Clinical Impact of Cytomegalovirus Infections of the Nervous System in Patients with AIDS

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Cytomegalovirus (CMV) causes at least five distinct neurological syndromes in patients with AIDS; these syndromes include retinitis, myelitis/polyradiculopathy, encephalitis with dementia, ventriculoencephalitis, and mononeuritis multiplex. The clinical syndromes associated with CMV ventriculoencephalitis and diffuse encephalitis in patients with AIDS have only recently been clearly described despite the fact that multiple neuropathologic descriptions of CMV in the brain have been published over the past decade. Even more-subtle levels of cognitive impairment have been detected in patients with CMV retinitis who are also at increased risk of developing diffuse CMV encephalitis. Demonstration of CMV DNA in the CSF with use of the polymerase chain reaction may provide both a sensitive and specific method for diagnosis of these syndromes. The effectiveness of aggressive early treatment of CMV syndromes in the nervous system, with the exception of retinitis, is unclear and warrants formal trials.

Cytomegalovirus (CMV) causes five distinct neurological syndromes in patients with AIDS: retinitis, myelitis/polyradiculopathy, encephalitis with dementia, ventriculoencephalitis, and mononeuritis multiplex. The incidence of retinitis has increased, but trends for the other syndromes (e.g., encephalitis) have not been well documented because they are uncommon or difficult to diagnose before death. For example, in one study the 2-year probability of developing CMV disease among persons beginning zidovudine therapy who had CD4 cell counts of <0.1 × 10⁹/L was 21.4% [1]. The most common syndromes were as follows: retinitis (85% of patients); esophagitis (9%); colitis (7%); and gastritis, hepatitis, and encephalitis (1% each). Autopsy studies result in the identification of neurological CMV infections more frequently than do clinical studies. During 101 necropsies of adult AIDS patients that were performed at Cornell Medical Center (New York), unsuspected CMV infections were found in 49 patients, 19 of whom had encephalitis [2]. An earlier report from the same institution documented CMV encephalitis (CMV-E) in 30 (28%) of 107 neurological autopsies [3]. Thus, most CMV-E has been unrecognized clinically, and its role in causing the dementia associated with AIDS has only recently been well documented [4].

The role of HIV—in contrast to that of CMV—in dementia and minor cognitive and motor disorder (MCMD) has been well documented and widely accepted [5, 6]. HIV-associated dementia (HAD) and MCMD are more common in patients with advanced disease, but they may occur before other manifestations of AIDS in a minority of patients [7]. The neuropathology of HIV encephalitis has been well described [8, 9]. HIV appears to invade the CNS early and frequently [10], and correlations between cognitive impairment and levels of HIV in the brain have been established [11, 12]. The pattern of dementia seen in HIV disease has been likened to that in Huntington’s chorea: it is subcortical rather than cortical (Alzheimer-like) [13]. While this pattern is consistent with the distribution of histopathy and HIV in the brain, neuronal loss in the cerebral cortex also has been well documented [14, 15].

Because patients with advanced AIDS (who are at high risk of developing CMV-E) are surviving longer, an increase in the incidence of dementia attributable to CMV-E would be anticipated. However, the incidence of HIV-associated dementia in the Multicenter AIDS Cohort Study remained constant (1.76 cases per 100 patient-years) from 1988 to 1992 [16]. In contrast, the incidence of three opportunistic neurological infections (toxoplasmic encephalitis, cryptococcal meningitis, and progressive multifocal leukoencephalopathy) as well as that of primary CNS lymphoma and neuropathy all increased over the same period. After adjustment for increasing immunosuppression among patients in the cohort, it was found that the incidence of dementia may have decreased slightly, while the incidence of other diagnoses have remained constant. Increased use of antiretrovirals could result in a decrease in the incidence of dementia by inhibiting the replication of HIV, which is probably the major cause of dementia in AIDS. Thus, an increasing rate of dementia attributable to CMV-E may be masked by a decline in the incidence of HAD. Because dementia caused by CMV-E is rarely clinically separated from HAD, overall incidence rates of dementia may not reflect the component attributable to CMV-E.

