Hyphal and Yeast Forms of Histoplasma capsulatum Growing within 5 Days in an Automated Bacterial Blood Culture System

An afebrile, 37-year-old, HIV-positive man, noncompliant with antiretroviral therapy, presented to the emergency department (ED) complaining of shortness of breath for 3 weeks. After an unremarkable chest radiograph, a bronchoalveolar lavage (BAL), and the collection of other diagnostic specimens, he left against medical advice. His CD4 count was 22/ml and his HIV viral load was 459,000 genomes/ml. Bacterial and viral cultures of the BAL fluid were negative. The BAL fluid was negative for Pneumocystis jirovecii by direct fluorescent antibody staining (DFA; Meridian Bioscience, Cincinnati, OH). DFA (Scimedx, Denville, NJ) and culture of the BAL fluid were also negative for Legionella pneumophila, as was the urinary antigen (Alere, Scarborough, ME). No fungal culture was ordered. Three bacterial blood culture sets were incubated in the Bactec 9240 system (Becton, Dickinson, Sparks, MD) at 35°C. We incubate such cultures for 5 days before discarding the negatives. Two sets were discarded as negative at 5 days. At 4 days, 23 h, and 18 min, the Bactec system flagged the aerobic bacterial blood culture bottle from the third set as positive. Gram stain revealed small budding yeast cells. Subcultures at 35°C grew small, budding yeast cells, while those incubated at 25°C grew hyphal forms with echinulate macroconidia, consistent with Histoplasma capsulatum. This identity was confirmed by DNA probe (GenProbe, San Diego, CA) and by conversion of the yeast form to the hyphal form upon incubation at 25°C. The fungal blood culture, collected in an Isolator 10 lysis-centrifugation tube (Wampole, Cranbury, NJ), also grew H. capsulatum after 2 weeks of incubation. Multiple unsuccessful attempts were made to locate the patient.

Four months later, he was brought unconscious to our ED and died within 6 h. Autopsy was not performed. Tests obtained at our hospital prior to death included a blood count with differential and three bacterial blood culture sets. The differential smear contained intracellular budding yeast (Fig. 1A). All three aerobic blood culture bottles turned positive with incubation times between 4 days, 5 h, and 4 days, 22 h. Gram stains of fluid from the positive bottles (Fig. 1B) exhibited both budding yeast and hyphal elements. Subcultures grew H. capsulatum, the identity of which was confirmed as described above.

This case has several unusual features. Intracellular budding yeast forms were seen on the hematology differential smear of the blood sample drawn just before the patient’s death. This has been previously reported, albeit rarely (1, 5). We were unable to find literature reports of the growth of H. capsulatum in the aerobic bacterial blood culture bottle within the standard 5-day incubation. However, there are reports of its growth in the radiometric Bactec mycobacterial culture system which was incubated longer (3, 4).

After 4 months of presumptive fungemia, this severely immunocompromised patient, who was not known to have received any antifungal or antiretroviral medications, had a high organism load at the time of death: this was evidenced by the presence of yeast in the predeath hematology smear. That high organism load, combined with more than 4 days of replication, apparently allowed enough metabolic activity to trigger the detection system in the Bactec instrument. The presence of both hyphal and yeast forms

FIG 1 Histoplasma capsulatum as seen in specimens collected on the patient’s second visit. (A) Peripheral blood smear stained with Wright-Giemsa, with the black arrow pointing to the intracellular budding yeast. (B) Gram stain of blood from the aerobic bacterial blood culture bottle when it turned positive at 4 days and 22 h. Black and white arrows point to the budding yeast and hyphal elements, respectively. Original magnification, ×1,000.
in the premortem blood culture bottles is unexpected as *H. capsulatum*, a thermally dimorphic fungus, should grow only as a yeast at this temperature (2, 5). These observations suggest that dimorphism can occur in response to stimuli other than temperature changes, perhaps including organism factors, components of the blood culture medium, the patient’s advanced immunodeficiency, or the unusually high number of organisms in the liquid culture medium.

ACKNOWLEDGMENT

We thank Robert Mitchell for the photography.

REFERENCES


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