**Clostridium glycolicum** Bacteremia in a Bone Marrow Transplant Patient

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We describe a case of **Clostridium glycolicum** bacteremia and septic shock in an adult woman with a recent bone marrow transplant for relapsed Hodgkin’s disease. The bacterium was identified by 16S rRNA gene sequencing. This is the first published report of the recovery of this organism from human clinical material.

**CASE REPORT**

The patient was a 43-year-old woman with biopsy-proven nodular sclerosing Hodgkin’s disease diagnosed in early 2003 after she presented with progressive left anterolateral chest discomfort, chest wall swelling, and eventually, dyspnea. She was found to have a 10-cm mediastinal mass associated with left axillary lymphadenopathy, a left pleural effusion, and involvement of the left anterior chest wall. Despite completing eight cycles of chemotherapy with doxorubicin-bleomycin-vinblastine-dacarbazine, she failed to achieve a remission. She eventually underwent an unsuccessful autologous stem cell transplant in February 2004, after which she required radiotherapy and a 6-month course of chemotherapy to help control her disease, but her symptoms persisted. She received an allogeneic bone marrow transplant in October 2005 after marrow ablation with fludarabine, busulfan, and antithymocyte globulin but developed septic shock on day 1 posttransplantation, necessitating transfer to the intensive care unit (ICU). In addition to supportive measures, empirical therapy with intravenous vancomycin, gentamicin, and ciprofloxacin was initiated after three sets of blood samples cultured with the BacT/Alert (bioMerieux Inc., Durham, NC) FA (aerobic) and FN (anaerobic) systems were collected. Within 24 h, all three anaerobic blood culture bottles were positive for large, gram-positive, rod-shaped bacteria resembling **Clostridium** spp., while two blood culture sets also demonstrated the presence of gram-positive cocci resembling streptococci. Forty-eight hours after subculture to brucella blood agar plates (PML Microbiologicals, Wilsonville, OR) incubated anaerobically at 35°C, tiny colonial growth (colonies approximately 2 mm in diameter) of a gray-white, nonhemolytic, motile, obligately anaerobic gram-positive bacillus with terminal endospores was observed. These observations, along with the results of other biochemical tests, confirmed the identity of the organism as a member of the genus **Clostridium**, although definitive identification to the species level relied on the results of partial sequencing of the 16S rRNA gene with MicroSeq 500 kits and an ABI Prism 3100 sequencer (Applied Biosystems, Foster City, CA). A BLAST search of the GenBank database and detailed phylogenetic analysis supported an identification of **Clostridium glycolicum**, based on 99.0% to 99.7% sequence identity of our 387-bp sequence (GenBank accession no. DQ986354) to those of four other strains of **C. glycolicum** in the GenBank database. The isolate was susceptible to penicillin G (MIC = 0.125 μg/ml), clindamycin (MIC = 0.064 μg/ml), and metronidazole (MIC = 0.19 μg/ml) by Etest methodology. Additionally, a gram-positive coccus identified as an **Enterococcus** sp. (ampicillin susceptible) was recovered aerobically and anaerobically from two blood culture sets. After the blood culture Gram stain results were reported, and the patient’s antibiotics were changed to intravenous ampicillin, aztreonam, and metronidazole. After the susceptibility test results were available, the antibiotics were switched to ampicillin, gentamicin, and metronidazole to complete a 2-week course of therapy. After 36 h in the ICU, she was transferred to the general medical ward. Her clinical condition gradually improved over the course of her stay in hospital, and she eventually demonstrated evidence of bone marrow engraftment but required ongoing standard post-bone marrow transplant medical care.

**Discussion.** The genus **Clostridium** is a group of anaerobic, endospore-forming gram-positive rod-shaped bacteria with various phenotypic characteristics (1). Over 150 species of **Clostridium** have been described to date (13), and while most have typically been considered harmless soil saprophytes or inhabitants of the human or animal gut, an increasing number are being reported as causes of human disease (1, 8–11, 16). Most human clostridial infections are endogenous, usually occurring secondary to the local or widespread dissemination of gut-colonizing strains as a result of perturbed host defenses caused by trauma, hypoxia, diabetes mellitus, alcoholism, chemotherapy, radiotherapy, and/or malignancy (1, 22).

