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Letters to the Editor

An Invasive Isolate of *Neisseria meningitidis* Showing Decreased Susceptibility to Quinolones

Antibiotic resistance in *Neisseria meningitidis* has not yet significantly compromised antibiotic treatment of invasive meningococcal disease (IMD) with penicillin or chloramphenicol but has developed more fully against agents used for chemoprophylaxis. Sulfonamides and tetracyclines can no longer be used for this purpose, and rifampin-resistant meningococci have also been encountered. The quinolones are also used for prophylactic purposes, particularly in adults. Recently, a serogroup B meningococcus, carried in the oropharynx of a sexually transmitted disease patient in Paris, was shown to have decreased ciprofloxacin susceptibility (I. Casin, B. Gandry, F. Lassau, M. Janier, P. Lagrange, and E. Collatz, Abstr. 39th Intersci. Conf. Antimicrob. Agents Chemother., abstr. 2101, 1999). We report what we believe is the first instance of a meningococcus from a patient with IMD showing decreased quinolone susceptibility.

In December 1998, a serogroup C meningococcus was cultured from the blood and cerebrospinal fluid of a 19-year-old female nursing student in Wollongong, New South Wales, Australia. Treatment with ceftriaxone and benzyl penicillin effected a clinical cure without complications. Close contacts were given rifampin prophylaxis, but throat swabs were not obtained. All isolates from IMD patients in Australia are examined for their susceptibility to antibiotics used for treatment and prophylaxis of meningococcal infection (1). By using a standard agar plate dilution technique (3), the Wollongong isolate was found to have decreased susceptibility to ciprofloxacin (MIC, 0.25 mg/liter). All other isolates examined in Australia since 1994, including those tested subsequent to the isolation of the Wollongong strain, have had ciprofloxacin MICs of $\leq$0.03 mg/liter (1). The MIC of penicillin G for the Wollongong meningococcus was also slightly increased—0.06 mg/liter—but those of chloramphenicol, rifampin, and ceftriaxone were not elevated. There was no history of prior antibiotic exposure to quinolone antibiotics in the patient. However, an elderly relative living with the patient had been given long-term intermittent norfloxacin for urinary tract infection prophylaxis and treatment.

Ciprofloxacin resistance in the closely related organism *Neisseria gonorrhoeae* is chromosomally mediated. Alterations in the 244-nucleotide quinolone resistance determining region (QRDR) of the *N. gonorrhoeae gyrA* gene increase resistance to quinolones (2). The *N. meningitidis gyrA* gene shares 95% identity with the *N. gonorrhoeae gyrA* gene. PCR amplification and sequencing of the equivalent region of two susceptible strains of *N. meningitidis* revealed three nucleotide differences. One of these encoded a conservative threonine amino acid substitution at position 91; *N. gonorrhoeae* has serine at the equivalent position. The other two changes were synonymous. The QRDR from the resistant *N. meningitidis* contained a mutation which resulted in an Asp95-to-Asn change. This is a recognized alteration in the QRDR of the *N. gonorrhoeae gyrA* gene that increases ciprofloxacin MICs to levels similar to those described for this strain (2). The alteration in the strain from the meningococcal carrier in France was Asp95-to-Gly (Casin et al., 39th ICAAC). Recognition of a different mutation in a strain from an IMD patient indicates that invasive meningococci can also become resistant to quinolone antibiotics by mechanisms known to exist in other organisms. Although slow to emerge thus far, if strains such as this become more prevalent or if levels of resistance increase further, options for chemoprophylaxis of meningococcal infection will be curtailed.

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