Urinary tract infection by atypical uropathogens in dogs

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Summary
Bacterial urinary tract infection (UTI) is a common condition affecting dogs. Urine culture and antimicrobial susceptibility test, associated with the identification of underlying cause, are of primary importance in order to select a correct treatment, especially in presence of comorbidities. Two cases of immunecompromised dogs affected by urinary tract infection (UTI) have been described: the first, probably immunosuppressed due to old age, was in poor body condition, with severe odontolithiasis and periodontitis; the second was affected by chronic kidney disease in advanced stage. Urine cultures isolated two rare and atypical pathogens, *Moellerella wisconsensis* and *Brevundimonas vesicularis*, both showing sensitivity versus floroquinolones which were selected for the treatment. After a 4 weeks treatment, a second culture demonstrated the resolution of infection in both cases, in absence of clinical signs.To date neither of the two bacteria have been reported as cause of UTI in dog.

Introduction

Bacterial urinary tract infection (UTI) is a common condition affecting dogs presented to first opinion and specialist practitioners. UTIs occur in approximately 14% (5-27%) of dogs in their lifetime with variable age of onset, especially in presence of predisposing factors and/or comorbidities (Wong *et al.* 2015). UTIs are a major reason for improper antibiotic prescription in small animal practice and the responsible bacterial populations have evolved with increasing resistances to many antimicrobials. International Society for Companion Animal Infectious Diseases (ISCAID) published guidelines to promote a cautious and reasoned use of antibiotics in cases of UTIs pointing out the importance of microbiological culture and the identification of underlying causes in order to select a correct treatment (Weese *et al.* 2019).

Escherichia coli is the most commonly isolated pathogen, followed by other species such as *Staphylococcus* spp., *Enterococcus* spp., *Streptococcus* spp., *Proteus* spp., *Pseudomonas* spp. and *Klebsiella* spp. (Wong *et al.* 2015, Hall *et al.* 2013). Other minor species, including *Acinetobacter* spp., *Bacillus* spp., *Bacteroides* spp., *Citrobacter* spp., *Clostridium* spp., *Corynebacterium* spp., *Lactobacillus* spp., *Morganella morganii, Pasteurella multocida* and anaerobic bacteria are rarely recognized in dog (Ball *et al.* 2008).

Case description

Case 1

A 14-year-old male Poodle was examined as suffering asthenia, anorexia and ataxia since few days. The clinical examination revealed a poor body condition score, dehydration, muscle atrophy, bilateral congiuntivitis and otitis, severe periodontitis and odontolithiasis. The ultrasound examination showed signs of chronic nephropathy, bilateral pyelonephritis, and prostatic hyperplasia. A bilateral hip luxation was identified by X-ray. Serum creatinine was increased (1.9 mg/dL) and urinalysis evidenced a significant proteinuria [urinary protein : creatinine ratio (UPC) 1.40], leukocyturia (10/hpf) and bacteriuria.

Sample for urine culture was inoculated on blood agar as well as MacConkey agar and incubated at 37 °C for 24 hours or 48 hours in negative cases. Growth of a single organism with a count of ≥ 10^5 colony-forming units (CFU)/ml was considered to represent the infection and the bacteria was identified using appropriate routine identification

Table I. *Results of the complete urinalysis of case 1.*

Parameter	Result	RV
Color	yellow	
Clarity	subclear	
USG	1,016	> 1,030
pH	5.5	5.5-7
Protein	++	
Glucose	negative	
Ketones	negative	
Bilirubin	+	
Blood	+++	
Hemoglobin	+++	
Nitrite	negative	
RBC	occasional	< 5/hpf
WBC	10/hpf	< 5/hpf
Epithelial cells	absent	
Casts	absent	
Bacteria	rods	
Crystals	absent	
UPC	1.40	< 0.5

RV = Reference value; USG = Urine specific gravity; RBC = Red blood cells; WBC = White blood cells; UPC = Urine protein : creatinine ratio; hpf = High power field.

methods including colony morphology, Gram-stain and biochemical characteristics of isolates. The bacterium identified with API 20E (bio-Mèrieux SA, Marcy l'Etoile, France) was *Moellerella wisconsensis* (API cod. 1244060, 99.9% identification).

