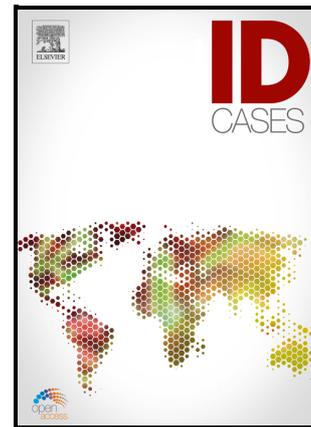


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Triple-Valve Endocarditis due to *Lysinibacillus sphaericus* Infection  
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Abstract: *Lysinibacillus sphaericus* is an environmental organism often considered a contaminant when isolated from patient specimens due to its rare association with human disease. Here we report a case of triple valve endocarditis caused by *L. sphaericus* infection. To the authors' knowledge, this is the first documented case of endocarditis caused by this bacterium.

Keywords: Endocarditis, *Lysinibacillus, sphaericus*, Triple-valve, bacteremia

## Introduction

*Lysinibacillus sphaericus* is a gram-positive bacillus characterized by a terminal endospore, the capability to utilize acetate as a sole carbon source, and the presence of lysine and aspartic acid in the cell wall peptidoglycan [1]. The binary toxin produced by this organism in the final stages of sporulation is larvicidal and used in vector-control programs that target mosquitos carrying malaria, filariasis, yellow fever, dengue, and West Nile [1], [2]. There are relatively few case reports and case series detailing human infection with *L. sphaericus* [3], [4], [5]. This case report describes a patient with triple-valve endocarditis (TVE) due to *L. sphaericus* and provides a literature review of human infection associated with this uncommon human pathogen.

## Case Report

A 74-year-old man was transferred from an outside hospital where he had presented with complaints of fatigue and malaise. Past medical history included former tobacco use, COVID-19 infection in October 2022, osteoarthritis, spinal stenosis, primary hypertension, and anemia of unspecified etiology. He was a retired truck driver and house painter.

The patient had been discharged ten days prior from the same outside hospital from which he was transferred. He had been hospitalized after he presented with fatigue and a forty-pound weight loss due to a lack of appetite for three months. One bottle from each of the two blood culture sets collected on the day of his admission to that hospital became positive on day three of hospitalization with *L. sphaericus* and no other organisms. The organism was sensitive to all tested antibiotics, including erythromycin, gentamicin, penicillin, rifampin, tetracycline, and vancomycin. A transthoracic echocardiogram (TTE) was obtained and showed TVE with involvement of the aortic (AV), mitral (MV), and tricuspid valves (TV). The ejection fraction (EF) was reduced at 30-35%. He had no known previous history of heart disease. He was discharged home on ampicillin-sulbactam and daptomycin via tunneled right internal jugular catheter for an anticipated six-week course, as well as losartan, metoprolol, and dapagliflozin. Once home, he noticed a progressive swelling of his abdomen and shortness of breath when walking short distances. Six days after discharge, he developed acute shortness of breath at rest and called EMS for transport back to the outside hospital. Laboratory work on arrival was significant for creatinine 3.1 mg/dl (baseline, 0.9 mg/dl three months earlier), potassium 3 mmol/L (normal range 3.5 – 5.3 mmol/L), D-dimer >25,000 FEU/ml (normal  $\leq$  500 FEU/ml) and BNP >5,000 pg/ml (normal < 125 pg/ml). COVID-19 PCR, Influenza A and B PCRs, *Streptococcus pneumoniae* antigen, and *Legionella* antigen in urine were all negative. Computed Tomography Angiography (CTA) of the chest showed no pulmonary embolism but did show bilateral pleural effusions and reflux of the contrast into hepatic veins suggestive of right heart strain. He underwent a right thoracentesis with the removal of 2 liters of fluid. Blood cell count and differential showed 114 white blood cells (54% lymphocytes, 32% monocytes) and 9,000 red blood cells. No organisms were identified on Gram stain, and cultures were negative for bacterial growth. Creatinine worsened to 4.0 mg/dl, potassium increased to 6.2 mmol/L and, despite continuous bumetanide infusion, he experienced persistent volume overload. Consequently, a right tunneled femoral dialysis catheter was placed, and hemodialysis was initiated. Antibiotics were changed to ceftriaxone and daptomycin per the consulting Infectious Disease physician. On day four of hospitalization, he was transferred to our facility for a cardiothoracic (CT) surgery evaluation of refractory heart failure.

