Clinical Utility of Broth Cultures of Cerebrospinal Fluid from Patients at Risk for Shunt Infections

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For patients with cerebrospinal fluid (CSF) shunts, culture of the CSF remains the most valuable tool in the evaluation of suspected shunt infections. To detect anaerobic Propionibacterium sp., a well-described cause of these infections, many clinical microbiology laboratories routinely employ a broth medium as an adjunct to solid media. The use of broth, however, creates a diagnostic dilemma since many contaminants also are isolated from broth cultures. Therefore, we retrospectively reviewed the records of 59 patients with CSF shunts in whom an organism was isolated from only broth cultures to assess their utility for the diagnosis of shunt infection. We found that no single clinical or laboratory parameter, including fever, leukocytosis, pleocytosis, or CSF protein and glucose, could reliably predict or exclude a shunt infection. Isolation of coagulase-negative staphylococci only in broth, in the absence of growth on solid media in concurrent or immediately preceding cultures, virtually always represented contamination. The isolation of Propionibacterium sp. from broth only usually represented contamination; however, infection could not be excluded without a repeated CSF culture, even in the absence of pleocytosis. We recommend that specific comments be appended to laboratory reports for isolates from CSF in broth only as an aid to the physician in interpreting the clinical importance of such isolates.

Culture of cerebrospinal fluid (CSF) is essential in the evaluation of suspected CSF shunt infection. Although the majority of these infections are caused by aerobic bacteria, including staphylococci and gram-negative bacilli, anaerobic bacteria, including Propionibacterium sp., are recognized as an increasingly common cause of shunt infections (1, 3, 4, 10, 11). Routine aerobic cultures of CSF often are inadequate to detect these slowly growing organisms. Therefore, most microbiology laboratories employ additional methods such as anaerobic solid media or thioglycolate broth to detect these organisms in patients who are at risk for shunt infection (2). The increased sensitivity, however, also leads to an increased yield of contaminants that may create a dilemma as to the interpretation of the clinical significance of these broth-only isolates (BOI). In a previous study of the clinical impact of BOI from all clinical specimens, only 2 of 88 BOI from CSF were found to be clinically relevant (7). To further study this issue, we retrospectively reviewed the charts of 59 patients with CSF shunts in whose CSF a BOI was identified over a 2-year period. We examined the clinical significance of these isolates and attempted to determine whether clinical parameters such as fever, peripheral leukocyte count, or CSF indices could reliably predict or exclude a CSF shunt infection in a patient in whom a BOI was identified.

MATERIALS AND METHODS

Patient population. Duke University Medical Center is a 750-bed tertiary-care hospital in which about 190 CSF shunts are placed yearly.

Specimen processing. All CSF specimens were centrifuged and planted on sheep blood agar and chocolate agar and kept for 48 h. Specimens that were labeled as originating from a patient with a shunt or labeled with the name of a physician who routinely cared for patients with shunts were also centrifuged, and up to 1 ml of the sediment was inoculated into tubes of thioglycolate broth that were kept for 14 days and examined daily for growth.

Clinical evaluation. All CSF specimens collected from January 1995 through December 1996 with a final result of a BOI were identified by a computerized search of microbiology records. All available charts from these patients were reviewed for the following information: patient name, age, and sex; presence of a CSF shunt; evidence of shunt malfunction; temperature; total peripheral leukocyte (WBC) count on the date of CSF specimen acquisition; CSF indices; relevant clinical data; if the culture result was acknowledged by the clinical team; assessment of the isolate by the clinical team; whether recovery of the isolate affected patient management; and outcome. Outcome was evaluated, if possible, on the basis of follow-up CSF cultures in the absence of antibiotics. If no further CSF was obtained, patient records were reviewed for 6 months following the date when the BOI was obtained for evidence of subsequent CSF shunt infection.

Definitions. Determinations of whether an isolate represented a true infection versus contamination and clinical significance were made by an infectious disease clinician. A BOI was deemed to be a true cause of infection if (i) ≥2 CSF specimens were positive for the organism or (ii) a single CSF specimen was positive for the organism, systemic signs and clinical course were compatible with infection, and there was no other obvious etiology of the clinical syndrome. A single BOI without a clinical course consistent with infection was classified as a contaminant. Cases in which a determination could not be made were designated unknown. Outcome was reviewed for 6 months from the date when the BOI was obtained to ensure that an infection due to a BOI judged to be a contaminant did not become clinically apparent at a later date. True isolates were deemed clinically significant if (i) they prompted an appropriate change in patient management or (ii) defined the clinical importance of the episode. A pleocytosis was defined as >5 WBC/mm³ of CSF (9). Fever was defined as an oral temperature exceeding 37.7°C (5).