Antimicrobial susceptibility of *M. wisconsensis* was tested by the disk diffusion method using the Mueller-Hinton agar (Kirby-Bauer method). Antimicrobial agents tested were amikacin (AK), ampicillin (AMP), amoxicillin clavulanate (AMC), cephalexin (CL), cefoperazone (CFP), cefovecin (CVN), cefuroxime (CXM), doxycycline (DO), enrofloxacin (ENR), gentamicin (CN), nitrofurantoin (F), oxacillin (OX), trimethoprim/ sulfamethoxazole (SXT). The isolated bacterium was sensitive to CFP, ENR and CN.

After a few days of antibiotic treatment (enrofloxacin 5 mg/kg SID for 3 days, prosecuted at home for 4 weeks) and supportive care, clinical conditions improved and the dog was discharged as normoazotemic.

Case 2

A 7-year-old female Labrador Retriever was referred for a second consultation after a diagnosis of chronic kidney disease (CKD). At clinical examination the dog was in good general condition with pale mucous membranes. The diagnostic investigations allowed to stage CKD in stage 3 *vs* 4 (serum creatinine 4.3 mg/dL), normotensive; the substaging based on proteinuria (UPC 1.0[6]) was dubious due to the presence of an ongoing infection. A moderate anaemia (red blood cells 3.93 x 10^6/µL, haemoglobin 9.7 g/dL haematocrit 27.5%) and mild hyperphosphataemia (serum phosphate 4.9 mg/dL) were thought to be the consequences of CKD, associated with the presence of anaemia of chronic disease. Urinalysis showed a low urine specific gravity (USG - 1,007), proteinuria (UPC 1.06), leukocyturia (100/hpf) and bacteriuria.

Table II. *Result of the antimicrobial susceptibility test of case 1.*

Antibiotic	Result
Amikacin	I
Amoxicillin clavulanate	R
Ampicillin	R
Cefovecin	R
Cephalexin	R
Ceftriaxone	I
Doxycycline	I
Enrofloxacin	S
Gentamicin	S
Nitrofurantoin	R

S = Susceptible, standard dosage regimen; I = Susceptible, increased exposure; R = Resistant.

The procedures for bacterial identification and evaluation of antimicrobial susceptibility were the same reported in Case 1. The bacterium identified with API 20NE (bio-Mèrieux SA, Marcy l'Etoile, France) was *Brevundimonas vesicularis* (API cod. 0441004, 91.5% identification). Antimicrobial agents tested were amikacin (AK), ampicillin (AMP), amoxicillin clavulanate (AMC), cephalexin (CL), cefoperazone (CFP), cefovecin (CVN), cefuroxime (CXM), doxycycline (DO), enrofloxacin (ENR), gentamicin (CN), marbofloxacin (MAR), oxacillin (OX), trimethoprim/ sulfamethoxazole (SXT). The isolated bacterium was sensitive to AK, CFP, ENR, CN, MAR and SXT.

The dog was treated with marbofloxacin (2 mg/kg for 4 weeks) according to antimicrobial sensitivity test and two weeks later urinalysis and culture showed the resolution of infection with the persistence of low USG (1,010) and proteinuria (UPC 1.19), probably due to underlying CKD.

