Short Communication

*Mycobacterium chelonae* Complex Bacteremia from a Post-Renal Transplant Patient: Case Report and Literature Review

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SUMMARY: In this report we present a case of a young lady with abdominal abscesses and septicemia caused by *Mycobacterium chelonae* complex. Identification of the organism and initiation of the appropriate antimicrobial therapy was delayed, resulting in significant morbidity and multiple hospital admissions. Gram staining of these organisms from blood culture can be easily overlooked or confused with either debris or diptheroids. We concluded that detection of Gram-positive rod colonies should prompt an acid-fast stain to distinguish diphtheroids from rapidly growing mycobacteria in immunosuppressed patients.

Non-tuberculous *Mycobacterium* (NTM), which are rapidly growing mycobacteria, were previously called atypical mycobacteria or mycobacteria other than tuberculosis. The improvement in mycobacterial cultures and the development of new molecular techniques resulted in a dramatic expansion in the number of identified mycobacterial organisms, now including over 100 different species (1). Rapidly growing mycobacteria of Runyon group IV produce mature growth on agar plates within 7 days. They include a clinically insignificant pigmented group and a non-pigmented group that includes the *Mycobacterium fortuitum* complex (*Mycobacterium chelonae*/*abscessus*) (2,3).

We report a case of a 27-year-old female with abdominal sepsis due to *M. chelonae*. The patient had end-stage renal disease requiring dialysis for the last 7 years. She underwent renal transplantation in the Philippines on the 9th of February 2008. This was complicated by acute rejection requiring nephrectomy 2 weeks later. She had continuous intermittent fever following surgery.

The patient was admitted to our institution on the 11th of March 2008 for an arteriovenous fistula insertion of a permanent catheter. On the first post-surgical day, she developed a high-grade fever reaching 39°C. On examination, she was afebrile and hemodynamically stable. Apart from tenderness in her right lower abdominal quadrant, her physical examination was unremarkable. The transplant surgical scar appeared healthy, with no sign of infection. Her initial laboratory tests were as follows: hemoglobin, 109 g/L; leukocyte, 3.0; platelets, 197; neutrophils, 82.7%; lymphocytes, 2.1%; and monocytes, 11.7%. Urea was 11.3 mmol/L, creatinine was 1,025 mmol/L, and electrolytes were normal. Albumin was 26 g/L. Liver enzymes and the coagulation profile were normal. Blood cultures were collected on the 11th, 14th, and 15th of March 2008, and all were positive for long thin-beaded Gram-positive bacilli. The organism grew on a blood agar plate and was resistant to all the routinely used antibiotics for Gram-positive bacteria (penicillin, all cephalosporins, erythromycin, clindamycin, tetracycline, and vancomycin).

Modified Kinyoun staining was done on the 23rd of March and showed acid-fast bacilli (AFB) in all positive blood culture samples. The plates were then moved to a level III laboratory. Ziehl-Neelsen (ZN) staining was repeated on all positive blood cultures, and all were positive for AFB (Figure 1). The result was reported to the treating physician. The standard solid and liquid mycobacterial media were inoculated. On the day of admission, the 11th of March, she was started empirically on ceftazidime. After the results of the blood cultures were obtained, vancomycin was added. The fever persisted despite this antibiotic coverage. Abdominal ultrasonography (US) revealed a left iliac fossa collection. A US-guided pigtail catheter was inserted and 250 cc of pus was drained. The pus was sent for microbiological investigation including ZN staining and mycobacterium cultures. Piperacillin/tazobactam 2.25 mg intravenously (i.v.) every 8 hours was added.
and the fluid from the right iliac fossa shown in Figure 1 by ZN staining. The isolates from the blood, abdominal fluid, Bacterial Growth Indicator Tube (MGIT), flagged the blood beaded bacilli. On the 2nd of April a liquid medium, the Myco-
were positive and showed Gram-positive long filamentous
3.7 cm (Figure 2).

weeks later, she was readmitted with high-grade fever reaching 40°C, accompanied by vomiting, sweating, and chills. An abdominal ultrasound examination was performed that revealed a considerably large, oval serous area with posterior acoustic enhancement indicating loculated fluid collection in the left iliac fossa measuring 6.2 × 3.8 × 4.7 cm (Figure 2).

Blood and peritoneal fluid cultures were requested. Both were positive and showed Gram-positive long filamentous beaded bacilli. On the 2nd of April a liquid medium, the Mycobacterial Growth Indicator Tube (MGIT), flagged the blood culture as positive, and the results were confirmed as AFB by ZN staining. The isolates from the blood, abdominal fluid, and the fluid from the right iliac fossa shown in Figure 1 were similar and all were identified as M. chelonea complex by the following tests: growth on para-aminobenzoic acid containing Lowenstein-Jensen (LJ) medium, MacConkey agar at 28°C, positive arylsulfatase test, negative nitrate reduction and iron-uptake tests at 28°C, negative 5% NaCl tolerance test, and no pigment production. Although the 5% NaCl tolerance test and the positive test for citrate utilization at 28°C presumptively identified this isolate as M. chelonea and differentiated it from M. abscessus, the final identification we got from the molecular method was M. chelonea complex using INNO-LIPA MYCOBACTERIA v2 (Innogenetics, Ghent, Belgium).

The organism had the following MIC results: ciprofloxacin, 32 μg/ml; clarithromycin, 0.5 μg/ml; amikacin, 1.5 μg/ml; tetracycline, 8 μg/ml; and linezolid, 16 μg/ml. The antibiotic treatment was revised and the patient was started on i.v. amikacin 400 mg post-dialysis, ciprofloxacin 500 mg orally once a day, and clarithromycin 250 mg orally twice a day. Two weeks later, the patient was seen in the outpatient clinic in stable condition and was totally asymptomatic. The patient was followed up multiple times during and after 6 months of treatment, and she remained asymptomatic, with no treatment-related side effects.

