

Two Cases of *Listeria monocytogenes*-Induced Infective Endocarditis

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Abstract: *Listeria monocytogenes* is a prevalent gram-positive intracellular zoonotic pathogen that is frequently associated with foodborne illnesses and opportunistic infections. This bacterium is responsible for causing various clinical manifestations, including bacteremia, meningitis, and encephalitis, and is primarily transmitted through contaminated food consumption. This study presents two cases of severe endocarditis in patients with heart valve disease caused by *L. monocytogenes*. Infection was confirmed by blood culture and pathogen culture of the valve pus. Early detection, clinical suspicion, and appropriate treatment are crucial for improving the prognosis of patients with listeriosis. The combination of ampicillin and aminoglycosides remains the most effective treatment for listeriosis.

Keywords: infective endocarditis, *Listeria monocytogenes*, heart valve disease

Introduction

Infective endocarditis (IE) is a microbial infection affecting the heart valves or endocardial surface, often resulting in the formation of vegetation on the valves and potentially leading to myocardial abscesses, significant valve regurgitation, systemic embolism, and may ultimately culminate in heart failure or mortality.¹ IE initiates with the adhesion of bacteria to tissues within the circulatory system. This process is facilitated by various predisposing factors, including rheumatic heart disease, prosthetic heart valves, residual intra-cardiac shunts, congenital heart anomalies, and ventricular assist devices.² *Listeria monocytogenes*, a gram-positive zoonotic intracellular pathogen, is a notable foodborne bacterium with conditional pathogenicity that causes listeriosis.³ Clinical manifestations of *L. monocytogenes* infection include bacteremia, meningitis, and encephalitis primarily transmitted through contaminated food sources, resulting in a high hospitalization rate and a mortality rate near 50%.⁴ The infection primarily affects elderly individuals, pregnant women, patients with malignancies, immunosuppressed individuals, and those with compromised immune systems while also causing self-limiting febrile gastroenteritis in healthy individuals.⁵ However, cases of IE attributed to *L. monocytogenes* are infrequent. In this study, we present two instances of heart valve disease induced by *L. monocytogenes*.

Case I

A 62-year-old male patient was admitted to the hospital due to sudden onset of blurred vision in his right eye persisting for 20 days. Upon physical examination, the patient exhibited a temperature of 36.3°C and presented with symptoms of acute illness, including an enlarged cardiac sector, arrhythmia, a systolic blowing murmur in the apical region, and a mid-to-late diastolic rumbling murmur. The patient had a 12-year history of heart valve disease with postactivity cardiac fatigue that worsened two years ago and had been managed with digoxin, aspirin, and spironolactone over an extended period. Transesophageal echocardiography revealed irregular thickening and severe stenosis of the mitral valve, severe regurgitation, irregular thickening of the aortic valve with mild stenosis, mild regurgitation of the tricuspid valve, and

a large left atrium (Figure 1). An electrocardiogram (ECG) indicated atrial fibrillation with left ventricular high voltage at a rate of 77 beats per minute. Laboratory tests conducted upon admission revealed significant elevations in the leukocyte count ($10.71 \times 10^9/L$), neutrophil granulocyte count ($7.83 \times 10^9/L$), C-reactive protein level (47.80 mg/L), and sedimentation rate (68.0 mm/h), which were indicative of inflammation. Additionally, the N-terminal pro-B-type natriuretic peptide (NT-ProBNP) concentration was 2007 ng/L, the troponin T concentration was 117.8 ng/L, the lactate dehydrogenase concentration was 265 IU/L, and the hydroxybutyrate dehydrogenase concentration was 221 IU/L, all of which showed varying degrees of increase.