Clinical Syndromes

Retinitis. Cytomegalovirus retinitis (CMV-R) is the most common opportunistic neurological infection in patients with
AIDS; it affects from 12% to 46% of these patients. CMV-R usually begins in the peripheral retina, causing symptoms of floaters or peripheral blind spots [17]. Severe visual dysfunction is usually caused either by extension of infection to the fovea or by retinal detachment. The diagnosis is made clinically by fundoscopic examination on the basis of characteristic edematous and hemorrhagic lesions with actively extending borders and a pallid, necrotic center. Involvement of the optic nerve (papillitis) is uncommon, but peripapillary retinitis is not an uncommon consequence of disease progression.

Although CMV-R has not been regarded as a harbinger of other neurological diseases, a recently published study of autopsy findings for 47 patients with AIDS has shown a strong association between CMV-R and CMV-E [18]. Overall, 10 (42%) of 24 patients with CMV-R and 9 (75%) of 12 patients with peripapillary CMV-R also had CMV-E. The association with peripapillary disease did not represent direct extension from the eye to the brain, since the optic nerve was usually spared. Thus, the presence of CMV-R markedly increases the likelihood (RR, 9.5) of finding CMV-E at autopsy, but the temporal sequence of involvement of the eye and brain remains unclear.

Myelitis/polyradiculopathy. The syndrome of CMV myelitis/polyradiculopathy presents with the subacute onset (mean duration of symptoms, 2.1 weeks; range, 0.3–6 weeks) of weakness, areflexia, and variable sensory loss in the legs in association with bladder or anal sphincter dysfunction. The disease evolves as an ascending paraparesis that mimics Guillain-Barré syndrome [19]. CMV infection of the ventral and dorsal rootlets of the cauda equina and/or the adjacent spinal cord produces severe inflammation and axonal necrosis [20].

Typically, marked pleocytosis consisting of hundreds to thousands of predominantly polymorphonuclear leukocytes in the CSF mimics the pattern of acute bacterial meningitis. The ascending paresis, marked pleocytosis, and an association with ventriculoencephalitis (see below) all suggest that CMV may spread to adjacent nerve rootlets via the CSF, perhaps transported by polymorphonuclear leukocytes [21]. As discussed below, the diagnosis is based on clinical and CSF findings and on detection of CMV in CSF by culture or specific DNA hybridization after amplification with use of PCR. Only about one-half of patients with typical clinical and CSF findings are culture positive, and the sensitivity of PCR is unclear. An MRI may reveal enlargement of the conus medullaris, clumping of the lumbosacral rootlets, or gadolinium enhancement of the leptomeninges of the lower spinal cord [22].

Acute lumbosacral polyradiculopathy due to CMV must be differentiated from several other similar syndromes. A less dramatically progressive form of acute lumbosacral polyradiculopathy of unknown cause has recently been described [19]. The CSF pleocytosis is predominantly mononuclear (i.e., lymphocytes and macrophages are present), and clinical stabilization occurs without treatment for CMV infection. Despite the fact that this condition is associated with a more benign neurological course, its overall course is similar (mean survival time, 2.7 months; range, 1–20 months) to that of polymorphonuclear (CMV) pleocytosis. Syphilis, lymphomatous involvement of the lower cord, or toxoplasmic myelitis have been implicated in a few clinically similar cases [23–25].

Treatment of patients with CMV myelitis/polyradiculopathy has been reviewed recently [26, 27]. Half of 17 treated patients survived the acute illness (median survival time, 11 weeks) [27], but all seven untreated patients died within 4 weeks of onset. Neurological stabilization or functional improvement occurred in half of the treated patients, with improvement sometimes delayed by several months. Responders had a higher degree of pleocytosis than did nonresponders. The authors hypothesize that recovery may be biphasic. Nerves that have been only slightly damaged may recover in weeks, but regrowth and remyelination of more heavily damaged axons may require months. The role of foscarnet in treating this syndrome is uncertain because most experience has been with the use of ganciclovir.

Diffuse and micronodular encephalitis. Two syndromes associated with CMV-E, diffuse micronodular encephalitis and ventriculoencephalitis, are clinically and neuropathologically distinguishable [3, 4, 28]. The more common syndrome is a multifocal and diffusely scattered micronodular encephalitis that resembles HIV encephalitis on histologic examination. Findings include small microglial nodules and inclusion-bearing cytomegalic cells that are more concentrated in the grey matter than the white matter. Their wide distribution in the cortex, basal ganglia, brain stem, and cerebellum suggests that CMV reaches the brain from the blood.