Atypical mycobacteria are found in soil, dust, water, ani-
mals, hospital water systems, and hemodialysis and dental devices. Low nutrients, low pH, and temperature extremes as well as biofilm formation on rubber and plastic are all successful survival strategies for these very hydrophobic organisms. In addition, they are resistant to standard disinfectants such as chlorine, organomercurials, and alkaline glutaraldehydes (4–6).

NTM can cause pseudo-infection due to laboratory cross-contamination, contaminated instruments, or contaminated solutions. A single isolate from a sterile body site or multiple isolates from a non-sterile site should be considered significant, especially in immunocompromised hosts. Although they have low pathogenicity, they can result in serious infection when introduced to sterile body sites (7,8).

In dialysis patients, colonization of potable water or reused hemodialysis filters can lead to M. fortuitum peritonitis in patients on continuous ambulatory peritoneal dialysis (CAPD) (9–12).

In surgical patients, M. fortuitum and M. chelonea are associated with sternal wound infection and endocarditis following cardiac surgery (13–16). M. chelonea led to pericarditis and endocarditis following porcine valve implants (17–19). It has also been associated with vein graft harvest site infection after cardiac bypass surgery (20). In addition, it can colonize hospital water systems. A reported outbreak of infection with this organism occurred in 22 cases of post-rhinoplasty cellulitis due to inadequate sterilization of surgical equipment (21). M. fortuitum and M. chelonea were also responsible for the majority of the NTM infections seen after augmentation mammoplasty (22–25). They also lead to wound infections after minor dermatological or laparoscopic surgery (26–28). Other NTM infections have been associated with invasive procedures such as bronchoscopy (29–32) or due to contamination of histopathological specimens (33).

Although most of the disseminated NTM infections have been reported in immunocompromised patients such as solid organ transplant patients (34), it has also been reported in immunocompetent patients. A recent review of 129 cases demonstrated aggressive diseases related to these species, suggesting the potential role of genetic, geographic, and immunologic factors in the disease outcome (35).

Although there is a lack of clinical correlation studies between susceptibility testing and clinical outcome (except for rifampin in the case of M. kansasii and clarithromycin for M. avium complex [MAC]), susceptibility testing is indicated to optimize selection of appropriate therapeutic regimens, in addition to variability in the susceptibility profiles according to the species. M. abscessus is considered more resistant than M. fortuitum and M. chelonea (36). There is inter-laboratory variation especially with imipenem due to variations in the level of experience. Other antibiotics tested by this method include quinolones, telithromycin, and linezolid (37–39).

Susceptibility testing of the commercially available Sensititre microplate (Trek Diagnostic Systems, Cleveland, Ohio, USA) was also employed for this purpose.

The E-test is another method to test the susceptibility to these organisms (AB Biodisk, Solna, Sweden) (40). Susceptibility testing is done by microdilution broth using a microtiter plate and inocula prepared in Mueller-Hinton (MH) or 7H9 broth followed by assessing the MIC at 72 h (41). Clinical and Laboratory Standards Institute (CLSI) interpretive criteria to assess broth microdilution for rapidly growing mycobacteria is available (41,42).

The in vitro susceptibility patterns of rapidly growing
mycobacterium that has been reported are unpredictable, and they are indicated for clinically significant isolates after the patient has been started on empirical treatment (43). Clarithromycin resistance and therapeutic failure resulting from a point mutation at position 2058 of 23S rRNA has been reported in patients with disseminated cutaneous infections who had clarithromycin monotherapy (44). Combined surgical and antimicrobial therapy may be required for treatment of these organisms. Both clarithromycin and azithromycin have been used successfully for durations of 4–6 months in case of skin infection (45). However, in cases of serious infection such as that of bone, amikacin and imipenem or cefoxitin can be added for the first 2–6 weeks (46). Linezolid can also be used in case of resistance to clarithromycin or in combination with other drugs in aggressive infections (38).

Unlike the M. tuberculosis complex, atypical mycobacteria, including rapidly growing mycobacterium, do not spread from one patient to another. The control of atypical mycobacteria in general is challenging due to their high lipid content, formation of biofilm, and resistance to disinfectants, high temperature, and UV light. Semicritical devices need cleaning and terminal rinsing with 2% glutaraldehyde for 20 min at 20°C (47). Other agents, such as 0.2–0.35% peracetic acid, 0.5% glutaraldehyde, 0.03% phenolic compounds, and alkyl compounds are also effective (48,49). In an outbreak situation, adequate surveillance of environmental sources by infection control teams is indicated. Application of molecular typing to identify the source, the institution of the environmental infection control measure, and decontamination of the equipment and plumbing fixtures may be required. Regular maintenance of the hospital water system, using sterile water and single-use devices, will help prevent infection by these organisms (50).

In conclusion, the appearance of beaded Gram-positive rods from blood culture and other sterile sites should prompt ZN staining to distinguish diphtheroids from rapidly growing mycobacteria in immunosuppressed patients. Identification of the M. fortuitum complex includes growth on MacConkey agar without crystal violet within 7 days and with a positive 3 days arysulfatase. Iron-uptake and nitrate-reduction tests can distinguish between M. fortuitum and M. chelonae, only the latter of which is negative for these two tests. Molecular methods play an important role in the definite identification of these organisms. To identify these organisms, susceptibility testing is indicated if rapidly growing mycobacterium is isolated from a sterile site (51).

REFERENCES


