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Acute Transverse Myelitis Caused by Herpes simplex Virus

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Case Report

A 42-year-old man presented with dysesthesia and palsy of the right upper limb and developed a complete tetraplegia with sensory loss below the level of C6, bowel and bladder dysfunction within 10 days. There was no stiffness of the neck or disturbance of consciousness. The tendon reflexes were first absent and then became hyperactive. Babinski's sign was found on the right side. No herpetic cutaneous or genital lesions were found. On the basis of the PCR results (see below) the patient was treated with dexamethasone 24 mg/day i.v. and acyclovir 750 mg 3 times a day i.v. Within 10 weeks motor function of both legs and of the left arm recovered almost completely whereas the right arm remained mildly paretic. Bowel and bladder function were normal. A sensory disturbance below the level of T8 remained.

Methods

Immunoglobulins and albumin in serum and CSF were measured by laser nephelometry and evaluated according to Reiber and Felgenhauer [1]. The specific IgG synthesis against herpes simplex virus antigen was detected by ELISA measuring serum and CSF samples at an identical IgG concentration of 1 mg/dl [2]. Higher titers in the CSF indicate an intrathecal specific synthesis. PCR was performed on CSF samples. After treatment with SDS and proteinase K, viral DNA was extracted using the phenol-chloroform method. The DNA was precipitated in cold ethanol after addition of yeast t-RNA. A nested-primer method was used to amplify a 221-bp-long DNA fragment (first PCR) and a 138-bp-long fragment (second PCR) from the glycoprotein D gene of the herpes simplex virus [3]. The amplified DNA was electrophoretically separated in agarose gel, stained with ethidium bromide and visualized under a short wave transilluminator. In addition, a dot-blot of the amplified DNA was hybridized with a specific digoxigenin-labeled DNA probe and detected by the che-moluminescent reaction of alkaline phosphatase-labeled digoxigenin antibodies with AMPPD on X-ray film.

Fig. 1. Gel electrophoresis (A) and dot-blot (B) of amplified herpes simplex virus DNA. N: Negative control, P: positive control, M: molecular weight marker VIII (Boehringer Mannheim), 1,2, 3: samples of the patient taken on day 1, 8, and 89 of the disease, 138: length of amplification product in base pairs.

Findings

Laboratory studies were normal. The serum titer of IgG antibodies against *Borrelia burgdorferi* was 1:25,600 (normal lower than 1:400) using a test according to Rhese-Kipper and Ackermann [4] but there was no intrathecal antibody synthesis. PCR of *B. burgdorferi* DNA was negative in the CSF. CSF cell count was 3–7 cells/ul. CSF glucose levels ranged between 65 and 98 mg/dl. Total CSF protein levels were elevated to 61–70 mg/dl (normal 15–40 mg/dl). The ratio of serum albumin and CSF albumin was lower than 150, indicating a disturbed blood brain barrier. There were no oligoclonal IgG bands in the isoelectric focussing of CSF and serum but the ELISA revealed a specific intrathecal antibody production against HSV with increasing titers in the course of the disease (1:2 on day 1 and 8, 1:16 on day 89). No other specific IgG production could be detected in the CSF. Viral and bacterial cultures were negative. The PCR for HSV from CSF was positive (fig. 1). The MR examination revealed a swelling of the spinal cord at the level C2–C5. Increased signal intensity due to inflammation was detected in the central portion of the spinal cord on T2-weighted spin-echo images. Four weeks later the top of the lesion had ascended to the medulla oblongata and showed a subtle contrast medium enhancement. Six months after onset of the disease cervical MR images were normal (fig. 2).

Discussion

The patient presented with an acute ascending transverse myelitis. HSV was detected in the CSF by PCR at day 8 of the disease and disappeared after treatment. Intrathecal antibody production against HSV with a 3-fold rise of antibody titers in the CSF was detected 3 months after onset of symptoms. Transverse myelitis is of viral etiology in up to 40% of the cases, but the virus is rarely detected [5]. Until now 8 reports of transverse myelitis due to HSV are known [6–13]. Only in 5 cases the virus was detected directly: 3 times by positive cultures and twice at autopsy. As is illustrated by our case, CSF pleocytosis is not a constant feature in HSV myelitis and virus-specific intrathecal IgGproduction may be absent in the early phase of the disease. However, early diagnosis is essential since in infections with HSV, VZV and CMV specific therapy is available. So PCR offers the opportunity to improve the prognosis of certain viral CNS disorders by starting an early specific treatment.

References

- 1 Reiber H, Felgenhauer K: Protein transfer at the blood cerebrospinal fluid barrier and the quantitation of the humoral immune response within the central nervous system. Clin Chim Acta 1987;163:319–328.
- 2 Felgenhauer K, Nekic M, Ackermann R: The demonstration of locally synthesized herpes simplex IgG antibodies in CSF by Sepharose 4B linked enzyme immunoassay. J Neuroimmunol 1982;3:149–158.
- 3 Aurelius E, Johansson B, Skoldenberg B, Staland A, Forsgren M: Rapid diagnosis of herpes simplex encephalitis by nested polymerase chain reaction assay of cerebrospinal fluid. Lancet 1991;337:189–192.
- 4 Rhese-Kipper B, Ackermann R: Demonstration of locally synthesized Borrelia antibodies in cerebrospinal fluid. Zentralbl Bakt Hyg A 1986;263: 407–411.
- 5 Tyler KL, Gross RA, Cascino GD: Unusual viral causes of transverse myelitis: Hepatitis A virus and Cytomegalovirus. Neurology 1986;36:855–858.
- 6 Britton CB, Mesa-Tejado R, Fengglio CM, et al: A new complication of AIDS: Thoracic myelitis caused by herpes simplex virus. Neurology 1985; 35:1071–1074.
- 7 Craig CP, Nahmias AJ: Different patterns of neurologic involvement with herpes simplex virus types 1 and 2: Isolation of herpes simplex virus type 2 from the buffy coat of two adults with meningitis. J Infect Dis 1973;127: 365–372.

Fig. 2. Sagittal T2-weighted MR images of the cervical spine 4 weeks (A) and 6 months (B) after onset of the disease (TR: 1,800 ms, TE: 100 ms, Philips Gysroscan 15).

- 8 Handler CE, Perkin GD: Radiculomyelopathy due to genital herpes. Lancet 1982;i:987–988.
- 9 Klastersky J, Cappel R, Snoeck JM, et al: Ascending myelitis in association with herpes simplex virus. N Engl J Med 1972;287: 182–184.
- 10 Maida E, Traugott U, Eibl M: Transfer-Faktor-Therapie bei einem Fall von chronischer Herpes-simplex-Myelitis. Nervenarzt 1978;49:671–673.
- 11 Koskiniemi M-L, Vaheli A, Manninen V, Nikki P: Ascending myelitis with high antibody titer to herpes simplex virus in the cerebrospinal fluid. J Neurol 1982;227:187–191.
- 12 Shyu W-C, Lin J-C, Chang B-C, et al: Recurrent ascending myelitis: An unusual presentation of herpes simplex virus type 1 infection. Ann Neurol 1993;34:625–627.
- 13 Tucker T, Dix RD, Katzen C, et al: Cytomegalovirus and herpes simplex virus ascending myelitis in a patient with AIDS. Ann Neurol 1985;18:74–79.