In a series of 30 patients with CMV-E (defined as the presence of nuclear or cytoplasmic inclusion-bearing cells and microglial nodules within the brain parenchyma at autopsy), 23 (77%) had microglial nodules containing CMV inclusion-bearing cells, and seven (23%) had CMV inclusions only in cells outside the nodules. Additional findings included focal parenchymal necrosis in four (13%) of the 30 patients, and either ventriculoencephalitis or radiculomyelitis in three patients (10%) each. Immunocytochemical staining for CMV antigens and cell-specific proteins showed CMV primarily in astrocytes, occasionally in neurons, and never in macrophages. Only two of nine antemortem CSF cultures yielded CMV; both specimens were from patients with radiculomyelitis.

A distinct clinical syndrome of dementia associated with CMV-E has recently been distinguished from HAD. In a retrospective review, 14 autopsy-confirmed cases of CMV-E were compared with 17 cases of HAD [4]. The dementia of CMV-E differed from HAD in clinical presentation, course, associated electrolyte disturbances, and MRI findings. The patients with CMV-E had had AIDS for longer periods than those with HAD (mean duration of illness, 16 months vs. 3.6 months, respectively) and had lower mean CD4 cell counts (0.013 × 10^9/L vs. 0.164 × 10^9/L) at presentation. Encephalopathic symptoms had been present in the patients with CMV-E for a shorter period before evaluation than in patients with HAD (mean duration, 3.5 weeks vs. 18 weeks, respectively). Patients with
CMV-E had the following signs more frequently that did those with HAD: delirium and confusion (90% vs. 27%, respectively); apathy and withdrawal, (60% vs. 9%, respectively); and focal neurological signs, (50% vs. 12%, respectively). In contrast, CMV-E patients and HAD patients did not differ with respect to complaints (60% vs. 64%, respectively) and signs (71% vs. 59%, respectively) of memory impairment, psychomotor retardation (57% vs. 76%, respectively), and mean scores on the minimental status examinations (24 correct responses vs. 25.5 correct responses, respectively, to 30 questions). The patients with CMV-E as well as those with HAD developed intermittent delirium and died, but survival was markedly shorter for patients with CMV-E (median survival, 8.5 weeks vs. 45 weeks, respectively). Strikingly high incidences of hypotension (54%), hyperkalemia consistent with an Addisonian state (23%), dilatatory hypotension with hypo-osmolality (38%), and hypernatremia from dehydration (30%) were found exclusively among patients with CMV-E. These metabolic findings may provide valuable differential diagnostic clues.

Although MRIs of the brain were available for only a minority of the 30 patients, this diagnostic modality may assist in making the diagnosis. Meningeal enhancement following injection of gadolinium (with a pattern suggestive of ventriculitis) appeared to be more common in cases of CMV-E (three of six patients) than in cases of HAD (none of five patients). Periventricular enhancement of the brain itself in patients with CMV-E was common, both in those patients with severe histopathology (six of eight patients) and in those with milder histopathology (three of six patients). While ventriculitis could have accounted for these MRI findings, the CSF findings for several of the 14 patients with CMV-E suggest that most did not have ventriculitis. Only two patients had pleocytosis (in both cases, predominantly lymphocytic), and only four of 12 patients had CMV DNA detected by PCR testing of the CSF. Thus, periven-

tricular inflammation may characterize both the diffuse micronodular and ventricular forms of CMV-E.

Ventriculoencephalitis. Ventriculoencephalitis was recently reviewed in a series that included seven new cases and 15 previously reported cases [28]. All cases occurred in patients with CD4 cell counts of \(<0.05 \times 10^9/L\). Antecedent CMV-R was noted in 11 (50%) of 22 patients, and 7 (64%) of these 11 patients were receiving ganciclovir or foscamet for treatment of retinitis at the onset of ventriculoencephalitis. The route of CMV invasion appears to be through the CSF; invasion of the brain occurs via the ependymal cells lining the ventricles. Necrosis of cranial nerves and of the periventricular parenchyma produces a rapidly fatal syndrome that consists of delirium, cranial nerve deficits, nystagmus, and progressive enlargement of the ventricles, as seen on neuroimaging studies [28].

