Case Report Rapport de cas

Urinary tract infection caused by methicillin-resistant *Staphylococcus pseudintermedius* in a dog

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Abstract — A young neutered male pug dog was presented for evaluation of acute onset pollakiuria and hematuria. Culture and susceptibility testing of urine identified a methicillin-resistant *Staphylococcus pseudintermedius,* which was susceptible to only tetracycline among commonly used antimicrobials. Treatment with doxycycline led to bacteriological cure and resolution of clinical signs.

Résumé — Infection des voies urinaires causée par *Staphylococcus pseudintermedius* résistant à la méthicilline chez un chien. Un jeune chien Pug mâle stérilisé a été présenté pour l'évaluation de l'apparition aiguë de pollakiurie et d'hématurie. Une culture d'urine et une épreuve de sensibilité ont mis en évidence un *Staphylococcus pseudintermedius* résistant à la méthicilline, qui a été susceptible seulement à la tétracycline parmi les antimicrobiens fréquemment utilisés. Le traitement avec la doxycycline a produit une guérison bactériologique et une résolution des signes cliniques.

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A 16-month-old dog was presented for evaluation of hematuria and pollakiuria. Following culture and susceptibility testing, the dog was diagnosed with a urinary tract infection caused by methicillin-resistant *Staphylococcus pseudintermedius* (MRSP). No presumptive risk factors for acquisition of MRSP were identified indicating that the infection was community acquired. Following a 7-day course of doxycycline (NuPharm, Richmond Hill, Ontario), 5 mg/kg bodyweight (BW), clinical signs resolved and bacteriological cure was achieved. This is the first report of a canine urinary tract infection caused by MRSP. Community acquired MRSP infections are increasingly common and practitioners should ensure that appropriate antimicrobial susceptibility tests are conducted on *S. pseudintermedius* isolates.

Case description

A 16-month-old neutered male pug dog was presented on emergency to the Western College of Veterinary Medicine (WCVM) Veterinary Teaching Hospital (VTH) for evaluation of hematuria and pollakiuria of 2-days duration. The owner reported inappropriate urination on the day of presentation.

Previously, its regular veterinarian had treated the dog for a superficial corneal ulcer, which at the time of presentation was resolved. The owner reported only using topical medications; no systemic antimicrobials were employed. There was no other medical or surgical history. The dog was not receiving any medications and had a normal activity level and appetite. The owner reported no coughing, sneezing, vomiting, or diarrhea and there were no abnormal findings on physical examination.

Samples for urinalysis and culture were collected via ultrasound-guided cystocentesis. Ultrasonographic examination revealed a small bladder with substantial echogenic material along the dependent wall. No echogenic structures with distinct shadows were seen. Abdominal radiographs did not identify radio-opaque uroliths.

The urine was cloudy and yellow. A specific gravity of 1.027 and pH of 6.0, 1+ proteinuria and 4+ blood were identified on a reagent strip (Chemstrip 10A; Roche, Mannheim, Germany). Examination of urine sediment revealed 3 to 6 WBC/high power field (hpf), 25 to 30 RBC/hpf, and 0 to 2 epithelial cells. Scant struvite crystalluria and debris were noted.

Pending culture and susceptibility results, empiric treatment for a presumptive urinary tract infection (UTI) was started with amoxicillin (Pfizer, Kirkland, Ontario) at a dose of 21 mg/kg BW, PO, 3 times daily. After 3 d of therapy clinical signs had not improved. A pure culture of *S. pseudintermedius* (recently identified as distinct from *S. intermedius*) was isolated from the urine and identified using standard biochemical tests including the ability to ferment maltose and mannitol, and the production of acetoin, DNase, coagulase, and hyaluronidase (1,2). Antimicrobial minimum inhibitory concentrations (MICs) were determined by broth micro-dilution (Sensititre, Trek Diagnostic Systems, Cleveland, Ohio, USA) according to the Clinical and Laboratory Standards Institute (CLSI) and manufacturer guidelines (3). The isolate was resistant to many of the antimicrobials commonly used in canine practice (Table 1), and was identified

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Table 1. Antimicrobial susceptibility profile of a *Staphylococcus pseudintermedius* isolate from the urine of a dog with a urinary tract infection

Drug	Minimum inhibitory concentration (μg/mL)	Resistance breakpoint (μg/mL)	Susceptible (S)/ Resistant (R)
Ampicillin[a]	≥ 16	≥ 0.5	R
Ceftiofur[a]	≥ 16	≥ 8	R
Oxacillin[a]	≥ 16	≥ 4	R
Penicillin[a]	≥ 16	≥ 0.25	R
Erythromycin[a]	≥ 8	≥ 8	R
Clindamycin[a]	≥ 32	≥ 4	R
Telithromycin[b]	≥ 4	≥ 4	R
Ciprofloxacin[b]	≥ 4	≥ 4	R
Danofloxacin[a]	≥ 2	≥ 0.5	R
Enrofloxacin[a]	≥ 4	≥ 4	R
Moxifloxacin[b]	≥ 4	≥ 2	R
Gentamicin[a]	≥ 32	≥ 16	R
Trimethoprim/ sulfamethoxazole[a]	≥ 8/176	≥ 4/76	R
Chloramphenicol[a]	≥ 16	≥ 32	R
Rifampin[b]	≥ 4	≥ 4	R
Tetracycline[a]	≤ 2	≥ 16	S
Nitrofurantoin[b]	≤ 32	≥ 128	S
Quinupristin/ dalfopristin[b]	≤ 0.5	≥ 4	S
Vancomycin[b]	≤ 1	≥ 16	S
Daptomycin[b]	≤ 0.5	≥ 2	S
Linezolid[b]	≤ 1	≥ 8	S

