

# Extensively drug-resistant *Myroides odoratimimus* – a case series of urinary tract infections in immunocompromised patients

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**Purpose:** We report an outbreak of urinary tract infections (UTIs) caused by *Myroides odoratimimus*, which occurred in the largest clinical hospital in western Romania.

**Patients and methods:** From June to August 2017, four strains of *M. odoratimimus* were isolated from the urine samples of patients hospitalized in the urology, diabetes, and surgery departments. Hospital records of all patients whose urine cultures were positive for *M. odoratimimus* were reviewed retrospectively. We also reviewed the cases reported in the literature.

**Results:** All UTIs, except one, were hospital-acquired infections. All patients with *M. odoratimimus* UTIs were immunocompromised. Three patients underwent urinary catheterization with a Foley’s catheter upon admission in the emergency department and one presented for replacement of ureterostomy tubes. All *Myroides* isolates were resistant to almost all the tested antibiotics. Two patients were successfully treated with tigecycline and one was receiving antimicrobial treatment for another infection at the time of isolation of the microorganism.

**Conclusion:** Although *M. odoratimimus* is an uncommon pathogen, clinicians should be aware of its ability to cause UTI outbreaks, especially in the immunocompromised population. Due to its multi-drug resistance, it is important to rapidly identify *Myroides* spp. in order to choose the best treatment regimen.

**Keywords:** *Myroides odoratimimus*, urinary tract infection, resistance, outbreak

## Introduction

The *Myroides* genus was created in 1996<sup>1</sup> for *Flavobacterium odoratum* species which were excluded from the *Flavobacterium* genus by Bernardet et al<sup>2</sup> due to important genomic and phenotypic differences. The new *Myroides* genus comprises two species, *Myroides odoratus* (former *F. odoratum*) and *Myroides odoratimimus*, which are Gram-negative rods, strictly aerobic, non-motile, with yellow pigmentation and a characteristic fruity odor.<sup>1</sup>

*Myroides* spp. are commonly found in environmental sources, particularly in soil<sup>3,4</sup> and water,<sup>5,6</sup> but have also been isolated from seafood products,<sup>7</sup> meat-processing plants,<sup>8</sup> and the gut of adult flesh flies.<sup>9</sup>

Members of the *Myroides* genus also behave as low-grade opportunistic pathogens, causing community-<sup>10</sup> or hospital-acquired<sup>11–13</sup> infections. *Myroides* spp. have been found to be responsible for cases of soft tissue infections,<sup>10,14</sup> septic shock and pneumonia,<sup>14,15</sup> systemic infections,<sup>11,12,16,17</sup> necrotizing fasciitis,<sup>18</sup> urinary tract infections (UTIs),<sup>19,20</sup> or erysipelas.<sup>16</sup>

We report an outbreak of UTIs caused by *M. odoratimimus* in a Romanian hospital, which is, to our knowledge, the first outbreak recorded in our country and the third described in the literature to date.<sup>19,20</sup>

## Patients and methods

### Study population

During a 3-month period (from June to August 2017), four isolates of *Myroides* spp. were identified among the 333 positive urine cultures analyzed in the Microbiology Laboratory of the “Pius Brînzeu” Emergency Clinical County Hospital, Timișoara, Romania. This institution is a 1,173-bed, tertiary care, university-affiliated hospital providing health care services for the western region of Romania. The study was approved by the Hospital Ethics Committee. Patients signed an informed consent upon admission, which included the fact that data recorded during hospitalization could be used for future research studies.

### Microbiological analysis and data collection

All isolates were first identified as *Myroides* spp. using the VITEK® 2 GN ID cards (BioMérieux, Marcy l’Etoile, France) and then confirmed as *M. odoratimimus* by the matrix assisted laser desorption/ionization-time of flight mass spectrometry (Bruker Daltonics, Bremen, Germany) system.

