

Received: 2021.03.25

Accepted: 2021.08.23

Available online: 2021.09.02

Published: 2021.10.09

Edwardsiella tarda Native Valve Infective Endocarditis in a Young and Non-Immunocompromised Host: A Case Report

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection GABCDEF 1 **Masamichi Koike**ABCDEF 1 **Takahiro Doi**ABCDEF 2 **Yutaka Iba**ABCDEF 1 **Satoshi Yuda**

1 Department of Cardiology, Teine Keijinkai Hospital, Sapporo, Hokkaido, Japan

2 Department of Cardiovascular Surgery, Teine Keijinkai Hospital, Sapporo, Hokkaido, Japan

Corresponding Author: Takahiro Doi, e-mail: doitaka518@yahoo.co.jp**Financial support:** None declared**Conflict of interest:** None declared**Patient:** Female, 28-year-old
Final Diagnosis: Infective endocarditis
Symptoms: Fever
Medication: —
Clinical Procedure: —
Specialty: Cardiology • Infectious Diseases**Objective:** Rare disease**Background:** Infective endocarditis (IE) is an infectious disease that occurs in valves, centered on the endocardium and ventricular septal defects. It is a serious disease that is easily misdiagnosed and has a high mortality rate if left untreated. *Edwardsiella tarda* is an extremely rare cause of IE, especially in young and non-immunocompromised hosts.**Case Report:** A woman in her 20s presented to our hospital with fever of unknown cause and liver dysfunction. She was admitted to the Department of Gastroenterological Medicine owing to suspicion of gastrointestinal infection. Gastrointestinal examination, including contrast-enhanced computer tomography and endoscopic ultrasonography, was performed; however, there were no significant findings. Liver dysfunction improved spontaneously, but her fever did not improve with antibiotic treatment. Transthoracic echocardiography was performed on day 9 of hospitalization because *E. tarda* was detected in a blood culture test, revealing vegetation at the mitral valve. Asymptomatic cerebral infarction was shown by brain magnetic resonance imaging, and mitral valvuloplasty was performed on day 14. After surgery, transthoracic echocardiography was performed on day 22, showing no vegetation or mitral regurgitation. However, postoperative transesophageal ultrasonography performed on day 29 revealed severe mitral regurgitation. Redo mitral valvuloplasty was performed on day 38. She clinically improved and was discharged on day 67.**Conclusions:** This is the first case in which *E. tarda* was diagnosed as the causative agent of IE on a native valve in a young and non-immunocompromised host. Aggressive source control resulted in a good clinical outcome.**Keywords:** Mitral Valve • Endocarditis • Young AdultFull-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/932387>

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Background

Worldwide, the top 3 species of bacteria that cause community-acquired infective endocarditis (IE) in a native valve are viridians group streptococci, staphylococcus, and enterococcus [1]. Gram-negative bacilli are rarely the causative agent of IE. The HACEK (*Haemophilus*, *Aggregatibacter*, *Cardiobacterium*, *Eikenella*, and *Kingella*) group of organisms consists of gram-negative bacilli with low pathogenicity and accounts for only about 1% of all of the causative bacteria of IE. Cases of IE caused by gram-negative bacteria other than HACEK bacteria are even rarer [1-3]. *Edwardsiella tarda* is a gram-negative bacillus and a rare cause of IE. IE, in which *E. tarda* is the causative agent, usually occurs in prosthetic valves and immunocompromised hosts. Furthermore, *E. tarda* is usually a summer organism.

We describe a rare case in which *E. tarda* caused IE in a young, non-immunocompromised host with native valves in the winter. The causative agent, *E. tarda*, had good antibiotic sensitivity; however, stroke occurred in the patient after hospitalization. She was also young, wanted to conceive, and was not menopausal. Considering her wish to conceive and the effects of potential treatments on perinatal fluid management, we decided that surgical intervention was necessary. Since there would be the possibility of fetal malformation during pregnancy, easy bleeding during menstruation, recurrence of IE, and new onset of heart failure, we decided to perform mitral valvuloplasty instead of mitral valve replacement so that the patient would not have to take warfarin for the rest of her life.