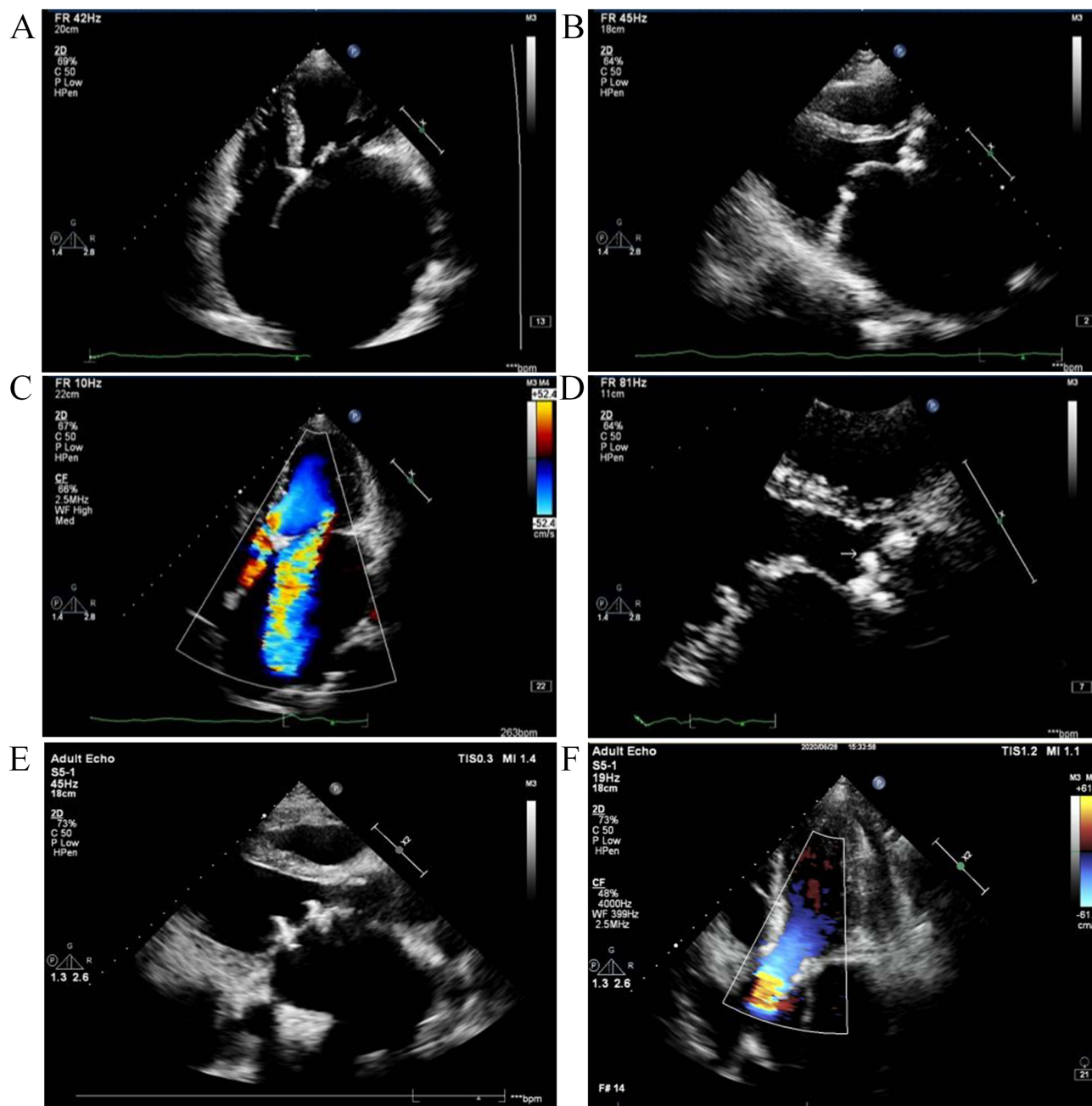


Figure 1 (A–F) Transesophageal echocardiography results before and after surgery. **(A)** Enlarged left atrium with normal left ventricular systolic function; **(B and C)** The mitral valve exhibited irregular thickening and severe stenosis with severe regurgitation, along with irregular thickening of the aortic valve; **(D)** The presence of echogenic flopping on the aortic valve with mild stenosis and mild tricuspid regurgitation; **(E and F)** No notable irregularities were observed in prosthetic bioprosthetic valve function or left ventricular systolic function measurements after surgery.

On the first day of hospitalization, the patient was suspected to have infective endocarditis following diagnostic evaluations. Consequently, two vials of blood culture were sent for examination, and a dose of 15 mg/kg vancomycin hydrochloride was administered every 12 hours (q12h) as an empirical treatment. On the third day of hospitalization, the patient underwent mitral valve and aortic valve replacement and tricuspid valvuloplasty. During the surgical intervention, approximately 50 mL of yellowish fluid was observed, with no pericardial adhesion noted. The heart exhibited enlargement, particularly affecting the left side. The mitral valve leaflet displayed thickening, calcification, and adhesion at the junction, resulting in severe stenosis and insufficient closure. The aortic and right coronary valves showed mild narrowing with a 1 cm × 1 cm vegetation, while the tricuspid annulus was enlarged with mild closure insufficiency. Furthermore, a 2 cm × 2 cm abscess was identified at the junction of the left coronary sinus, and pus samples were collected for further analysis.

