Rifampicin-Resistant Serotype B *Neisseria meningitidis:* First Case in Portugal

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Neisseria meningitidis is a common cause of bacterial meningitis[1] and early treatment is mandatory for a better outcome. In order to prevent secondary cases, chemoprophylaxis is indicated in close contacts. In Portugal, as in many European countries, rifampicin is the first-line drug recommended for prophylaxis.[2] Rifampicin efficacy in eliminating the meningococcal carrier state was first demonstrated in 1969[3] and resistant strains were also reported long ago.[4] The mechanism of the resistance is linked to point mutations in the *rpo*B gene.[5,6] Even though this resistance still remains rare, this is an important issue because resistant strains may cause chemoprophylaxis failure.

We present the first case of rifampicin-resistant *Neisseria meningitidis* serotype B in Portugal. In February 2018, a previously healthy 8-month-old infant was hospitalized with a fever, vomiting, and petechia. Evolution to sepsis with hemodynamic instability and disseminated intravascular coagulation occurred. Meningococcemia was suspected and she was started on ceftriaxone 100 mg/kg/dose, once daily. No cerebrospinal fluid was collected, and blood cultures were negative. Prophylaxis with rifampicin was prescribed for close contacts and the health delegate was notified. Four days after the hospitalization of the index-case and one day after a course of prophylactic rifampicin, fever and vomiting developed in the index-case 3-year-old sister. Lumbar puncture was performed, blood cultures were obtained, and she was started on ceftriaxone 100 mg/kg/dose, once daily. She also presented evolution to sepsis with hemodynamic instability and hemorrhagic dyscrasia. Cerebrospinal fluid cultures were positive for *Neisseria meningitidis* ceftriaxone-sensitive (Etest®, minimum inhibitory concentration 0.016 µg/mL),[7] with intermediate sensitivity (susceptible, increased exposure according to the new definition) to penicillin (Etest®, minimum inhibitory concentration 0.25 µg/mL)[7] and resistant to rifampicin (Etest®, minimum inhibitory concentration > 32 µg/mL).[7] Serotyping identified *Neisseria meningitidis* serotype B. Household contacts again received chemoprophylaxis, this time with ciprofloxacin (children and pregnant contacts received prophylaxis with ceftriaxone). The genotype analysis did not show any mutation in the *rpoB* gene that would be linked to the rifampicin resistance, so there must be an unknown mechanism of resistance. The evolution was favorable and without acute sequela. A follow-up study was normal in both cases.

The aim of this paper is to raise concerns about rifampicin-resistant *Neisseria meningitidis* and its implications for chemoprophylaxis. Although this resistance seems to be a rare event, since it is a severe disease, it is very important to monitor changes in the level of antibiotic susceptibility among clinical isolates. A few cases of meningococcal resistance to ciprofloxacin have also been reported,[8] which is one of the alternative chemoprophylaxis recommended in our country. Given the small number of rifampicin-resistant isolates, it is perhaps not the right time to change the recommendation of rifampicin as the first line drug for prophylaxis, but we do need to keep in mind the possibility of this occurrence and closely monitor close contacts after chemoprophylaxis. It is also important to continue monitoring the trends of *Neisseria meningitidis* susceptibility profiles to the recommended antibiotics for chemoprophylaxis and treatment.

Keywords: Carrier State/drug therapy; Drug Resistance, Microbial; Infant; Meningitis, Meningococcal/prevention & control; Neisseria meningitidis, Serogroup B; Portugal; Rifampin/therapeutic use

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

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