Aerococcus Urinae Aortic Valve Endocarditis with Kissing Aortic Wall Ulcer: A Case Report and Literature Review

Patient: Male, 55-year-old
Final Diagnosis: Aerococcus urinae endocarditis • infective aortic wall ulcer • infective endocarditis
Symptoms: Shortness of breath
Medication: —
Clinical Procedure: —
Specialty: —
Objective: Rare disease
Background: Initially presumed as nonpathogenic, the bacterial genus aerococcus now includes 7 distinct virulent and avirulent species. Aerococcus urinae first isolated in 1992 is an uncommon cause of urinary tract infection (UTI) and is seen in only 0.15% to 0.8% of cases. A. urinae associated invasive bacteremia and systemic infection are extremely rare entities. Less than 50 cases of A. urinae associated with infective endocarditis (IE) have been reported in the literature, with the prevalence being 3 per 1 million.

Case Report: A 59-year-old male presented to our hospital with exertional dyspnea and new-onset atrial flutter. Prior to his current admission patient was treated for A. urinae associated UTI with levofloxacin for 10 days. A trans-thoracic echocardiogram revealed severe aortic regurgitation with aortic valve endocarditis, which was subsequently confirmed on transesophageal echocardiogram. Blood cultures displayed gram-positive cocci in clusters, ultimately identified as A. urinae. The patient was treated with intravenous vancomycin and underwent surgical aortic valve replacement along with patch repair for underlying aortic wall ulcer.

Conclusions: To the best of our knowledge, this is the first-ever reported case of A. urinae associated IE complicated by an aortic wall ulcer. Male gender, age >65 years, and preexisting urinary tract pathology have all been implicated as risk factors for aerococcus infection. A. urinae is almost always sensitive to penicillin, carbapenem, and aminoglycosides.

MeSH Keywords: Aerococcus • Aortic Diseases • Aortic Valve Insufficiency • Endocarditis

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Background

The annual incidence of infective endocarditis (IE) is on the rise and is estimated between 1.5 to 11.6 cases per 100 000 person-years [1,2]. The incidence increases by 2-fold in patients with traditional risk factors such as advanced age, intravenous drug use, dental infection, and structural heart disease [3]. Cardiac complications of IE include most commonly heart failure, perivalvular abscess, pericarditis, and intracardiac fistula. The 3 most frequently identified organisms implicated in IE are staphylococcus, followed by streptococcus and enterococcus [4,5]. Aerococcus is a gram-positive, alpha-hemolytic, and catalase-negative cocci first described in 1938 [6]. Initially presumed as nonpathogenic, the bacterial genus aerococcus now includes 7 distinct virulent and avirulent species. Aerococcus urinae first isolated in 1992, is an uncommon cause of urinary tract infection (UTI) and is seen in only 0.15% to 0.8% of cases [7–9]. Invasive bacteremia and systemic infection from A. urinae are extremely rare entities. Less than 50 cases of IE caused by A. urinae have been reported in the literature [10]. Here, we present a sporadic case of a healthy young male who initially presented with constitutional complaints of weight loss, dyspnea and was found to have A. urinae associated IE complicated by aortic wall involvement. To the best of our knowledge, this is the first-ever reported case of A. urinae associated IE complicated by an aortic wall ulcer.

Case Report

A 59-year-old Caucasian male with a past medical history of hypertension was referred to the emergency department (ED) of our facility from outpatient clinic due to exertional dyspnea and new-onset atrial flutter (AF). Associated symptoms included diarrhea, fatigue, and 13-pound weight loss over the last 2 weeks. Prior to his current admission, the patient was started on a 10-day course of levofloxacin for a UTI with urinary cultures isolating greater than 100 000 A. urinae colonies per mL. The patient was an active 1 pack per day cigarette smoker with no history of alcohol or illicit drug abuse. Other medical history was notable for penicillin allergy as a child. The patient denied previous genitourinary surgery, instrumentation, or anatomical abnormalities. On presentation, the patient had a low-grade temperature of 100.7°F (38.2°C); his blood pressure was 106/55 mmHg, heart rate 113 beats per minute, respiratory rate 20 breaths per minute, and oxygen saturation 93% on room air. Cardiac auscultation revealed an irregularly irregular heart rate with no murmur, rubs, or gallop. The rest of the physical examination was unremarkable.

An electrocardiogram performed in the ED confirmed the diagnosis of AF with variable atrioventricular (AV) block. Laboratory investigations revealed leukocytosis (white blood cells 14 700 cells per µL), mild anemia (hemoglobin 12.7 g/dL), and thrombocytopenia (platelets 126 000 per µL). The patient had elevated lactate (2.0 mmol/L) with normal serum chemistry, troponin, and brain natriuretic peptide (BNP) levels. Urinalysis repeated during current admission demonstrated improved microscopic white blood cells and bacterial count. He tested negative for stool clostridium difficile infection and was given one dose of intravenous (IV) vancomycin to finish his remaining course of A. urinae UTI treatment. There was no evidence of pulmonary congestion or infectious process on chest radiograph. Blood cultures were drawn, and the patient was started on IV ditiazem and heparin drip for AF. The following day both sets of blood culture displayed colonies of gram-positive cocci at about 20 hours for which he was continued on IV vancomycin.

