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Azithromycin Treatment Failure in *Mycoplasma genitalium*-Positive Patients with Nongonococcal Urethritis is Associated with Induced Macrolide Resistance.

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BACKGROUND: *Mycoplasma genitalium* is a common cause of nongonococcal urethritis. Treatment trials have shown that doxycycline is inefficient, whereas a 5-day course of azithromycin eradicates the bacterium from 95% of infected men. The aim of the study was to establish the reason for the occasional treatment failures.

METHODS: Seven *M. genitalium* strains isolated from men who experienced azithromycin treatment failure were tested for in vitro susceptibility to macrolides with use of a cell culture-based method. The genetic basis for the drug resistance was established by sequencing parts of the 23S ribosomal RNA gene and the genes encoding the L4 and L22 proteins. Nine sets of specimens obtained before and after treatment from patients who experienced azithromycin treatment failure were examined with use of sequencing of polymerase chain reaction products.

RESULTS: The 7 strains that were isolated from patients who experienced treatment failure with azithromycin had minimum inhibitory concentrations >8 microg/mL for azithromycin and erythromycin. Three different mutations at positions 2058 and 2059 (*Escherichia coli* numbering) in region V of the 23S rRNA gene were found. Of the 9 patients with specimens obtained before and after treatment, only 2 had an initial specimen in which the mutation was present, indicating that drug resistance was induced as the result of an inappropriate dosage of azithromycin.

CONCLUSION: Development of macrolide resistance was shown to correlate with subsequent azithromycin treatment failure. The genetic basis for the drug resistance was shown to be mutations in region V of the 23S rRNA gene, which is well described in other Mollicutes. These findings raise concern about the use of single-dose azithromycin treatment of nongonococcal urethritis of unknown etiology.

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