Several clinical features of ventriculoencephalitis distinguish it from diffuse micronodular encephalitis. These features include: (1) a more acute onset (median duration of onset, 2 weeks) of lethargy, disorientation, cranial nerve palsies, and nystagmus; (2) ventriculomegaly, seen on CT or MRI of the brain; and (3) the presence of CSF pleocytosis. Despite almost uniformly abnormal findings in CSF (i.e., pleocytosis, elevated protein, and a decreased glucose concentration), the CSF profile was highly variable among these patients and did not distinguish CMV ventriculoencephalitis from a variety of acute and subacute opportunistic infections or lymphoma of the CNS.

Death ensued quickly (median duration of illness, 5 weeks), and autopsies revealed periventriculitis, ependymal and subependymal necrosis, and associated inclusion-bearing cytomegalic cells. Orderly layers of viral invasion throughout the ventricular surfaces were demonstrated histopathologically in one well-studied case [29]. These layers included necrotic ependyma, gliotic subependyma containing CMV inclusion-bearing cells, and histologically normal cells that expressed CMV antigens at the advancing borders of the infection. None of the six newly described patients with neuropathology had microglial encephalitis, a finding suggesting that CMV did not enter the CSF via the brain parenchyma [28]. The association of one-third (7 of 22) of these cases of ventriculoencephalitis with ascending weakness suggests that, in some cases, polyradiculo-litis may be the source of CMV that enters the CSF.

Treatment of encephalitis and ventriculoencephalitis. In one early report [30], clinical responses were noted in two of three patients with acute meningoencephalitis that the authors attributed to CMV; however, five patients treated for polyradiculo-

litis did not respond to ganciclovir or foscamet used for induction therapy. CMV-E is untreatable with the higher doses of ganciclovir or foscamet used for induction therapy.

Role of CMV in Minor Cognitive and Motor Dysfunction in Patients with Advanced AIDS

The early stages of both diffuse micronodular CMV-E and of HIV encephalitis can cause mild cognitive dysfunction in some patients with advanced AIDS, but evidence for a role of CMV-E has only recently been obtained. Because of the strong association of CMV-R with CMV-E observed at autopsy, investiga-

tors at the HIV Neurobehavioral Research Center (San Diego) postulated that some patients presenting with CMV-R would have neurocognitive impairment caused by the presence of subclinical CMV-E [32]. To address this possibility, we compared neuropsychological test results for 16 CMV-R patients with those for 32 AIDS patients without CMV-R (this comparison included two controls per case patient); the patients were
Diagnostic and Immunological Data for Case Patients with CMV-R vs. Matched Controls

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients with CMV-R (n = 16)</th>
<th>Matched controls (n = 32)</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
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<tr>
<td>Age (y)*</td>
<td>37.5 ± 1.4</td>
<td>36.3 ± 1.0</td>
<td>.5</td>
</tr>
<tr>
<td>Education (y)*</td>
<td>14.1 ± 0.4</td>
<td>14.3 ± 0.3</td>
<td>.81</td>
</tr>
<tr>
<td>Race (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>81</td>
<td>91</td>
<td>.35</td>
</tr>
<tr>
<td>Other</td>
<td>19</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Gender (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>88</td>
<td>94</td>
<td>.45</td>
</tr>
<tr>
<td>Female</td>
<td>12</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Medical and immunological data*</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>CD4 cell count (×10⁶/mm³)</td>
<td>26 ± 4</td>
<td>26 ± 3</td>
<td>.96</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>31.3 ± 1.2</td>
<td>37.0 ± 0.86</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Serum β₂-microglobulin level (mg/L)</td>
<td>5.6 ± 0.5</td>
<td>4.1 ± 0.3</td>
<td>.01</td>
</tr>
<tr>
<td>Serum albumin level (g/dL)</td>
<td>3.8 ± 0.12</td>
<td>4.0 ± 0.08</td>
<td>.29</td>
</tr>
<tr>
<td>Total serum globulin level (g/dL)</td>
<td>3.5 ± 0.21</td>
<td>3.3 ± 0.15</td>
<td>.44</td>
</tr>
<tr>
<td>CDC classification (%)</td>
<td>C3 (100)</td>
<td>C3 (97)</td>
<td>.47</td>
</tr>
</tbody>
</table>