Antimicrobial susceptibility tests (AST) were performed using the VITEK 2 GN AST-N222 cards by determination of the minimum inhibitory concentration (MIC) and classification into resistance phenotypes. The following antimicrobial agents were tested: ticarcillin, piperacillin, piperacillin/tazobactam, ceftazidime, cefepime, aztreonam, imipenem, meropenem, amikacin, gentamicin, tobramycin, ciprofloxacin, pefloxacin, minocycline, colistin, and trimethoprim-sulfamethoxazole. MIC results were interpreted according to the Clinical and Laboratory Standards Institute criteria. Extensive drug resistance was defined as acquired resistance to at least one agent in all, but two or fewer antimicrobial categories.<sup>21</sup>

Hospital records of all patients with positive *M. odoratimimus* urine cultures were reviewed retrospectively. The collected data included the demographic characteristics of the patients, comorbidities, and the presence of an indwelling urinary catheter. The antimicrobial treatment and the clinical outcomes were individually reviewed.

## Results

Four cases of *M. odoratimimus*-positive urine cultures were identified in the Microbiology Laboratory of the “Pius

Brînzeu” Emergency Clinical County Hospital, Timișoara, between June and August 2017. The isolates were recovered from patients admitted to the departments of urology (two cases), surgery (one case), and diabetes (one case), respectively.

Demographics and clinical data of the patients are shown in Table 1. Three (75%) patients were males and one (25%) was a female. The mean age was 56 years (range 36–72). The patient hospitalized in the surgery department (C1) had a case history of kidney transplantation for chronic glomerulonephritis and was under immunosuppressive treatment. He was also suffering from anal condylomatosis, for which he underwent multiple surgical interventions (the last one 4 days before presentation at the emergency room). He was admitted for abdominal pain and anuria. The female patient (C2) had diabetes mellitus and was hospitalized for diabetic ketoacidosis. One of the patients admitted to the urology department (C3) had a case history of transurethral resection of the prostate for benign prostatic hyperplasia and was suffering from COPD, for which he was on long-term corticosteroid treatment; he was admitted for acute urinary retention. The other patient from the urology department (C4) had undergone a radical cystectomy with bilateral cutaneous ureterostomy for a muscle-invasive bladder cancer 3 months earlier. He was admitted for the replacement of the ureterostomy tubes.

Three cases (C1–C3) underwent urinary catheterization with a Foley’s catheter on presentation at the emergency room (one for acute urinary retention and two for accurate monitoring of urinary output). These patients also complained of symptoms characteristic of UTI (fever, flank pain, costovertebral angle tenderness, or pelvic discomfort) and their urinalysis showed the presence of nitrites, leukocyte esterase, and more than five white blood cells per high-power field. All these cases were hospital-acquired UTIs, with a mean duration of hospitalization of 11 days (range 2–23) before isolation of the uropathogen.

AST and the determination of MICs revealed that all *M. odoratimimus* isolates were sensitive only to minocycline and were resistant to beta-lactams (including extended-spectrum cephalosporins and beta-lactamase inhibitors), monobactams, carbapenems, aminoglycosides, fluoroquinolones, polymyxins, and sulfonamides. One isolate demonstrated intermediate susceptibility to piperacillin/tazobactam. MICs of the antimicrobial agents are shown in Table 2.

Two patients (C2 and C3) received tigecycline for the treatment of UTIs with a good clinical response. One patient (C1) had been receiving antibiotic treatment for a pelvic

**Table 1** Clinical characteristics and treatment of the four cases of UTIs due to *Myroides odoratimimus*

Case no., age (years)/gender	Department admitted to	Admission date	Collection date	Days of hospitalization	Comorbidities	Presence of an indwelling device	Prior antibiotic treatment	Type of infection	Treatment for <i>Myroides</i> UTI	Outcome
C1 36/M	Surgery	May 30, 2017	June 22, 2017	43	Pelvic abscess, anal condylomatosis, kidney transplantation, hepatitis B infection	Urethro-vesical catheterization	Imipenem, amikacin, colistin	UTI	None	Cured
C2 59/F	Diabetes	June 19, 2017	June 27, 2017	9	Diabetes mellitus, above-knee left amputation for PAD, obesity, hypertension	Urethro-vesical catheterization	None	UTI	Tigecycline	Good clinical response
C3 72/M	Urology	June 24, 2017	June 26, 2017	10	TUR-P for BPH, BNI for bladder neck obstruction, COPD	Urethro-vesical catheterization	None	UTI	Tigecycline	Good clinical response
C4 57/M	Urology	August 3, 2017	August 3, 2017	2	Radical cystectomy for high-grade papillary urothelial carcinoma stage pT2, obesity, hypertension	Bilateral cutaneous ureterostomy	None	Bladder colonization	None	Favorable