Prompt and aggressive source control and surgical intervention with antibiotic treatment in our patient were effective for achieving a good outcome as well as midterm family planning, including pregnancy and childbirth, good long-term quality of life, and good prognosis.

Case Report

A woman in her 20s presented to our hospital with fever of unknown cause in the winter. Her past medical history included a diagnosis of ovarian endometriotic cysts and endometriosis 2 years prior, and she had been taking low-dose norethisterone and ethinyl estradiol after ovary-sparing surgery, in which only ovarian lesions were removed laparoscopically. On arrival at the hospital, the patient was conscious, and her vital signs were as follows: body temperature 38.9°C, blood pressure 103/58 mmHg, pulse 138 beats/min, respiratory rate 18 breaths/min, and oxygen saturation 96%. On physical examination, there was tenderness only in the mid-upper abdomen to the right costal region. Blood samples showed a markedly high white blood cell count of $15.0 \times 10^3/\mu\text{g}$ and C-reactive protein level of 31.2 mg/dL. In addition, levels of aspartate aminotransferase, glutamic-oxaloacetic transferase, lactate dehydrogenase, and bilirubin were high. Therefore, contrast-enhanced computed tomography and endoscopic ultrasonography were performed owing to suspicion of gastrointestinal disease; however, there were no specific clinical findings. The patient was empirically treated with cefmetazole (1 g) by intravenous (i.v.) injection every 6 h. The liver dysfunction improved spontaneously, but her fever did not improve. Two blood cultures obtained by a

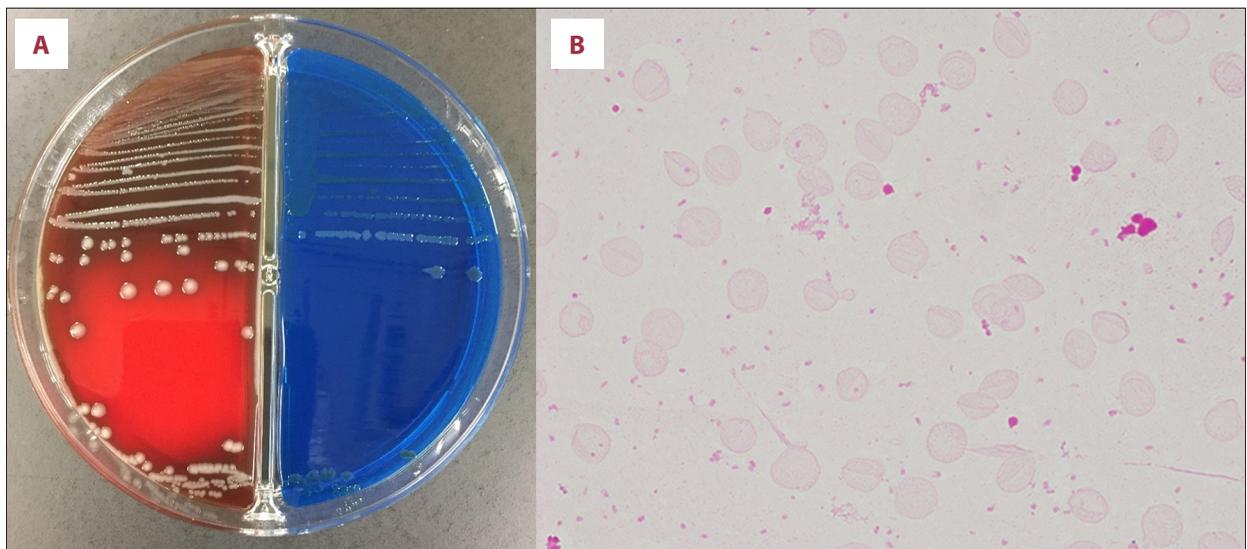


Figure 1. (A) The red medium is trypticase soy agar II sheep blood agar, and the blue medium is bromothymol blue lactose agar. The bacterial cells produced indole, and β -hemolysis was observed. Since there was no H_2S production in *Salmonella-Shigella* agar medium, the bacterium was considered to be *Edwardsiella* of biogroup 1 rather than wild type. (B) The bacterium was a gram-negative short rod bacterium typical of *Edwardsiella tarda* and showed an *Enterobacteriaceae*-like morphology.

