Catheter Sepsis Due to Mycobacterium chelonae

We read with interest the recent article by Hsueh et al. on catheter sepsis due to Mycobacterium chelonae (3).

In the antimicrobial susceptibility section, the clarithromycin MIC is reported to be 1.5 to 2.0 μg/ml. The authors later state, “...our isolates were not susceptible to any of the antibiotics tested, including clarithromycin.” In another study (1), which found 100% of M. chelonae isolates to be susceptible to ≤1.0 μg of clarithromycin per ml (by a different susceptibility method), resistance is defined as >4 μg/ml. This breakpoint for rapidly growing mycobacteria, although not approved by the National Committee for Clinical Laboratory Standards (NCCLS), has been proposed (2). Thus, we would consider these isolates to be susceptible to clarithromycin and suspect the somewhat higher MICs than reported by Hsueh et al. (3) could be method dependent (E test versus broth microdilution). Thus, clarithromycin likely contributed to the clinical and microbiologic response of the patient.

REFERENCES

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Authors’ Reply

We thank Drs. Wallace and Brown for their interest in our paper and for their concern about the susceptibility of the Mycobacterium chelonae isolates to clarithromycin (4). The letter from Drs. Wallace and Brown addresses two important questions that deserve more attention and need more study. First, the M. chelonae isolates for which E-test clarithromycin MICs were 1.5 to 2 μg/ml should be considered susceptible. Second, clarithromycin likely contributed to the clinical and microbiologic responses of the patient.

Before we respond to their comments, we should give a more detailed description of our patient. In the paper, we stated that the patient had a satisfactory response to treatment with clarithromycin (500 mg every 12 h), ciprofloxacin (300 mg every 12 h), and amikacin (750 mg every 12 h) for 1 month, followed by 2 months’ treatment with clarithromycin (500 mg every 12 h) and ciprofloxacin (300 mg every 12 h). We discontinued the antibiotics because the patient suffered severe gastrointestinal upset and abnormal liver function was noticed. Follow-up examinations disclosed the disappearance of the lesions over the right lung and the right subclavian vein. However, 2 months after the discontinuance of antimicrobial therapy, the patient had a fever and developed a subcutaneous mass (2 by 3 cm) over her left leg. Cultures of the aspirate specimen also yielded the M. chelonae isolate with two morphotypes. The clarithromycin E-test MIC (2 μg/ml) and the random amplified polymorphic DNA patterns (with five primers) of the isolates were identical to those of isolates A to D described previously (4). A whole-body gallium scan revealed no evidence of other foci of infection. The patient underwent surgical debridement and is now on the third month of treatment with clarithromycin (500 mg every 12 h) and ciprofloxacin (300 mg every 12 h).

Determination of MIC breakpoint criteria to define susceptibility for an antimicrobial agent-microorganism combination is based on pharmacokinetic data, population distribution of MICs, and studies of clinical efficacy. As Drs. Wallace and Brown mentioned, the MIC breakpoint criteria for susceptibility of M. chelonae to clarithromycin (susceptible, ≤2 μg/ml; intermediate, 4 μg/ml; resistant, ≥8 μg/ml) have not been approved by the NCCLS. The interpretive values that appeared in the ASM handbook were obtained from Abbott Laboratories, Abbott Park, Ill. (3). However, different MIC breakpoint criteria for rapidly growing mycobacteria (susceptible, ≤1 μg/ml; moderately susceptible, 2 μg/ml; resistant, ≥4 μg/ml) were also suggested by other investigators (2). Furthermore, these other investigators found that for 51 (51%) of 100 isolates of rapidly growing mycobacteria, clarithromycin E-test MICs were 1 to 3 log₂ dilutions lower than MICs determined by the reference agar dilution method (2).

Until now, no large-scale controlled clinical trials have documented the clinical efficacy of clarithromycin for treating invasive infections caused by M. chelonae, and the appropriate regimen for this infection remains undetermined (1). In a study regarding the clinical efficacy of clarithromycin monotherapy for treatment of 14 patients with cutaneous (disseminated) M. chelonae infections, 1 patient was initially given clarithromycin at a dosage of 1.0 g twice a day, because of a high clarithromycin MIC of 1 μg/ml (5). The remaining 13 patients, who received clarithromycin at a dosage of 500 mg or 1 g twice a day, all had isolates for which clarithromycin MICs were ≤0.25 μg/ml (5). On the other hand, the clarithromycin MIC for the isolate recovered from our patient was 2.0 μg/ml. The contribution of clarithromycin only at the prescribed dosage to the clinical and microbiologic responses of our patient remains questionable. In this situation, defining an isolate as susceptible or resistant to clarithromycin according to the previously declared or suggested criteria might be inappropriate.

Maybe we should change the statement “In contrast, our isolates were not susceptible to any of the antibiotics tested, including clarithromycin,” to “In contrast, all antibiotics tested except for clarithromycin had poor activities against our isolates.”

REFERENCES


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