Clarithromycin-Resistant *Mycobacterium avium* Strain in a Clarithromycin-Naive AIDS Patient

Disseminated *Mycobacterium avium complex* (MAC) infection occurs frequently in patients in the late stage of HIV disease. The recent introduction of clarithromycin has been a major advance for the treatment of MAC infection. However, clarithromycin-resistant MAC strains have emerged in AIDS patients during prophylaxis and treatment [1]. To our knowledge, we describe the first case in which a clarithromycin-resistant MAC strain was isolated from a patient who was not treated with this drug.

A 37-year-old HIV-infected patient with cerebral toxoplasmosis had been treated with pyrimethamine (50 mg/d) and clindamycin (2,400 mg/d) since May 1995. His CD4 cell count was 13/mm$^3$. In August 1995, he was admitted to the hospital with asthenia and fever but had no significant clinical findings on physical examination. A MAC strain, identified by the Gen-Probe (San Diego, CA) hybridization method, was isolated from two blood samples. The MIC for clarithromycin was determined by radiometric Bactec (Becton Dickinson, Le Pont de Claix, France) and Etest (AB BIO-DISK, Solna, Sweden) methods at a pH of 7.4 [2]. This strain was resistant to clarithromycin (MIC $\geq$ 256 $\mu$g/mL).

This patient had been followed up exclusively in our institution since 1991. An extensive search revealed that he had never received clarithromycin or any other macrolide. Although nosocomial transmission of MAC has not previously been reported, we searched for other patients who had acquired resistant MAC strains during the same period. Only one other MAC isolate was found in our patient’s unit, and typing of both strains by pulsed-field gel electrophoresis revealed different genomic profiles, ruling out the possibility of nosocomial transmission. Finally, careful analysis of our patient’s drug regimen showed that he had received only clindamycin for toxoplasmosis.

Although lincosamides have poor in vitro activity against MAC [3], it is possible that because these antibiotics are at a high concentration in MAC-infected macrophages, they may select for clarithromycin-resistant strains [4]. It is of interest that the clarithromycin-resistant MAC isolate harbored a point mutation in the peptidyl domain of the 23S ribosomal RNA gene, as has been found in clarithromycin-resistant strains selected after clarithromycin therapy [5].

Our report emphasizes that clarithromycin-resistant MAC strains may be found in patients who have not been treated with clarithromycin and that these strains may be selected by lincosamide treatment. These findings may suggest that MAC isolates should be tested for clarithromycin susceptibility by using recently described in vitro methods [2].

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**References**


The Hidden Danger of Primary Fluconazole Prophylaxis for Patients with AIDS

The use of primary fluconazole prophylaxis has significantly reduced the prevalence of oropharyngeal candidiasis and has essentially eliminated cryptococcosis in HIV-infected patients [1]. We recently encountered two patients with AIDS who developed cryptococcal meningitis while receiving primary fluconazole prophylaxis. Both patients had advanced AIDS, with CD4 cell counts of 14/mm$^3$ and 22/mm$^3$, respectively. They had been receiving fluconazole prophylaxis on a continuous basis for 4 years (dose: 100 mg/d) and 17 months (dose: 400 mg/d), respectively. One patient’s compliance in taking fluconazole was confirmed by pharmacy refill records. One patient presented to the hospital with ataxia and confusion, and the other presented with fever and headache.

*Cryptococcus neoformans* was recovered from the CSF of both patients. Fluconazole MICs for these two isolates were 16 $\mu$g/mL and $\geq$32 $\mu$g/mL, respectively [2]. The first patient received a 3-day course of amphotericin B (0.6 mg/kg) followed by fluconazole (600 mg/d). The second patient received a 2-week course of amphotericin B (0.6 mg/kg) and flucytosine (100 mg/kg) followed by...