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Case report

Aerococcus urinae endocarditis – A case report.

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ABSTRACT

Aerococcus urinae is a gram-positive coccus bacterium with a previously underestimated prevalence due to morphological similarities to other gram-positive cocci. Development of newer diagnostic technologies (such as matrix-assisted laser desorption ionization time-of-flight mass spectrometry MALDI-TOF) led to increased recognition of *Aerococcus urinae* as causative organism mainly for urinary tract infections. Its antibiotic susceptibility poses some challenges, with resistance to some drugs of choice for urinary tract infection. We report a case of a 69-year-old male with infective endocarditis of the mitral valve, who initially presented with fever and shoulder pain to the emergency department. The patient reported an episode of obstructive renal infection two weeks earlier, which was treated with trimethoprim-sulfamethoxazole. The unusual presentation with shoulder pain and a new heart murmur led to suspicion of endocarditis. Urine and blood cultures were positive for *Aerococcus urinae*, echocardiography revealed vegetations on the mitral valve with severe mitral insufficiency. After two weeks of antibiotic treatment, mitral valve replacement was performed, from which the patient recovered. Reports of *Aerococcus urinae* endocarditis are still limited in number. On the other side, *Aerococcus urinae* is an emerging bacterial uropathogen with greater relevance than previously believed. We review the case reports of *Aerococcus urinae* endocarditis and newest literature about its presentation, course, and clinical management.

Introduction

Aerococcus urinae is a gram-positive cocci bacterium growing in pairs or tetrads [1]. Due to its morphological similarities to other gram-positive cocci, it was an underestimated human pathogen. Recently, more widespread use of mass spectroscopy-based identification techniques (mainly matrix-assisted laser desorption ionization time-of-flight mass spectrometry MALDI-TOF) led to increased recognition of *Aerococcus urinae* in medical laboratories [2]. For instance, its prevalence in urinary tract infections in newer literature is reported around 20 % [3–5].

The antibiotic susceptibility of *Aerococcus urinae* leads to challenges. A resistance to fluoroquinolones was reported with a sensitivity to ciprofloxacin between 50–90 % [2,6]. Furthermore, *Aerococcus urinae* is resistant to sulfamethoxazole [7,8]. These resistances are very important in the clinical context, as trimethoprim-sulfamethoxazole and ciprofloxacin are often drugs of choice for urinary tract infections. Being an emerging and underrecognized urinary tract pathogen, undiagnosed patients can suffer complications such as bacteremia or endocarditis due to wrong antibiotic choice.

We here describe a patient with infective endocarditis with *Aerococcus urinae*. Initially, this patient suffered from urogenital tract infection with *Aerococcus urinae*. Sterile urine culture led to antibiotic treatment with trimethoprim-sulfamethoxazole, which was inadequate and presumably allowed bacterial dissemination leading to endocarditis. Case reports of *Aerococcus urinae* endocarditis are still limited in number, despite *Aerococcus urinae* being an emerging uropathogen.

We review existing case reports and provide and update of the current literature about presentation, course, and clinical management of *Aerococcus urinae* endocarditis. We hereby aim to fill the knowledge gap of the clinical importance of *Aerococcus urinae* existing among clinicians.

Abbreviations: MALDI-TOF, matrix-assisted laser desorption/ionization-time of flight; COVID-19, Corona-Virus-Disease 2019.

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Case

A 69-year-old Caucasian male presented to our emergency department with fever and shoulder pain. He reported of an episode of renal infection caused by obstructive nephrolithiasis two weeks earlier, which was diagnosed and treated by his general practitioner. He was intolerant to the initially prescribed ciprofloxacin, triggering vomiting. The treatment was therefore changed to trimethoprim-sulfamethoxazole, which was taken for 7 days. No bacteria were detected in the urine culture.

Fever returned soon after initial improvement. At time of presentation at our hospital, he complained of fever with temperatures above 40 °C in the evenings. In addition, his left shoulder was painful. He reported having pollakiuria, but no dysuria, hematuria, nor symptoms of an upper respiratory tract infection.

