ASAT 18N, gamma-GT normal, and alkaline phosphatases 1.5 N); ESR was normal. Tissue-specific antibodies (smooth muscle, mitochondria and liver kidney microsomes) were negative. Alpha-1 antitrypsine was normal. Viral hepatitis screens (HAV, HBV, HCV, and HEV serologies, and HCV PCR) were negative. HIV serology was negative. Antinuclear antibodies were weakly positive (titer 1/80, speckled pattern), and dsDNA antibodies were negative. A hepatobiliary ultrasonography was normal. Her symptoms and abnormal liver test results spontaneously decreased within 2 weeks.

One month later the patient's acne worsened and she re-started minocycline 100 mg/day. After 4 weeks she developed inflammatory polyarthralgia affecting the small joints of the hands, the wrists, the shoulders and the ankles, with myalgia and fatigue but no fever. Despite the administration of naproxen, her symptoms became so severe that she was re-admitted 4 months later.

On physical examination, the patient had tenosynovitis of the left hand and tender metacarpophalangeal joints. Laboratory abnormalities included an ESR of 22 mm/hr and CRP 12.5 mg/l. Renal and liver tests were normal. Antinuclear antibodies were 1/800 (speckled pattern), dsDNA antibodies were 64 UI (Farr test) and myeloperoxidase antibodies were 97 U (N < 20). Antibodies to extractable nuclear antigen, cANCA, smooth muscle, mitochondria, and liver kidney microsomes were negative. Anticardiolipin IgG antibodies were weakly positive (19 UGPL, N < 15). Human leukocyte antibody typing was positive for A1, A2, B8, B60, Bw6, DRB1*15, DRB1*04, DRB5*0101, DRB4*01. Hand and wrist X-rays were normal. Minocycline was stopped and her symptoms dramatically improved over one week with no adjuvant therapy.

To the best of our knowledge this represents the first description of highly positive dsDNA antibodies in a typical case of minocycline-induced lupus. Although dsDNA positive antibodies may indicate idiopathic SLE rather than drug-induced lupus, their presence does not eliminate the diagnosis of minocycline-induced lupus.

F. TUBACH, MD
G. KAPLAN, *MD, Professor*
F. BERENBAUM*, *MD, PhD*

Department of Rheumatology, Saint-Antoine Hospital, 184 rue du faubourg Saint-Antoine, 75012 Paris, France.
**To whom correspondence should be addressed.*

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Leucocytoclastic vasculitis in a young body builder

Sir,

A 19-year-old male was admitted for severe inability to walk for the last 2 days. There were no systemic complaints. He was previously healthy and the family history was not contributory. Recent previous trauma or infection were ruled out. For the last 4 years he had been engaged in regular and intensive (2 - 3 hrs every day) body building exercises. He denied consuming anabolic steroids or other illicit drugs. During the week before his admission he had been involved in intense body-building activity including stressful exercises to build up the muscles of the thighs and calves.

Physical examination showed a muscular young man. The BP was 130/80, the pulse was regular (80 per minute), and the body temperature was normal. Purpuric lesions and erythema were present on the lower part of the thighs, calves and ankles, but not on the buttocks. All of these areas and the feet were swollen, warm and highly sensitive on palpation. There was no neurological deficit. The patient could not walk.

His ESR was 60 mm/1st hr (Westergren). A complete blood count, serum biochemistry and thyroid function tests, proteins, protein-electrophoresis and urine analysis were normal. Creatinine phosphokinase (CPK) was 713 U/L (30 - 280). A urine examination for myoglobin was negative. ANA, anti-ds DNA antibodies, RF, anti-RNP, anti-cardiolipin, C- and P-ANCA were all negative. The serum levels of C3, C4 and CRP were within normal limits. A chest X-ray was normal.

A skin biopsy from the right ankle area revealed acute leucocytoclastic vasculitis. As anamnesis, physical examination and laboratory investigations failed to provide the etiology of the vasculitis, the possibility of prolonged and intensive physical exercise as the pathogenetic mechanism was considered. During 3 days of complete rest the purpuric lesions, erythema, swelling and limb pain gradually disappeared, and the patient was able to walk again.

Our patient's elevated serum CPK levels were attributed to his intense regimen of physical training. A pre-discharge blood test showed the normalization of all values. The patient was advised to rest for an additional week and to substantially reduce his future physical activities. Nevertheless, a few days later later, a new (but milder) episode of calf and ankle pain and swelling occurred, following the resumption of exercise. They rapidly subsided after rest.

Leucocytoclastic vasculitis has been associated with a cohort of pathological conditions including collagen, infectious and malignant diseases, hypersensitivity to drugs, and other conditions (1). Sporadic cases of exercise-induced purpura (2-4), as well as one case of exercise-induced leucocytoclastic vasculitis in a patient with urticarial vasculitis (5), have been reported. The association of prolonged exercise with skin leucocytoclastic vasculitis was established by a clinical pathological study in subjects who developed purpuric lesions and vasculitis on the lower legs after engaging in long distance walking (6).

The pathogenetic mechanism of exercise-induced leucocytoclastic vasculitis is still unclear. An altered cutaneous microcirculation (7), transient alterations in immunological and/or biochemical parameters (8, 9), and activation of the complement cascade system by endurance exercise (10) are possible explanations. We propose that prolonged and strenuous physical exercise should be included among the various etiologies of leucocytoclastic vasculitis.

D. SCHAPIRA[1] Y. BRAUN[1]
R. BERGMAN[2] M. NAHIR[1]

Departments of Rheumatology[1] and Dermatology[2], Rambam Medical Center and Faculty of Medicine, Technion; Institute of Technology, Haifa, Israel.

Please address correspondence to: Dr. Daniel Schapira, The B. Shine Department of Rheumatology, Rambam Medical Center, Haifa 31096, Israel.
(Reprints will not be available from the author.)

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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).

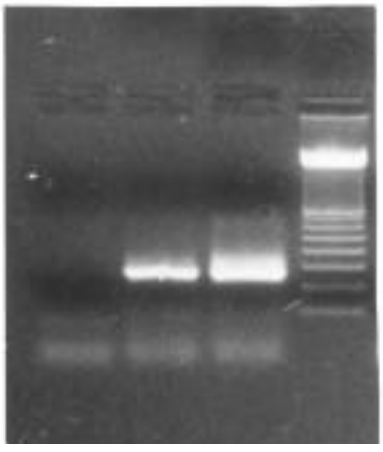

Fig. 1. Nested PCR analysis of DNA from HHV-7. Products of HHV-7 were visualized by electrophoresis on 2% agarose gel. **Lane 1**: negative control; **lane 2**: patient's sample; **lane 3**: positive control; **M**: molecular weight marker.

G. TACCETTI, *MD* — S. CAMPANA, *MB*
T. REPETTO, *MD* — F. FALCINI*, *MD*
L. MARIANELLI, *MD* — E. PROCOPIO, *MD*

*Cystic Fibrosis Center, Meyer Hospital, University of Florence, Italy; *Department of Pediatrics, University of Florence, Italy. Address correspondence and reprint requests to: Giovanni Taccetti, MD, Cystic Fibrosis Center, Meyer Hospital, via L. Giordano 13, 50132 Florence, Italy.*

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