**Abbreviations:** BNI, bladder neck incision; BPH, benign prostatic hyperplasia; PAD, peripheral artery disease; TUR-P, transurethral resection of prostate; UTI, urinary tract infection.

abscess (with imipenem, amikacin, colistin) for 22 days at the time the microorganism was isolated in urine, with a favorable outcome.

In accordance with the European Association of Urology guidelines,<sup>22</sup> C4 did not receive antibiotic treatment as no symptoms were present in this patient.

## Discussion

*Myroides* spp. are Gram-negative bacilli frequently encountered in the environment, usually in sources such as water and soil.<sup>3-6</sup> They are uncommon pathogens in humans, having been reported as causing opportunistic infections, most often in severely immunocompromised hosts.<sup>11,23-25</sup> Only rarely have they been identified in immunocompetent patients.<sup>10,14</sup>

The present outbreak of UTIs due to *M. odoratimimus* is the third described in the literature to date. We reviewed the cases reported in literature to date (Table 3). Holmes et al<sup>26</sup> first reported these isolates from UTIs, describing 18 strains of *F. odoratum* isolated from urine.<sup>27</sup> *M. odoratimimus* has been previously identified as an etiologic agent for UTIs in two nosocomial outbreaks among urologic patients.<sup>19,20</sup> Ktari et al<sup>19</sup> reported seven cases of UTIs due to *M. odoratimimus* in the urology unit of a Tunisian hospital, all of them (except one) in patients who underwent endourological surgeries and had urinary calculi. The available clinical data in the Turkish report of Yağci et al<sup>20</sup> covering a 3-year period showed that patients with *F. odoratum* UTIs were catheterized and had either neoplasia of the urinary tract or urinary calculi. In the current report, two of the four patients had urological comorbidities (transurethral resection of the prostate for benign prostatic hyperplasia and cystectomy with bilateral cutaneous ureterostomy for bladder cancer). The four *M. odoratimimus* cases reported in this study were urinary sources only, although it appears this pathogen may be potentially isolated in other sites. A recently published Indian case report discussed isolating *M. odoratimimus* from both urine and blood cultures of a patient with anaplastic astrocytoma.<sup>28</sup>

All our patients with *M. odoratimimus* UTIs had an indwelling urinary device and all except one (C4) have been hospitalized for lengthy periods. The most important predisposing factor for hospital-acquired UTIs is urinary catheterization, which reduces host defense mechanisms and offers easier access of germs to the bladder.<sup>29</sup> It is possible that C4 acquired the uropathogen prior to admission, most probably 3 months earlier during his previous hospitalization for radical cystectomy, when he had ureterostomy tubes placed.

We suspect that the current outbreak arose in the emergency room where patients underwent urinary catheterization,

