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Human herpesvirus-7 infection in a patient with systemic lupus erythematosus

Sir,

Infections represent the major cause of morbidity and mortality in systemic lupus erythematosus (SLE) patients (1). Corticosteroid therapy and immunosuppressive medications improve patients' survival but increase the risk of opportunistic infections (1, 2). The newly discovered herpes viruses have a wide range of clinical manifestations which for the present remain poorly defined (3-6). We report the case of a 14-year old SLE patient with HHV-7 infection.

The patient, affected by a severe form of SLE for 5 years characterised by renal involvement, autoimmune haemolytic anemia and thrombocytopenia, was hospitalised in February 1996 for intermittent fever lasting 8 days. The patient had been on therapy with prednisone (0.5 mg/kg/day), aspirin (3 mg/kg/day) and for 2 years had been treated regularly with cyclophosphamide 0.5 g/m^2 i.v. every 3 months.

Upon admission no cutaneous rash was present and the blood pressure was normal. Laboratory exams showed leucopenia (WBC 1,700 mm^3, N 65%, L 32%, M 3%), mild normocytic anemia (Hb 10.9 g/dl) and thrombocytopenia (96,000 mm^3). The erythrocyte sedimentation rate was 125 mm/hr, C-reactive protein 2 mg/dl, ALT 36U/l (normal < 45), AST 42 U/l (normal < 45), C3 60 mg/dl (normal 83 - 177), and C4 4.5 mg/dl (15 - 45). Immunoglobulin levels, urea nitrogen and creatinine levels were within normal limits; urinalysis showed granulous hyaline casts in the sediment.

Antinuclear antibodies (immunofluorescence on HEp-2 cells) were positive 1: 640, homogeneous pattern (normal < 1:40), anti-dsDNA (immunofluorescence on *Crithidia luciliae*) were positive at 1:80; anticardiolipin antibodies (ELISA) were negative while lupus anticoagulant was positive (coagulation diluted tissue thromboplastin inhibition test and Russell's viper venom time test).

Due to suspected infection, further examinations including blood and urine cultures were performed but no bacteria were isolated. Echocardiogram, chest X-ray and abdominal and pelvic sonograms were normal and serological tests for typhus, brucellosis, toxoplasmosis, herpes simplex virus, Epstein-Barr virus and parvovirus B19 showed no active infections.

Cytomegalic antibodies were detected (ELISA: IgG 162 UA/ml, IgM negative) and an ophthalmologic exam showed retinitis, suggesting cytomegalovirus infection in the left eye. Further serological investigations revealed the presence of antibodies to human herpesvirus (HHV)-6 (indirect immunofluorescence for HHV-6: IgG 1: 40, IgM 1: 10) and HHV-7 (indirect immunofluorescence for HHV-7: IgG 1: 80 and IgM 1: 20).

Due to the clinical suspicion of herpes virus infection, treatment with gangciclovir (10 mg/kg/24 hr i.v. for 21 days) without modification of the prednisone and aspirin therapy was begun. On the 8th day of therapy the fever disappeared, while the retinitis regressed completely in two weeks.

On the 15th day of therapy a further assay of antiherpes virus antibodies and viral DNA was carried out by polymerase chain reaction (PCR). Cytomegalovirus, Epstein-Barr and herpes simplex virus antibody titres were not substantially modified, whereas HHV-7 antibody titres were significantly increased (IgG 1: 640 and IgM 1: 40). A search for HHV-7 DNA by PCR, using the method of Iuliano *et al.* (7), indicated the presence of viremia (Fig. 1). HHV-6 DNA was not detected by PCR.

Infectious complications are the principal cause of morbidity and mortality in SLE patients (1). While immunosuppressive therapy with cyclophosphamide has improved the efficacy of medical treatment and reduced the daily prednisone dose necessary to control the disease, the risk of infections is increased since this drug can cause leucopenia (2). As the causative pathogens responsible for infection can change over time (1), we would advise that a careful search be made for opportunistic agents during the course of immunosuppressive therapy (2). While opportunistic infections in SLE caused by herpesvirus are well known, the role of the new herpesviruses (HHV-6 and HHV-7) requires further study (1, 4) . The case which we have described here adds yet another pathogen to the list of those responsible for opportunistic infections in SLE, and represents the first recorded case of retinitis attributable to HHV-7, a type of virus hitherto considered responsible for exanthem subitum (3).

The finding in this patient of increased anti-HHV-6 IgM titres during a primary HHV-7 infection has led us to re-assess the interpretation of serologic tests in light of the cross-reactivity existing between the new herpesviruses (3).

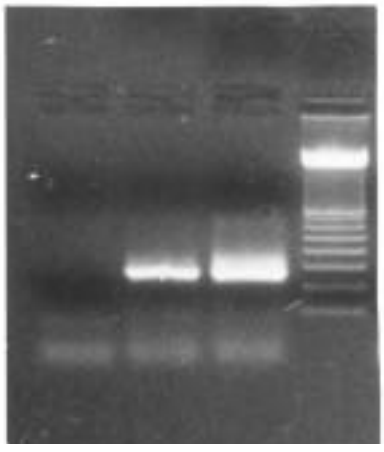

Fig. 1. Nested PCR analysis of DNA from HHV-7. Products of HHV-7 were visualized by electrophoresis on 2% agarose gel. **Lane 1**: negative control; **lane 2**: patient's sample; **lane 3**: positive control; **M**: molecular weight marker.

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