

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

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

We report here the characterization of an *L. monocytogenes* human clinical isolate (CLIP 2009/01237) highly resistant to rifampin. A 68-year-old male had a protracted intramedullary 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 4 weeks later with fever and pus flow emitting from the operative site. As pneumonia was suspected, he received ceftriaxone and ciprofloxacin for 48 h. A collection in the femoral region formed, and surgical debridement was performed. Pus grew *L. monocytogenes*. As for most sporadic cases of listeriosis, the contamination source was not identified. Amoxicillin (6 g/day) was prescribed.

L. monocytogenes identification was confirmed using the API *Listeria* system (bioM erieux, Marcy l’Etoile, France) and the strain typed as belonging to genosero-group IVb (6). Susceptibility to antibiotics was determined by the disk diffusion assay according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines (3, 7, 8). The strain was resistant to high levels of rifampin but otherwise susceptible. The MIC of rifampin was >32 µg/ml, as determined by the Etest (bioM erieux).

Resistance to rifampin is mediated mostly by mutations in *rpoB*, which encodes the β-subunit of the RNA polymerase, and mutations in *rpoB* have been associated with resistance to rifampin (9–11). The *rpoB* gene (3,555 bp) of this rifampin-resistant isolate was amplified and sequenced. Comparisons with *rpoB* of the susceptible strain (12) identified missense mutation S488L in a conserved domain previously shown to be associated with rifampin resistance (resistance locus) in both *Escherichia coli* and *L. monocytogenes* 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 rifampin-resistant *Mycobacterium tuberculosis* (11). Another nonsynonymous mutation was detected at codon 1178 (A1178T).

To our knowledge, S488L and A1178T substitutions have not been described for *L. monocytogenes* (14). This strain is the only

one displaying high resistance to rifampin among the 5,114 human isolates tested in the NRCL since 1994. A single isolate from another patient for which the rifampin MIC was borderline (4 µg/ml) did not exhibit any mutation in the *rpoB* resistance locus (our unpublished data).

According to the information that we have, this patient was not exposed to rifampin, arguing for a mechanism reminiscent of that causing spontaneous *M. tuberculosis* resistance to rifampin in infections with a large inoculum (11). The mutations in *rpoB* reported here may also be a consequence of the patient’s previous exposure to ciprofloxacin, which has been shown to promote mutations associated with rifampin resistance in *Staphylococcus aureus* (15). To our knowledge, we provide here the first report of a highly rifampin-resistant *L. monocytogenes* human clinical isolate.

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