Nongonococcal Urethritis and Antibiotic-Resistant Mycoplasma genitalium Infection

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The finding of Mycoplasma genitalium in the urethra of men with nongonococcal urethritis (NGU) [1, 2] and its later unequivocal and significant association, not only with NGU as a whole, but also with chlamydia-negative NGU [3], has at least partially filled the void in our understanding of the etiology of NGU in men. Although tetracyclines (in particular, doxycycline) were the antibiotics of choice for the treatment of NGU before the finding of M. genitalium, it has become apparent that they are not the antibiotics of choice for M. genitalium–associated urethritis. Indeed, this mycoplasma was often found to persist in the urethra of men treated with tetracyclines [4, 5], and it became clear that tetracycline treatment was responsible for some, if not all, cases of persistent or chronic NGU. Fortunately, it seemed, azithromycin was available for the treatment of NGU before the finding of M. genitalium, and it has become apparent that they are not the antibiotics of choice for M. genitalium–associated urethritis. Indeed, this mycoplasma was often found to persist in the urethra of men treated with tetracyclines [4, 5], and it became clear that tetracycline treatment was responsible for some, if not all, cases of persistent or chronic NGU. Fortunately, it seemed, azithromycin was available for the treatment of Chlamydia trachomatis infection; azithromycin was more active in vitro than the tetracyclines, had superior mucosal cell penetration, and could be given effectively as a single dose. When azithromycin was given to M. genitalium–positive men with urethritis, the organisms were eliminated from the genital tracts of almost all patients; the patients responded accordingly, without the development of chronic disease [6]. In hindsight, this should not have been surprising, because the in vitro activity of tetracyclines against M. genitalium is poor, and the macrolides have far greater activity, with azithromycin being the most effective [7]. Interestingly, a similar antibiotic profile is seen with Mycoplasma pneumoniae, which is closely related antigenically to M. genitalium.

Thus, the notion that NGU of chlamydial or mycoplasmal etiology can be dealt with by a single antibiotic, namely azithromycin, has had considerable clinical appeal. Admittedly, Ureaplasma species are not very susceptible to azithromycin; however, that aside, our understanding of the etiology of NGU and the development of a rational treatment for the disease had progressed. Now, we learn that strains of M. genitalium have developed (and, doubtless, continue to develop) resistance to azithromycin through mutations in region V of the 23S ribosomal RNA gene [8]. This is a potentially serious matter because of the possibility that extensive use of single-dose azithromycin for treatment of C. trachomatis or for presumptive treatment of NGU might lead to the development of widespread resistance in M. genitalium strains and, therefore, to worsening disease in both men and women.

What measures might be taken to prevent an increase in the prevalence of resistance to azithromycin? Clinicians should realize that single-dose therapy for NGU may create the problem of resistance and that spreading the dosage over several days may overcome the problem. If this is not effective and there is evidence that chronic disease is developing, thought should be given to administering a course of moxifloxacin [9], which has potent activity against M. genitalium [10]. Hopefully, in the future, most clinicians will be able to rely on the assistance of laboratory analysis, which will enable them to make a sensible choice of antibiotic and dosage.

The treatment of NGU in patients who are also HIV positive is also uncharted territory. There is some evidence that such subjects are more susceptible to infection due to M. genitalium than are individuals who are HIV negative [11]. Furthermore, animal experiments have clearly shown that a fully functioning immune system is required for the elimination of mycoplasmas (as opposed to simply suppression of their growth) after antibiotic therapy [12]. It remains to be seen whether this is another hurdle that has to be faced in the
treatment of HIV-positive men who have NGU.

Acknowledgments


References