A transthoracic echocardiogram (TTE) was done, which revealed an ejection fraction (EF) of 55% to 60%, no wall motion abnormalities, moderate mitral valve regurgitation, severe aortic valve regurgitation, and approximately 1 cm sized mobile aortic valve lesion. Subsequently, transesophageal echocardiography (TEE) was pursued that established the presence of sizeable mobile vegetation on the aortic valve with a mean regurgitant flow of 409 cm/second. The aortic root was normal size with no evidence of aneurysm or dissection. Preliminary blood cultures identified GPC as alpha-hemolytic streptococcus and given his penicillin allergy patient was continued on IV vancomycin. Cardiothoracic surgery was consulted for possible aortic valve replacement, and a diagnostic cardiac angiogram was scheduled. Cardiac catheterization revealed no epicardial coronary artery disease with left ventricular end-diastolic pressure (LVEDP) of 26 mmHg. Once the patient was afebrile and surveillance blood cultures remained negative, the patient underwent surgical aortic valve replacement. Prior to the surgery patient had finished 1-week course of IV vancomycin. The surgery identified large mobile vegetations involving all 3 aortic valve leaflets, which were all resected. Dissection of the left coronary cusp uncovered a 1 cm x 1 cm aortic valve ulceration just below the sinus of Valsalva. The ulcer was irrigated and covered with a bovine patch followed by placement of a 23 mm Inspiris Carpentier-Edwards tissue valve. The patient did well postoperatively and was transitioned out of the intensive care unit. Occasional paroxysms of atrial fibrillation were managed with oral amiodarone, and anticoagulation was achieved with warfarin. Due to the symptomatic nature of atrial fibrillation, rhythm strategy was opted, and the patient was continued on amiodarone and warfarin. Final blood cultures were reported as A. urinae, and due to presumed susceptibility to penicillin, sensitivity was deferred. The patient had 3 sets of negative surveillance blood cultures, and he was discharged to a skilled nursing facility to finish a total of 6 weeks of IV vancomycin from the date of his first negative blood culture. Repeat TTE performed after 1 month of surgery showed no evidence of vegetation with the resolution of severe aortic regurgitation (Figure 4),
A. urinae is a gram-positive alpha-hemolytic coccus commonly misidentified as streptococcus or staphylococcus. The cluster colonies of A. urinae can simulate staphylococcal growth; however, aerococcus does not share the catalase positivity of staphylococcus. Male gender, age >65 years old, and preexisting urinary tract pathology have all been implicated as risk factors for aerococcus infection. Other than the male status, our patient belonged to a relatively younger age group and

Discussion

A. urinae is a gram-positive alpha-hemolytic coccus commonly misidentified as streptococcus or staphylococcus. The cluster colonies of A. urinae can simulate staphylococcal growth; however, aerococcus does not share the catalase positivity of staphylococcus. Male gender, age >65 years old, and preexisting urinary tract pathology have all been implicated as risk factors for aerococcus infection. Other than the male status, our patient belonged to a relatively younger age group and
carried no traditional genitourinary risk factor. Less than 50 cases of *A. urinae* related IE have been reported in the literature; this is primarily due to the misdiagnosis as either streptococcus or staphylococcus infection [10]. Two aerococcus species, in particular, *A. urinae* and *A. sanguinicola*, have been associated with invasive human infections.

Endothelial injury secondary to turbulent blood flow, diseased heart valves, structural lesion, and iatrogenic trauma from intravascular devices are the primary inciting event leading to IE [11]. Intact endothelium is usually resistant to bacterial impaction. The disrupted endothelial lining is either directly infected by bacteria or can act as a nidus for the aggregating platelet and fibrin, often referred to as nonbacterial thrombotic endocarditis (NBTE). Clinical conditions such as valvular heart disease, rheumatoid arthritis, systemic lupus erythematosus, and malignancy are commonly associated with NBTE. Transient bacteremia can invade either the exposed endothelial lining or the nonbacterial thrombus via adhesin matrix molecules expressed by microbial pathogens giving rise to “vegetations” [12]. The surface of such vegetations consists predominantly of proliferating microbes which are continuously shredded into the bloodstream causing persistent fevers and constitutional symptoms. The pathophysiology behind *A. urinae* associated IE is fundamentally related to the pathogen’s ability to form biofilm and induce platelet aggregation [13]. Transient bacteremia in most cases of aerococcus results from genitourinary infection.

