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

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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 Adult

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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. 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 15.0×10³/μg 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 H₂S 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.
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.

**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.
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 bacteraemia 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**

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**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.
References:

1. Habib G, Erba PA, Jung B, et al. Clinical presentation, aetiology and outcome of infective endocarditis. Results of the ESC-EORP EURO-ENDO (European infective endocarditis) registry: A prospective cohort study. Eur Heart J. 2019;40:3222-32

2. Nakatani S, Mitsutake K, Ohara T, et al. Recent picture of infective endocarditis in Japan – lessons from Cardiac Disease Registration (CADRE-IE). Circ J. 2015;77:1558-64

3. Morpeth S, Murdoch D, Cabell CH, et al. Non-HACEK gram-negative bacillus endocarditis. Ann Intern Med. 2007;147:829-35

4. Litton KM, Rogers BA. Edwardsiella tarda endocarditis confirmed by indium-111 white blood cell scan: An unusual pathogen and diagnostic modality. Case Rep Infect Dis. 2016;2016:1082160

5. Nettles RE, Sexton DJ. Successful treatment of Edwardsiella tarda prosthetic valve endocarditis in a patient with AIDS. Clin Infect Dis. 1997;25:918-19

6. Janda JM, Abbott SL. Infections associated with the genus Edwardsiella: The role of Edwardsiella tarda in human disease. Clin Infect Dis. 1999;17:742-48

7. John AM, Prakash JA, Simon EG, Thomas N. Edwardsiella tarda sepsis with multiple liver abscesses in a patient with Cushing’s syndrome. Indian J Med Microbiol. 2012;30:352-54

8. Wang IK, Kuo HL, Chen YM, et al. Extraintestinal manifestations of Edwardsiella tarda infection. Int J Clin Pract. 2005;59:917-21

9. Nelson JJ, Nelson CA, Carter JE. Extraintestinal manifestations of Edwardsiella tarda infection: A 10-year retrospective review. J La State Med Soc. 2009;161:103-6

10. Spencer JD, Hastings MC, Rye AK, et al. Gastroenteritis caused by Edwardsiella tarda in a pediatric renal transplant recipient. Pediatr Transplant. 2008;12:238-41

11. Auwarter, PG. Edwardsiella Spp. Johns Hopkins ABX Guide, The Johns Hopkins University, 2020. Johns Hopkins Guide. Available from: www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540736/all/Edwardsiellaspp

12. Stock I, Wiedemann B. Natural antibiotic susceptibilities of Edwardsiella tarda, E. ictaluri, and E. hoshiniae. Antimicrob Agents Chemother. 2001;45:2245-55