Aerococcus urinae: Severe and Fatal Bloodstream Infections and Endocarditis[▽]

Margriet F. C. de Jong,^{1*} Robin Soetekouw,¹ Reinier W. ten Kate,¹ and Dick Veenendaal²

Department of Internal Medicine, Kennemer Gasthuis, Boerhaavelaan 22, 2035 RC Haarlem, Netherlands,¹ and
Department of Medical Microbiology, Streeklaboratorium voor de Volksgezondheid, Kennemerland,
Boerhaavelaan 26, 2035 RC Haarlem, Netherlands²

Received 27 April 2010/Returned for modification 2 June 2010/Accepted 12 July 2010

***Aerococcus urinae* is a pathogen that rarely causes severe or fatal infections. We describe four cases of severe *A. urinae* bloodstream infections. All patients had underlying urologic conditions. Urine cultures, however, were negative.**

CASE REPORTS

Patient A, an 81-year-old man with a history of benign prostatic hyperplasia, was admitted to our department because of fever. He had been home for 4 days after a 2-week admission for *Aerococcus urinae* bacteremia for which no source could be identified. Transesophageal echocardiography (TEE) showed no vegetations. The fever responded well to a 10-day course of high-dose intravenous penicillin, and blood cultures were negative on the last day of admission. At readmission, the patient showed no clinical signs of heart failure and no heart murmurs were heard on auscultation. Electrocardiography (ECG) was normal. Laboratory findings showed an erythrocyte sedimentation rate of 54 mm/h, a white blood cell count of 15.4×10^9 /liter, and a C-reactive protein (CRP) level of 138 mg/liter. Urinalysis did not show white blood cells or nitrite, and urine cultures performed before the initiation of antibiotic treatment were negative. The chest radiograph and ultrasound examination of the abdomen were normal. The blood cultures drawn on the day of admission showed growth with Gram-positive cocci resembling staphylococci, and intravenous flucloxacillin was subsequently started. However, subinoculation onto blood agar showed alpha-hemolytic colonies resembling viridans streptococci which were identified as *A. urinae* using the Vitek system (99% reliability; bioMérieux, France) and 16S rRNA PCR (97 to 99% reliability). The antibiotic treatment was switched to penicillin after sensitivity testing showed a MIC of 0.023 mg/liter. Repeated TEE demonstrated a vegetation on the mitral valve with regurgitation and prolapse. The patient was treated with 12 million IU/day intravenous penicillin for 6 weeks and 3 mg/kg of body weight gentamicin once a day for 2 weeks. He declined mitral valve surgery.

Patient B, a 78-year-old man with a history of ischemic heart disease and polymyalgia rheumatica, was recently diagnosed with stage IV non-small cell lung carcinoma. After two courses of chemotherapy (carboplatin/gemcitabine), he refrained from further treatment. One day after suprapubic catheterization of

the bladder, the patient became septicemic. His temperature was 39.6°C, and he was hypotensive, with a blood pressure of 65/40 mm Hg and a heart rate of 92 beats per minute (b/min). After performing blood and urine cultures, fluid resuscitation was immediately started, as well as intravenous cefuroxime administration on the presumptive diagnosis of a urinary tract infection. An ECG was normal. The laboratory findings showed a CRP level of 46 mg/liter, sodium 140 mmol/liter, potassium 3.5 mmol/liter, urea 9.0 mmol/liter, and creatinine 107 μ mol/liter. Cefuroxime was replaced with flucloxacillin when Gram-positive organisms, thought to be staphylococci, were identified in the blood cultures. However, after growth on blood agar, the alpha-hemolytic colonies resembled viridans streptococci. Using the Vitek system and 16S rRNA gene sequence analysis, the organisms were identified as *A. urinae*. A transthoracic echocardiogram (TTE) showed a possible vegetation on the aortic valve, and the antibiotic treatment was switched to high-dose penicillin (12 million IU/day). Because the patient had a poor prognosis, he did not consent to a TEE. Because the patient's condition deteriorated, treatment was discontinued. He was transferred to a hospice.