In most cases, the diagnosis of IE is made before the causative agent is identified. The diagnosis of IE is based on the presence of clinical features, evidence of bacteremia on blood cultures, and confirmation of vegetation on echocardiography. The widely accepted Duke’s criteria for IE stratifies patients into 3 categories using major, minor, and pathological criteria:

![Figure 3. 1×1 cm kissing aortic ulcer as evident (B) after dissecting aortic valve with vegetations involving all three leaflets (A).](image1)

![Figure 4. Follow up transthoracic echocardiogram (TTE), 1 month after surgical aortic valve replacement showing no evidence of aortic valve regurgitant blood flow on colored doppler.](image2)
a) definitive IE, b) pathologically proven IE, and c) possible IE. The negative predictive value of Duke’s criteria, as calculated in a study where 58 cases of “rejected IE” were followed for 3 months, was 98% [14]. In our case, the patient demonstrated both major clinical criteria (positive set of blood cultures with echocardiographic evidence of vegetation) with absent minor clinical criteria (fever, predisposing risk factors, immunologic/vascular phenomenon, or microbiological evidence) making the diagnosis of IE definitive.

A negative TTE (as opposed to our case) should prompt evaluation with TEE if the suspicion for IE is high. Both TTE and TEE have high specificity; however, the diagnostic sensitivity of TEE is far superior, 87% to 100% compared to 44% to 66% for TTE [15]. The presurgical accuracy of TEE in detecting the location and extent of vegetations is improved when performed closer to the surgery [16]. Laboratory identification of A. urinae can be challenging, and due to similarities with other bacteria, the true incidence is underestimated. The standard gold test to identify aerococcus species remains 16S ribosomal RNA gene sequencing. However, the use is limited due to cost and limited availability. The use of matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) has replaced the more expensive gene sequencing. Due to the lack of uniform testing and morphological similarities to staphylococcus or streptococcus species, there remains a potential for the under-estimation of aerococcus due to erroneous diagnosis.

Aside from developing better diagnostic modalities, or novel medical/surgical interventions for the treatment of IE, complications from IE are of major interest to clinicians and researchers alike. Some of the common sequela from IE include stroke, embolization, heart failure, intracardiac abscess, and new conduction abnormalities [17]. In our case, unfortunately, along with aortic valve vegetation resulting in severe aortic regurgitation, interestingly, we also found kissing ulceration involving the aortic wall. Aortic ulcer secondary to IE has been reported in isolated cases previously; however, there have been no cases of infectious aortic ulcer secondary to A. urinae bacteraemia [18]. The pathophysiology behind the peri-annular extension of IE is related to the anatomic vulnerability of through the most susceptible part of the annulus near the membranous septum [17]. The disruption of the vessel endothelium secondary to the constant insult from the vegetation irritating the vessel wall is responsible for the superficial kissing ulcer. The high intravascular pressure can further worsen and extend the ulcer. Late or under-diagnosis of the ulceration in the aortic wall can potentially lead to abscess formation, which may result in intracardiac or pericardial fistula formation, ultimately leading to death. Treatment is usually necessitating surgical excision of necrotic tissue, drainage of any visible abscess cavities, and replacement of the injured valve. Due to the metabolic inactivity of the organism deep inside the vegetation core, complete eradication of the bacteria warrants either prolonged antibiotic therapy or surgical removal of the vegetation. The selection of antibiotics is dictated predominantly on the blood culture, which is positive in 90% of IE cases. Antibiotic sensitivity can vary based on the different aerococcus species. A. urinae is almost always sensitive to penicillin, ampicillin, carabapenem, and aminoglycosides [8]. Studies have shown a synergistic effect of penicillin and aminoglycosides in aerococcal infections [19]; however, these results were not correlated in newer studies. In cases with penicillin allergy, a 4-week course of vancomycin with 14 days of gentamycin have shown similar results [20]. In our patient with life-threatening penicillin allergy, vancomycin was successfully used, and gentamycin was avoided due to the latter’s side effect profile [20].

Similar to other infective pathologies, IE is associated with a significant systemic inflammatory response, which is evident with high levels of inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). The patients with left-sided IE are at an increased risk of developing new-onset atrial fibrillation. Studies have looked into the association between new-onset atrial fibrillation and its correlation with the inflammatory response mounted during IE. Ferrera et al. reported that the presence of new-onset atrial fibrillation is an independent predictor of heart failure and in-hospital mortality in patients with IE [21]. In our case, although the patient had other risk factors implicating his new-onset atrial fibrillation, the presence of heightened inflammatory state along with concomitant aortic regurgitation heightened his risk of atrial fibrillation. Managing heart failure as a consequence of new-onset atrial fibrillation can become challenging. IE associated with severe valvular dysfunction or new-onset heart failure needs surgical evaluation. A multidisciplinary approach in such cases is advocated.

Conclusions

A. urinae associated UTI is encountered in male patients with advanced age and predisposition to urinary pathology. The utilization of MALDI-TOF MS has improved the identification and diagnosis of A. urinae. Invasive bacteraemia due to A. urinae should prompt further investigation with TTE and TEE to rule out underlying IE. Penicillin, carabapenem, and aminoglycosides usually provide adequate coverage. The role of combination therapy with penicillin and aminoglycosides needs further clarification. A. urinae associated IE can lead to valvular abnormalities, which can extend beyond the valvular apparatus to involve the aorta and surrounding structures as depicted in our case.
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Conflict of interest

None.

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