After 22 hours, the blood culture yielded a positive result, with the bacterial colonies observed on the blood agar exhibiting characteristics of being small, white, and smooth (Figure 2). *L. monocytogenes* was determined through mass spectrometry analysis, confirming the diagnosis of IE caused by this pathogen. In vitro drug sensitivity tests revealed that *L. monocytogenes* was sensitive to ampicillin, erythromycin, meropenem, and penicillin G but resistant to cotrimoxazole and sulfamethoxazole-trimethoprim. The treatment of *Listeria* endocarditis involved the administration of 2 g of ampicillin q8h. The patient experienced recurrent fever during the treatment period, with a peak temperature of 38.5°C. Consequently, further efforts were undertaken to administer 1000 mg of meropenem q8h or 3000 mg of piperacillin-tazobactam sodium for antimicrobial therapy at different stages. Ocular examination did not reveal any significant lesions in the right eye, suggesting that the observed blurred vision may be attributed to the heart condition.

After 5 weeks of active anti-infection therapy, the patient exhibited a normal body temperature and improved symptoms. Examination of cerebrospinal fluid and blood pathogen cultures yielded negative results. Markers of infection returned to normal levels; imaging examinations, including magnetic resonance imaging (MRI) of the head and computed tomography (CT) scanning, revealed no signs of infection, indicating successful treatment of the patient's *Listeria* endocarditis. Furthermore, transesophageal echocardiography revealed normal left ventricular systolic function and proper functioning of bioprosthetic valves, with no significant postoperative complications (Figure 1). The patient was discharged on the 39th day with a favorable recovery outcome. Subsequent follow-up over a 2-year period postoperation revealed no recurrence of the condition.

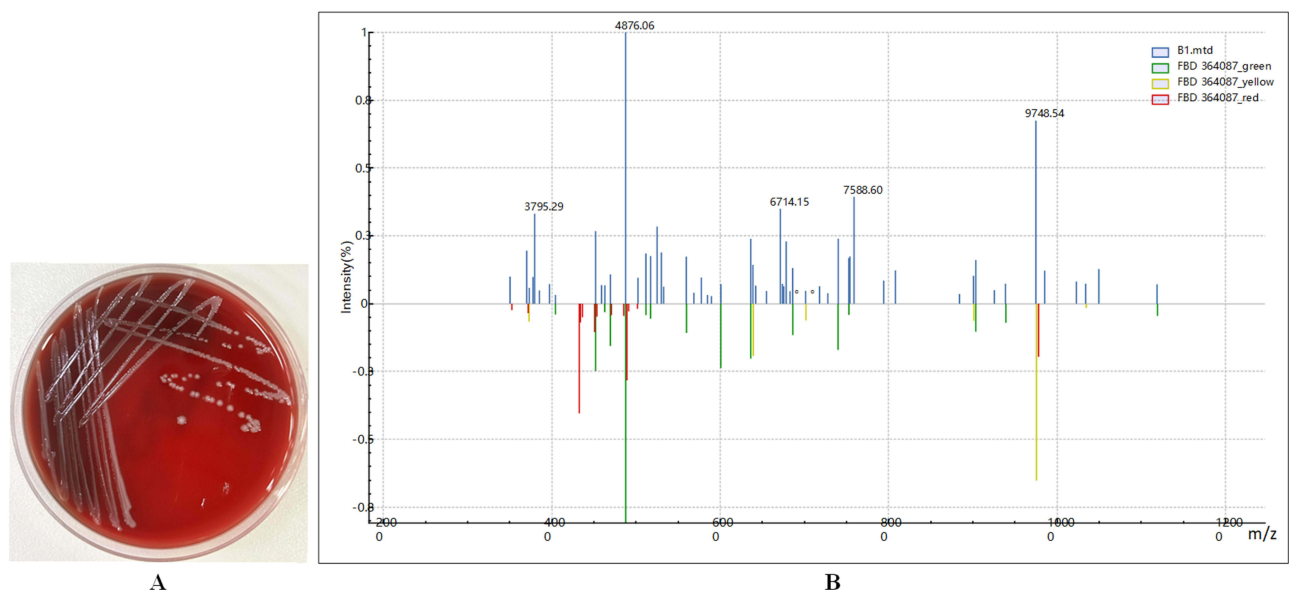


Figure 2 Colonies of *L. monocytogenes* on blood agar and mass spectrometry results. (A) Colonies are small, white, and smooth on the blood agar. (B) Diagram of mass spectrum peaks, with the color blue indicating the strain that was detected.

