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Letter to the Editor

# Hospital-associated meticillin-resistant *Staphylococcus pseudintermedius* in a French veterinary hospital

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*Sir,*

*Staphylococcus pseudintermedius* is an opportunistic pathogen causing various infections in cats and dogs. Recently, the rapid emergence of meticillin-resistant *S. pseudintermedius* (MRSP) isolates was reported in pets from several European countries and North America [1]. Moreover, the MRSP phenotype was frequently associated with resistance to nearly all available antibiotics in veterinary medicine, leading to serious therapeutic challenges and to the tempting option for veterinarians to treat MRSP infections with critically important antimicrobials in human medicine [1]. Although *S. pseudintermedius* is not a common human pathogen, cases of meticillin-susceptible *S. pseudintermedius* and MRSP infections have been reported, possibly correlated with the growing reservoir of this pathogen in the dog population [2].

Two lineages of resistant MRSP clones were reported to disseminate throughout Europe and North America, namely the ST71(MLST)–J(PFGE)–t02(*spa*)–II/III(SCC*mec*) and ST68–C–t06–V lineages, where MLST stands for multilocus sequence typing, PFGE for pulsed-field gel electrophoresis and SCC*mec* for staphylococcal cassette chromosome *mec*. This dissemination was mainly observed in individual animals and was most likely acquired from different sources, as suggested by diverse PFGE patterns [1]. However, MRSP with high PFGE similarity were also reported in veterinary hospitals, suggesting the clonal spread of specific strains [3,4].

In France, 15 MRSP isolates were recovered in a veterinary hospital from the Hérault district (southern part of France) between 2007 and 2009. Strains were isolated during post-surgical examination from dogs that presented no signs of bacterial infection prior to surgery. These MRSP, which presented a specific multiresistant profile, were increasingly identified over the years (one in 2007, four in 2008 and ten in 2009). They represented 4%, 11% and 17% of annual staphylococcal isolates reported in this hospital during the 2007–2009 time period, and ca. 50% of the post-surgical MRSP infections. Since all dogs developed a surgical-site infection, the presence of a hospital-associated strain was suspected. For the purpose of the study, MRSP 'hospital-associated, community onset' infections were defined as 'probable' when the disease onset ranged from 48 h after admission up to 30 days after hospitalisation, and as 'possible' when the onset occurred later but within 12 months after hospitalisation [5,6]. Following these definitions, 11/15 cases can be considered of 'probable' nosocomial origin (Fig. 1) and 2/15 of 'possible' nosocomial origin (#23253 and #23239). Contrarily, infections due to isolates #21972 (unknown time interval) and #23341 (surgery in another hospital) were considered indeterminate [5].

Antimicrobial susceptibility was tested by the disk diffusion method on Mueller–Hinton agar and was interpreted according to the clinical breakpoints recommended by the Antibiogram Committee of the French Society of Microbiology (http://www.sfm-microbiologie.org). The 15 isolates presented resistance to erythromycin, lincomycin, kanamycin, gentamicin, tobramycin, chloramphenicol or fluoroquinolones (Fig. 1). Outside resistance to broad-spectrum cephalosporins and fluoroquinolones, no resistance was detected to other critically important antimicrobials in human medicine (i.e. pristinamycin, vancomycin or teicoplanin), even though they were occasionally prescribed. Despite antibiotic treatment, the recovery time was long (Fig. 1).

All MRSP strains belonged to *spa* type t06 and harboured an SCC*mec* type II/III with positive amplifications for *mecA*, *mecI* and *ccrA3* but not for cadmium resistance, a lineage rarely reported in Europe. PFGE analysis (Fig. 1) was performed according to a previously published method with slight modifications (pulse time of 1–30 s during 23 h) [7]. Results showed that the 13 probable/possible hospital-associated MRSP isolates were genetically linked