**Clostridium glycolicum** is a species that was first described in 1963 by Gaston and Stadtman (15). Those investigators reported the isolation of a unique anaerobic gram-positive bacterium from a specimen of mud obtained from a pond in Maryland (15). Their isolate was a long, slender, motile, gram-positive endospore-forming rod-shaped bacterium capable of utilizing ethylene glycol as a source of energy and carbon, hence the species name (15). **Clostridium glycolicum** has since been recovered from a variety of soils and environmental niches in different geographic regions of the world (4, 6, 20, 23). The organism has also been isolated from human and...
bovine feces (7). In 1987, the first and only published report of animal infection due to C. glycolicum was described in a young addax with myonecrosis of the buttock and hind legs (17). As far as we know, there are no published reports of C. glycolicum human infection in the world literature, although the recovery of this organism from clinical sources (wounds, peritoneal fluid) has previously been documented in published texts (1, 12).

Microscopically, C. glycolicum is a gram-positive straight or slightly curved motile, rod-shaped bacterium (0.3 to 1.3 μm wide by 2 to 15 μm long) that occurs singly or in pairs and that commonly displays subterminal or terminal endospores (4, 5, 12, 15, 18, 20, 24). Colonies are approximately 2 mm in diameter and are typically flat and round with smooth symmetrical borders (15). Virtually all strains demonstrate strict anaerobic growth properties (4, 5, 18), although an aerotolerant strain of C. glycolicum recovered from sea grass roots has been reported (20). Phenotypically, C. glycolicum is a nonhemolytic, weakly saccharolytic organism which demonstrates negative tests for lecithinase and lipase production, gelatin liquefaction, nitrate reduction, catalase production, and esculin hydrolysis, characteristics that differentiate it from most other clinically important Clostridium spp. except C. symbiosum, from which it may be distinguished by gas-liquid chromatography (4, 5, 15, 19, 24). An additional taxonomically recognized characteristic of C. glycolicum is its ability to metabolize cinnamic acids (4). However, reliance on an extensive battery of biochemical and other phenotypic tests for organism identification may be considered too time-consuming and labor-intensive in today’s clinical microbiology laboratory. Molecular techniques, such as automated DNA sequencing, are playing an increasingly important role in infectious disease diagnostics worldwide. Many laboratories are resorting to 16S rRNA gene sequencing for the definitive identification of bacteria that cannot easily be identified to the genus or species level by the use of standard phenotypic tests.

Although C. glycolicum was recovered from three consecutive blood culture sets from our patient, the concomitant recovery of an Enterococcus sp. from two of these two sets may obscure the potential clinical importance of C. glycolicum in humans. Like many Clostridium spp., Enterococcus spp. are also found as normal inhabitants of the human colon and may similarly cause bacteremic disease in patients with perturbed host defense mechanisms (22). Polymicrobial bacteremia is frequently observed in patients with Clostridium bloodstream infections, particularly in the setting of severe sepsis or septic shock (2, 21, 22, 25), whereby Clostridium spp. and infectious agents such as Enterococcus spp. may act as copathogens. Severe sepsis or septic shock occurs in approximately 40% of patients with Clostridium bacteremia and, in this setting, is associated with a mortality rate of over 50% (3). Patients with hematological malignancies, particularly those experiencing partial failure of chemotherapy, have been shown to be at increased risk for Clostridium bacteremia, with or without sepsis or septic shock (2, 3, 25). The rigorous chemotherapeutic regimens used for the treatment of hematological malignancies are typically associated with damage to the mucosa of the gastrointestinal tract, leading to potential translocation of anaerobic bacteria such as Clostridium spp. from the gut to the bloodstream (3, 25). Presumably, the source of our patient’s C. glycolicum was the gastrointestinal tract, although this remains to be proven. Further study, presumably by use of an animal model, is required to determine the true pathogenic potential of C. glycolicum, although the clinical importance of this organism in our patient appears to be supported by the patient’s clinical presentation and the recovery of the organism from multiple blood collections.

Limited information is available regarding the putative antimicrobial susceptibility profiles of C. glycolicum strains. However, Finegold and colleagues reported agar dilution susceptibility results for nine fecal isolates of C. glycolicum, with all strains demonstrating susceptibility to amoxycillin-clavulanate, clindamycin, metronidazole, and vancomycin (14). In a similar regard, our isolate was susceptible to penicillin G, clindamycin, and metronidazole, which is typical of most Clostridium spp. Phylogenetically, C. glycolicum does not display very close 16S rRNA gene relationships with other Clostridium species of known medical importance.

In summary, C. glycolicum is an anaerobic gram-positive rod-shaped bacterium that may be implicated as a cause of bacteremia and septic shock in immunocompromised patients. The clinical significance and pathogenic potential of C. glycolicum, however, awaits further study.

**Nucleotide sequence accession number.** The rRNA gene sequence of the C. glycolicum isolate evaluated in this study has been placed in GenBank under accession no. DQ986354.

**REFERENCES**


