Paraneoplastic necrotising myelopathy in a case of AIDS with lymphoma

Paraneoplastic necrotizing myelopathy is a rare and still obscure neurological complication of malignancy.1 Spinal cord affection is common in patients with HIV infection, but necrosis of the spinal cord in AIDS is rare and usually caused by opportunistic infections.2 Our patient had AIDS and immunoblastic lymphoma with a necrotizing myelopathy, not due to an infectious or vascular cause.

A 29 year old male homosexual patient had been known to be HIV positive since 1987. In 1990 he developed AIDS and Pneumocystis carinii pneumonia. Azithromycin had to be discontinued due to anaemia. In December 1991 he started complaining of a slowly ascending numbness, which began in both feet and reached the T10 level in April 1992. At the same time he developed a weakness in his legs, dull pain on the right, and reduced pain and temperature sensation in the left leg, as well as a maxillary and mandibular herpes zoster. Lumbar puncture showed 43 cells/μl, mostly lymphocytes, plasma cells, and several cosinophilic granulocytes, and protein (59 g/l). The serum/CSF protein ratio indicated a severe disturbance of the blood-brain barrier. T2 weighted spinal MRI showed thickening and enhanced water content of the thoracic cord, maximum at the T12 level. A spinal infiltration of a lymphoma was suspected, but examinations of bone marrow, repeated lumbar punctures, or radiographs of the lungs did not show evidence for a lymphoma at that time. Repeated serological tests for neurotropic viruses (borreliosis, syphilis, varicellzoster, and candidiasis) were negative in serum and CSF. The neurological deficits were rapidly progressive and treatment with acyclovir and corticosteroids had no effect. Further MRI a month later no longer showed the intramedullary lesion. The patient was discharged six weeks after admission with a diagnosis of parasite myelitis, an incomplete loss of sensibility below T8, and complete incontinence.

At the end of September 1992 he was readmitted with a lymphoma of the lung and cerebral involvement. The paraplegia had become spastic and the level of sensibility loss was now at T6. He was still completely incontinent and had decubitus ulceration. The lymphoma was not treated and the patient died two months later of respiratory failure due to pulmonary problems.

Postmortem examination showed an immunoblastic infiltration of both lung bronchopneumonia of the left lung, and pleural effusions on both sides. There was cerebral involvement of the lymphoma in both hemispheres but no opportunistic infections of the brain and no signs of increased intracranial pressure. The thoracic meninges stuck to the cord, which was very soft in the thoracic region. Microscopic examination revealed diffuse infiltration of the spinal cord. On both ends of the softened part of the cord there was a roughly 1cm long region of pencil-like softening. There was no macroscopic evidence for angioma, vascular obstruction, or tumour infiltration. Histologically, the thoracic cord displayed the aspect of complete coagulation necrosis with few macrophages. No vascular disease, tumour, or viral, bacterial, fungal, or parasitic cause was found in the spinal cord. No fibrin thrombi were seen despite a study of numerous sections. Only a few mononuclear inflammatory infiltrates were present; these were generally well preserved, whereas the anterior roots showed a substantial loss of myelinated nerve fibres (figure). In the cervical cord, the fasciculus gracilis exhibited a complete loss of myelinated nerve fibres, whereas the fasciculus cuneatus was not affected. The lumbar and sacral cord was well preserved. Immunohistochemistry for herpes simplex 1 and 2 viruses and cytomegalovirus as well as hybridisation for herpes simplex, JC, and varicella zoster viruses were negative. No viruses were found on electron microscopy.

Tumour infiltration, a vascular cause, especially Polia-Alagiauant's syndrome, and an infectious aetiology can be ruled out on serological, histological, and electron microscopic grounds. In particular a herpes simplex infection can be excluded on the basis of preserved JC virus inclusions. Although the lymphoma was not discovered at the first admission, it is likely to have existed at that time. To our knowledge paraneoplastic necrotizing myelopathy has not been described in AIDS before.

L M DRACH
Neurológisches Institut (Edinger-Institut)
WENZENSBERGER
Klinik für Neurologie
T FABIAN
G GERMANN
Zentrum der Pathologie Klinikum der Johann Wolfgang Goethe-Universität, Frankfurt/M, Germany

Correspondence to: Dr Lutz M Drach, Neurologisches Institut (Edinger-Institut), Deutschordensstrasse 46, D-60528 Frankfurt/Main, Germany.


Total tau protein immunoreactivity in lumbar cerebrospinal fluid of patients with Alzheimer's disease

Alzheimer's disease is the most frequent cause of dementia in elderly people. The definite diagnosis can only be established by (semi) quantitative histopathological examination of neuritic plaques and neurofibrillary tangles. Neurofibrillary tangles are composed of bundles of paired helical tangles, the main component of which is the microtubule associated tau protein in a pathologically hyperphosphorylated form. Because valid biological markers for the in vivo diagnostic of Alzheimer's disease are not available, the recent development of assays allowing the detection of tau protein in CSF is of much interest.1,2 The diagnostic value of these assays needs further validation.

We have measured total tau protein immunoreactivity in a series of 73 lumbar CSF specimens with a modified version of a specific sandwich enzyme linked immunosorbent assay (ELISA, Innogenetics, Belgium).3 Informed consent was obtained before lumbar puncture. The patients were subdivided into five groups:

(1) 16 patients (10 women, 6 men, mean age 72.3 years) with definite Alzheimer's disease according to the NINCDS-ADRDA criteria; (2) 20 patients (11 men, 9 women, mean age 58.7 years) with other neurology disorders without Alzheimer's disease (cerebrovascular disease, 4 and 5) 16 young subjects (2 women, 14 men, mean age 37.8 years) 5 years younger than patients in group (4 and 5) 16 young subjects (5 men, 11 women, mean age 62.3 years) 5 years older than patients in group (4 and 5).

For the immunological test anti-human tau protein monoclonal antibodies (1B5 1B6) were used. The specificity of the antibodies was confirmed by immunohistochemical analysis. The immunoreactivity of tau protein was detected directly in the supernatant of a homogenate of the lumbar CSF in a standardized two-sandwich ELISA using a peroxidase labeled anti-mouse IgG (ICN Diagnostics, Costa Mesa, CA). The titer of tau protein in each sample was expressed as the OD500 nm of the test sample divided by the OD500 nm of the control sample.

The results obtained were compared with the mean tau protein concentration of normal control subjects (group 1) by the Wilcoxon signed rank test. The significance of differences between the various groups was estimated by the Mann-Whitney test.

In 33% of the Alzheimer's disease patients a significant increase in tau protein concentration was observed compared with the normal control group. In all other groups the number of elevated tau protein concentrations was not significant. These data indicate that tau protein is a potential marker for Alzheimer's disease.