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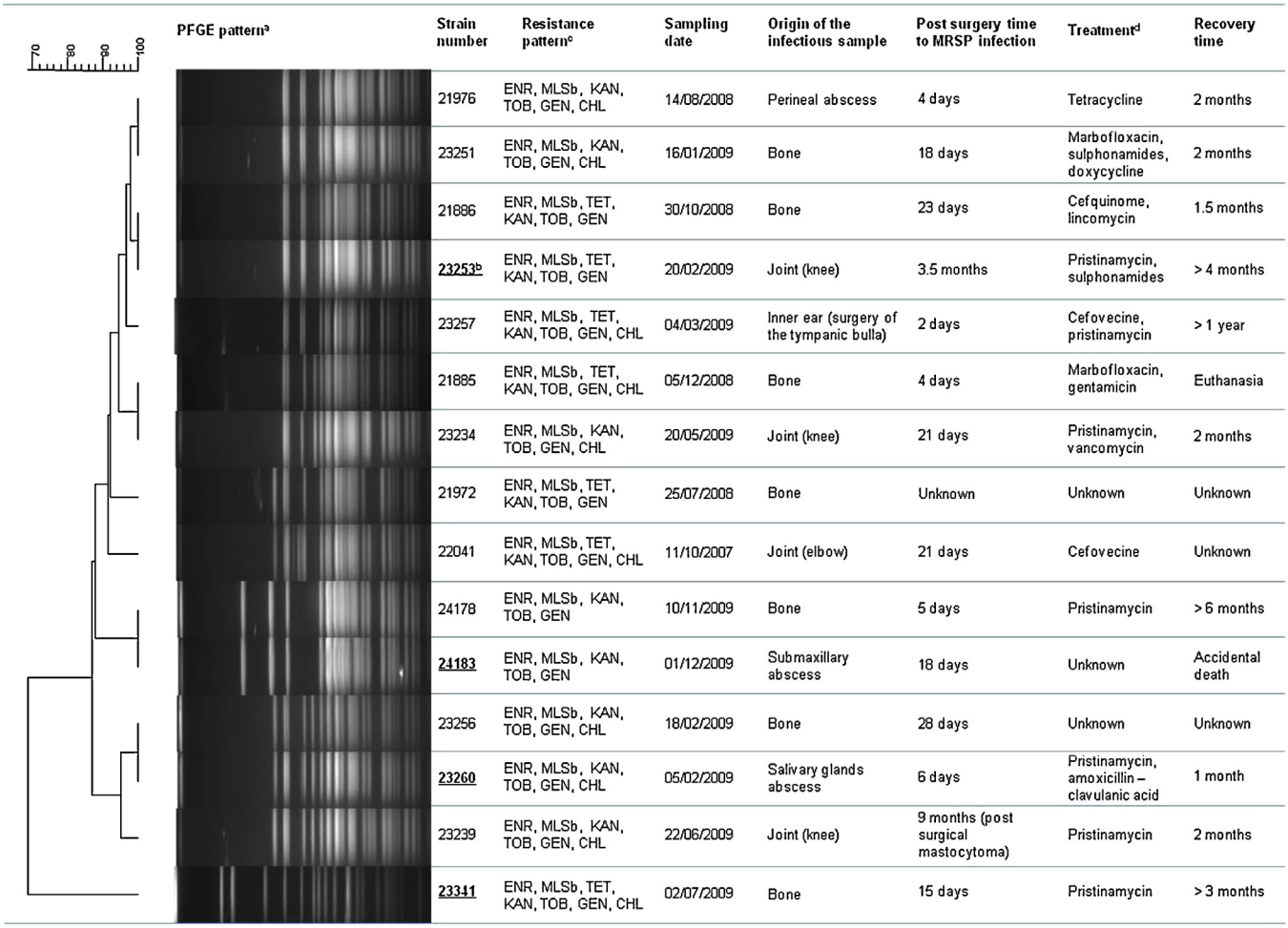


| PFGE pattern[a] | Strain number | Resistance pattern[c] | Sampling date | Origin of the infectious sample | Post surgery time to MRSP infection | Treatment[d] | Recovery time |
|---|---|---|---|---|---|---|---|
| | 21976 | ENR, MLSb, KAN, TOB, GEN, CHL | 14/08/2008 | Perineal abscess | 4 days | Tetracycline | 2 months |
| | 23251 | ENR, MLSb, KAN, TOB, GEN, CHL | 16/01/2009 | Bone | 18 days | Marbofloxacin, sulphonamides, doxycycline | 2 months |
| | 21886 | ENR, MLSb, TET, KAN, TOB, GEN | 30/10/2008 | Bone | 23 days | Cefquinome, lincomycin | 1.5 months |
| | **23253**[b] | ENR, MLSb, TET, KAN, TOB, GEN | 20/02/2009 | Joint (knee) | 3.5 months | Pristinamycin, sulphonamides | > 4 months |
| | 23257 | ENR, MLSb, TET, KAN, TOB, GEN, CHL | 04/03/2009 | Inner ear (surgery of the tympanic bulla) | 2 days | Cefovecine, pristinamycin | > 1 year |
| | 21885 | ENR, MLSb, TET, KAN, TOB, GEN, CHL | 05/12/2008 | Bone | 4 days | Marbofloxacin, gentamicin | Euthanasia |
| | 23234 | ENR, MLSb, KAN, TOB, GEN, CHL | 20/05/2009 | Joint (knee) | 21 days | Pristinamycin, vancomycin | 2 months |
| | 21972 | ENR, MLSb, TET, KAN, TOB, GEN | 25/07/2008 | Bone | Unknown | Unknown | Unknown |
| | 22041 | ENR, MLSb, TET, KAN, TOB, GEN, CHL | 11/10/2007 | Joint (elbow) | 21 days | Cefovecine | Unknown |
| | 24178 | ENR, MLSb, KAN, TOB, GEN | 10/11/2009 | Bone | 5 days | Pristinamycin | > 6 months |
| | **24183** | ENR, MLSb, KAN, TOB, GEN | 01/12/2009 | Submaxillary abscess | 18 days | Unknown | Accidental death |
| | 23256 | ENR, MLSb, KAN, TOB, GEN, CHL | 18/02/2009 | Bone | 28 days | Unknown | Unknown |
| | **23260** | ENR, MLSb, KAN, TOB, GEN, CHL | 05/02/2009 | Salivary glands abscess | 6 days | Pristinamycin, amoxicillin – clavulanic acid | 1 month |
| | 23239 | ENR, MLSb, KAN, TOB, GEN, CHL | 22/06/2009 | Joint (knee) | 9 months (post surgical mastocytoma) | Pristinamycin | 2 months |
| | **23341** | ENR, MLSb, TET, KAN, TOB, GEN, CHL | 02/07/2009 | Bone | 15 days | Pristinamycin | > 3 months |

