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First Report of Macrolide Resistance in a *Mycoplasma pneumoniae* Isolate Causing Community-Acquired Pneumonia in Spain

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Mycoplasma pneumoniae is a common cause of community acquired pneumonia (CAP) (1). Macrolides are first-choice agents, but resistance is possible by point mutations in domain V of the 23S rRNA gene (1, 2). Asiatic countries have the highest proportion of macrolide resistance, but in Europe it still seems low (3–9). We present the first report in our country of a macrolide-resistant *M. pneumoniae* (M^RMpn) strain with a point mutation in its 23S rRNA isolated from an adult patient with CAP.

On September 2012, a previously healthy 23-year-old Chinese female presented to our hospital's emergency department with an 8-day history of fever and respiratory symptoms. The patient had been studying in Spain for 1 year, and she returned from a 1-month trip to China and Korea 13 days before the onset of symptoms. Clinical examination and laboratory findings were consistent with severe pneumonia, and a chest ray demonstrated bilateral alveolar infiltrates in her lower right lobe and upper left lobe.

Sputum and serum samples were sent for microbiological diagnosis of CAP. Sputum was seeded in conventional media and in *M. pneumoniae* media. Total DNA from sputum was extracted, and specific real-time PCR schemes for *M. pneumoniae* and for influenza virus and other respiratory viruses were performed. Serological studies included the detection of specific antibodies against *M. pneumoniae*, *Chlamydophila pneumoniae*, *Legionella pneumophila*, and the agent of Q fever by enzyme-linked immunosorbent assay methods.

Common causative agents of CAP were excluded after negative results were obtained for conventional sputum cultures, serology, and specific PCRs. Diagnosis of *M. pneumoniae* was established on the basis of positive PCR results (day 7 after admission) and confirmed by positive *M. pneumoniae* culture (10 days after sputum reception) and serological tests (IgM antibodies in the acute-phase serum sample and positive seroconversion in IgG antibody titers between samples of the acute and convalescent phases).

Antibiotic susceptibility tests of the isolate were performed by the diffusion gradient test, as previously described for *Mycoplasma hominis* and *Ureaplasma* spp. (10). The isolate showed a high level of resistance to erythromycin and azithromycin (MIC values $\geq$ 256 mg/liter) and was susceptible to tetracycline, levofloxacin, and moxifloxacin (MICs values of 0.094, 0.064, and 0.016 mg/liter, respectively) according to the recent Clinical and Laboratory Standards Institute breakpoints (11). Although this method is not yet validated for *M. pneumoniae*, these results were consistent with our molecular findings.

The 23S rRNA gene was amplified as previously described (12) from DNA obtained from culture. Amplicons were purified, sequenced, and compared with the 23S rRNA genes of susceptible reference strains (FH, M129) in the GenBank database. The only discrepancy observed was an A→G transition located at position 2063 (2058 by *Escherichia coli* numbering), which is the most frequent mutation associated with macrolide resistance (2–5).

Initially, the patient received a single dose of ceftriaxone and levofloxacin empirically, but an urticaria-like rash appeared, so treatment was changed to meropenem plus azithromycin. Over the next 7 days, her respiratory status declined, with worsening hypoxemia and persistency of symptoms, so when *M. pneumoniae* CAP was diagnosed (day 7 after admission), treatment was changed to doxycycline due to the high rates of resistance to macrolides in China and Korea (4, 5). Her clinical status markedly improved, and she was discharged on day 13 after admission.

Macrolide resistance may present problems in the future. M^RMpn CAP suspicion was based on the patient's travel history and on azithromycin treatment failure. Clinicians should be aware of respiratory infections in Asiatic patients, travelers, and native patients not responding quickly to macrolide therapy. Rapid methods for detection of macrolide resistance based on quantitative PCR or pyrosequencing are described in the literature (9, 12) and may be performed in this subset of patients. Treatment with quinolones or tetracyclines, especially in severe cases, should be considered.

ACKNOWLEDGMENTS

We are grateful to Luis de Rafael and María Isabel Morosini for technical support.

This study was supported by the Ministerio de Economía y Competitividad, Instituto de Salud Carlos III, and cofinanced by the European Development Regional Fund (A Way To Achieve Europe) (ERDF) and the Spanish Network for Research in Infectious Diseases (grant REIPI RD12/0015).

We have no conflicts of interest to declare.

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Published ahead of print 2 December 2013

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doi:10.1128/AAC.02325-13

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