Highly Rifampin-Resistant Listeria monocytogenes Isolated from a Patient with Prosthetic Bone Infection

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Highly rifampicin-resistant *Listeria monocytogenes* isolated from a patient with prosthetic bone infection

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Listeriosis is a rare but severe foodborne infection due to *Listeria monocytogenes* (*Lm*). *Lm* is naturally susceptible to a wide range of antibiotics, including penicillins, aminoglycosides, tetracyclines, macrolides, co-trimoxazole, linezolid, moxifloxacine, glycopeptides and rifampicin but not to cephalosporins (1-3). *Lm* resistance to antimicrobials is rare; it was estimated around 1.3% from 4,668 clinical isolates tested in the National Reference Centre for *Listeria* (NRCL) (3), involving mostly fluoroquinolones, but not rifampicin (1, 3-5).

We report here the characterization of a *Lm* human clinical isolate (CLIP 2009/01237) highly resistant to rifampicin. A 68-year-old male had protracted intra-medullar femoral nail infection. His history included radiotherapy for femoral plasmocytoma with subsequent fractures. He presented with pain and instability, and was afebrile. A purulent collection was evidenced and the prosthetic device removed, albeit incompletely. Pus cultures remained sterile and he was discharged without treatment. He was readmitted four weeks later with fever and pus flow emitted from the operative site. As pneumonia was suspected, he received ceftriaxone and ciprofloxacin for 48 hours. A collection in the femoral region formed, and surgical debridement was performed. Pus grew *Lm*. As for most sporadic cases of listeriosis, the contamination source was not identified. Amoxicillin 6g/d was prescribed.

Lm identification was confirmed using the API *Listeria* system (bioMérieux, Marcy l'Etoile, France) and the strain typed as belonging to genoserogroup IVb (6). Susceptibility to antibiotics was determined by disk diffusion according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines (3, 7-8). The strain was resistant to high-levels of rifampicin but otherwise susceptible. The MIC of rifampicin was > 32 µg/ml, as determined by Etest (bioMérieux).

Resistance to rifampicin is mostly mediated by mutations in *rpoB*, which encodes the β-subunit of the RNA polymerase, and mutations in *rpoB* have been associated with

resistance to rifampicin (9-11). The *rpoB* gene (3,555 bp) of this rifampicin-resistant isolate was amplified and sequenced. Comparisons with *rpoB* of susceptible strain (12) identified missense mutation S488L in a conserved domain previously shown to be associated with rifampicin resistance ("resistance locus") in both *E. coli* and *Lm* mutants obtained *in vitro* (13). A similar substitution (S531L) has been reported in the central region of the β-subunit of the RNA polymerase of rifampicin-resistant *M. tuberculosis* (11). Another non-synonymous mutation was detected at codon 1178 (A1178T).

To our knowledge, S488L and A1178T substitutions have not been described in *Lm* (14). This strain was the only one displaying high resistance to rifampicin among the 5,114 human isolates tested in the NRCL since 1994. A single isolate from another patient with a borderline rifampicin MIC (4µg/ml) did not exhibit any mutation in the *rpoB* resistance locus (our unpublished data).

According to the information we have, this patient was not exposed to rifampicin, arguing for a mechanism reminiscent to spontaneously arising *M. tuberculosis* resistance to rifampicin in infections with large inoculum (11). Mutations in *rpoB* reported here could also be the consequence of the previous ciprofloxacin-exposure, which has been shown to promote mutations associated with rifampicin-resistance in *Staphylococcus aureus* (15). To our knowledge, we provide here the first report of a highly rifampicin-resistant *Lm* human clinical isolate.

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