Case 2

A 38-year-old male patient was admitted to the hospital because of avulsion of aortic valve prosthesis. The individual had previously undergone aortic valve and root replacement surgery eight years before due to aortic aneurysm. Upon admission, the patient exhibited stable vital signs, with a normal heart boundary and no abnormalities in the precordial area. A systolic murmur was detected in the aortic valve region, along with arrhythmia and irregular heart sounds. Transesophageal echocardiography revealed a separation between the artificial aortic valve and the native aortic annulus, accompanied by considerable regurgitation surrounding the prosthetic valve (Figure 3). Computed tomography (CT) results indicated left ventricular enlargement and mild pericardial effusion (Figure 4). ECG revealed atrioventricular block and ST-T changes. Initial laboratory tests revealed significant increases in leukocyte count ($10.04 \times 10^9/L$), neutrophil granulocyte count ($7.11 \times 10^9/L$), C-reactive protein level (43.40 mg/L) and sedimentation rate (48.0 mm/h), which are indicative of inflammation. Concentration of NT-ProBNP (28163 ng/L) and troponin T (279.3 ng/L) reached critical values.

On the seventh day following admission, the leukocyte count ($11.29 \times 10^9/L$) and predominant neutrophilic nucleated granulocyte count ($10.24 \times 10^9/L$) indicated a worsening infection. Blood cultures revealed the presence of gram-positive bacilli identified as *L. monocytogenes*, which were sensitive to ampicillin, meropenem, penicillin G, and the compound sulfamethoxazole. Vancomycin (15 mg/kg, q12h) was administered for initial anti-infection treatment, and the medication regimen was changed to ampicillin (2 g, q8h) after detecting *L. monocytogenes*. Modified cabrol surgery was performed on the tenth day. Transesophageal echocardiography revealed extensive adhesion in the pericardium and significant tissue proliferation around the ascending aorta with pus at the root. The artificial mechanical valve frame was