On arrival, the patient was alert, able to converse, and hemodynamically stable with oxygen saturation > 92% on room air. Laboratory work showed creatinine of 1.88 mg/dl, white blood cell count of 6.3 K/ $\mu$ L (normal range 4.0 - 10.5 K/ $\mu$ L), platelet count of 97, 000 K/ $\mu$ L (normal range 130 – 400 K/ $\mu$ L), potassium 3.3 mmol/L, and BNP 34,461 pg/ml. Ceftriaxone and daptomycin were continued. Because creatinine was still elevated above baseline and in anticipation of left and right heart catheterization, continuous intravenous fluids were administered. A nephrologist evaluated the patient and diagnosed him with multifactorial acute tubular necrosis secondary to losartan, dapagliflozin, contrast-induced nephropathy, and cardio-renal syndrome. Since creatinine was improved from pre-dialysis levels and the patient had a large urine output, hemodialysis was not re-started, and the dialysis catheter was removed. The Infectious Disease team was consulted and discontinued ceftriaxone and daptomycin after confirming the blood culture results and susceptibility profile from the outside hospital. Penicillin G 4 million units every four hours was started which the patient tolerated well. A TTE revealed an EF of 25 -30%, moderate AV and MV regurgitation, and severe TV regurgitation. Two large mobile echodensities were identified on the TV measuring 0.85cm x 0.86cm and 2.2cm x 1.64cm. A mobile echodensity measuring 1.79cm x 0.82cm on the AV was also identified. The patient underwent a left heart catheterization on day three of hospitalization and was found to have severe calcific three-vessel coronary artery disease including subtotal occlusion of the right coronary artery in the mid-segment. Duplex imaging of his lower extremities revealed that he had no adequate venous conduit for coronary artery bypass graft surgery. The CT surgeon had a discussion with the patient and his family detailing that surgery for his cardiac conditions would involve triple valve surgery and quadruple bypass surgery in the setting of significantly reduced left ventricular function with likely no conduit for complete revascularization. The patient and his family elected for extirpation of the TV vegetation to mitigate the risk for embolization, chest tube placement for the right pleural effusion which had recurred, and to continue an extended penicillin treatment course. Further surgical intervention would be discussed after the antibiotic course was completed.

The patient underwent the planned procedures on day six of hospitalization. Transesophageal echocardiogram confirmed the TTE findings of two large irregular mobile masses attached to the atrial side of the TV and the smaller mobile irregular mass on the aortic side of the AV leaflets. It also showed a small irregular mobile mass on the atrial side of MV posterior leaflet, establishing the diagnosis of triple-valve endocarditis. The TV had no residual vegetation after extirpation but still showed severe regurgitation. Unfortunately, on arrival at the intensive care unit after surgery, the patient developed bradycardia and then asystole. Advanced life support measures were initiated but the patient never regained a cardiac rhythm and his family eventually asked for resuscitative efforts to cease.

## Discussion

*L. sphaericus* (previously *Bacillus sphaericus*) is a gram-positive spore-forming bacterium [1] that naturally occurs in soil and aquatic habitats [6]. On Gram stain, vegetative cells are gram-positive but sporulating cells are gram-variable. Some strains are toxic to mosquito larvae of the *Culex* spp., *Anopheles* spp., and *Psorophora* spp. In 1980, entomocidal *B. sphaericus* strains SSII-I, 1404-9, and 1593-4 were used to inoculate rodents. No animals became clinically ill or died; the authors concluded that these strains were safe to use in environments with high human exposure [7]. Certain entomocidal strains of *Lysinibacillus* are now used in mosquito-control programs targeting mosquitos carrying malaria, filariasis, yellow

fever, dengue, and West Nile. While ubiquitous in the environment, *L. sphaericus* has also been isolated in hospital microbiological laboratory waste, clinical sharp waste, and clinical solid waste from hospital isolation wards [8]. When isolated in microbiology laboratories, this organism is often considered an environmental contaminant but, with documented cases of *L. sphaericus* causing human disease, its pathogenicity can be ambiguous [5].

There were two reported cases of *B. sphaericus* bacteremia between 1932 and 1969 [9]. In 1969 Allen and Wilkinson reported a case of meningitis due to *B. sphaericus* [10]. In 1976, Isaacson et al described a large pseudotumor of the left lung from which *B. sphaericus* was isolated [4]. In the 1980s, two patients with cancer were found to have central venous catheter-related bacteremia attributed to *B. sphaericus* [11], [12]. There were 12 cases of *B. sphaericus* bacteremia in children with cancer or receiving bone marrow transplants between 1989 and 1999 at one children's hospital in Genoa, Italy [3]. Half of these cases were central venous catheter-related, five infections were in patients with neutropenia, and one infection was in a patient with mucosal barrier damage due to intestinal graft versus host disease. This gastrointestinal mucosal damage was theorized to possibly have caused bacteremia, although whether *B. sphaericus* is a colonizer of the gut has not yet been established [3]. In 2015, Wenzler et al described a case of severe sepsis due to polymicrobial bacteremia which included gram-variable rods that were eventually identified as *L. sphaericus* using 16s rDNA sequencing [5]. This case demonstrated the critical importance of accurate laboratory techniques in the diagnosis of infections caused by uncommonly isolated microorganisms so that treatment is not delayed.

Most *Bacillus* species are susceptible to vancomycin, clindamycin, fluoroquinolones, aminoglycosides, and carbapenem antibiotics while susceptibilities to penicillins and cephalosporins are variable [5], [13]. The patient reported by Wenzler et al was given ertapenem and vancomycin as empiric therapy, with a subsequent switch to ampicillin-sulbactam after both *Lysinibacillus* species were determined to be penicillin-sensitive. The strain of *L. sphaericus* identified in our patient was also susceptible to standard antibiotics including penicillin. Because of the genetic similarity of *Lysinibacillus* spp. to other *Bacillus* spp., empiric treatment may be selected according to the standard susceptibility profile for *Bacillus* species and subsequently adjusted as appropriate based on the results of susceptibility testing.

## Conclusion

*Lysinibacillus sphaericus* is a gram-positive bacillus with larvicidal activity used in many vector-control programs to reduce the transmission of mosquito-borne diseases to humans. It has been associated clinically with bacteremia, meningitis, and pulmonary pseudotumor but to the authors' knowledge, this is the first reported case of endocarditis due to *L. sphaericus*. While infection with this bacterium is uncommon, this patient's case highlights how accurate laboratory diagnosis, prompt susceptibility-guided antibiotic treatment, and source control if possible are essential for patient care.

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Declaration of Competing Interest

The authors have no conflicts of interest to report.