False positive results for antibody to HIV in two men with systemic lupus erythematosus

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Abstract

False positive results were obtained for HIV tests in two men with active systemic lupus erythematosus (SLE) who were suspected of being infected with HIV because of fever, weight loss, lymphadenopathy, and inflammatory myopathy. Enzyme linked immunosorbent assays (ELISAs) for HIV were twice positive when tested three times over a period of six months. Western blot analysis showed reactivity against the gp41 band in patient 1. False positive results for HIV tests can occur in patients with SLE, potentially leading to an erroneous diagnosis of HIV infection.

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Previous studies have addressed the potential role of infectious agents in the aetiopathogenesis of systemic lupus erythematosus (SLE).¹ Common clinical and immunopathological features of HIV infection and autoimmune diseases² have renewed interest in examining the participation of this or a closely related agent in the aetiology of SLE. Antibodies to human T cell leukaemia virus type I have been reported in SLE by some workers³ but not others.^{4,5} Two previous reports have shown false positive results for antibodies to HIV in patients with SLE.^{6,7} The pathogenic significance of these antibodies in SLE remains to be established. Their presence may impede the diagnosis of coexisting HIV infection in patients with clinically active SLE. We here report two patients with active SLE and positive results for antibody to HIV by enzyme linked immunosorbent assay (ELISA) in whom HIV infection was suspected on clinical grounds but was unconfirmed by western blot analysis.

Case reports

PATIENT 1

A 30 year old male Hispanic college student with no history of intravenous drug abuse, blood transfusion, or high risk sexual behaviour was admitted to hospital in October 1990. He had had fever, myalgias, dyspnoea, weight loss (about 5 kg), mouth ulcers, and arthritis in his legs for four months before admission. Physical examination showed high blood pressure, diffuse lymphadenopathy, left pleural effusion, hepatomegaly, ascites, tibial oedema, synovitis in his knees and ankles, and symmetrical proximal muscle weakness.

Laboratory tests showed haemoglobin 60 g/l, packed cell volume 0.19, white blood cell count $5.3 \times 10^9/l$ with 18% lymphocytes, platelet

count $146 \times 10^9/l$, and erythrocyte sedimentation rate (ESR) 100 mm/hour (Westergren). Blood chemistry was normal except for aspartate transaminase 233 U/l, alanine transaminase 159 U/l, creatine kinase 240 U/l, urea 69.6 mmol/l, and serum creatinine 173 $\mu\text{mol/l}$. Urine analysis showed 4+ proteins, red blood cells 20-40/high power field and cellular casts. The 24 hour protein urinary excretion and the creatinine clearance were 4.13 g and 34 ml/minute respectively. A percutaneous renal biopsy sample showed proliferative diffuse glomerulonephritis (class IV, WHO). Antinuclear antibodies and antibodies to DNA were positive at 4+; the CH50 was <50 U/ml, C3 189 mg/l, C4 80 mg/l and other autoantibodies were absent (table 1). Hepatitis anticore antibodies were positive and antibodies to HBsAg negative. IgM antibodies to cytomegalovirus were detected at 1/512 dilution. Antibodies to HIV were twice positive by ELISA (DuPont Laboratories, Wilmington, DW, USA) at a one month interval. The western blot (DuPont Laboratories) analysis gave positive results for the gp41 band. The lymphocyte phenotypic profile was normal (table 1). Six months later the ELISA and western blot results were negative. The patient showed improvement of renal function with monthly intravenous pulses of cyclophosphamide and prednisone 60 mg/day by mouth.

Table 1 Immunological features in patients with SLE with false positive results for antibody to HIV. Antibodies to HIV were detected by enzyme linked immunosorbent assay (ELISA) and western blot analysis

Test	Patient 1	Patient 2
Antinuclear antibodies	4+ (speckled)	4+ (diffuse)
Antibodies to DNA	4+	4+
CH50	Low	Low
C3	Low	Low
C4	Low	Low
Antibodies to Sm	Negative	Negative
Antibodies to ribonucleoprotein	Negative	Negative
Antibodies to SS-A	Negative	Negative
Antibodies to SS-B	Negative	Negative
Lymphocyte subpopulation (%) [*]		
CD3	60.9 (NS)†	21.6 (p<0.01)†
CD4	34.0 (NS)	4.2 (p<0.01)
CD8	24.3 (NS)	8.4 (p<0.01)
CD16	14.3 (NS)	2.4 (p<0.01)
CD25	3.8 (NS)	11.9 (NS)
slg	23.4 (NS)	58.3 (p<0.01)
HLA-DR	18.9 (NS)	14.2 (NS)
Monocyte/macrophage	22.4 (NS)	16.4 (p<0.05)
HIV (ELISA)	Positive	Positive
HIV (western blot)	gp41 band	Negative

^{*} 1×10^6 peripheral blood mononuclear cells were labelled with an optimum dilution of unconjugated or FITC conjugated monoclonal antibodies and proportions of positive cells were determined by flow cytometry (EPIC V, Coulter Electronics, Hialeah, FL, USA).