Patient C, an 87-year-old man, was admitted for progressive dyspnea. Physical examination revealed an elevated jugular venous pressure, a grade IV/VI holosystolic heart murmur on the apex, and late inspiratory crepitations at the lung bases. The patient's blood pressure was normal, and he did not have fever. He had a history of basal cell carcinoma, glaucoma, bifascicular block, lower-urinary-tract symptoms, and heart failure. An ECG showed a sinus rhythm of 84 b/min and right bundle branch block configuration. A chest radiograph showed signs of pulmonary congestion. A TTE was performed because of the new heart murmur and showed poor left ventricular function with an ejection fraction of 40 to 50%, a severe tricuspid valve regurgitation, and severe mitral valve regurgitation with a flail of the hindmost valve and a possible vegetation on the valve. The right atrium and ventricle were dilated. Blood and urine cultures were performed, and the patient was transferred to the coronary care unit but shortly thereafter went into cardiac arrest. After successful cardiopulmonary resuscitation, mechanical ventilation, hemodynamic support, hypothermia, and antibiotic treatment were initiated on the intensive care unit. Considering the very poor prognosis,

* Corresponding author. Mailing address: Department of Internal Medicine, Kennemer Gasthuis, Boerhaavelaan 22, 2035 RC Haarlem, the Netherlands. Phone: 31-23-5453545. Fax: 31-23-5453759. E-mail: Jongdem1@kg.nl.

[▽] Published ahead of print on 21 July 2010.

treatment was discontinued, and the patient died. Urine cultures were negative, but blood cultures obtained at admission were positive for *A. urinae* identified by Vitek (bioMérieux, France). Autopsy was denied.

Patient D, a 78-year-old woman, was admitted for septic shock. One day earlier, she had undergone flexible ureteroscopy with laser lithotripsy and ureteral stent implantation. Cefazolin and gentamicin had been administered preoperatively. Besides a renal calculus and recurring urinary tract infections, the patient had a history of aortic valve sclerosis, slight mitral and tricuspid valve regurgitation with good left and right ventricular function, hypertension, and diabetes mellitus. On physical examination, she was febrile (39.1°C) and hypotensive (80/50 mm Hg). On auscultation, a systolic heart murmur was heard on the second intercostal space on the right side of the sternum. The white blood cell count was $15.7 \times 10^9/\text{liter}$, and the CRP level was 157 mg/liter. The serum creatinine level was 185 $\mu\text{mol/liter}$. Serum levels of sodium and potassium were normal. Repeated urinalysis showed a few white blood cells but no nitrite, and urine cultures performed before the initiation of antibiotic treatment were negative. The chest radiograph was normal except for a slight cardiomegaly. The patient was treated with intravenous fluid administration and antibiotics. The antibiotic regimen consisted of cefuroxime and vancomycin. The latter was added because previous urine cultures yielded *Enterococcus faecalis* and allergy to amoxicillin was recorded. Vasoactive agents were required to treat refractory shock. Ultrasound examination of the abdomen showed normal-sized kidneys without signs of obstruction. Over the course of 14 days, the patient recovered. Blood cultures were positive for *A. urinae* and *Escherichia coli*.

Aerococcus urinae is a Gram-positive, catalase-negative coccus that was first described in the 1990s as a causative organism of urinary tract infections (1). *A. urinae* levels of 0.3 to 0.8% in urine specimens are reported, with a preponderance in patients with underlying urologic conditions (6, 8). Although the organism is considered to be of low pathogenicity and may not always need to be treated (6, 8), there are descriptions of severe, sometimes fatal infections, such as endocarditis (2–4, 6–9, 11), but often in the presence of urinary tract infections or symptoms typical of this infection (12). The mortality rate of *A. urinae* endocarditis is high, but the virulence factors are as yet unknown. Old age and underlying urologic conditions, such as prostatic hyperplasia, seem to be risk factors for infection (2, 6, 7).

Microbiology. Isolates of *A. urinae* may easily be mistaken for staphylococci in the Gram stain, because they appear as Gram-positive cocci that are arranged in tetrads or clusters (12). Colonies on blood agar may be mistaken for streptococci, because these show alpha hemolysis and are catalase negative, resembling viridans streptococci and some enterococci (5, 12). Primary identification is based upon Gram stain of alpha-hemolytic colonies which are catalase negative. *Aerococcus* species will appear as Gram-positive cocci in clusters, which differentiates these species from streptococci and enterococci (12). Differentiation between *A. urinae* and *Aerococcus viridans* can be done by testing for pyrrolidiny aminopeptidase (PYR), which is only positive for *A. viridans*, and leucine aminopepti-

TABLE 1. Antibiotic sensitivity of *A. urinae* isolates from cases and overall in our laboratory from 2004 to 2009

Antibiotic	Sensitivity ^a in isolate from patient:				No. of sensitive isolates/no. of isolates tested (%)
	A	B	C	D	
Penicillin	S	S	S	S	171/171 (100)
Amoxicillin	S	S	S	S	171/171 (100)
Clindamycin	S	S	S	R	162/171 (95)
Doxycycline	S	S	R	S	22/26 (85)
Vancomycin	S	S	S	S	20/24 (83)
Erythromycin	S	S	R	R	165/170 (97)

^a S, sensitive; R, resistant.