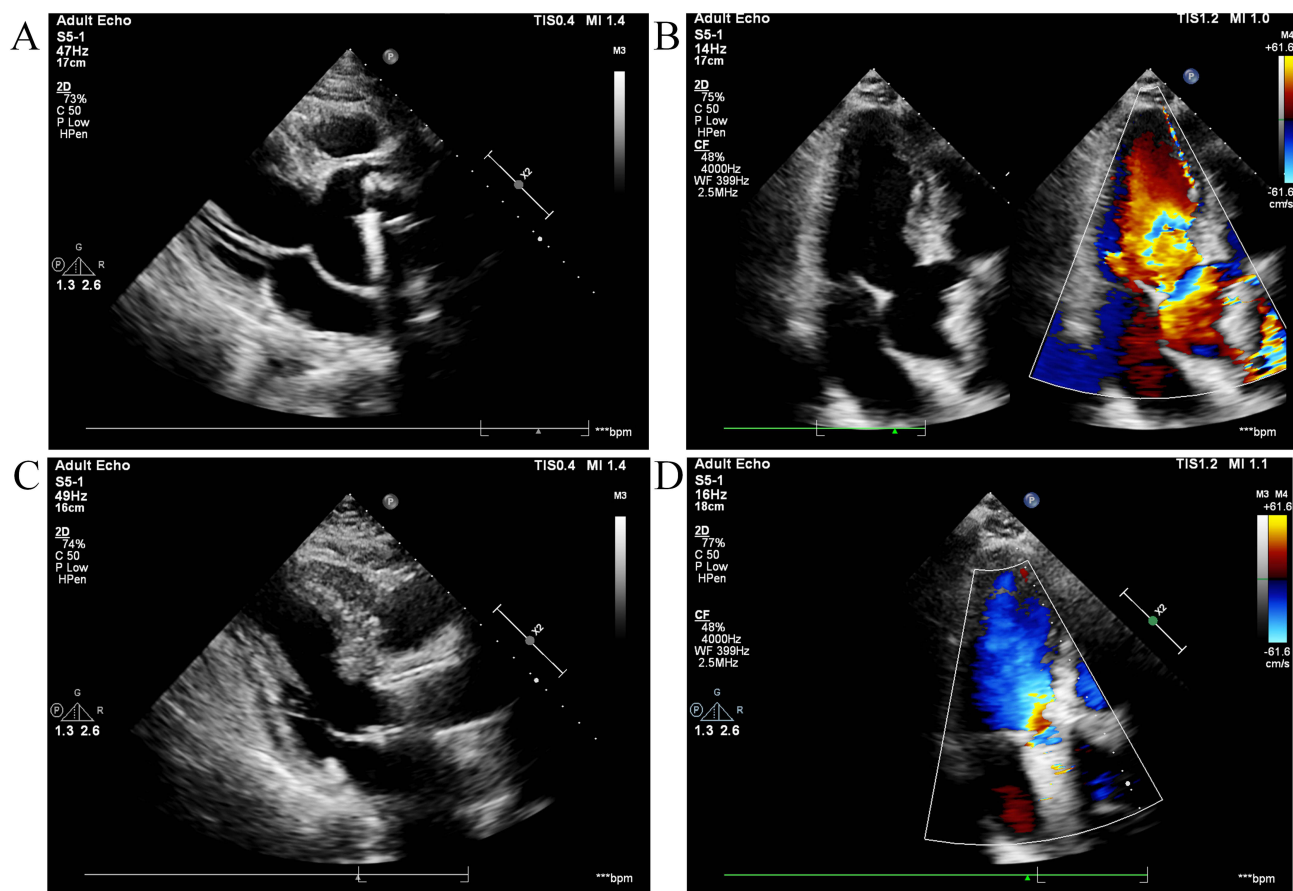


Figure 3 (A–D) Transesophageal echocardiography results before and after surgery. **(A)** Artificial aortic valve detached from the intrinsic aortic annulus. **(B)** Significant paravalvular regurgitation. **(C)** Artificial aortic valve was functioning normally. **(D)** Normal blood flow observed in the artificial ascending aorta.

