False-Positive Cryptococcal Antigen Test Associated with Use of BBL Port-A-Cul Transport Vials

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A total of 52 residual CSF and serum specimens, which were originally negative with the Cryptococcal Antigen Latex Agglutination System (CALAS), were shown to become falsely positive after placement in BBL Port-A-Cul anaerobic transport vials. This transport device, although excellent for specimen transportation for subsequent culture, should not be used if cryptococcal antigen testing is needed.

Cryptococcal antigen detection (CAD) tests are highly sensitive and specific assays that are clinically relied upon for the rapid diagnosis of cryptococcal meningitis (7, 8). The detection of a positive cryptococcal antigen test is a significant clinical finding. It suggests that the etiologic agent of disease is Cryptococcus neoformans and implies the likelihood of an immunocompromised state (3). The consequences of a false-positive CAD test are significant for a variety of reasons. This type of misdiagnosis could lead to inappropriate therapy for the actual cause of meningitis. In addition, when a confirmatory culture is not present, subsequent ancillary tests, such as additional lumbar punctures and radiologic scans, may be performed in an attempt to achieve a confirmed diagnosis. Fortunately, the causes of false-positive CAD tests are few. Likely the most noted cause is an infection and cross-reaction with a Trichosporon species (4, 5). Rarely, other causes, such as starch, disinfectants, and soap, have been reported to cause false-positive CAD results (1, 2, 6).

The Cryptococcal Antigen Latex Agglutination System (CALAS; Meridian Bioscience, Inc. Cincinnati, OH) is the assay used in our laboratory for the detection of the cryptococcal antigen. It employs latex particles that are coated with antibodies directed against an antigen present on the polysaccharide capsule of Cryptococcus neoformans. A positive reaction is heralded by clumping of the latex particles and a clearing of the normally milky background. Although cerebrospinal fluid (CSF) specimens are usually transported to the laboratory in three separate plastic tubes, which are available from a number of vendors, for chemistry, cell count, and microbiology analysis, occasionally this specimen may be transported to the laboratory in another transport device. This may particularly occur in neurosurgery as part of the assessment of the functioning of an indwelling intraventricular shunt. There was an event in our laboratory wherein a CSF obtained in surgery during the assessment of an intraventricular shunt was submitted to microbiology for culture and CAD testing, the latter of which was falsely positive. It was hypothesized that the false positivity was possibly due to submission of the CSF in a BBL Port-A-Cul anaerobic transport device (BD Diagnostic Systems, Sparks, MD).

We, therefore, sought to determine if the material present in the BBL Port-A-Cul anaerobic transport vial could cause culture and CAD-negative CSF and serum specimens to become falsely positive in the CAD assay. Serum was tested only to determine if false-positive results were specific to specimen type, since serum is not received in this specimen container. A total of 52 clinical specimens that were CAD and culture negative and 3 clinical specimens that were CAD and culture positive for C. neoformans by routine testing were studied; these consisted of 29 CSF specimens and 26 serum specimens. This was performed over a 3-month period. The residual specimens were inoculated into transport vials using a tuberculin syringe; the inoculum volume varied depending upon the amount of residual specimen, but it ranged from 150 to 500 µL. The inoculated vials were held at room temperature for 1.5 to 5 h. All specimens were then tested per the routine CALAS protocol.

All of the 55 specimens that were placed into the BBL Port-A-Cul Transport vial and tested for the presence of the cryptococcal antigen using the CALAS CAD test were positive, with reaction strengths of 2+ or 3+. Three of the falsely positive samples were diluted to obtain a titer; two samples were positive at a 1:64 dilution, and one was positive at a 1:32 dilution.

In addition, five mock specimens that consisted of saline were tested; for these, saline was introduced into the BBL Port-A-Cul anaerobic transport device, as described above. The same saline control was CAD negative prior to introduction to the BBL Port-A-Cul anaerobic transport device. These five mock specimens were also falsely positive for the presence of the cryptococcal antigen.

In summary, this study demonstrated that the BBL Port-A-Cul anaerobic transport device is an inappropriate specimen container for CSF that will be tested for the presence of the cryptococcal antigen using the CALAS CAD test. This study demonstrates the importance of thoroughly assessing preanalytic components associated with testing (e.g., a transport container in this instance), as these may affect both the analytic and postanalytic phases of testing.

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REFERENCES