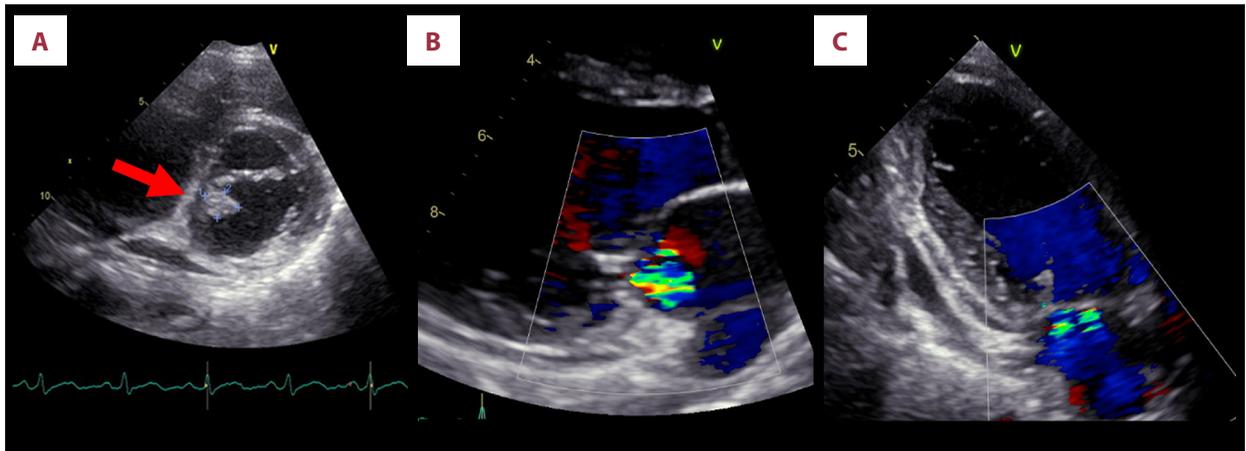


Figure 2. Transthoracic echocardiography. (A) A mass (13×10 mm) was attached to the posterior commissure of the mitral valve with high mobility. Arrow shows the vegetation. Mild-to-moderate mitral regurgitation was detected. (B) Parasternal long-axis view. (C) Two-chamber view.

