 8 Masi A T, Eisenstein B. Disseminated gonococcal infection (DGI) and gonococcal arthritis (GCA). II. Clinical manifestations, diagnosis, complications, treatment and prevention. *Semin Arthritis Rheum* 1981; **10**: 173-97.
- 9 Brogadir S P, Schimmer B M, Myers A R. Spectrum of the gonococcal arthritis-dermatitis syndrome. *Semin Arthritis Rheum* 1979; **8**: 177.
- 10 Hook E W, Holmes K K. Gonococcal infections. *Ann Intern Med* 1985; **102**: 229-43.