The Role of Lumbar Puncture in the Management of Elevated Intracranial Pressure in Patients with AIDS-Associated Cryptococcal Meningitis

Sir—we read with great interest the study by Graybill et al. [1] regarding the diagnosis and management of elevated intracranial pressure in patients with AIDS and cryptococcal meningitis, and we agree that high intracranial pressure without any evidence of obstructive hydrocephalus is a frequent complication of cryptococcal meningitis and is associated with a poor prognosis and more-severe symptoms. However, it seems to us that the authors’ recommendation that an “opening pressure $>$250 mm H$_2$O be treated with large-volume CSF drainage” needs to be considered with caution, despite their observation that this practice was not associated with any major adverse reactions.

From January 1986 through December 1999, 470 consecutive HIV-infected patients were evaluated for neurological disorders at the Infectious Diseases Institute of Milan, in Milan, Italy, and underwent a lumbar puncture (LP) as part of the workup. Table 1 shows the final diagnoses and the number of LPs performed. Fatal brain herniation was observed in 2 patients affected by cryptococcal meningitis, both of whom underwent multiple LPs that were aimed at reducing intracranial pressure by means of CSF drainage.

Patient 1 was a 26-year-old male injection drug user who had cryptococcal meningitis diagnosed in March 1989 and who experienced a clinical and mycological relapse in November of the same year. The results of a brain CT scan were normal. From 6 November through 11 November, the patient underwent 3 LPs, the last 2 of which were done to treat elevated intracranial pressure. After the third LP was performed (opening pressure, 600 mm H$_2$O), he went into a coma, in association with mydriasis and an absence of response to pain stimuli, and he died 8 h later. Autopsy revealed meningoencephalitis with marked cerebral edema and bulbar-cerebellar herniation.

Patient 2 was a 33-year-old homosexual man with AIDS (cutaneous Kaposi’s sarcoma) who presented in March 1990 with fever, headache, rigor nucalis, and an altered mental status. The results of a brain CT scan were normal, and an LP revealed the presence of Cryptococcus neoformans. After a second LP was performed 3 days later (opening pressure, 450 mm H$_2$O),

<table>
<thead>
<tr>
<th>Evaluation for</th>
<th>Diseases associated with focal brain lesions</th>
<th>Diffuse disease or meningitis, no. patients/ no. LPs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final diagnosis</td>
<td>No. patients/ no. LPs</td>
<td>Lesions detected by CT and/or MRI, median no. (range)</td>
</tr>
<tr>
<td>Aspergillosis</td>
<td>1/1</td>
<td>—</td>
</tr>
<tr>
<td>Astrocitoma/glioblastoma</td>
<td>3/3</td>
<td>2 (1–3)</td>
</tr>
</tbody>
</table>
| Bacterial meningitis | — | — | 7/10
| CMV encephalitis | — | — | 49/54
| CMV plus other OI$^a$ | — | — | 5/23
| Cryptococcosis | 6/45 | 2 (1–4) | 67/263$^b$
| Encephalopathy, unknown origin | 6/7 | 1 (1–2) | 36/41
| Herpetic meningoencephalitis | — | — | 8/10
| HIV encephalopathy | — | — | 74/87
| HIV encephalopathy plus other OI$^c$ | — | — | 2/3
| Primary brain lymphoma | 15/16 | 1 (1–2) | — |
| PML | — | — | 67/78
| Syphilis | — | — | 11/14
| Systemic non-Hodgkin’s lymphoma | 3/6 | 2 (1–3) | 1/3
| Toxoplasmosis | 74/91 | 3 (1–5) | — |
| Toxoplasmosis plus other OI$^d$ | 10/17 | 2 (1–4) | — |
| Tuberculosis | 3/7 | 3 (1–5) | 20/25
| Tuberculosis plus other OI$^e$ | — | — | 2/3
| Total | 121/193 | 349/614 |

NOTE. CMV, cytomegalovirus; HSV, herpes simplex virus; OI, opportunistic infection; PML, progressive multifocal leukoencephalopathy.

$^a$ Type and no. of OIs were as follows: HSV, 1; cryptococcosis, 1; PML, 2; and tuberculosis, 1.

$^b$ Included 2 cases of herniation.

$^c$ Type and no. of OIs were as follows: PML, 1; and CMV encephalitis, 1.