[a] CLSI M31-A3. Performance standards for antimicrobial disk and dilution susceptibility tests for bacterial isolates from animals.
[b] CLSI M100-S18. Performance standards for antimicrobial susceptibility testing.

as MRSP. Methicillin-resistance was confirmed by polymerase chain reaction (PCR) amplification of *mec*A, the gene conferring methicillin-resistance, using previously published primers (4). *Staphylococcus aureus* ATCC 43300 and 29213 were used as positive and negative controls in the detection of *mec*A. The MRSP reported here did not possess Panton-Valentine leukocidin (PVL), a toxin produced by staphylococci that is active against neutrophils (5). *Staphylococcus aureus* ATCC 49775 and 29213 were used as positive and negative controls in screening for PVL; previously published primers were used (6).

The unusual resistance profile of this isolate prompted further questioning of the owners to elucidate possible risk factors for the acquisition of MRSP. No humans in the household or in close contact with the dog were on antibiotics or had medical problems. The owner's sister-in-law lived in the same apartment building and worked in a nursing home. Her Labrador retriever had had contact with the dog, although her dog had no pertinent medical history such as recent hospitalization or antimicrobial use. No other animals lived in the house with the dog. The origin of this organism remains unknown.

Based on antimicrobial susceptibility results, therapy was changed to doxycycline (NuPharm) 5 mg/kg BW, PO, twice daily for 10 d. The owner reported resolution of clinical signs within 2 d of beginning therapy with doxycycline.

Seven days after completion of the doxycycline regimen the dog was presented to the WCVM for recheck evaluation. Clinical signs remained resolved and physical examination findings were within normal limits.

Ultrasound-guided cystocentesis was attempted, but no urine could be collected due to a small bladder. No echogenic material was seen in the bladder. A 5 French feeding tube (Med-Rx, Oakville, Ontario) was passed using sterile technique to obtain a urine sample.

The urine was bright yellow and slightly cloudy. A specific gravity of 1.044 and pH of 6.5, 1+ proteinuria and 1+ bilirubinuria were noted on the reagent strip (Chemstrip 10A; Roche); 3–5 epithelial cells and mild debris were noted on sediment examination. No organisms were cultured from the urine.

Discussion

In this case, the recognition of clinical signs characteristic of UTIs and a lack of findings suggestive of underlying predisposing causes, prompted empiric antimicrobial therapy pending culture and susceptibility and urine analysis results. Empiric therapy is appropriate in patients with first time UTIs that have not received antimicrobials during the previous 4 to 6 wk (7,8).

The most common bacteria isolated from canine UTIs at the WCVM are *Escherichia coli* and *Staphylococcus* spp., occurring in 51.1% and 16.5% of infections, respectively; other organisms including *Enterococcus* spp. (10.6%), *Proteus* spp. (5.9%), and streptococci (4.6%) are also encountered (9).

There are increasing reports of MRSP infections in companion animals. Resistance to methicillin confers resistance to all β-lactam drugs, rendering many of the common treatment options for staphylococcal infections ineffective (10). While risk factors for the acquisition of MRSP remain ill-defined, our current knowledge of MRSA suggests that patients with recent antimicrobial use, hospitalization, or compromised defenses may be predisposed (11). None of these presumptive risk factors were present in this patient. Currently, there are no published reports of canine UTIs with MRSP, although feline cases have been documented (12). The organism isolated here is remarkable in its extended resistance profile. Simultaneous resistance to the aminoglycosides, trimethoprim/sulfamethoxazole, rifampin, and chloramphenicol has not been reported in MRSP. While this isolate remained susceptible to a number of drugs, many of them are used exclusively in human medicine (quinupristin/dalfopristin, vancomycin, daptomycin, and linezolid) for treating infections caused by multidrug resistant organisms. Doxycycline was the most rational therapeutic choice in this case.

Despite pharmacokinetic studies demonstrating doxycycline's potential for the treatment of canine UTIs, this application is limited in practice. Four hours after oral administration, urinary doxycycline concentration was 52.4 μg/mL +/− 24.1 μg/mL (13). A concentration at the low end of this range would vastly surpass the MIC of the MRSP reported here (tetracycline MIC ≤ 2). The overwhelmingly high concentrations reported compared to the organism's MIC, combined with resolution of clinical signs and bacteriological cure indicate that doxycycline was effective in this case.

With the emergence of MRSP as a cause of canine infections, practitioners should consider the possibility of these organisms in refractory cases or those with unusual susceptibility profiles. Oxacillin- or methicillin-resistance is routinely determined and isolates that are resistant to these agents are resistant to all β-lactam antimicrobials: the penicillins (including amoxicillin/clavulanic acid), cephalosporins, and carbapenems. This case

highlights the possibility of community-associated MRSP infections in previously healthy dogs. Although *S. pseudintermedius* infrequently causes infections in humans, zoonotic MRSP transmission from dogs is reported, demonstrating the potential occupational and public health hazards of this organism (14,15). Currently, the prevalence of antimicrobial resistance among *S. pseudintermedius* from healthy dogs in western Canada is unpublished; these data would be useful in the development of empiric therapy guidelines and for monitoring the dissemination of antimicrobial resistance.

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