On physical examination, we saw a fully oriented patient in good general condition. Examination of the lungs was normal. A systolic murmur radiating to the axillary region, compatible with mitral insufficiency was noted. Abdominal examination was unremarkable and there was no tenderness in the renal area. No edema or signs of hypervolemia were observed.

The laboratory analysis showed inflammation with elevation of c-reactive protein (130 mg/l, reference range <5 mg/l), leukocytosis (15·9 Giga/l, reference range 2·6–7·8 Giga/l) with neutrophilia (12·75 Giga/l, reference range 0·9–4·5 Giga/l), and slightly elevated procalcitonin (0·47 µg/l, reference <0·25 µg/l). SARS-CoV-2-RNA PCR in the nasopharyngeal swab was positive. Urine sample showed mild leukocyturia (6–10 cell counts per field view, reference 0–5) and bacteriuria, but was also positive for squamous cells.

The systolic murmur and shoulder pain did not fit to an infection with COVID-19 and led us to suspect infective endocarditis. The patient was admitted to our hospital for further diagnostic workup. The following day, a transthoracic echocardiography described suspected vegetation on the mitral valve. Further evaluation with transesophageal echocardiography showed vegetations on the posterior leaflet of the mitral valve (2 × 9 mm). In addition, severe insufficiency of the mitral valve with suspected perforation of the posterior mitral valve leaflet were seen.

At the same time, results from culture of the blood and urine sample were positive for *Aerococcus urinae*. Two days after presentation, red, macular and non-tender lesions were observed on both palms and interpreted as Janeway lesions. International Society of Cardiovascular Infectious Diseases ISCVID / Duke criteria [9] were met with one major criterion (vegetation on echocardiography) and three minor criteria (fever > 38.0 °C, vascular phenomena with Janeway lesions, microbiologic evidence of *Aerococcus urinae* in two sets of blood cultures) and endocarditis on mitral valve position was diagnosed. The susceptibility pattern of the detected bacterium showed sensitivity to amoxicillin, ampicillin, penicillin and vancomycin. Intravenous antibiotic treatment was initially started with co-amoxicillin and switched to penicillin according to the susceptibility pattern. The antibiotics were continued for 6 weeks. In a computed tomography of the shoulder, a minimal swelling of the left shoulder joint was described, but no specific cause could be identified. No shoulder tap was performed.

During the course of the hospitalization, the patient suffered congestive heart failure due to decompensated mitral valve regurgitation. An interdisciplinary decision for biological mitral valve replacement was made. The operation was successfully performed two weeks after initial presentation. Histology of the mitral valve confirmed chronic and focal acute inflammation and aggregation of coccoid bacteria.

The patient was discharged to a cardiac rehabilitation clinic, where antibiotic treatment was continued for a total of six weeks. In a follow-up examination six months after operation, echocardiography showed a normal function of the left ventricle and the biological mitral valve. The patient reported to be in good health.

Discussion

Aerococcus urinae is a catalase negative, gram-positive coccus producing alpha-hemolytic colonies on blood agar [1,10]. Due to their similar morphologic and biochemical properties, aerococci were long misidentified as streptococci and granulicatella [11]. The development of newer technologies for pathogen identification, such as matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF), next-generation sequencing or broad-range PCR, have enabled fast and accurate identification of aerococci, while minimizing the risk of confusion with streptococci.

The most reported origin of bacteremia with *Aerococcus spp*. is urinary tract infection, typically in older men with underlying urinary tract disorder [2]. Very recent studies identified *Aerococcus urinae* in around 15–20 % of urinary tract infections, making *Aerococcus urinae* one of the top 3 emerging bacterial uropathogens [3–5]. Significantly higher prevalence of the bacterium was found in women with urinary incontinence compared to controls without urinary incontinence [5]. The pathogen can also cause invasive infection, such as urosepsis or endocarditis. Some factors contributing to persistence and virulence of the pathogen are its ability to develop biofilms [10,12] and to activate platelet aggregation [12].