Statistical methods. All clinical data were collected on data sheets and entered into a database for analysis. Statistical analysis was performed with a statistical software package (JMP; SAS Institute, Cary, N.C.). A P value of 0.05 was used to establish statistical significance.

RESULTS

Of 1,188 CSF specimens processed in accordance with the above-described protocol for CSF shunt patients from January 1995 through December 1996, 212 cultures were positive and 976 were negative. Of the 212 positive cultures, 87 from 63 patients with CSF shunts were positive only in thioglycolate broth. The charts of 59 patients with 83 BOI were available for review.
Clinical significance. Twenty-three BOI from 10 patients were deemed true causes of infection, representing 11 episodes of CSF shunt infection; 57 isolates were judged to be contaminants. In three cases, a determination could not be made. In 9 of 11 episodes of true infection, the causative organism was isolated from at least one additional culture. In the two remaining episodes, CSF was not submitted for repeat culture. In a single patient, two CSF specimens separated by 2 weeks yielded Propionibacterium sp. organisms which were felt to be contaminants, as the patient received no antibiotics and repeated cultures were negative. The 11 episodes of true infection were caused by Propionibacterium sp. in five cases and coagulase-negative staphylococci in six cases. In all six cases in which a coagulase-negative staphylococcus BOI was judged to represent true infection, the organism had been isolated on solid media from one or more previous CSF specimens. The most frequent contaminant was Propionibacterium sp. (63%), followed by coagulase-negative staphylococci (21%).

Eleven of 23 true BOI from six patients were determined to be clinically significant, and 12 were judged to be not clinically significant. Three clinically significant BOI from two patients were designated as such because they prompted a change in patient management. The remaining eight significant BOI defined the clinical importance of the episode.

Outcome. There was adequate clinical information to assess outcome for 22 of 23 truly pathogenic BOI and 51 of 57 contaminants. In no case did an organism deemed to be a contaminant cause infection within 6 months of when the initial BOI was obtained.

CSF parameters. A pleocytosis of >5 WBC/mm³ of CSF was present in the CSF of 10 (59%) of 17 truly pathogenic BOI for which the specimen was also submitted for analysis of the cell count (several specimens were submitted for culture only). These isolates represented 70% of the episodes of true shunt infection. The CSF WBC count of all truly pathogenic BOI had a range of 0 to 1,800 WBC/mm³ of CSF and a mean of 260 WBC/mm³. A pleocytosis was present in 16 (35%) of 46 contaminant BOI for which CSF was submitted for cell count determination. The mean CSF WBC count was 23 WBC/mm³ for contaminants, compared to 260 WBC/mm³ for truly pathogenic BOI (P = 0.01), and the range was 0 to 260 WBC/mm³. A one-way analysis of variance (ANOVA) was used to compare the CSF WBC counts. All contaminant specimens with a CSF pleocytosis were also accompanied by >500 erythrocytes (RBC)/mm³, with all but one accompanied by >2,000 RBC/mm³ (mean, 19,396 RBC/mm³).

Seven truly pathogenic BOI from three patients were not accompanied by a CSF pleocytosis. Of these, five BOI from three patients were judged to be clinically significant. In two of these patients, the isolate prompted a change in patient management; in the third patient, repeated isolation of the organism strengthened the diagnosis of shunt infection.

There was no significant difference between the mean CSF protein concentration of truly pathogenic BOI (88.5 mg/dl) and that of contaminants (80.0 mg/dl) (P = 0.97). The mean glucose concentration in the CSF was not significantly decreased when an isolate was judged to be a true pathogen (57 mg/dl) versus a contaminant (59 mg/dl) (P = 0.88). The one-way ANOVA was used for both of these comparisons.

Clinical parameters. Fever was present in only 4 of 11 episodes of shunt infection due to a BOI. Neither the presence of fever (P = 0.39), compared by using the Pearson correlation coefficient, nor an elevated peripheral leukocyte count (P = 0.86), compared by one-way ANOVA, was significantly associated with a truly pathogenic BOI compared with a BOI representing contamination.

Management. All 10 patients in whom a BOI was judged to be a true cause of infection were managed appropriately. As previously mentioned, in only four of these patients did the BOI have an effect on patient care, either by defining the infection (3) or by prompting a modification of therapy (1). All patients with BOI judged to be contaminants were managed appropriately; however, the BOI prompted acquisition of additional CSF cultures from six patients for evaluation of the possibility of a true infection. In a single patient with a Propionibacterium sp. BOI of unknown clinical significance, the shunt was immediately removed without a repeat culture to assess the possibility that the isolate represented contamination.