NOTE. CDC = Centers for Disease Control and Prevention; CMV-R = cytomegalovirus retinitis.
* Numbers are mean ± SD.

matched for age (± 5 years), education (± 1 year), and CD4 cell counts (± 20 cells) (table 1). Patients with CMV-R were more frequently impaired in terms of the following functions: global cognitive functioning (69% vs. 37%, respectively; P = .04); attention (73% vs. 22%, respectively; P < .001); and verbal fluency (33% vs. 10%, respectively; P = .04) (table 2). On the basis of data on a limited number of patients in each group, it can be concluded that neither antecedent differences in cognitive capacity nor levels of anxiety or depression after diagnosis of CMV-R appeared to account for these differences. MRIs revealed central volume loss and patchy hyperintensities, both of which are consistent with encephalitis, more frequently in patients with CMV-R than in patients without CMV-R (77% vs. 23%, respectively; P < .001; and 23% vs. 3%, respectively; P = .04). Although infection with either CMV or HIV could account for these differences, the findings are consistent with the presence of CMV-E in a substantial fraction (about one-third) of patients who present with CMV-R. Another one-third are impaired—presumably as a direct result of HIV infection—and the other one-third are not impaired.

Thus, the finding of cognitive impairment in patients who present with CMV-R supports the hypothesis that CMV causes mild cognitive dysfunction as well as dementia. A study of the reversibility of cognitive impairment during treatment with ganciclovir, which inhibits CMV but not HIV, would further advance this hypothesis.

Diagnosis of Neurological Syndromes Due to CMV

Presumptive clinical diagnosis of some CMV-induced syndromes in the nervous system can be made from signs and symptoms, imaging of the brain or spinal cord, and the magnitude and type (polymorphonuclear or lymphocytic) of pleocytosis. For example, both ventriculitis and polyradiculopathy present as specific neurological syndromes and are associated with specific imaging patterns, and polyradiculopathy usually causes polymorphonuclear pleocytosis. In contrast, the delirium and/or dementia associated with CMV-E may be difficult to differentiate clinically from that associated with HIV encephalitis or other opportunistic infections.

Culture of CMV from CSF appears to be a specific but insensitive procedure, even for those syndromes (i.e., ventriculitis and polyradiculopathy) in which direct invasion of CSF is the postulated mode of spread. For example, in a recent review only 8 (57%) of 14 AIDS patients with polyradiculopathy syndrome and polymorphonuclear pleocytosis were culture positive [19]. Despite these limitations, culture of CSF should be done routinely for patients with AIDS who are suspected of having a neurological syndrome due to CMV, preferably with use of a rapid detection (shell vial) technique [33].