**Table 2** In vitro susceptibility testing of the *Myroides odoratimimus* isolates

Antibiotic	C1		C2		C3		C4	
	MIC value (µg/mL)	Interpretation (S, I, R)	MIC value (µg/mL)	Interpretation (S, I, R)	MIC value (µg/mL)	Interpretation (S, I, R)	MIC value (µg/mL)	Interpretation (S, I, R)
Ticarcillin	≥128	R	≥128	R	≥128	R	≥128	R
Piperacillin	≥128	R	≥128	R	≥128	R	≥128	R
Piperacillin/tazobactam	64	I	≥128	R	≥128	R	≥128	R
Ceftazidime	≥64	R	≥64	R	≥64	R	≥64	R
Cefepime	32	R	≥64	R	≥64	R	≥64	R
Aztreonam	≥64	R	≥64	R	≥64	R	≥64	R
Imipenem	≥16	R	≥16	R	≥16	R	≥16	R
Meropenem	≥16	R	≥16	R	≥16	R	≥16	R
Amikacin	≥64	R	≥64	R	≥64	R	≥64	R
Gentamicin	≥16	R	≥16	R	≥16	R	≥16	R
Tobramycin	≥16	R	≥16	R	≥16	R	≥16	R
Ciprofloxacin	≥4	R	≥4	R	≥4	R	≥4	R
Pefloxacin	8	R	8	R	8	R	≥16	R
Minocycline	2	S	2	S	2	S	≥1	S
Colistin	≥16	R	≥16	R	≥16	R	≥16	R
Trimethoprim-sulfamethoxazole	≥320	R	≥320	R	≥320	R	≥320	R

**Abbreviations:** I, intermediate; MIC, minimum inhibitory concentration; R, resistant; S, susceptible.

although the normal hospital environmental screening did not reveal any contamination with *Myroides* spp. In many cases, the source of *Myroides* spp. infection remains unknown, although water in the hospital environment is often suspected of carrying the microorganism.<sup>20,30</sup>

In the current outbreak, all the patients who developed *M. odoratimimus* UTIs were immunocompromised. Diabetes mellitus, chronic corticosteroid treatment for COPD, and liver cirrhosis have all been previously identified as causes of immunodepression in patients with *Myroides* spp. infections.<sup>11,23–25</sup>

*Myroides* spp. are known to be resistant to a wide range of antimicrobial agents, including beta-lactams, monobactams, carbapenems, and aminoglycosides.<sup>27</sup> The resistance to beta-lactams is due to the production of chromosome-encoded metallo-beta-lactamases, TUS-1 for *M. odoratus* and MUS-1 for *M. odoratimimus*.<sup>13</sup> Due to their multiple antibiotic resistance mechanisms,<sup>31</sup> a fast and reliable identification method for *Myroides* spp. is needed. Schrottner et al showed that the VITEK 2 diagnostic system is suitable for identifying bacteria at the genus level, but cannot differentiate between species. In contrast to this, matrix assisted laser desorption/ionization-time of flight mass spectrometry and 16S rDNA are methods capable of distinguishing between *M. odoratus* and *M. odoratimimus*.<sup>32</sup>

Choosing the appropriate antimicrobial treatment for *Myroides* infections can be quite challenging because of the limited clinical experience. All *M. odoratimimus* isolates reported in the present paper were extensive drug resistance

strains, sensitive only to minocycline and resistant to all the other tested antimicrobials. Two of our patients were successfully treated with tigecycline. Previous studies reported quinolones combined with rifampicin as optimal therapeutic regimens for treating *M. odoratimimus* UTI.<sup>19</sup> Other sites of *Myroides* spp. infections benefited from treatment with cotrimoxazole, meropenem, or piperacillin/tazobactam,<sup>12,14,17</sup> with favorable clinical responses.

One limitation of the present study could be the lack of pulsed-field gel electrophoresis tests to confirm the outbreak and trace the source of genetically related strains.

## Conclusion

Although *Myroides* spp. are uncommon pathogens, clinicians should be aware of the ability of *M. odoratimimus* to cause prolonged UTI outbreaks, especially in the immunocompromised population. It is important to identify *Myroides* spp. infections rapidly in order to choose the best therapeutic regimen, considering the wide range of antibiotic resistance of these microorganisms.

