Case Report

High anti-double-stranded DNA antibodies and progressive multifocal leukoencephalopathy in a patient with systemic lupus erythematosus

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Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease with protean manifestations and an unpredictable course. Treatment is determined mainly by the extent of disease manifestations. Severe systemic, renal or neurological impairment may necessitate long-term immunosuppressive therapy. The clinical management of lupus patients is challenging. During its early course, it may be difficult to make the diagnosis of SLE. During its later course, it remains difficult to differentiate disease progression or relapse from treatment complications or opportunistic infections.

Case

A 51-year-old Caucasian woman was known to have severe SLE since 1986. In 1991 she had a severe SLE flare-up with fever, leukopenia (2000–4000 leukocytes/mm³), pericarditis, high titres of anti-double-stranded DNA antibodies and a diffuse intracapillary proliferative glomerulonephritis with focal extracapillary proliferation. Treatment with high-dose steroids and cyclophosphamide pulse therapy (9.7 g cumulative dose) was instituted. Due to persistent disease activity and deterioration of the renal function, cyclophosphamide was switched to cyclosporin A in 1996. Despite continued therapy, the patient suffered progressive deterioration of the renal function. Cyclosporin A was stopped in November 1998. Peritoneal dialysis was started in May 2000. The institution of dialysis induced a marked amelioration of other clinical lupus manifestations and a decrease in anti-double-stranded DNA antibodies (Farr).

In October 2003 the patient had an asymptomatic increase in Farr. At the end of December 2003, she presented with recent-onset concentration problems and a right hemi-anopsia. A magnetic resonance imaging (MRI) scan suggested a parieto-occipital infarction. Cerebral angiography and lumbar puncture were reassuring. Because of the clinical suspicion of cerebral lupus, therapy with mycophenolate mofetil was instituted in December 2003. A few months later, the patient presented with ongoing and progressive complaints of memory loss, walking difficulties and anorexia with involuntary weight loss. Clinical examination revealed poor language and a discreet neurological deficit in the right arm. The patient had an erythrocyte sedimentation rate of 53 mm/h and a normal C-reactive protein. The white cell count was decreased (3300/mm³). The patient had a marked lymphopenia of 693 cells/mm³ with only 143 T4 cells/mm³ (20.6%). HIV serology was negative. Anti-double-stranded DNA antibody titre (Farr) was > 100 IU/ml (normal range: ≤7 IU/ml). MRI of the brain demonstrated new, T2 hyperintense lesions in the frontal and parietal white matter and subcortical regions and several non-specific lesions in the remaining white matter. Lumbar punctures revealed no cells and normal protein content. Enzyme-linked immunosorbent assay for Borrelia, Treponema pallidum and Cryptococcus, cultures for bacteria, fungi and mycobacteria and quantitative polymerase chain reaction for Herpes simplex, H. zoster and Toxoplasma were all negative. Two million copies of polyoma DNA was found per ml of cerebrospinal fluid. The tentative diagnosis of progressive multifocal leukoencephalopathy (PML) was made. Brain biopsy demonstrated focal areas of demyelination with relative preservation of the axons and with enlarged oligodendrocytes with a prominent nuclear membrane and a central ground glass appearance. Staining for polyoma virus was strongly positive (Figure 1).
Treatment with cidofovir was started. Despite this therapy, the patient deteriorated and died 5 weeks after admission to the hospital.

Discussion

PML is a deadly, infectious disease caused by the polyoma virus JC that occurs exclusively in severely immunosuppressed patients [1]. PML is characterized by progressive focal and global neurological deficits, leading almost invariably to death [2]. PML occurs almost exclusively in patients with AIDS [3] and has been reported only sporadically in patients with SLE [3–7]. No effective treatment exists for PML, except in the context of antiretroviral therapy in HIV [1].

Several experimental and epidemiological data indicate a relation between polyoma virus and the initiation of the production of anti-double-stranded DNA and antihistone antibodies [8–11]. In one study, polyoma viruses were recovered persistently in the urine of 16 out of 20 patients diagnosed with SLE [8]. In our patient, the increase in anti-double-stranded DNA antibodies initially suggested a false diagnosis of a relapse of SLE. Nevertheless, brain biopsy confirmed the final diagnosis of PML and did not show vasculitis. Given the possible relations between SLE and polyoma virus infections, it may be prudent to test systematically for PML in SLE patients with unexplained and progressive neurological deficits.

Conflict of interest statement. None declared.

References


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