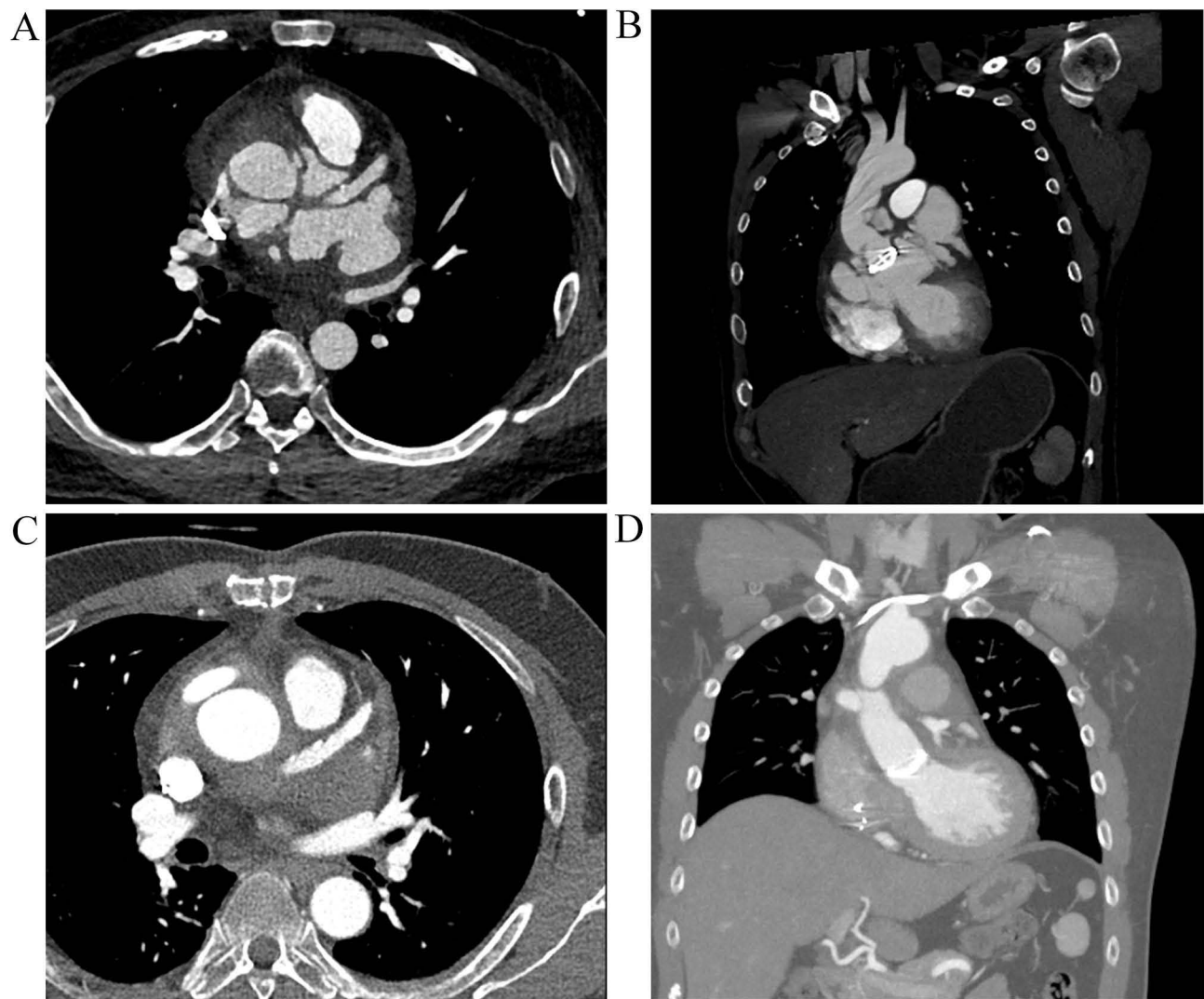


Figure 4 Computed tomography (CT) scans were performed during both the infection and recovery stages. (A and B) During the infection phase, CT revealed left ventricular enlargement and mild pericardial effusion. (C and D) During the recovery phase, the aortic valve orifice was free of obstruction, and there was a decrease in the accumulation of fluid in the pericardial cavity.

completely removed, and proliferation of fibrous tissue formed under the original valve annulus. Purulent samples were collected and subjected to microbiological testing.

After surgery, the patient experienced fever along with elevated levels of inflammatory markers and subsequent treatment with piperacillin-tazobactam at a dosage of 4500 mg q8h or meropenem at a dosage of 1000 mg q8h for antimicrobial purposes at various stages. Afterward, the patient's health condition remained stable, with no signs of infection. On the 25th day, a permanent dual chamber pacemaker was implanted. The patient was discharged on the 30th day. A follow-up examination conducted 4 months later indicated that the artificial aortic valve was functioning normally, with normal blood flow observed in the artificial ascending aorta (Figure 3). CT imaging revealed a significant decrease in localized fluid accumulation in the pericardial cavity (Figure 4). Subsequent follow-up over an 11-month period postoperation revealed no recurrence of the condition.

Discussion

Endocarditis caused by *L. monocytogenes* is a rare but serious disease characterized by a high fatality rate. Among the aforementioned patients, two had a prolonged history of heart valve disease and were predisposed to *L. monocytogenes* infection. Two patients had chronic postactivity cardiac fatigue without significant fever, localized pain or other typical

symptoms of endocarditis on admission, which was consistent with limited systemic inflammation associated with invasive listeriosis.⁶ Presently, the diagnosis of listeriosis relies on the isolation and identification of *L. monocytogenes* from biological specimens, including blood cultures or cerebrospinal fluid.⁷ In our patients, *L. monocytogenes* was detected simultaneously in heart valve pus obtained intraoperatively and in peripheral blood cultures, elevated inflammatory markers, and recurrent fever, which led to the final determination of heart valve disease combined with *L. monocytogenes*-induced endocarditis. Studies have confirmed that endovascular infections such as endocarditis are not linked to specific *L. monocytogenes* clones and that genomic sequence diversity reflects the overall distribution of isolates causing sporadic listeriosis.⁸ In cases where a heart murmur is not readily apparent, IE may be obscured by the primary infection, leading to a heightened risk of misdiagnosis. It should be differentiated from influenza, acute arthritis, acute purulent meningitis, acute pyelonephritis, etc. Artificial valve replacement surgery, hemodialysis, or congenital heart disease correction surgery all increase the risk of endocardial infection.⁹ For patients with these risk factors, attention should be paid to changes in cardiac auscultation, skin bleeding points, and embolism. An echocardiogram should be performed, and blood samples should be obtained to check for the presence of bacteria.