†Statistical analysis by unpaired Student's *t* test comparing mean (SEM) (%) in patients and healthy subjects. NS=not significant.

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PATIENT 2

A 26 year old male Hispanic construction worker was diagnosed as having SLE in 1988 based on malar rash, photosensitivity, persistent leucopenia, and positive antibodies to DNA. He also developed sensitive polyneuropathy due to peripheral nerve vasculitis which was proved by taking a biopsy sample. He did not report a history of intravenous drug abuse, blood transfusion, or high risk sexual behaviour. He was being treated with prednisone 40 mg/day and monthly intravenous cyclophosphamide. In 1989 he was treated for pulmonary tuberculosis. He was admitted to hospital in August 1990 with fever, abdominal pain, weight loss (about 6 kg), myalgias, and proximal and distal muscle weakness. Physical examination showed a malar rash, diffuse alopecia, mouth ulcers, and white plaques in his mouth mucosae, enlarged lymph nodes, jaundice, and a tender hepatomegaly. In January 1991 he developed monarthritis of the right knee and secondary osteomyelitis due to *Staphylococcus aureus* coagulase positive infection. He showed an improvement after treatment with oxacillin, open drainage, and rehabilitation.

The laboratory tests showed haemoglobin 80 g/l, packed cell volume 0.26, white blood cell count, $3.2 \times 10^9/l$ with 12% lymphocytes, platelets $198 \times 10^9/l$, aspartate transaminase 781 U/l, and alanine transaminase 190 U/l. Tests for hepatitis A and B were negative and a percutaneous liver biopsy sample showed diffuse hepatocellular damage and fibrosis. Antinuclear antibodies and antibodies to DNA were positive 4+, CH50 was <50 U/ml, C3 370 mg/l, and C4 110 mg/l; other autoantibodies were absent (table 1).

The patient tested positive twice for antibodies to HIV by ELISA with a two month interval, but was negative by Western blot analysis. Six months later both tests were negative. The lymphocyte phenotypic profile showed a marked decrease of CD3+ cells affecting both CD4+ and the CD8+ subpopulations. There was also enhanced expression of CD25 molecules of the interleukin 2 receptor and the number of CD16+ cells was significantly reduced. One year later the patient was well while receiving prednisone 15 mg/day.

Discussion

These two cases illustrate the potential difficulties associated with diagnosing HIV infection in patients with SLE. The two types of disorder share clinical and immunological features such as skin rash, arthritis, lymphadenopathy, myositis, leucopenia, thrombocytopenia, hypergammaglobulinaemia, and high levels of circulating immune complexes.⁸ The appearance of low titres of antinuclear antibodies in patients infected with HIV raises further difficulties in the differential diagnosis.

Our patients had unequivocal SLE as they fulfilled six (patient 1) and seven (patient 2) American Rheumatism Association criteria⁹ (table 2) including high titres of antibodies to DNA and reduced serum complement levels. Both patients were men and presented with

Table 2 American Rheumatism Association (ARA) criteria for systemic lupus erythematosus present in patients with false positive results for antibody to HIV

Characteristic	Patient 1	Patient 2
Age (years)	30	26
Sex	Male	Male
ARA criteria		
Malar rash	Absent	Present
Photosensitivity	Absent	Present
Mouth ulcers	Present	Present
Arthritis	Present	Present
Serositis	Present	Absent
Renal disease	Present	Absent
Leukopenia	Absent	Present
Thrombocytopenia	Absent	Absent
Antinuclear antibodies	Present	Present
Antibodies to DNA	Present	Present
Antibodies to Sm	Absent	Absent

fever, significant weight loss, lymphadenopathy, and inflammatory myopathy, features that are common in patients infected with HIV.²

Serum samples from patient 1 were initially positive for the gp41 band in western blot analysis. The accepted international criteria require the presence of antibodies to p24, p31 and to gp41 and gp120/gp160 to confirm the diagnosis of HIV infection, however.¹⁰ In rare instances western blot tests can yield false positive results in healthy donors. False positive reactivity to band gp41 such as seen in our patients is exceptional in healthy subjects, however.¹¹

Interestingly Golding *et al*¹² showed cross reacting antibodies recognising the HIV gp41 protein and the $\beta 1$ domain of human major histocompatibility complex class II molecules in serum samples from patients with AIDs. Okudaira *et al*¹³ have reported the presence of antibodies to HLA-DR molecules in serum from patients with SLE. It is possible that serum samples from patient 1 had this pattern of cross reacting antibodies in the absence of HIV infection. Antibodies to the p24 gag protein of HIV-1 have also been reported in patients with SLE.¹⁴ Whether these antibodies arise by molecular mimicry to homologous host proteins or reflect viral infection remains to be established.

The diagnosis of HIV infection should always be considered in patients presenting with clinical symptoms suggestive of a systemic autoimmune disease. The use of rigorous confirmatory testing by western blot analysis or immunofluorescence assay is therefore mandatory. More sensitive assays such as gene amplification by the polymerase chain reaction may be necessary to confirm the presence of HIV infection in patients with unclear serological reactions.

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