DISCUSSION

Infection remains a major complication of CSF shunts. Despite an operative incidence of <4% in recent studies, 8 to 40% of patients with shunts can expect at least one shunt infection during their lifetimes (4). Unfortunately, the diagnosis of shunt infection may be difficult due to few or inapparent symptoms, which may be insidious, lasting from weeks to months before the diagnosis is established. Fever is not a universal sign, and its absence does not rule out infection (4). In our subset of patients with BOI, there was no significant difference between patients with and without CSF shunt infection in terms of the presence of either fever or peripheral leukocytosis. Signs of shunt malfunction, occurring in 65% of patients with documented infection, are also not a dependable indicator of infection (4). Examination of the CSF remains the most useful tool in the diagnosis of CSF shunt infections.

In patients without prosthetic material in the central nervous system, pleocytosis is a sensitive indicator of inflammation. Several previous reports, however, have noted that pleocytosis may not be a reliable indicator of infection in patients with CSF shunts (3, 6, 8, 10, 11). Unfortunately, these reports gave little information on these few patients and no details about the clinical significance of the specimens which failed to show pleocytosis. In our study, pleocytosis was present in the majority (70%) of episodes of true CSF shunt infection. Only 35% of contaminants were accompanied by pleocytosis, and all of these were also accompanied by >500 RBC/mm³ of CSF. However, as in previous studies (3, 6, 8, 10, 11), we noted several patients (3) in whom a true BOI infection was not associated with pleocytosis. In addition, the isolation of these organisms was clinically significant and had a positive impact on patient care. Therefore, although a finding of pleocytosis was more likely to reflect a true infection, the absence of pleocytosis did not reliably exclude infection. Neither the CSF protein nor glucose was helpful in discriminating whether a BOI represented a true infection versus contamination.

Anaerobes, including Propionibacterium sp., have been well described as the cause of 1 to 14% of CSF shunt infections (1, 4, 10). Many microbiology laboratories routinely inoculate broth as an adjunct to direct plating to improve the yield of these slowly growing organisms (2). The improved sensitivity, however, is not without cost, since contamination with a single organism will lead to a positive culture. In addition, the inoculation of a broth medium precludes the use of quantitation as a guide to significance. The increased recovery of contaminants creates a dilemma for the clinician: does this BOI represent a true infection or contamination?

In patients without CSF shunts, a BOI is indicative of contamination. Therefore, these cultures should be either not processed at all or reported as consistent with (or indicative of) contamination. In patients with CSF shunts, a single BOI of a
coagulase-negative staphylococcus, in the absence of growth on solid media, virtually always represents contamination. In every case of true infection due to coagulase-negative staphylococci, the BOI was accompanied by growth on solid media from either a concurrent or an immediately preceding culture. This finding is not surprising, since this organism grows easily on most aerobic media. Therefore, the isolated finding of a BOI of coagulase-negative staphylococci is not indicative of infection and should not prompt the acquisition of additional cultures, almost always represents contamination.

Although the vast majority of Propionibacterium sp. isolates from the CSF of patients with CSF shunts represent contamination, infection cannot be excluded in the setting of a single specimen submitted for culture, even in the absence of pleocytosis. We suggest the following statement to accompany such isolates: in patients with CSF shunts, Propionibacterium sp. often represents contamination, but infection cannot be excluded. Please submit repeat specimen for culture if infection is suspected.

Recent data from Sturgis et al. (12) support our conclusions about BOI of coagulase-negative staphylococci. Their study, however, did not adequately assess the role of Propionibacterium sp., since thioglycollate broth was incubated for only 48 h. Previous data have shown that this organism routinely requires 4 to 7 days for growth, with some isolates requiring up to 9 days (1). For this reason, many laboratories routinely keep broth cultures of CSF for 14 days for patients with shunts. In addition, the study by Sturgis et al. did not address the subject of patients with CSF shunts, the patient population in which Propionibacterium sp. can cause CSF shunt infections (12).

In accord with the results of a study by Morris and colleagues (7), we found that broth cultures were helpful in relatively few patients (only six in this study). Moreover, seven other patients were negatively impacted by the isolation of an organism in broth only. However, for the six patients on whose care the identification of a BOI had a positive impact, the timely identification of the etiology of the infection avoided further diagnostic maneuvers, including repeated lumbar puncture or multiple revisions of the CSF shunt. We feel that these benefits outweighed the negative impact of the need for repeated lumbar puncture of patients from whom contaminants were isolated. Note that five of these six episodes of shunt infection were caused by Propionibacterium sp. detected only by broth culture. Thus, suspected CSF shunt infection may be one of the few remaining clinical scenarios in which the use of a broth medium for culture may be helpful to the clinician. Consequently, we recommend the continued use of broth medium for the culture of CSF from patients with CSF shunts to exclude the possibility of an infection caused by Propionibacterium sp. The clinical utility of this practice, however, can be augmented by issuing an interpretative report as to the likely meaning of an organism isolated only from broth cultures of the CSF.

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REFERENCES