**Fig. 1.** Pulsed-field gel electrophoresis (PFGE) profiles, resistance patterns and characteristics of the 15 *spa* type t06 meticillin-resistant *Staphylococcus pseudintermedius* (MRSP) isolates. [a]PFGE-based dendrogram and *Sma*I macrorestriction. Analysis was performed using the Dice coefficient with an optimisation set at 0.5% and a position tolerance at 1.5%. [b]Underlined bold numbers indicates strains on which multilocus sequence typing (MLST) was performed. All four strains belong to ST71 (allelic profile 3/9/1/2/1/2/1). [c]ENR, enrofloxacin; $MLS_b$, erythromycin and lincomycin; KAN, kanamycin; TOB, tobramycin; GEN, gentamicin; CHL, chloramphenicol; TET, tetracycline. [d]A 7-day post-surgical antibiotic treatment with cefalexin or marbofloxacin was administered to all dogs in addition to the antibiotic described here.

(≥85% of homology), which is in favour of the persistence of a unique clone inside the hospital. Moreover, thorough decontamination and promotion of good practices for nosocomial infection control (including hand hygiene, use of personnel protective equipment, limited access to the surgical unit and disinfection of its environment) was set up early in 2010, and MRSP surgical infections substantially decreased until the hospital closed at the end of 2010. Furthermore, no MRSP with such a multiresistant pattern was reported from neighbouring veterinary settings over the 3-year period.

Interestingly, the subclustered PFGE patterns observed in this *spa* type t06–SCC*mec* II/III clone, with many isolates (or clusters of isolates) that do not share more than 85–90% homology (Fig. 1), suggest that it may have undergo microevolutions due, for example, to the introduction of random mutations in the *Sma*I restriction site or to the acquisition or loss of mobile genetic elements. Moreover, isolate #23341 showed a completely different PFGE profile, suggesting another origin; indeed, this strain was recovered from a dog that had previously been operated in another hospital before being treated in the Hérault veterinary hospital. However, MLST (http://pubmlst.org) performed on four strains representative of the different PFGE profiles showed that they all belonged to the European ST71 type.

In conclusion, this study describes the occurrence of *spa* type t06 MRSP associated with hospital-associated infections in a district in Southern France. Although this *spa* type has rarely been described in MRSP infections in Europe, it belonged to the widespread ST71 European epidemic lineage.

It remains unclear whether this specific ST71–t06–II/III MRSP clone was selected due to specific veterinary antibiotic usage, and its capacity to persist over years remains to be investigated. Considering that this *spa* type has been considered atypical in Europe and is usually associated with the North American epidemic clone ST68–V, MLST is deemed necessary in future studies to correctly infer relationships among clones and lineages in different geographic areas in order to have a deeper insight into the epidemiology of this pathogen.

Therapeutic and surgical antibiotic prophylaxis guidelines on these multiresistant pathogens are also needed in order to control their dissemination and to avoid the emergence of bacterial resistance to all (or nearly all) veterinary-licensed antibiotics. Indeed, this study proves that the multiresistant character of MRSP tempts some veterinarians to use antimicrobials that are critically important in human medicine and have until now been reserved for human life-threatening infections.

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## Competing interests

None declared.

## Ethical approval

Not required.

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