Diagnosis of Cytomegalovirus Meningoencephalitis by Polymerase Chain Reaction in an Immunocompetent Infant Who Recovered After Treatment with Ganciclovir

Cytomegalovirus (CMV) infection of the CNS is rarely observed in immunocompetent infants after the first month of life [1]. Until recent molecular techniques became available, this infection was diagnosed exclusively on the basis of the results of CSF culture and of immunohistochemical studies of a brain biopsy specimen. The outcome of this infection was poor in most instances but improved when ganciclovir became available. We describe a patient with CMV encephalitis who recovered after receiving treatment with ganciclovir.

A 6-week-old boy was born in the city hospital of Sint Nicolas after a normal term delivery. His mother had been treated with amoxicillin/clavulanic acid for postpartum endometritis; her bacterial cultures were negative. The infant was breast-fed during the first week of life. From the age of 5 weeks, convulsions of the right arm and leg were noted; these convulsions evolved to generalized convulsions.

Laboratory investigations at the age of 5 weeks revealed a normal complete blood cell count and an increased level of C-reactive protein (25 mg/L). Examination of the CSF revealed a WBC count of 2/mm³, an increased protein level (472 mg/dL), and a low glucose level (3 mg/dL). No C-reactive protein was found in CSF, and bacterial cultures were sterile. The serum CMV IgM titer was 1.5 AU/mL (positive, >0.5 AU/mL), and the CMV IgG titer was 73.4 AU/mL (immune, >15 AU/mL).

The patient’s clinical condition did not improve after iv treatment with cefotaxime, dexamethasone, and phenobarbital was administered, and the infant was transferred to our hospital. A physical examination revealed fever (temperature, 38°C), generalized hypotonia, and frequent myoclonic convulsions of the right arm. The WBC count and serum C-reactive protein level were within normal limits. Examination of the CSF revealed a WBC count of 940/mm³ (47% monocytes, 27% lymphocytes, 24% neutrophils, and Zolo plasma cells) and confirmed the high protein (708 mg/dL) and low glucose (2 mg/dL) concentrations. Antibiotic treatment consisted of cefotaxime (50 mg/kg every 6 hours), ampicillin (25 mg/kg every 6 hours), and a 4-day course of tuberculosstatic drugs for possible bacterial meningitis.

A CT scan of the brain showed ventricular dilatation and a periventricular low-density lesion in the deep white matter of the right parieto-occipital region that was confirmed by an MRI scan. Bacterial and viral cultures (including those for CMV) of urine, saliva, and CSF as well as PCR for detection of herpes simplex in the CSF remained negative. An electroencephalogram showed bilateral high voltage paroxysmal discharges. The patient had progressive hydrocephaly and protracted convulsions. Nine days after admission, cultures of saliva yielded CMV. On day 11, CMV was detected in the CSF by PCR (this procedure was previously described by Bale et al. [2]).

Antibiotic treatment was stopped, and therapy with ganciclovir (5 mg/kg every 12 hours) was started. No side effects were observed during 31 days of treatment. During antiviral treatment, the convulsions disappeared, CSF values progressively normalized, and the epileptic discharges on the electroencephalogram disappeared. The child had no neurologic impairments at the age of 3 years. Serum CMV IgM antibodies were not detected 8 weeks postpartum, although CMV IgG antibodies were detected in the mother. The patient’s immunoglobulins, IgG subclasses, and T cell subsets were normal; antibodies to HIV were not detected.

In our patient’s case, the diagnosis of CMV meningoencephalitis was suggested by the periventricular lesion found on the CT and MRI scans, the CSF findings, and the positive specific serum IgM titers; however, this diagnosis was questioned because serial viral cultures of urine, saliva, and CSF remained negative and because CSF findings were compatible with bacterial meningitis. CSF findings in immunocompetent patients with CMV encephalitis are variable, and the absence of viruria does not rule out CNS infection [3]. Recently, identification of viral DNA in CSF by PCR, as was done in our case, has proved to be a reliable marker of CNS involvement [4] and has replaced more cumbersome and invasive methods [5].

Since no cultures were performed in the first 2 weeks of life, the etiology of our patient’s infection remains uncertain. The absence of periventricular calcifications suggests a postnatal infection or a congenital infection during late pregnancy. In the event of a congenital infection, the absence of viruria and generalized infection and the regression of the neurological symptoms would be unusual. It is unlikely that our patient acquired CMV infection postnatally through breast milk since he was nursed for a short period; like nosocomial infection, CMV infection acquired postnatally usually remains asymptomatic [1, 6]. Although ganciclovir therapy is not efficacious in AIDS patients, it has been shown to be efficacious in immunocompetent patients with CMV encephalitis [3, 5, 7].

The present case illustrates that CMV encephalitis should be considered in the differential diagnosis for patients with protracted convulsions even if CSF findings suggest bacterial infection and viral cultures remain negative. Our case highlights the value of PCR for establishing the diagnosis of CMV encephalitis and demonstrates that immunocompetent patients with this infection may be successfully treated with ganciclovir.
Mental Neuropathy in Patients with AIDS-Associated Malignant Lymphoma

Cranial neuropathy associated with a malignancy is unusual, but when this condition is present, most reported cases have involved patients with lymphoma [1]. Williams et al. [2] described an incidence of ~1.2% for isolated cranial nerve involvement in their review of 5,778 cases of lymphoma and leukemia. Therefore, the incidence of neuropathic involvement of one cranial nerve subdivision, the mental nerve, should be uncommon. Despite its rarity, involvement of the mental nerve can be of clinical importance. Nobler [1] described eight cases of mental nerve palsy in patients with malignant lymphoma, which he found was a hallmark of rapidly progressive, fatal disease.

The incidence of malignant lymphoma related to HIV infection is increasing [3]. We describe two cases of HIV-associated lymphoma and mental neuropathy, a complication that has been described only once before [4].

Case 1. A 27-year-old female presented to the emergency department with a 1-month history of a left neck mass and a 2-day history of horizontal diplopia, paresthesias, and bilateral numbness of the chin and lower lip. She was found to have a right sixth cranial nerve palsy and bilateral mental neuropathy. MRI of the head showed an enhanced soft-tissue thickening of the falx (figure 1). CT of the neck showed extensive bilateral cervical adenopathy (figure 2). Serological testing showed the presence of antibodies to HIV and Epstein-Barr virus (EBV), and examination of lymph node biopsy specimens confirmed the diagnosis of AIDS-related lymphoma (small noncleaved cell type B).

Treatment with methotrexate, bleomycin, doxorubicin, cyclophosphamide, vincristine, and dexamethasone (m-BACOD) and with intrathecal cytosine arabinoside resulted in resolution of her mental neuropathy; however, her highly aggressive disease relapsed, and she died 2.5 months after initial presentation.

Case 2. A 45-year-old male with a distant history of transverse myelitis and mononucleosis antibodies to EBV and was found to be positive for HIV in May 1987 and was treated with zidovudine monotherapy. In August 1994, he developed chills and fever, and examination of a biopsy specimen from a rapidly enlarging axillary lymph node revealed B cell–type, immunoblastic lymphoma. One month after therapy with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) was initiated, he returned to the hospital with bilateral mental neuropathy, with numbness over the chin and anterior jaw, which spontaneously resolved in 2 weeks. Three months after it had initially regressed, the tumor recurred.

Figure 1. Coronal T1-weighted contrast-enhanced MRI of the head shows enhanced soft-tissue thickening of the falx in a patient with mental neuropathy due to AIDS-associated lymphoma (arrow).