Discussion

Moellerella wisconsensis is a rare Gram-negative bacillus belonging to the family of *Enterobacteriaceae*, named definitively in 1984. Its pathogenic rule remains nowadays unclear due to two factors: *Moellerella* is rarely identified in clinical

Table III. *Results of the complete urinalysis of case 2.*

Parameter	Result	RV
Color	pale yellow	
Clarity	clear	
USG	1,007	> 1,030
pH	5.5	5.5-7
Protein	+	
Glucose	negative	
Ketones	negative	
Bilirubin	negative	
Blood	++	
Hemoglobin	negative	
Nitrite	negative	
RBC	occasional	< 5/hpf
WBC	100/hpf	< 5/hpf
Epithelial cells	transitional	
Casts	absent	
Bacteria	rods	
Crystals	absent	
UPC	1.06	< 0.5

RV = Reference value; USG = Urine specific gravity; RBC = Red blood cells; WBC = White blood cells; UPC = Urine protein : creatinine ratio; hpf = High power field.

Table IV. *Result of the antimicrobial susceptibility test of case 2.*

Antibiotic	Result
Amikacin	S
Amoxicillin clavulanate	R
Ampicillin	R
Cefadroxil	R
Cefovecin	I
Cephalexin	R
Ceftriaxone	S
Doxycycline	I
Enrofloxacin	S
Gentamicin	S
Marbofloxacin	S
Nitrofurantoin	S
Trimethoprim-sulphonamide	S

S = Susceptible, standard dosage regimen; I = Susceptible, increased exposure; R = Resistant.

samples and only a few numbers of case report in humans and animals are available; belonging to the group of *Enterobacteriaceae* is probably a natural inhabitant of gastrointestinal tract and the pathogenic role is evident only if predisposing factors are present (Cardentey-Reyes *et al.* 2009). In humans, *Moellerella* has been identified in cases of diarrhoea, cholecystitis, in a bronchial aspirate and in a blood culture; in animals it has been reported in faecal samples of captive raptors and in the oral cavity of a wild raccoon in USA, in a lung of a goat and in poultry meat in Italy, in liver and kidney from a cow in Portugal (Cardentey-Reyes *et al.* 2009, Bangert *et al.* 1998, Sandfort *et al.* 2002, Casalinuovo and Musarella 2009, Anastácio and Leão 2016). Moreover, a case reported a *Moellerella* infection in a dog with a clinically relevant chronic vaginal discharge in Poland (Zielińska *et al.* 2015).

Moellerella is generally susceptible to most antibiotics that are active against Gram-negative bacteria; however, in the case reported in dog the bacteria showed significant resistances versus amoxicillin clavulanate, ampicillin, sulphonamides and trimethoprim and resulted sensible to amikacin, gentamicin and fluoroquinolones (Cardentey-Reyes *et al.* 2009, Zielińska *et al.* 2015). Interestingly, these results are similar those observed in our case..

To the best of our knowledge, this is the first isolation of *Moellerella wisconsensis* in a clinical case of UTI.

Brevundimonas vesicularis, named definitively in 1994, is an aerobic Gram-negative rod belonging to the *Caulobacteraceae* family and is the main representative of genus *Brevundimonas*, currently composed by 25 species. It is considered an opportunistic pathogen able to cause severe and invasive infections in presence of underline predisposing conditions and/or coinfections. *Brevundimonas vesicularis* is the most isolated pathogen in human medicine and it has been found primarily in patients with bacteraemia but also in eye, urine, wounds, central nervous system, heart, joints, liver, cervical specimens and also in the lung sputum of a cystic fibrosis patient (Ryan and Pembroke 2018). To date, only few cases have been described in animals (Carnevia *et al.* 2013, Suchodolski *et al.* 2010).

The treatment of *Brevundimonas* spp. infections is frequently difficult because these bacteria can be resistant to many antibiotics including β-lactams and fluoroquinolones; however, in our case, the isolation showed sensitivity versus some cephalosphorines and fluoroquinolones and the antibiotic treatment was effective (Carnevia *et al.* 2013).

To the best of our knowledge, this is the first isolation of *Brevundimonas vesicularis* in a clinical case of UTI.

The reported cases reinforce the importance of the execution of performing urine culture and antimicrobial susceptibility in all cases of suspected UTI.

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