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**Table 3** Reported cases of *Myroides* spp. strains isolated from the urine, as found in the USA National Library of Medicine (PubMed) database (May 12, 2017)

Case no.	Gender/age (years)	Clinical condition/indwelling device	Antibiotic resistance status	Treatment for <i>Myroides</i> UTIs	Outcome	Report/year/reference
1	M/66	Bilateral hydronephrosis, bilateral ureteric stones/left DJ stent	Resistant to all beta-lactam and non-beta-lactam antibiotics,	Imipenem, colistin	Failure	Ktari et al/2012/19
2	M/44	Bilateral hydronephrosis, bilateral ureteric stones, left kidney stone/bilateral DJ stent	including imipenem, vancomycin, ciprofloxacin, chloramphenicol	No treatment (bladder colonization)	Favorable	Ktari et al/2012/19
3	M/44	Left ureteric stone/left DJ stent		No treatment (bladder colonization)	Favorable	Ktari et al/2012/19
4	M/47	BPH, bladder calculi		No treatment (bladder colonization)	Favorable	Ktari et al/2012/19
5	M/77	Right hydronephrosis, right ureteric stone/right DJ stent		Rifampicin + ciprofloxacin	Cured	Ktari et al/2012/19
6	M/65	BPH, bladder calculi, prostatitis		Rifampicin + ciprofloxacin	Cured	Ktari et al/2012/19
7	M/80	Bladder cancer		Rifampicin + ciprofloxacin	Cured	Ktari et al/2012/19
8–11 (four cases)	ND/ND	Neoplasia of the urinary tract/catheterization	Resistant to all 12 antimicrobial agents tested (amikacin, aztreonam, cefoperazone, ceftazidime, ceftriaxone, ciprofloxacin, gentamicin, imipenem, piperacillin, tetracycline, tobramycin, trimethoprim-sulfamethoxazole)	ND	ND	Yağci et al/2000/20
12–20 (nine cases)	ND/ND	Urinary calculi/catheterization		ND	ND	Yağci et al/2000/20
21–29 (nine cases)	ND/ND	ND		ND	ND	Yağci et al/2000/20
30	F/48	Cystitis (contaminant)	Fully resistant to clinically obtainable levels of streptomycin, kanamycin, gentamicin, tobramycin, amikacin,	Furadantin	ND	Holmes et al/1979/27
31	F/59	ND (contaminant)		ND	ND	Holmes et al/1979/27
32	F/ND	Urinary retention (not clinically significant)		ND	ND	Holmes et al/1979/27
33	ND/ND	Not known		ND	ND	Holmes et al/1979/27
34	F/67	Total cystectomy, ileal loop urethrotomy (mixed culture)	ampicillin, carbenicillin, chloramphenicol,	ND	ND	Holmes et al/1979/27
35	M/48	Renal insufficiency, pyelonephritis, renal calculi (mixed culture)	tetracycline, polymyxin B, and erythromycin	ND	ND	Holmes et al/1979/27
36	M/54	ND (very scanty numbers)	Resistant or moderately sensitive to sulfamethoxazole,	ND	ND	Holmes et al/1979/27
37	M/87	ND (mixed culture)		ND	ND	Holmes et al/1979/27
38	M/46	ND (Mixed culture)	cotrimoxazole,	ND	ND	Holmes et al/1979/27
39	M/59	ND (mixed culture)	cephaloridine and nalidixic acid	ND	ND	Holmes et al/1979/27
40	F/ND	ND (mixed culture)		ND	ND	Holmes et al/1979/27
41	M/67	Multideficiency syndrome, pyelonephritis, liver disease (mixed culture)		ND	ND	Holmes et al/1979/27
42	M/38	Relapsing UTIs, bladder carcinoma		ND	ND	Holmes et al/1979/27
43	ND/ND	ND		ND	ND	Holmes et al/1979/27
44	M/ND	Syringomyelia/indwelling catheter		ND	ND	Holmes et al/1979/27
45	F/ND	Relapsing urinary infection, renal insufficiency, hypertension		ND	ND	Holmes et al/1979/27
46	M/19	Spina bifida/permanent catheter		ND	ND	Holmes et al/1979/27
47	ND/ND	ND		ND	ND	Holmes et al/1979/27

**Abbreviations:** BPH, benign prostatic hyperplasia; DJ, double-J; ND, not described; UTI, urinary tract infection.

## Disclosure

The authors report no conflicts of interest in this work.

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### Infection and Drug Resistance

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