The first-line antibiotic treatment for *Aerococcus urinae* reported in literature is penicillin [13]. The known susceptibility pattern of *Aerococcus spp.* includes benzylpenicillin, ampicillin, meropenem, rifampicin, nitrofurantoin and vancomycin, resistance is known to ciprofloxacin [6]. The combination of penicillin with an aminoglycoside such as gentamicin have shown in vitro activity leading to synergistic effects [14]. The addition of an aminoglycoside may be particularly favorable where a biofilm has already been formed [10] and should be

Table 1
Summary of case reports in literature. IQR = interquartile range.

	All **n = 82**	**Male** **78% (n = 64)**	**Female** **12% (n = 18)**
Age (median)	75 years (IQR 56·5 - 80·75 years)	75 years (IQR 57·25 - 81 years)	78.5 years (IQR 57·25 - 80 years)
Urinary tract pathology*	41·5% (n = 34)	43·8% (n = 28)	33·3% (n = 6)
Surgical management (valve replacement or repair)	Surgery: 36·6% (n = 30) (including 1 pacemaker extraction) *Mortality: 6.7% (n = 2)*	Surgery: 39·1% (n = 25) (including 1 pacemaker extraction)	Surgery: 27·8% (n = 5)
	No surgery: 51·2% (n = 42) *Mortality: 45.2% (n = 19)*	No surgery: 46·9% (n = 30)	No surgery: 66·6% (n = 12)
	Unknown: 12·2% (n = 10) *Mortality: 50% (n = 5)*	Unknown: 14·1% (n = 9)	Unknown: 5·6% (n = 1)
Outcome	Died: 31·7% (n = 26) Survived: 67·1% (n = 55) Unknown: 1·2% (n = 1)	Died: 35·9% (n = 23) Survived: 62·5% (n = 40) Unknown: 1·6% (n = 1)	Died: 16·7% (n = 3) Survived: 83·3% (n = 15)

* Urinary tract infection or recent operation

Table 2
Collection of Case Reports.

