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Distinguishing between Chemical and Bacterial Meningitis in Patients Who Have Undergone Neurosurgery

Str—We are writing to express our concerns about the potentially fatal consequences of adopting the recommendations made by Forgacs et al. [1]. On the basis of the results of what we regard as a flawed study, the authors concluded that patients who have undergone neurosurgery and have chemical meningitis can be distinguished postoperatively, on an individual basis, from such patients who have bacterial meningitis, thereby avoiding the unnecessary administration of antibiotics to patients in the former group.

Forgacs et al. [1] retrospectively reviewed the clinical characteristics, results of radiological studies, and CSF profiles of 70 patients with postneurosurgical meningitis in an attempt to identify variables that could be used prospectively to differentiate patients with bacterial meningitis from those with noninfectious meningitis. Of the 70 patients with postoperative meningitis, 30 were categorized as having chemical meningitis (defined as negative CSF Gram staining and culture results for a patient who recovered without antibiotic therapy), 20 were categorized as having bacterial meningitis (defined as CSF culture that yielded a significant pathogen) and 20 were categorized as having disease of indeterminate etiology (defined as negative CSF Gram staining and culture results for a patient who had received antibiotics after a lumbar puncture).

For all of the variables evaluated by Forgacs et al. [1], in particular the CSF profiles (which consisted of WBC counts and glucose and protein concentrations), the results for infected patients overlapped markedly with those for noninfected patients. The authors themselves acknowledged that the findings were similar for both groups. Nonetheless, they drew attention to the observation that WBC counts were >7500 × 10⁶ cells/L in 4 patients in the infected group and in no patients in the noninfected group. However, this represented only 20% of patients in the infected group. Similarly, they pointed out that a glucose concentration of <10 mg/dL was not found in a single patient with chemical meningitis; yet this low concentration was detected in only 1 of 20 patients with bacterial meningitis. Not one of the variables evaluated by the investigators had sufficient specificity and sensitivity to be used to discriminate accurately between bacterial and aseptic meningitis at the time of presentation.

The desirability of avoiding unnecessary administration of antibiotics to patients who have aseptic meningitis has prompted a search for diagnostic tests that can reliably and rapidly distinguish between patients with and without infection. Many such tests have been evaluated [2], but, with one exception, none has been shown to have had sufficient specificity and sensitivity to allow it to be used for this purpose. In a retrospective study, Leib et al. [3] demonstrated that CSF lactate concentrations of ≥4 mM have high sensitivity, specificity, and positive and negative predictive values for diagnosis of bacterial meningitis in patients who have undergone craniotomy. However, these observations have not yet been validated by prospective studies. The serum procalcitonin concentration also shows promise as a means of distinguishing bacterial from aseptic meningitis, but it has not yet been assessed in patients who have undergone neurosurgery.

For the time being, therefore, isolation of a pathogen from the CSF of patients with postneurosurgical meningitis must remain the definitive diagnostic test, although this means that the diagnosis can be made only retrospectively. Because of the difficulties of accurately identifying patients with bacterial meningitis prospectively, and because of the morbidity and mortality that result from delays in initiating therapy, we and others have concluded that all patients who present with the clinical and laboratory features of postoperative meningitis should receive empirical antibiotic therapy [2, 4]. If the CSF is subsequently found to be sterile (usually after 2–3 days), antibiotic therapy can be discontinued, providing that it was not administered during the 24–48 h before the lumbar puncture was performed.

Forgacs et al. [1] dismissed this strategy as being an oversimplified approach to the management of patients with post-

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operative meningitis and claimed that patients with chemical meningitis “can often be differentiated from patients with bacterial meningitis” ([1], p. 185). We do not believe that this conclusion is justified by the evidence contained in their article, nor do we believe that they have identified variables that are capable of facilitating the distinction with the 100% accuracy that is required. Administering antibiotics to noninfected patients unnecessarily for 3 days is clearly undesirable, but the consequences of failing to administer these agents to patients who have received an incorrect diagnosis of aseptic meningitis can be devastating.

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References

Reply
Str—Brown et al. [1] express concern about not administering intravenous anti-
tibiotics empirically to patients who are believed to have a noninfectious meningitis (chemical meningitis) after a neurosurgical procedure. They have published guidelines on the management of postoperative meningitis (after we submitted our manuscript to Clinical Infectious Diseases) that recommend 2 or 3 days of empirical antibiotic treatment for all patients who have meningitis after neurosurgery, at which time antibiotic therapy should be discontinued for patients with negative results of CSF cultures [2]. They stated that their guidelines were not necessarily evidence based.

During the past 24 years, while administering clinical care to patients with meningitis after neurological surgery, we have asked ourselves, on a case by case basis, whether it is possible to conclude that a patient’s likelihood of having chemical meningitis is great enough that we could avoid administering antibiotic treatment at the time of their baseline evaluation. We have seen a large population of such patients who had not received antibiotic treatment. For our article [3], we decided to review data on this population and compare it with data on patients with definite bacterial meningitis (data for both groups were readily available for the 11 years of our study) to see whether it had been possible to distinguish these groups safely.

We concluded that there was a great deal of overlap in CSF test results for patients with chemical meningitis and for those with infectious meningitis, as mentioned by Brown et al. [1], and that findings of gram staining of CSF were often negative. We found that it had been possible to recognize chemical meningitis in 30 of 70 patients with meningitis, primarily on the basis of clinical characteristics, and so to avoid administering antibiotic treatment to these patients. Although no single clinical feature was present in all patients with infection or in all patients with chemical meningitis, the composite clinical aspects of the 2 populations were different. In patients with chemical meningitis, there were no wound infections, new focal findings, coma or new seizure disorders, or temperatures of >39.4°C, and CSF rhinorrhea and otottrhea were unusual. We had avoided antibiotic treatment in these patients safely. Nineteen of 20 patients who subsequently were found to have had a CNS infection began to receive antibiotics on the day that CSF examination was performed or earlier; treatment was begun later for 1 patient who had a temperature of ≤38°C without mental status change, who subsequently recovered.

Although the toxicity associated with treating every patient who has meningitis with iv antibiotics for 2 or 3 days is low, there are risks in addition to drug toxicity that are associated with empiric treatment. In patients with bacterial infections, it is not uncommon for the initial CSF culture to have a negative result, possibly because the patient received perioperative antibiotics or because of the presence of a parameningeal focus of infection. A short course of antibiotics may partially treat a bacterial CNS infection and make the subsequent diagnosis and management more difficult.

There are risks in not giving antibiotic treatment to a patient who has bacterial meningitis. Our intent was not to formulate a recommendation: it was rather to permit characterization of the entity of chemical meningitis and to permit decisions about treatment (by physicians experienced with the management of postoperative meningitis) that are based on data.

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References