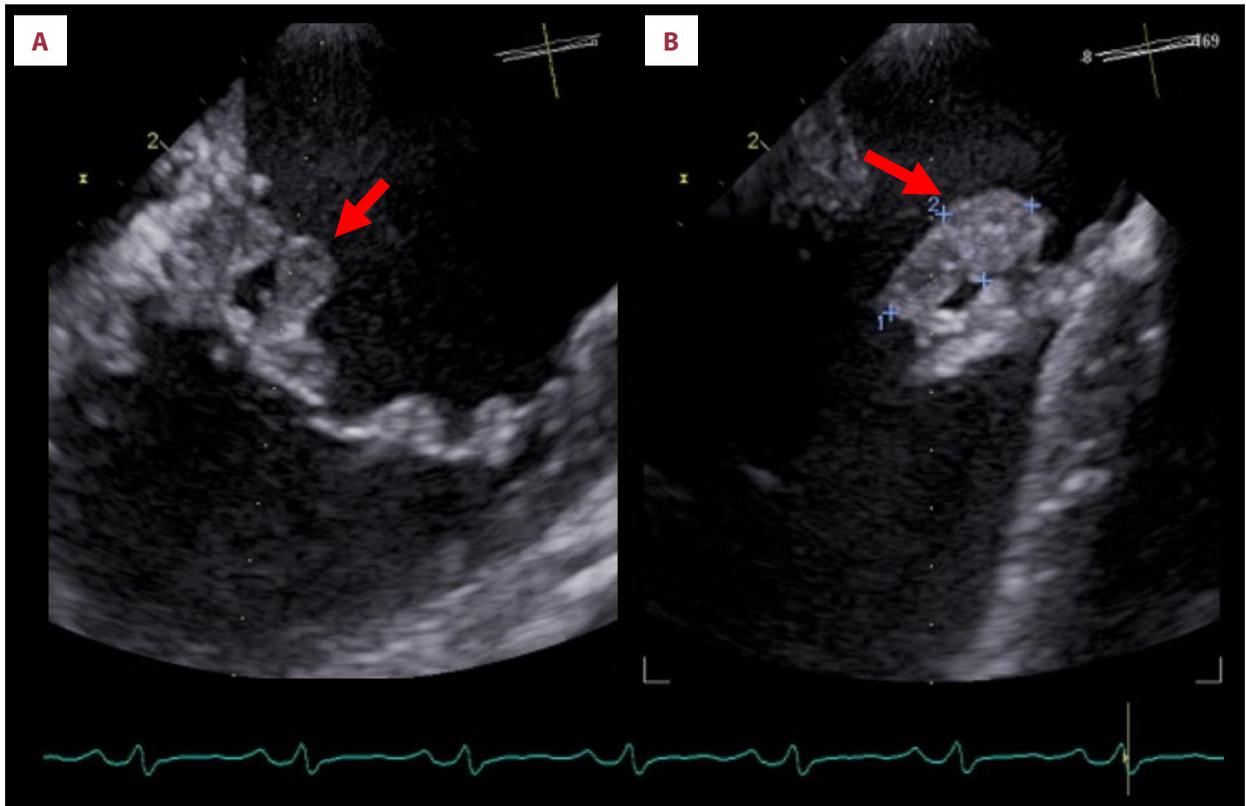


Figure 3. (A, B) Transesophageal echocardiography. A mass (15×7 mm) was attached to the posterior commissure of the mitral valve and medial site of the posterior mitral leaflet. Arrows show the vegetation.

single antecubital vein puncture revealed only *E. tarda* before the start of antibiotic treatment (Figure 1). Antibiotic treatment was changed from cefmetazole to ampicillin/sulbactam (3 g i.v. every 6 h) and gentamicin (300 mg i.v. every 24 h) based on the sensitivity. Transthoracic echocardiography was performed on day 9 because the patient met 1 major and 1 minor criterion in the modified Duke diagnostic criteria and the

possibility of IE was strongly suspected. The echocardiography revealed a mass (13 mm × 10 mm) attached to the posterior commissure of the mitral valve with high mobility. Doppler echocardiography demonstrated mild-to-moderate mitral regurgitation. Left ventricular systolic function was preserved (ejection fraction, 67%). Transesophageal echocardiography performed on the following day revealed a mass (15×7 mm)

attached to the posterior commissure of the mitral valve and medial site of the posterior mitral leaflet (P3) (Figures 2, 3). No symptoms of heart failure were observed. Asymptomatic infarction was shown by magnetic resonance imaging, which was performed as a screening test.

We decided that early surgical therapy was appropriate, and surgical therapy was performed on day 14. Extensive vegetation was present at the posterior commissure and medial site of P3. These areas were destroyed, and the chordae tendineae under P3 had become edematous. The posterior commissure and half of P3 were resected and the subvalvular abscess was scraped. Annuloplasty of the mitral valve was also

performed. Histopathological features suggested that active IE included mitral valve vegetation with inflammation of subvalvular tissues (Figures 4, 5). *E. tarda* was not cultured from the surgical specimens.

After surgery, transthoracic echocardiography performed on day 22 showed no mitral regurgitation. However, transesophageal ultrasonography performed on day 29 revealed prolapse at the medial site of the anterior mitral leaflet and marked accelerated blood flow in the same site. Severe mitral regurgitation toward the medial wall and posterior wall of the left atrium was observed. Redo mitral valvuloplasty was performed for the mitral regurgitation on day 38. Bacteria were also not cultured from the surgical section of the mitral valve.