In this study, we examined cases of IE attributed to *L. monocytogenes* as reported in the PubMed database over the preceding five-year period (Table 1). The infected patients were predominantly male (71.4%, 5/7), with an average age of 60.4 ± 17.5 years. Symptoms commonly presented upon admission included sudden encephalopathy (42.9%, 3/7) and acute myocardial infarction with respiratory distress (28.6%, 2/7). A large majority of the patients had a prior history of heart disease or heart valve surgery (85.7%, 6/7). Upon detection of *L. monocytogenes*, patients exhibited various infection-related symptoms, such as elevated white blood cell count and proportion of multinucleated cells (57.1%, 4/7), increased levels of C-reactive protein (42.9%, 3/7), and fever (42.9%, 3/7). The most frequently administered antibiotics for treatment were ampicillin and gentamicin (57.1%, 4/7). Following the infection, two patients underwent surgical treatment after the infection, and two patients ultimately died (28.6%). The mortality rate among patients diagnosed with IE has been documented to be approximately 30%.¹⁰ A study examining 100 patients with *L. monocytogenes* endocarditis revealed that these patients had variable clinical presentations and that vascular phenomena were prevalent but caused milder symptoms with a lower incidence of fever and localized pain than other pathogens, such as *Staphylococcus aureus*, *Streptococcus spp.* and Enterobacteriaceae.^{3,6,7} The main predisposing factors associated with this condition include immunodeficiency, valvular disease, prosthetic devices, hypertrophic cardiomyopathy, and a history of endocarditis. Another study on 71 cases of *L. monocytogenes*-associated endovascular infections indicated that the presence of prosthetic devices, including those related to valvular, intracardiac, or vascular structures, was significantly correlated with an increased incidence of endocarditis and vascular infections among patients experiencing bacteremia.⁸ Aortic involvement was most frequently observed in patients with congenital valvular endocarditis, while mitral valve involvement was common in individuals with prosthetic hearts.³ In patients with prosthetic valve endocarditis, the combination of antibiotic therapy and valve replacement surgery has demonstrated an increased rate of successful treatment outcomes.¹¹ Notably, patients who present with endocarditis concurrent with *L. monocytogenes* encephalitis infection often had a poor prognosis, leading to a significant increase in mortality rates due to the rapid progression of the disease.^{12,13}

In cases of IE where patients present with acute symptoms, intravenous antibiotic therapy should be started immediately after obtaining blood samples for culture.¹⁴ The selection of antibiotics, along with their dosage and duration of administration, is contingent upon the minimal inhibitory concentrations (MICs) identified in blood cultures. Treatment strategies are informed by clinical presentations and serological assessments, and early surgical intervention is advisable in cases with significant valve dysfunction and a substantial presence of vegetations.¹⁵ Given the rarity of these infections, there are no established treatment protocols for *L. monocytogenes* endocarditis or vascular infections, with most patients typically receiving a combination of amoxicillin and aminoglycoside. The recommended duration of amoxicillin therapy is 6–8 weeks for prosthetic valve endocarditis and at least 4 weeks for native valve endocarditis, and the bactericidal efficacy of this combination has been demonstrated.^{7,8} According to the Sanford Guide for Antimicrobial Therapy (43rd edition), the standard treatment regimen for *L. monocytogenes* disease is ampicillin and gentamicin combined with methymycin/sulfamethoxazole or meropenem in cases of penicillin allergy.⁴ The combinations of ampicillin + ceftriaxone and ampicillin + daptomycin were each noted to have synergistic activity against

Table 1 Reported Cases of Infective Endocarditis Caused by *L. Monocytogenes* in the Past 5 Years