More recently, detection of CMV DNA in CSF by nucleic acid hybridization following amplification with use of PCR has been described by multiple investigators [4, 34–39]. While most investigators achieved a high level of sensitivity (80%–100%) and specificity (75%–100%) with this technique [34–36], others have reported decidedly different results [4, 39]. Achim and colleagues [39] compared the results of PCR analysis of CSF obtained at autopsy to those of neuropathologic examination; these authors achieved a sensitivity of 91% (10 of 11 patients with CMV-E were PCR positive) but a specificity of only 42% (10 of 24 patients without CMV-E were PCR positive). In contrast, Holland and colleagues [4] detected CMV...
Table 2. Summary of data on neuropsychological and psychiatric function of patients with CMV-R vs. matched controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients with CMV-R (n = 16)</th>
<th>Matched controls (n = 32)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuropsychological ratings (no. impaired/total no. of subjects)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global cognitive function</td>
<td>11/16 (69%)</td>
<td>12/32 (37%)</td>
<td>.04</td>
</tr>
<tr>
<td>Attention</td>
<td>11/15 (73%)</td>
<td>7/32 (22%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Verbal fluency</td>
<td>5/15 (33%)</td>
<td>3/31 (10%)</td>
<td>.04</td>
</tr>
<tr>
<td>Psychomotor</td>
<td>6/15 (40%)</td>
<td>5/32 (16%)</td>
<td>.06</td>
</tr>
<tr>
<td>Abstraction</td>
<td>6/15 (40%)</td>
<td>6/32 (19%)</td>
<td>.11</td>
</tr>
<tr>
<td>Motor function</td>
<td>8/13 (61%)</td>
<td>11/31 (35%)</td>
<td>.11</td>
</tr>
<tr>
<td>Learning</td>
<td>8/15 (53%)</td>
<td>10/32 (31%)</td>
<td>.14</td>
</tr>
<tr>
<td>Memory</td>
<td>2/15 (13%)</td>
<td>5/32 (16%)</td>
<td>.83</td>
</tr>
<tr>
<td>IQ scores†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WAIS-R Full Scale IQ</td>
<td>97.5 ± 4.2</td>
<td>101.5 ± 2.1</td>
<td>.39</td>
</tr>
<tr>
<td>WAIS-R Performance IQ</td>
<td>100.7 ± 4.9</td>
<td>101.9 ± 2.5</td>
<td>.82</td>
</tr>
<tr>
<td>WAIS-R Verbal IQ</td>
<td>96.3 ± 4.2</td>
<td>102.4 ± 2.1</td>
<td>.24</td>
</tr>
<tr>
<td>WAIS-R Vocabulary T-Score‡</td>
<td>50.9 ± 1.5</td>
<td></td>
<td>.27</td>
</tr>
<tr>
<td>Psychiatric ratings†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hamilton Depression Score</td>
<td>6.4 ± 1.5</td>
<td>7.0 ± 0.9</td>
<td>.74</td>
</tr>
<tr>
<td>Hamilton Anxiety Score</td>
<td>4.9 ± 1.4</td>
<td>5.5 ± 0.8</td>
<td>.73</td>
</tr>
</tbody>
</table>

NOTE. CMV-R = cytomegalovirus retinitis; WAIS-R = Wechsler Adult Intelligence Scale-Revised.
* Neuropsychological rating scores are standardized for age, education, and gender.
† Determined with use of the WAIS-R for 6 patients and 24 matched controls.
‡ WAIS-R Vocabulary T-Score range is between 0 and 100, with scores of 40–60 within the normal range; this score is the best predictor of premorbid IQ.
§ Hamilton Anxiety and Depression Scores, determined for 9 patients and 26 matched controls, range from 0 to 40; a score of 15 is the cutoff for clinical anxiety or depression.

DNA in only four of 12 patients with autopsy-proven CMV-E (sensitivity, 33%) and in none of eight controls without CMV-E (specificity, 100%).

Thus, most investigators who used PCR to analyze CSF obtained before death achieved good sensitivity, and all achieved good specificity, even when the patients had AIDS and CMV-R. The only study of CSF obtained at autopsy supported the sensitivity, but not the specificity, of this technique. Postmortem migration of cells containing CMV, or diffusion of CMV DNA into CSF, might account for the loss of specificity. PCR may provide rapidly-available, sensitive, and specific evidence of CMV encephalitis, ventriculitis, or polyradiculopathy/myelitis, but prospective testing of this procedure for each syndrome is needed to confirm the results of these retrospective studies. Quantitative PCR assays of CSF might help to monitor the virological effects of treatment and to differentiate disease limited to the brain parenchyma from that involving the CSF.

Summary and Future Directions

Neurological CMV infection is increasingly recognized as a cause of subacute delirium, dementia, and ascending paralysis in patients with advanced AIDS and may be treatable. The proportion of dementia and of mild cognitive and motor dysfunction in these patients that is attributable to CMV remains unclear, but it could be substantial. The development of topical treatment for CMV-R with implantable or injectable drugs that do not act systemically could increase the incidence of cognitive impairment from CMV-E dramatically [40–42]. Studies are needed to address this potential limitation of topical therapy.

Detection of CMV in CSF by PCR-based methods appears to provide a sensitive and specific method for diagnosing encephalitis and polyradiculopathy. Prospective studies of this technology, with neuropathologic confirmation of the results at autopsy, are needed to verify and resolve conflicting data from retrospective studies. Studies on treatment of CMV-E and of the mild cognitive motor defects found at presentation of CMV-R are needed to confirm the causal role of CMV and the responsiveness of CMV-E to treatment.

References

CID 1995;21 (Suppl 2)  CMV Neurological Infections in AIDS  S201