Postoperative treatment with ampicillin/sulbactam (3 g i.v. every 6 h) and gentamicin (300 mg i.v. every 24 h) was continued, and the patient achieved full recovery. She was followed up postoperatively and remained clinically stable with no clinical sequelae. Only mild mitral regurgitation was observed by transthoracic echocardiography performed on day 45, and she was discharged without any symptoms of heart failure on day 67.

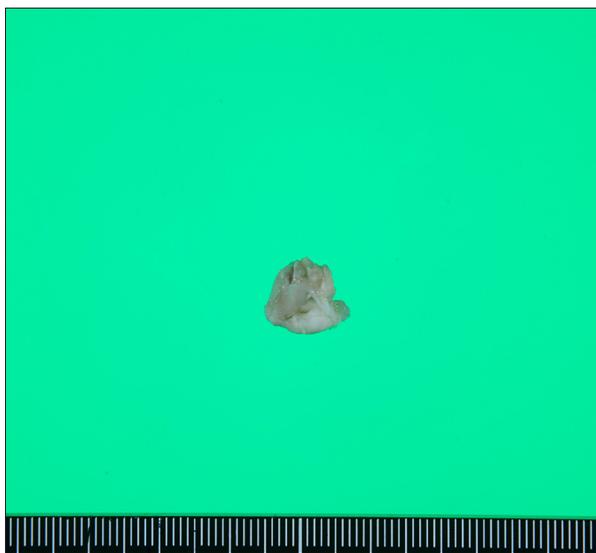


Figure 4. Image of a surgical section of the mitral valve. Vegetation (10×8×8 mm) attached to the mitral valve was resected during mitral valvuloplasty.

Discussion

To the best of our knowledge, this was a rare case of native valve IE caused by *E. tarda* in a young, non-immunocompromised host [4,5]. *E. tarda* is a gram-negative bacillus that belongs to the family *Enterobacteriaceae* but is not normally resident in the human intestine [6]. It is abundant in water systems such as freshwater and is well known as a pathogen of aquatic organisms [4,7]. *E. tarda* is non-motile and produces hydrogen sulfide and indole. The possible growth temperature is 15°C

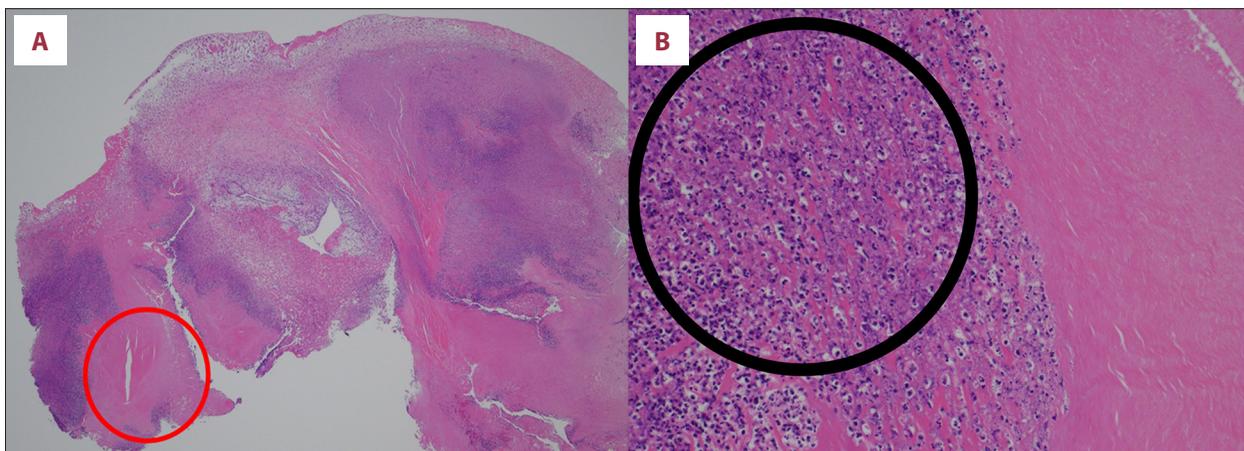


Figure 5. Imaging of hematoxylin and eosin staining of the mitral valve. A large number of neutrophils were found in pathological tissue of the mitral valve, a finding consistent with the development of infective endocarditis. (A) General view of the specimen. (B) The black circle shows the focused image of the inside of the red circle: neutrophils and crushed image of neutrophil nuclei.

to 42°C (optimal growth temperature of 30°C) and its growth salt concentration is 0% to 4%. Although this case occurred in winter, *E. tarda* infection often occurs when water temperatures are high, mainly from summer to autumn.