No.	First Author	Year	Affected Valve	Age	UTP	Sex	Surgery	Outcomes
1	Christensen	1991	MV	81	yes	m	-	†
2	Christensen	1995	*unknown*	78		m	*unknown*	†
		1995	*unknown*	81		m	*unknown*	†
		1995	AV	73	yes	m	-	†
		1995	*unknown*	81		m	*unknown*	†
		1995	MV and AV	55		f	-	†
		1995	*unknown*	78		m	*unknown*	recovered
3	Skov	1995	AV	81	yes	m	-	†
4	Kristensen	1995	AV	78		m	-	†
5	Zbinden	1998	MV	48		m	-	recovered
		1998	AV	79		f	-	recovered
6	Gritsch	1999	AV	43	yes	m	-	†
7	Schuur	1999	MV	89	yes	m	-	†
8	Ebnöther	2002	AV	75	yes	m	AVR	recovered
9	Perdekamp	2002	AV	18		m	-	†
10	Georgescu	2004	MV and AV	54		f	-	†
11	Slany	2007	AV	69	yes	m	AVR	recovered
12	Tekin	2007	MV	68		m	-	recovered
13	Kass	2008	AV	77		m	-	†
14	Allegre	2008	AV	79		f	AVR	recovered
15	Bruegger	2009	MV and AV	62		m	MVR and AVR	recovered
16	De Jong	2010	MV	81		m	-	recovered
		2010	AV	78		m	-	†
		2010	MV	87	yes	m	-	†
		2010	*unknown*	78	yes	f	-	recovered
17	Ho	2010	AV	80		m	AVR	recovered
18	Cabezas	2011	AV	33		f	AVR	recovered
19	Alozie	2012	AV	68		m	AVR	recovered
20	Gompelman	2014	AV	42		m	AVR	recovered
21	Westmoreland	2014	AV	49		m	*unknown*	*unknown*
22	Sunnerhagen	2015	MV	91		m	-	recovered
		2015	MV	91		m	-	recovered
		2015	MV	89		f	-	recovered
		2015	AV	86	yes	m	-	recovered
		2015	MV	83		m	MVR	recovered
		2015	MV	80		f	-	recovered
		2015	AV	77		m	-	recovered
		2015	MV	75	yes	m	MVR	recovered
		2015	*unknown*	74	yes	m	-	recovered
		2015	MV	65	yes	m	-	recovered
		2015	AV	53	yes	m	AVR	recovered
		2015	AV	49	yes	f	AVR	recovered
		2015	MV	81		m	-	recovered
		2015	AV	74		f	-	recovered
23	Melnick	2016	MV	74	yes	m	MVR	†
24	Siddiqui	2016	AV and TV	54	yes	m	-	†
25	Kotkar	2016	MV	54		m	MVR	recovered
26	Senneby	2016	MV	87		m	*unknown*	†
		2016	AV	77	yes	m	*unknown*	recovered
		2016	MV *	83		m	*unknown*	recovered
		2016	*unknown*	73		m	*unknown*	†
		2016	AV	88		f	*unknown*	recovered
27	Creed	2016	MV	75		m	-	recovered
28	Tathireddy	2017	AV *	69	yes	m	-	recovered
29	Adomavicius	2018	MV	49	yes	m	MVR	†
30	Yabes	2018	MV	43	yes	m	MVR	recovered
31	Samuelsson	2018	PM and TV	84	yes	m	PME	recovered
32	Adeel	2018	AV *	75		m	-	†
33	Figueroa Rodriguez	2019	MV	55	yes	m	MVR	recovered
34	Ludhwani	2020	AV	55	yes	m	AVR	recovered
35	Varughese	2020	AV **	43	yes	m	-	recovered
36	Rosborough	2020	MV	92		m	-	recovered
37	Martin-Guerra	2020	AV	61		m	AVR	recovered
38	Yaban	2020	MV	67	yes	m	MVR	recovered
			AV	86	yes	f	AVR	recovered
39	Khan	2021	AV	86	yes	f	-	†
40	Bradel	2021	AV	76		m	AVR	recovered
41	Ahmed	2021	AV	58	yes	m	AVR	recovered
42	Tai	2021	AV and MV	56		f	AVR	recovered
		2021	MV	54		m	MVR	recovered
		2021	MV	79		f	-	recovered
		2021	AV	72		f	-	recovered
		2021	AV and MV	46		m	-	†
		2021	MV	80		m	MVR	recovered

(*continued on next page*)

Table 2 (*continued*)

No.	First Author	Year	Affected Valve	Age	UTP	Sex	Surgery	Outcomes
		2021	MV	70		m	MVR	recovered
43	Akinboboye	2022	AV	48		m	-	†
44	Feghaly	2022	AV	79		m	-	†
45	Saeed Al-Asad	2022	AV	75	yes	m	-	†
46	Banerjee	2022	TV	61	yes	f	-	recovered
47	Tiong	2022	AV and ARU	82	yes	m	AVR	recovered
48	Yee	2023	AV	80	yes	f	-	recovered
49	Meyer	2024	MV	69	yes	m	MVR	recovered

Abbreviations: UTP = urinary tract pathology; m = male; f = female; AV = aortic valve; MV = mitral valve; TV = tricuspid valve; PM = pacemaker; ARU = aortic root ulcer; AVR = aortic valve replacement; MVR = mitral valve replacement; PME = pacemaker extraction; † = died; * = bio prosthetic; ** = prostethic.

considered for patients with endocarditis. *Aerococcus urinae* is further susceptible to meropenem, vancomycin, nitrofurantoin, and rifampicin [6]. With whole genome analysis, *Aerococcus urinae* could be even further differentiated into several genomic variants [1]. Future research will show, if these variants differ in pathogenicity and antibiotic susceptibility.

