LETTERS TO THE EDITOR

Relapsing polychondritis and Behçet's syndrome in a patient with HIV infection

Relapsing polychondritis is a systemic disorder characterised by recurrent inflammatory lesions involving cartilaginous structures, the cardiovascular system, the eyes, and the ears. Connective tissue diseases, dysmyelopoietic and myeloproliferative syndromes, ulcerative colitis, and thyroid diseases have been reported in association with relapsing polychondritis.¹ We present a patient with coexisting relapsing polychondritis, Behçet's syndrome, and infection with the human immunodeficiency virus (HIV).

A 25 year old man presented with a six month history of recurrent oral and genital ulcerations, followed by redness of his left eye and generalised polyarthrititis. There was a past history of intravenous drug abuse and hepatitis B infection. Two months later he developed pain and swelling of his left pinna and nasal cartilage, and necrotising skin lesions on his legs, fingers, and toes. On examination the left pinna was erythematous, swollen, and tender. Several ulcers were noted on the buccal mucosa and penis. There were signs of uveitis in the left eye and necrotising skin lesions suggesting vasculitis (fig 1). The characteristic saddlenose deformity was evident. Radiographs of the hands and knees were normal. Laboratory findings included: erythrocyte sedimentation rate 23 mm/1st h, haemoglobin 100 g/l, leucocyte count $10.4 \times 10^9/l$ with a normal differential count, platelet count $777 \times 10^9/l$. Tests that gave negative or normal results included serum creatinine, urine analysis, total

haemolytic complement, bilirubin, transaminases, alkaline phosphatase, hepatitis B surface antigen, hepatitis B surface antibody, Venereal Disease Research laboratory tests, rheumatoid factor and anticytoplasmic neutrophil antibodies. Hepatitis B core antibody and serology for HIV performed by enzyme linked immunosorbent assay were positive. The number of CD4 positive lymphocytes was $350/mm^3$. A biopsy specimen from the left pinna showed diffuse loss of basophilic staining of matrix (fig 2). Despite treatment with prednisone 60 mg/day and dapsone 100 mg/day, buccal, genital, and skin lesions persisted and methotrexate 15 mg/week was added; it was stopped four months later because of lack of efficacy. During the next two years, while receiving prednisone 5-30 mg/day and azidothymidine (AZT) 600 mg/day, the patient developed several flares of oral and genital ulcers, bilateral auricular chondritis, and oesophageal candidiasis; he eventually died from a pulmonary infection.

There is a broad spectrum of rheumatic manifestations associated with HIV infection;^{2,3} vasculitis is one of them.⁴ Relapsing polychondritis and Behçet's syndrome are multisystem diseases in which vasculitis appears to be an important factor. The coexistence of the two conditions has been reported previously,^{5,6} but not in patients infected with HIV. Our patient fulfilled the diagnostic criteria proposed by McAdam⁷ for relapsing polychondritis (bilateral auricular chondritis, nasal chondritis, uveitis, and polyarthrititis), and by the International Study Group for Behçet's disease (recurrent oral and genital ulcers, and uveitis).⁸ The relationship between HIV and connective tissue diseases is unknown. The development of the latter seems not to be affected by the stage of immunosuppression.⁹ It is possible that the HIV interacts with endothelial cells, leading to the release of chemotactic mediators, the development of vasculitis⁴ and, in this patient, relapsing polychondritis and Behçet's syndrome. The five year estimated survival rate of patients with relapsing polychondritis and systemic

vasculitis is 45%,¹ similar to that reported for polyarteritis nodosa.¹⁰ In patients with autoimmune diseases infected with the HIV, each case must be judged carefully, weighing the risks of immunosuppressive therapy in an immunodeficient patient.⁴ AZT has not been reported to be effective. In our patient, aggressive therapy was warranted to control the severe vasculitis. Antimicrobial prophylaxis (pentamidine, acyclovir, broad spectrum antibiotics) may be necessary for preventing infectious diseases.¹

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Figure 1 Necrotising vasculitic lesions on the patient's fingers.

Figure 2 Biopsy specimen of the left pinna, showing diffuse loss of basophilic staining of the matrix.

Human leucocyte antigen typing in rheumatoid arthritis/polymyositis overlap syndrome

Rheumatoid arthritis/polymyositis (RA/PM) overlap syndrome is an uncommon disorder.¹ One study of 76 patients with myositis found no cases of RA.² Halla *et al* first reported 'rheumatoid myositis', and noted that muscle necrosis was associated with mild synovitis.³ Non-erosive arthritis has been described in PM associated with the Jo-1 antibody.⁴ We describe five patients with erosive, seropositive RA, and electromyographically and biopsy proven PM, their autoantibodies and human leucocyte antigen (HLA) alleles.