$^d$ Type and no. of OIs were as follows: CMV encephalitis, 3; PML, 2; cryptococcosis, 1; HIV encephalopathy, 1; syphilis, 1; primary brain lymphoma, 1; and bacterial meningitis, 1.

$^e$ Type and no. of OIs were as follows: cryptococcosis, 1; and PML, 1.
the patient became unconscious and had bilaterally dilated and unreactive pupils and a vasomotor reaction throughout the trunk. Although iv mannitol was immediately administered and led to regression of the coma, it resulted in residual amaurosis. The patient was admitted to the intensive care unit, where he experienced several episodes of waxing and waning consciousness and finally died 3 days later. Autopsy revealed meningocencephalitis with marked cerebral edema and cerebellar herniation. Since then, we have stopped using CSF drainage to treat elevated intracranial pressure in patients with cryptococcal meningitis.

We believe that cryptococcal meningitis is associated with a higher risk of brain herniation than are any of the other CNS complications observed in patients with AIDS and that great caution is required when frequent LPs are performed to achieve mechanical decompression. Furthermore, the LP should be considered investigational until an “ad hoc” study is performed.

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Reference


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Reply

Sir—We appreciate the letter from Dr. Antinori et al. regarding our study “Diagnosis and Management of Increased CSF Pressure in Patients with AIDS and Cryptococcal Meningitis,” which was published in the January 2000 issue of Clinical Infectious Diseases [1]. The authors bring to our attention 2 patients who succumbed to the consequences of high intracerebral pressure resulting from cryptococcal meningitis. They attribute the cause of death to herniation caused by the lumbar punctures (LPs), and they recommend that this procedure be considered “investigational” until an “ad hoc” study is performed.

In effect, Dr. Antinori and his colleagues have raised 2 issues. The first is the presence or absence of elevated CSF pressure, and the second is the presence or absence of focal lesions that could cause or aggravate obstructive hydrocephalus from large-volume CSF drainage. Such lesions are common in cases of toxoplasmosis, aspergillosis, and lymphoma, as the authors noted. Imaging studies are often used to detect these lesions, and management is tailored to deal with the specific lesions. Focal findings and space-occupying lesions are associated with an increased risk of herniation after LP, and they may require neurosurgical consultation and intervention.

Although many of our patients had CT or MRI scans, there was no clear evidence of lesions that would preclude lumbar drainage. Indeed, both patients reported by Dr. Antinori et al. had normal CT scans, a finding that is consistent with our experience. What, then, caused their deaths? It is our suspicion that the patients may have had inadequate, rather than excessive, CSF drainage. The first patient had a CSF pressure >600 mm H2O after 3 LPs, and the second patient had a pressure of 450 mm H2O after 2 LPs.

In the setting of persistent high pressures and communicating hydrocephalus (as suggested by the normal CT scans), we have, at times, used drainage procedures more than once daily to reduce the pressures. We have tended to use large needles, rather than small ones, to create a larger rent in the dura mater so that fluid can leak out for some hours after the LP and thus contribute to keeping pressure down. However, the reduction of pressure during LP should be done at a controlled rate. For a few patients in whom pressures could not be normalized after 4–7 days, lumbar drains were temporarily placed as a way to keep the pressures down by draining more fluid than could be achieved with intermittent LPs. Finally, it is clear that a small number of patients will not respond to these methods and will require ventriculoperitoneal shunting. If left untreated, uncontrolled elevated intracranial pressure can cause herniation in its own right.

Another factor associated with LP-herniation risk is removal of CSF that is done too rapidly. Rapid uncontrolled decompression of extremely high pressure, similar to that described by Dr. Antinori et al., may precipitate herniation.

Dr. Antinori et al. have not suggested alternatives to CSF lumbar drainage. The patients that they reported may well have responded to ventricular drainage, but we doubt that they would have survived if nothing had been done to decompress the CSF pressure. Indeed, the early deaths of our patients were associated with extremely high CSF pressure. Among patients with normal or nonfocal CT scans, determining who might require ventricular drainage is an extremely difficult decision. However, we fear that deferring or avoiding lumbar drainage would carry a heavy price for a large number of patients. Given the paucity of such cases in North America and Europe, it is extremely unlikely that prospective randomized studies will ever be undertaken; therefore, retrospective data analysis of large case series has been the only way of extracting useful clinical data. We stand by our recommendation for CSF drainage.

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