The first reports of *Aerococcus urinae* isolated from patients with endocarditis were reported in 1967 by Colman, then named as "Aerococcus-like organisms" [15]. To identify published case reports, a literature search in PubMed was conducted (search string: "aerococcus urinae"[All Fields] OR "aerococcus-like organism"[All Fields]) AND ("endocarditis"[MeSH Terms] OR "endocarditis"[All Fields], last updated 25.04.2024). The literature search was restricted to adult patients, one case report was excluded due to Japanese language.

We identified 48 reports of infective endocarditis caused by *Aerococcus urinae*. A summary of important characteristics from the 48 case reports and the here presented patient can be found in Table 1, the complete collected information is presented in Table 2. Median age was 75 years, and similar in male and female patients. A urinary tract pathology (urinary tract infection or recent urinary tract surgery) was reported in 41·5% of all cases, but information about underlying pathologies were not available in all publications.

Surgical valve replacement was reported for 36·6% of all cases. Male patients had a higher percentage of surgical management (39·6% vs. 27·8%), an observation in accordance with previous reports of sex differences in surgical management in infective endocarditis [16]. The surgical management is lower than reported from registry-based studies [17], where around half of all patients undergo surgery during hospitalization. The overall mortality was high with 31.7%, and higher in male compared to female patients (35·9% vs. 27·8%). The high mortality is likely due to publication bias with only severe and special cases being published. This theory is supported by a study of the Swedish Endocarditis Registry published 2016, where none of the reported 14 cases had fatal outcomes [18]. Furthermore, the treatment of endocarditis may have improved over the last decades (17 out of 48 reports are from 2010 and older).

The frequency of *Aerococcus urinae* causing endocarditis could be higher than previously thought. An analysis of a Swedish registry [19] of patients with bacteremia showed a similar percentage of patients having infective endocarditis due to *Aerococcus urinae* compared to pathogens classified as "commonly causing infective endocarditis" (for example Granulicatella). The authors thus suggested a similar cardiotropic property of *Aerococcus urinae* and to include it as microorganisms that commonly causes infective endocarditis in the Duke-International Society for Cardiovascular Infectious Diseases Criteria. For this, however, further larger-scale epidemiological studies are required.

Sex differences have been demonstrated for the prevalence of infections with *Aerococcus urinae*. The detection rates of *Aerococcus urinae* in patients with suspected urinary tract infection was higher in female compared to male patients (female 20·3%, male 7·9%) [3]. However, male sex is a risk factor for dissemination and complications of *Aerococcus urinae* infection [4]. Accordingly, the case reports of *Aerococcus urinae* endocarditis are mainly from male patients (78%) of older age (median 75 years). The reason for this disparity between higher detection rate in female patients, but higher risk for complication in male patients remains unclear.

Conclusions

Our case report is a typical case for *Aerococcus urinae* endocarditis regarding the patient's male gender, age, and presence of urinary tract pathology. Although the presentation with positive COVID-19 and shoulder pain was unusual, new heart sounds should always raise suspicion for endocarditis. *Aerococcus urinae* is an increasingly recognized as urinary tract pathogen with an ability to cause invasive infection. Population-based epidemiological studies with newer identification techniques (such as MALDI-TOF) analyzing bacteremia and infective endocarditis are needed for better assessment of its true prevalence and cardiotropic characteristics. Furthermore, we suggest a sex-sensitive approach for future research, especially as sex differences in prevalence and complication rate are well described.

Ethical approval

Not applicable.

Consent

Written and signed informed consent from the patient is available.

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CRediT authorship contribution statement

Helene G. Meyer: Writing – original draft, Project administration, Methodology, Formal analysis, Conceptualization. **Prof. Balthasar Luzius Hug:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Conflict of interest

None.

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