Year	Country	Age/sex	Admission symptoms	Basic condition	Infective Symptoms	Complication	Surgical treatment	Antibiotics used	Outcome	Reference
2019	USA	66/female	Respiratory distress	Valvular heart disease, COPD, Hodgkin's lymphoma	WBC 18,000/ μ L, NEUT% 88.7%	Atrial ventricular block	/	AMP, GEN	Improved	Shobayo et al ¹⁷
2020	China	43/male	Chestpain, respiratory distress	Rheumatic heart disease	Recurrent fever	/	Mitral valve replacement, tricuspid valvuloplasty	TEC, MXF	Recovered	Zhao et al ¹⁸
2021	Italy	32/female	Cerebral hemorrhage	HUVS, valvular heart disease, pyelonephritis	Remittent fever	Encephalitis	/	AMP, LVX, LNZ	Dead	Scheggi et al ¹⁹
2022	France	75/male	Polyarthritits	Valvular heart disease, chronic alcoholism	CRP 78 mg/L	Spondylodiscitis, cerebral embolus	/	AMX, GEN	Improved	Randrianarisoa et al ⁷
2022	USA	77/male	Sudden onset altered mental status	Valvular heart disease, type I diabetes mellitus	WBC 13,200/ μ L, NEUT% 75%	Cerebral embolism	/	AMP	Recovered	Badar et al ²⁰
2023	Germany	74/male	High fever, disturbed coagulation	Valvular heart disease	High fever, CRP 170 mg/L, WBC 17,900/ μ L	/	Mitral valve surgery	AMP, RFP, GEN, VAN	Recovered	Marschner et al ²¹
2023	Malaysia	56/male	Slurring of speech and generalized body weakness	/	WBC 18,600/ μ L, CRP 40 mg/L	Pneumonia, encephalitis	/	PEN, GEN	Dead	Mohan et al ²²

Abbreviations: COPD, chronic obstructive pulmonary disease; WBC, white blood cell count; NEUT%, neutrophilic granulocyte percentage; HUVS, hypocomplementemic urticarial vasculitis syndrome; CRP, C-reactive protein; AMP, ampicillin; GEN, gentamicin; TEC, teicoplanin; MXF, moxifloxacin; LVX, levofloxacin; LNZ, linezolid; AMX, amoxicillin; RFP, rifampin; VAN, vancomycin; PEN, penicillin.

L. monocytogenes endocarditis isolates according to checkerboard assays.¹⁶ In the cases discussed, patients received ampicillin for the treatment of *L. monocytogenes* endocarditis. Subsequently, piperacillin and meropenem were utilized during different treatment phases in accordance with established clinical guidelines and the results of drug sensitivity testing.

In summary, endocarditis associated with *L. monocytogenes* is rare, yet healthcare providers should be cognizant of this severe and specific complication. Clinicians must thoroughly assess potential *L. monocytogenes*-associated endocarditis infections and promptly administer aggressive combined antimicrobial and surgical interventions. Therefore, timely and appropriate initiation of antimicrobial therapy is crucial for managing this disease and enhancing the clinical outlook for patients, particularly those who are elderly, have tumors, or suffer from immunodeficiencies. Diagnostic and therapeutic measures for listeriosis heavily rely on pathogenic bacterial culture and antimicrobial susceptibility test. Clinicians should increase the frequency of specimen collection and blood culture while ensuring an adequate treatment regimen. Our study provides an important perspective on *L. monocytogenes*-related IE, and we hope that the findings will provide a reference for clinicians to diagnose and treat *L. monocytogenes*-related IE in a timely manner.

Conclusion

This study reports the diagnostic and therapeutic course of *L. monocytogenes* as an example of endocarditis occurring in patients with a history of heart valve disease. Echocardiography serves as a diagnostic tool for the verification of implants, abscesses, valve perforations, or the detachment of artificial valves. Additionally, the identification of microorganisms and their susceptibility to antibiotics is essential for informing treatment strategies. The selection of antibiotics, along with their dosage and duration of administration, is contingent upon the MICs identified in blood cultures. The most effective treatment for listeriosis involves a combination therapy regimen comprising ampicillin and aminoglycosides.

Abbreviations

IE, infective endocarditis; ECG, electrocardiogram; NT-ProBNP, N-terminal pro-B-type natriuretic peptide; MRI, magnetic resonance imaging; CT, computed tomography; MICs, minimal inhibitory concentrations.

Ethical Approval and Informed Consent

The documentation and publication of the case were approved by the Ethics Review Committee of West China Hospital, Sichuan University (Approval Number: 20231974). Written informed consent for publication of their details was obtained from the patients. The subjects' rights were adequately protected, and there was no potential risk to the subjects.

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Author Contributions

All authors made a significant contribution to the work reported, whether in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

Disclosure

The authors have no conflicts of interest to declare in this work.

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