Human leucocyte antigen typing class I and class II of five patients with rheumatoid arthritis/polymyositis overlap syndrome

Patient	A loci	B loci	DRB1	DQA1	DQB1
1	1,11	8,35	0101,0407	101,301	501,301
2	29,31	63,71	1302,0701	102,201	502,303
3	1,11	8,14	0301,0301	501,501	201,201
4	2,68	42,63	0901,0802	201,401	301,201
5	2,74	8	0302,1304	401,501	301,402

Five patients seen at The University of Texas Medical Branch at Galveston satisfied the American Rheumatism Association criteria for RA⁵ and Bohan⁶ criteria for PM. Two white and two black women (mean age 54 years) and one black man (48 years of age) had disease ranging in duration from three to nine years. Clinical evaluation included medical histories, physical examinations, serum creatine phosphokinase levels, antinuclear antibodies (ANA) by indirect immunofluorescence on HEP-2 cells, antibodies to double stranded DNA using *Criethidia lucilae*, antiribonucleoprotein, and anti-Sm antibodies by immunofixation, latex fixation test for rheumatoid factor, HLA class I and class II typing, and radiographs of hands, wrists, feet, and ankles. Electromyography was performed and muscle biopsy specimens examined in all patients.

All the patients had RA, were older than 40 and were receiving disease modifying drugs and prednisone <7.5 mg/day before onset of PM. Nodules were present in four of the five. None had lung involvement. Two patients had positive ANA results, and skin biopsy proven dermatomyositis. One patient was previously exposed to penicillamine.

The table shows HLA typing results. A single patient had HLA DRB*0407, an allele not usually associated with RA, and DRB*0101, the only RA susceptibility gene found.⁷ HLA-B8, seen in patients with myositis,⁸ was present in three of the five patients, DRB1*03 in two of the five, and DQB 1*03 in four.

Patient 5 and anti-Jo-1 and PI-7 antibodies. Both of these antisynthetases are associated with HLA-DR3,⁹ HLA-DQA1*0401, and *0501 alleles,⁹ all present in this patient. Patient 3 was positive for anti-PM-Scl, SS-A, and homozygous for DRB1*0301.

There were no serological markers universally present. Although our population was small, the phenotypes and auto-antibodies resembled more closely those found in idiopathic PM than those in RA.

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Cytidine deaminase is not released from degranulating polymorphonuclear neutrophils

Cytidine deaminase (CD) is an enzyme involved in DNA metabolism which is particularly abundant in cytoplasm of polymorphonuclear neutrophils (PMN) and may be useful as a marker of granulocyte mediated inflammation.¹ In the inflamed joints of rheumatoid arthritis, PMN are the predominant cells in synovial fluid and release CD which diffuses into the blood and provides an integrated serum measure of overall synovitis.² Current theories argue that CD is released by cell lysis, by cell activation and degranulation, or by a combination of the two.³ We therefore examined these two possible mechanisms of CD release from normal PMN.

PMN were obtained from the peripheral blood of eight normal volunteers by a one step sodium metrizoate-Dextran 500 separation and used at concentrations of $2.5-9 \times 10^5$ cells/ml. Cell suspensions were subjected either to freeze-thawing in liquid nitrogen for varying times (0-50 seconds) to disrupt cell membranes and cause lysis of different proportions of cells, or to stimulation with formyl methionyl leucyl phenylalanine (FMLP) in varying concentrations (10^{-6} - 10^{-3} mol/l) to cause degranulation of different proportions of cells. Cells were spun down and supernatants collected for the assays shown below. After each procedure cells were resuspended, lysed by sustained freezing (which does not interfere with the assay for CD and lactate dehydrogenase (LDH)) and spun down.

In the case of the degranulation experiments, cells were resuspended, divided into two aliquots, lysed either by sustained freezing or by adding Triton X-100 (which ensures complete disruption of granules),

Figure 1 Correlation between cell lysis (death) and CD release.

Figure 2 Relationship between cell degranulation and CD release.

and spun down. These supernatants also were collected for assay.

The amount of cell lysis was assessed by measuring LDH⁴ released into the supernatant and comparing the value (after freeze-thawing) with the total LDH release after complete disruption of the cells and was expressed as a percentage of the total amount of LDH. The extent of PMN degranulation after stimulation was assessed by measuring myeloperoxidase (MPO) release from primary granules using standard methods⁵ and expressing it as a percentage of the total MPO released after lysis of all cells and granules by Triton X-100. CD concentrations were measured by standard methods.¹

The proportion of cells lysed by freeze-thawing varied between 0 (controls) and 98%, and this was mirrored by a similar range for CD release. The correlation between LDH release (cell lysis) and CD release was $r = 0.975$ ($p < 0.001$) (fig 1). The proportion of degranulation achieved varied between 0 and 35.2%, but in these experiments the maximum CD release was only 2.4% and release of CD did not correlate significantly with that of MPO ($r = 0.367$, $p > 0.05$) (fig 2).

These results confirm previous reports that PMN lysis causes CD release,² but also show that FMLP stimulated degranulation does not cause CD release. It seems unlikely that other stimuli to degranulation would cause CD release, although it might be valuable to confirm that immune complexes or aggregated IgG do not have this effect. Our findings support the notion that increased synovial fluid and serum concentrations of CD reflect intra-articular PMN lysis. It is possible that CD release might be caused by other stimuli to PMN activation within inflammatory synovial fluid which do not lead to degranulation. There also remains the possibility that PMN from synovial fluid in