dase (LAP), which is only positive for *A. urinae* (5, 12). Furthermore, automated systems like the Vitek system are reliable instruments for phenotypical identification, and 16S rRNA PCR may be used for genotypic confirmation. Sometimes blood cultures remain negative, in which case 16S rRNA PCR directly on a blood culture could reveal *A. urinae* (11). In our laboratory, urine cultures are routinely performed on blood agar and a chromogenic agar that is specific for Gram-negative species. Gram-positive cocci that grow in clusters and show alpha hemolysis on blood agar are further determined using the Vitek system. *Aerococcus* species are tested for sensitivity to penicillin, amoxicillin, clindamycin, doxycycline, vancomycin, and erythromycin. *A. urinae* is often sensitive to penicillin, amoxicillin, and quinolones, such as ciprofloxacin, but variably sensitive to clindamycin, erythromycin, and doxycycline. Strains are resistant to aminoglycosides and other antimicrobials used for treating urinary tract infections, including co-trimoxazole and trimethoprim (6, 10).

Incidence. A search in our laboratory database for urine and blood cultures positive for *A. urinae* showed 136 patients with a urinary tract infection and 7 patients with a bloodstream infection with this microorganism from November 2004 until December 2009. Since our hospital serves a population of about 500,000, the incidence of *A. urinae* urinary tract and bloodstream infections is estimated to be 54 and 3 per 1,000,000 per year, respectively. The percentages of antibiotic sensitivities of *A. urinae* isolates of the described cases and all blood and urine strains isolated from 2004 to 2009 are shown in Table 1.

In conclusion, urologic conditions predispose for infections with *Aerococcus urinae*. Generally considered to be of low pathogenicity, this microorganism may cause severe bloodstream infections, including endocarditis. The identification of *A. urinae* can be challenging. Physicians and microbiologists should consider endocarditis in patients when *A. urinae* is isolated from the blood.

REFERENCES

- Aguirre, M., and M. D. Collins. 1992. Phylogenetic analysis of some *Aerococcus*-like organisms from urinary tract infections: description of *Aerococcus urinae* sp. J. Gen. Microbiol. **138**:401–405.
- Ebnöther, C., M. Altwegg, J. Gottschalk, J. D. Seebach, and A. Kronenberg. 2002. *Aerococcus urinae* endocarditis: case report and review of the literature. Infection **30**:310–313.
- Kass, M., B. Toye, and J. P. Veinot. 2008. Fatal infective endocarditis due to *Aerococcus urinae*—case report and review of the literature. Cardiovasc. Pathol. **17**:410–412.
- Kristensen, B., and G. Nielsen. 1995. Endocarditis caused by *Aerococcus urinae*, a newly recognized pathogen. Eur. J. Clin. Microbiol. Infect. Dis. **14**:49–51.

5. **Ruoff, K. L.** 2002. Miscellaneous catalase-negative, Gram-positive cocci: emerging opportunists. *J. Clin. Microbiol.* **40**:1129–1133.
6. **Schuur, P. M., M. E. Kasteren, L. Sabbe, M. C. Vos, M. M. Janssens, and A. G. Buiting.** 1997. Urinary tract infections with *Aerococcus urinae* in the south of the Netherlands. *Eur. J. Clin. Microbiol. Infect. Dis.* **16**:871–875.
7. **Schuur, P. M. H., L. Sabbe, A. J. Van der Wouw, G. J. Montagne, and A. G. M. Buiting.** 1999. Three cases of serious infection caused by *Aerococcus urinae*. *Eur. J. Clin. Microbiol. Infect. Dis.* **18**:368–371.
8. **Sierra-Hoffman, M., K. Watkins, C. Jinadatha, R. Fader, and J. L. Carpenter.** 2005. Clinical significance of *Aerococcus urinae*: a retrospective review. *Diagn. Microbiol. Infect. Dis.* **53**:289–292.
9. **Skov, R. L., M. Klarlund, and S. Thorsen.** 1995. Fatal endocarditis due to *Aerococcus urinae*. *Diagn. Microbiol. Infect. Dis.* **21**:219–221.
10. **Skov, R., J. J. Christensen, B. Korner, N. Frimodt-Møller, and F. Espersen.** 2001. In vitro antimicrobial susceptibility of *Aerococcus urinae* to 14 antibiotics, and time-kill curves for penicillin, gentamicin and vancomycin. *J. Antimicrob. Chemother.* **48**:653–658.
11. **Slany, M., T. Freiberger, P. Pavlik, and J. Cerny.** 2007. Culture-negative infective endocarditis caused by *Aerococcus urinae*. *J. Heart Valve Dis.* **16**:203–205.
12. **Zhang, Q., C. Kwok, S. Attorri, and J. E. Clarridge, III.** 2000. *Aerococcus urinae* in urinary tract infections. *J. Clin. Microbiol.* **38**:1703–1705.