When pathogenic to humans, *E. tarda* infection often develops as enteritis; however, in patients with hepatobiliary system diseases, it can develop as biliary tract infection, liver abscess, and skin and soft tissue infections [8]. It also often takes the form of bacillemia [9,10]. Soft tissue infection can present with severe necrotizing fasciitis, and together with *Aeromonas hydrophila* and *Vibrio vulnificus* infections, it is known as an infection that is triggered by exposure to a water system.

Our patient had no history of traveling abroad and had never eaten snakes or eels. The average temperature in the month of onset in that year was -1.6°C. *E. tarda* developed during the cold winter months, which is extremely unfavorable for the growth environment. Previously reported cases of IE caused by *E. tarda* were cases in immunocompromised hosts with prosthetic valves [4,5]. There has been no report of a case of IE such as ours in a non-immunocompromised host who was young and had not undergone cardiac surgery.

The route of invasion of *E. tarda* in this case was not clear. However, for some reason, it invaded from the digestive tract and reached the liver from the portal vein. There was no specific findings on imaging, but hepatitis or cholecystitis developed. The hepatitis or cholecystitis may have exacerbated secondary bacteremia and caused IE.

E. tarda is susceptible to many antimicrobial agents, mostly β -lactamase-producing strains, but β -lactam resistance other than penicillin and oxacillin has not been reported. It is also susceptible to cephalosporins, aminoglycosides, fluoroquinolone ST-complexes, and tetracyclines. Although a synergistic effect has not been proven, severe cases such as meningitis and septicemia can be treated with beta-lactams plus aminoglycosides [11,12]. Therefore, we elected to treat synergistically with ampicillin/sulbactam and gentamicin in this case.

It is possible that IE caused by *E. tarda* in our case could have been cured by antibiotic treatment alone because of its good antibiotic sensitivity. However, during the course of the disease, our patient developed a stroke, which was most likely caused by the vegetation. Furthermore, she was young and wanted to conceive. Because pregnancy and delivery have the potential of perinatal fluid management, we decided that surgical

intervention was necessary for source control of the infection and management of mitral regurgitation. Also, since the patient was not menopausal, we opted for mitral valvuloplasty rather than mitral valve replacement, which would have required her to take warfarin for the rest of her life, which could have caused increased menstrual bleeding. Warfarin also passes through the placenta and affects the fetus. Anticoagulation of pregnant women carries the risk of maternal hemorrhage during pregnancy and delivery, fetal congenital abnormalities, fetal death, and neonatal death. This is also a reason why we chose mitral valvuloplasty. The possibility of developing recurrent IE and heart failure if there had been residual mitral regurgitation, regardless of pregnancy and delivery, was also a reason for surgical intervention.

Conclusions

IE can cause serious complications. Furthermore, even in non-immunocompromised hosts, IE should be considered when non-HACEK gram-negative rods such as *E. tarda* are detected in blood cultures. IE caused by gram-negative bacteria outside the HACEK group has been reported to have a poor prognosis. Prompt and aggressive source control and surgical intervention with antibiotics in our patient were effective for achieving a good outcome as well as midterm family planning, including pregnancy and childbirth, good long-term quality of life, and good prognosis.

Department and Institution Where Work Was Done

Department of Cardiology, Teine Keijinkai Hospital, Sapporo, Hokkaido, Japan.

Acknowledgements

The authors sincerely thank the staff of Teine Keijinkai Hospital (Sapporo), Hokkaido, Japan for their clinical services and technical assistance. In particular, we would like to thank Dr. Koki Kikuchi of the Department of Infectious Diseases at our hospital for his invaluable advice.

Declaration of Figures Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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