Fluoroquinolone-Resistant Mycoplasma genitalium, Southwestern France

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To the Editor: Mycoplasma genitalium is a sexually transmitted bacterium involved in nongonococcal urethritis in men and associated with cervicitis and pelvic inflammatory disease in women. Azithromycin regimens have been commonly used as a first-line treatment of these conditions, but a recent increase in M. genitalium with azithromycin resistance has been described worldwide; in 2012, resistance in the organism was detected in France at a prevalence of 14% (1). In case of azithromycin failure, moxifloxacin is a second-line treatment; however, moxifloxacin treatment failures have also been reported and are associated with mutations in ParC or GyrA (2).

Prevalence of M. genitalium infection was ≈4% in 2013–2014 at Bordeaux University Hospital (Bordeaux, France). To evaluate the prevalence of fluoroquinolone resistance in M. genitalium in southwestern France, we examined the quinolone resistance–determining regions (QRDRs) of the gyrA and parC genes in M. genitalium–positive specimens obtained during 2013–2014. We retrospectively collected (from the Department of Bacteriology, Bordeaux University Hospital) 369 M. genitalium–positive urogenital specimens and DNA extracts from 344 patients. The gyrA and parC QRDRs were amplified and sequenced as described (3,4). We also assayed macrolide resistance–associated mutations using real-time PCR and melting curve analysis (I). To determine resistant genotypes A2058G or A2059G, we sequenced PCR products. Nucleotide positions in the 23S rRNA and amino acid positions in GyrA and ParC were identified according to Escherichia coli numbering.

From the 344 M. genitalium–positive patients, 200 specimens underwent complete analysis for the gyrA and parC genes, specimens from 221 patients were investigated for macrolide resistance, and specimens from 168 patients were examined for 23S rRNA, gyrA, and parC genes. Unsuccessful amplifications could be attributed to low bacterial loads of M. genitalium or to the degradation of frozen DNA during storage. Strains from 12/200 patients (6%; 95% CI 3.47%–10.19%) had QRDR mutations, with rates of 6.4% (6/93) for 2013 and 5.6% (6/107) for 2014. This prevalence is in accordance with the 4.5% moxifloxacin resistance described in the United Kingdom in 2011 (3) but lower than prevalences found in small numbers of strains in Japan and Australia during 2006–2014, which ranged from 10% to 47% (4–8).

Strains from 11 patients (patient nos. 6, 8, 12, 20, 23, 28–31, 46, 47) harbored alterations in the ParC QRDR (Table) at positions 80 (Ser→Asn or Ile) or 84 (Asp→Tyr or Asn). These mutations have been previously described for M. genitalium (4,6–8). In addition, 1 new amino acid alteration, Asn–96→Ser (strain from patient 20), was found in ParC. We detected a GyrA modification with the Ala–93→Thr transition in a strain from 1 patient (patient 3). These 2 amino acid changes were not.

References

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previously reported; however, mutations at the next positions (97 in ParC and 95 in GyrA) have been described for *M. genitalium* (4,7), and these positions are within the QRDRs, suggesting their involvement in fluoroquinolone resistance. As previously described, *M. genitalium* ParC alterations predominate over GyrA alterations.

None of the 12 patients with strain *parC* or gyrA mutations had a history of fluoroquinolone treatment. Six patients received no treatment; 4 patients received azithromycin (1 g); 2 patients received extended azithromycin (1.5 g), 1 patient after azithromycin (1 g) failure, and 1 after receiving doxycycline for 7 days. Therapeutic outcomes were not available except for 1 patient, who experienced clinical failure after 2 azithromycin treatments.

Regarding macrolide resistance, 38 of 221 patients (17.20%); 95% CI 12.79%–22.72%) had *M. genitalium* with macrolide resistance–associated 23S rRNA mutations; prevalence was 17% (19/112) for 2013 and 17.4% (19/109)
for 2014. This prevalence is increasing compared to that described in France in 2012 (14%). We found 35 A-G substitutions at position 2058 or 2059, two A2062T mutations and one A2059C mutation (Table) (1,9). Notably, in patients 15 and 33, who were infected with strains with macrolide resistance–associated mutations, M. genitalium infection was unsuccessfully treated with azithromycin, with treatment failures after azithromycin (1 g) and extended azithromycin (1.5 g for 5 d), but moxifloxacin treatment was effective. Patient 15 had been treated 1 year earlier with azithromycin (1 g) for nongonococcal urethritis.

Among the 168 patients whose isolates were examined for the 23S rRNA, gyrA, and parC genes, strains from 2 patients (patients 3 and 6) had both macrolide- and fluoroquinolone-associated mutations (1.2%; 95% CI 0.33%–4.24%). Both patients received azithromycin (1 g), and patient 6 received additional azithromycin (1.5 g) after failure of azithromycin (1 g). Patient 6 experienced azithromycin failure again after the extended regimen. M. genitalium multidrug resistance is described in France at a prevalence of 1.2%, lower than prevalence described in Australia (7.5%) (7) and Japan (30.8%) (10).

In conclusion, M. genitalium fluoroquinolone resistance is emerging in France, with a prevalence of 6% in 2013–2014. Further, macrolide resistance also increased during this period, to a rate of 17.2%. Patients infected with M. genitalium strains containing both macrolide and fluoroquinolone resistance mutations associated with therapeutic failure raise concerns about untreatable M. genitalium infections.

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References


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Possible Transmission of mcr-1–Harboring Escherichia coli between Companion Animals and Human

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To the Editor: Plasmid-mediated, colistin-resistance mechanism gene mcr-1 was first identified in Escherichia coli isolates from food, food animals, and human patients in November 2015 (1). Reports on detection of mcr-1 in Enterobacteriaceae from humans and food animals

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